



# **The Health Impact Fund**

Making New Medicines  
Accessible for All

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Making New Medicines Accessible for All

A Report of *Incentives for Global Health*

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Lead Authors



### **Incentives for Global Health**

Incentives for Global Health is a nonprofit organization dedicated to developing market-based, systemic solutions to global health challenges.

Our main project, the Health Impact Fund, aims to increase access to medicines by creating additional incentives for innovation in the health sector.

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This book should be cited as:

Aidan Hollis and Thomas Pogge, *The Health Impact Fund: Making New Medicines Accessible for All* (Incentives for Global Health, 2008).

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# Preface

This book presents for public consideration a complement to the existing rules governing the development and distribution of new medicines. It shows that the proposed Health Impact Fund is feasible and that it would produce large gains in global public health and economic productivity at comparatively low cost. We ask readers for help in perfecting this proposal and for political support.

*Incentives for Global Health* is a nonprofit organization created by an international and interdisciplinary group of scholars and practitioners to promote the Health Impact Fund and other market-based solutions to public health problems. The following team members collaborated with us in writing this book: Christian Barry, Laura Biron, Leila Chirayath, Kieran Donaghue, Mike Ravvin, and Michael Selgelid. Many others have provided valuable comments during the writing process: Kalypso Chalkidou, Patrick Childress, Julian Cockbain, Peter Drahos, David Feeny, Jocelyn Finlay, Margot Kaminski, Miltos Ladikas, Carl Nathan, Noah Novogrodsky, Gorik Ooms, Matt Rimmer, Doris Schroeder, Devi Sridhar, Jie Tian, Ling Tong, Peter Tugwell, and Judith Whitworth. We have made presentations on this idea in universities and conferences around the world, and have immensely benefited from the many helpful comments and criticisms offered. Matt Peterson has, on a very short timeline, given us all the help needed to get the text ready for the printer.

In working out the details of the Health Impact Fund, we have learned from many other ideas and proposals, including those put forward by Michael Abramowicz, Michael Kremer, James Love, Steven Shavell, and Tanguy van Ypersele. Our ongoing work has also received crucial support from the Australian Research Council, the BUPA Foundation, the Canadian Social Sciences and Humanities Research Council, the Centre for Applied Philosophy and Public Ethics, and the Centre for the Study of Mind in Nature.

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# Executive Summary

The Health Impact Fund (HIF) is a new proposal based on two simple insights: (1) privately funded pharmaceutical R&D responds to incentives, and (2) new drugs can have a much larger impact if their prices are low. At present, the most profitable research efforts are not the ones most needed to alleviate the global burden of disease. And high prices often put new drugs out of reach of most of the world's population.

The HIF seeks to correct both of these failings by offering to reward any new medicine, if priced at cost, on the basis of its global health impact. Any firm receiving marketing approval for a new medicine would be offered a choice between (a) exercising its usual patent rights through high prices *or* (b) registering its product with the HIF. Registration would require the firm to sell its product worldwide at an administered price near the average cost of production and distribution. In exchange, the firm would receive from the HIF a stream of payments based on the assessed global health impact of its drug. The HIF is, in other words, an optional pay-for-performance scheme for new pharmaceuticals.

Innovative companies would benefit from this new option because they could profitably introduce important new medicines that are needed mainly by patients who cannot pay high prices. Patients—especially those in the developing world—would benefit through access to new drugs at low prices. By supporting the HIF, citizens and governments in all countries would reap large cost savings on medicines

as well as substantial reductions in the human and economic burdens of disease.

The chief problems with the present system governing the development and distribution of medicines are well known: despite relatively low manufacturing costs, patented medicines are often very expensive and are therefore unaffordable for most people; and diseases concentrated among the poor attract little or no pharmaceutical research. As a result of both factors, the disease burden among the poor is, avoidably, very high. Many diseases of the poor are communicable and expose all of humanity to the risk of new and virulent strains. These problems are further aggravated: by patients who, often deterred by high prices, fail to complete a full course of treatment; by lack of access to competent medical staff who would ensure that medicines are taken correctly; and by counterfeiters, often attracted by high prices, who may dilute a medicine's active ingredients. In addition, competitive marketing and litigation costs reduce the return from innovation, and make it a less attractive investment.

Each of these problems has provoked ideas and initiatives by academics, NGOs, governments, and international agencies. By supporting both innovation and real access, the Health Impact Fund extends the best of these ideas into one comprehensive, unified solution that makes substantial progress toward a rational system of developing and distributing worldwide the pharmaceuticals we all need.

This book explains how the HIF would work and why the world needs it. Chapter 1 provides a summa-

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ry overview. The next four chapters examine in detail how the HIF would operate. Chapter 2 discusses the proposed mechanism for deciding how much each innovative drug would earn based on its assessed health impact. Chapter 3 shows how health impact can be measured while also examining the difficulties such measurement would have to overcome. Chapter 4 explores the HIF's governance and administrative structure. Chapter 5 considers the commitment of funding partners.

The following four chapters explore the rationale for the HIF. Chapter 6 constructs a moral argument, based on widely recognized human rights, for implementing the HIF. Chapter 7 shows how the HIF would help address the important "last mile" problem of ensuring effective distribution and use of pharmaceuticals in poor countries. Chapter 8 shows, from an economic perspective, how the HIF would usefully supplement the patent system, and Chapter 9 examines the relationship between the HIF and other proposed reforms. Chapter 10 summarizes the above and shows how this new mechanism can be brought into being.

The HIF is a work in progress, to be further perfected and completed with the help of many stakeholders. This book's objective is to show that, and how, the existing rules governing the development and distribution of new medicines can be improved upon in ways that would dramatically enhance global public health. The Health Impact Fund is a *feasible* complement to the existing regime. Governments have decisive moral reasons to implement the HIF and citizens have decisive reasons to urge their governments to do so.

Most countries are unable to institute the HIF single-handedly. But governments can make a conditional commitment to participate if enough others are also willing. Given a threshold participation of states representing about one third of global income, the founding partner states can commence the Fund at a cost of 0.03 percent of their respective gross national products. The Fund would then become operational within three years and be enhanced thereafter as experience warrants. There is little to lose, much to gain, and no time to waste.

# I. The Health Impact Fund: A Summary Overview

## THE HEALTH IMPACT FUND: PAY-FOR-PERFORMANCE

The goal of pharmaceutical innovation is improved health. The Health Impact Fund will give innovative firms an option to be directly rewarded based on their contribution to this goal, without impeding access through high prices. It will thus be able to achieve the twin goals of stimulating pharmaceutical innovation in the most important therapeutic areas *and* enabling widespread access.

The integrated solution the HIF provides is global in scope. Many innovative firms have found it difficult to make money in poorer countries because the low prices required to generate substantial sales in those markets made it impossible to charge high prices to wealthier people in those and other markets. The HIF eliminates this problem by requiring a uniformly low price worldwide, while offering innovative companies direct payment based on the health impact of their innovations, no matter where the health impact occurs.

This approach will make it profitable to develop medicines for heretofore neglected diseases as well as medicines with global impact. And these medicines will be sold at low prices all over the world, while still generating a return for the shareholders of innovative pharmaceutical companies.

The essence of the proposal is to offer firms a share of a fixed fund for each of ten years, in proportion to the share of health impact of their registered product out of all registered products. For example, if all reg-

istered products were estimated to have saved twenty million “Quality-Adjusted Life Years” (or QALYs), a registered product which had saved two million of those QALYs would receive ten percent of the fund. This calculation would be performed every year, and each registered product would receive a payment based on this approach for ten years following market approval. In exchange, the firm would agree to sell its product worldwide at a specified low price, roughly equal to the average cost of manufacturing, and to offer a royalty-free open license for generic versions of the product following the ten-year reward period. Firms could choose whether to register any particular product for health impact rewards or to exploit their monopoly pricing privilege in the usual way.

Capitalism has improved the lives of billions of people ... But it has left out billions more. They have great needs, but they can't express those needs in ways that matter to markets. So they are stuck in poverty, suffer from preventable diseases and never have a chance to make the most of their lives. Governments and nonprofit groups have an irreplaceable role in helping them, but it will take too long if they try to do it alone. It is mainly corporations that have the skills to make technological innovations work for the poor. To make the most of those skills, we need a more creative capitalism: an attempt to stretch the reach of market forces so that more companies can benefit from doing work that makes more people better off.

Bill Gates

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Funds for the HIF will be provided by partner countries that agree to support it. The greater the support provided to the HIF, the more effective it will be in encouraging widely accessible innovations. The system can be scaled up as larger amounts of funding become available, but a reasonable starting level would be six billion dollars per year. At this scale, the HIF could support the development of about two new drugs per year, sustaining a stock of about twenty medicines.

The HIF is designed to use market forces to set the rate of payment made to innovators: the more patented medicines are registered with the HIF, the lower would be the payment for any given health impact. Market forces will also determine sales volumes of registered medicines without the monopoly price distortions that are otherwise typical of pharmaceutical markets. In many countries today, pharmaceutical pricing is to a large extent controlled by governments. The HIF would employ a method for determining payments to innovators that is more transparent and less subject to influence than the mechanisms used by state and private insurers today. And unlike systems in which research is funded directly, the HIF would not intervene at any stage in funding research: it would only reward successfully developed products based on their assessed impact. Difficult decisions about which molecules should be explored and tested, and how to allocate research funds among particular illnesses would be left to firms with a financial stake in the decision. The HIF is thus more market-oriented and less prone to creating distortions than are existing systems of financing pharmaceutical innovation. It pays strictly on the basis of performance.

### WHY THE HEALTH IMPACT FUND IS NECESSARY

The global pharmaceutical industry should serve two critical needs: to create new medicines that are important to global health, and to enable people all over the world to access these products once they are developed. A system that promotes innovation without also ensuring access is cruel to those who are excluded from medicines by high prices. And achieving

low drug prices is of little value if the most urgently needed remedies are not being developed.

The Health Impact Fund is specifically designed to address both those needs by rewarding pharmaceutical innovators directly on the basis of health impact, while requiring low prices to enable access. In addition, the HIF will create incentives for manufacturers to engage in facilitating the appropriate distribution of their products in poor as well as in wealthy countries, since improved (appropriate) use will increase the rewards they earn. Since the HIF will reward health impact on anyone in the world at an equal rate, innovators will find it profitable to develop medicines to treat even the poor – especially given that among them the greatest health impacts are waiting to be realized.

Our current systems of innovation are not fully achieving the needs of patients or even of investors in the pharmaceutical industry. They encourage drug firms to spend too much on developing minor modifications of existing drugs and on competitive marketing and patent litigation, instead of focusing their efforts on the innovations that would have the largest global health impact. This is not what patients need, it is not what the research scientists want, and it does not seem to be creating the returns that investors demand.<sup>1</sup> Firms are responding to the incentives they face, and doing the best they can given those incentives. Under the present system, firms have incentives:

1. to focus on the diseases of the people who can pay a lot of money when they get sick, even though those diseases tend to have many available treatments already, and the incremental health gains are typically small;
2. to extend the monopoly position of existing patented medicines by incremental changes; and
3. to duplicate other firms' blockbuster medicines by creating "me-too" drugs.

Of course, while those activities have some value, they may not have much effect on the overall health of the world's population.

The Health Impact Fund will offer innovators the option to be rewarded for global health impact, even

if most of the people consuming their products are poor and can only afford medicines priced near cost. This opens up a range of diseases and treatments which so far have been of only marginal interest to investors, since under the current system they have little prospect of benefiting from sales to the poor. The HIF will thus benefit investors, researchers, and wealthy and poor patients alike. Of course, these benefits come at a cost: governments and private foundations will have to finance the Fund for it to be able to reward innovators.

Currently, diseases concentrated among the poor are “neglected diseases.” An example is human African trypanosomiasis (sleeping sickness)<sup>2</sup> with about sixty thousand infections reported annually and perhaps ten times as many going unreported. Diagnosis of this disease is difficult, and current treatments have severe side effects and involve frequent infusions at a clinic.

There has certainly been welcome progress in addressing neglected diseases, much of it due to an increase in charitable contributions. PPPs (private-public partnerships) have successfully enhanced the rate of development of new drugs in the absence of significant new government incentives, through contributions from pharmaceutical companies and philanthropic foundations.<sup>3</sup> Despite these laudable efforts, the attention of pharmaceutical companies naturally continues to be focused on products which can be profitable to them. Unfortunately, while the poor are numerous, they cannot pay very much for drugs. It is therefore typically unprofitable to develop drugs for diseases concentrated among the poor. There are other obstacles as well: in the absence of well-developed primary care systems, diagnosis may be incomplete or absent; and distribution systems may be expensive, effectively impeding both demand and supply. For all these reasons, some pharmaceutical firms have shunned altogether the diseases of the poor.

With respect to drugs for global diseases, which affect people all over the world, manufacturers of patented products tend to set high prices which exclude some buyers, both in rich and in poor countries. Differential pricing between rich and poor consumers, between or within countries, is difficult: arbitrageurs<sup>4</sup> will try to buy the good cheaply and resell it at the

higher price. Even without parallel trade, there is a network of international price comparisons which makes it hard for firms to charge different prices in different countries or within the same country. But then, if the innovator firm sets a high price even in poor countries, its sales volume will be low and it may face a risk of compulsory licensing or of bad public relations.

Firms operating in other markets don’t usually face such problems. Few would demand that Siemens sell its refrigerators at low prices to the poor, but many people believe that Sanofi Aventis should sell its drugs at low prices to poor patients. Such atypical demands are directed at the pharmaceutical industry because this industry is in the business of saving lives. Under the prevailing rules, these ethical demands are in conflict with the for-profit nature of pharmaceutical firms, which have a legal responsibility to their shareholders.

These problems can be solved only through a mechanism such as the Health Impact Fund, which aligns the mission of pharmaceutical firms, to promote public health, with their responsibility to make money for their shareholders. The HIF is not a system which looks to the pharmaceutical companies for philanthropy: instead the idea is to offer them the opportunity for market-based rewards for the contribution their products make to improving global health.

We need a bolder effort to solve the global problem of drug pricing. Prescription drugs are truly global products today, and we need a global strategy to get the most benefit from new medications for all of the people of the world. Specifically, it's time for developed nations, recognizing their shared interest in bringing better treatments to market, to find ways to fairly share the cost of new drug treatments.

Mark McClellan –  
Commissioner of the US Food and Drug  
Administration 2002–2004

The HIF would not merely stimulate the development of medicines that are unprofitable in its absence. Products such as Plavix (which helps prevent heart attacks and strokes) could offer therapeutic



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value throughout the world, and yet their sales tend to be concentrated in the wealthiest countries due to relatively high prices. If rewarded under the HIF, such products could see enormously expanded sales volumes because of lower prices. Depending on the scale of funding of the HIF, this could be a more profitable way of selling such drugs—and it would be of tremendous value to patients all over the world.

### PROPERTIES OF THE HEALTH IMPACT FUND

The HIF approach to solving problems of innovation and access is straightforward: pay directly for what is valuable, and don't ration access on the basis of artificially high prices. This simple and intuitively compelling approach has many attractive characteristics.

- The mechanism of the HIF is designed to give incentives for innovation, the strength of which is proportional to the social value of the innovation, as measured by health impact. No other approach to paying for innovation has this desirable property. The patent system places a value on an innovation based on people's willingness to pay, which, for essential medicines, is closely related to their ability to pay. As a result, the patent system rewards innovation which addresses the health needs of the wealthy much more than those of the poor. The HIF redresses this imbalance and motivates firms to invest in research with the greatest impact on health.
- The HIF eliminates the need for high prices, which is of course a significant obstacle to making important drugs accessible to the poor. The savings from low drug prices, however, will accrue to everyone.
- The low price of HIF medicines reduces the incentives for counterfeiting, which is a blight on pharmaceutical markets, especially in developing countries. Counterfeit drugs harm not only manufacturers, but, when they fail to contain the correct amounts of the relevant active ingredients, may also harm patients and, in the case of communicable diseases, people everywhere (by causing development of disease-resistant strains).
- The HIF is ethically attractive because it solves the problem of obtaining innovation without blocking access through artificially high prices.
- The HIF is scaleable: if it works well, it can be expanded by increasing the amount of funding available.
- The HIF has a clear objective and straightforward rules. It requires relatively little administrative discretion.
- Because the HIF is an optional system, there is an automatic adjustment mechanism to ensure that the payments it makes are reasonable relative to the profits earned on other drugs not registered with the HIF: if payments get to be too high, more products will be registered with the HIF and payments will fall as funds are spread over more products. The reverse effect operates if payments fall too low. This not only limits the risks of insufficient payments faced by firms that register their products with the HIF, it also curtails the risk faced by funding partners of excessive payments.
- The HIF addresses the "last mile" problem of getting drugs to the poor who need them. While the present regime provides strong incentives to expose affluent people to patented medicines they do not need, it provides no incentives to ensure that poor people benefit from medicines they do need. However, in the HIF system, registrants will be financially motivated to encourage appropriate use of their products among both the rich and the poor, since the amount of health impact will in part depend on the number of people using the medicine effectively.
- The citizens of the wealthier countries benefit not only directly from lower drug prices and a greater industry focus on achieving actual health impact, but also indirectly from improved health in developing countries which has global benefits in terms of economic growth and reduction in the development and spread of harmful pathogens.
- The HIF can reduce expenditures by pharmaceutical companies on promotional activities and litigation. To the extent that pharmaceutical companies can reduce such wasteful competitive expenses, they will obtain higher profits and will

be more strongly motivated to innovate and to register their products with the HIF.

It is instructive here to compare the HIF to the Advance Market Commitments (AMCs) espoused by the G8 finance ministers. What makes the HIF different is that (1) it applies to all kinds of pharmaceutical products that improve human health, and not just a particular prespecified vaccine for a neglected disease; (2) it doesn't require a body of experts to set a price, since the reward paid under the HIF arises endogenously from choices by firms about which products to register in the HIF; (3) it can offer incentives for R&D at an early stage because it isn't exclusive about the products that can be registered; and (4) it rewards the innovator not by subsidizing sales but on the basis of the health benefits this medicine actually brings to patients. For supporting R&D on specific vaccines, AMCs are an effective mechanism. But for pharmaceuticals generally, the HIF is arguably the best mechanism for inducing innovations that will be widely accessible.

In summary, as a mechanism for incentivizing innovation of and access to essential medicines, the HIF has a unique combination of advantages which the succeeding chapters lay out in greater detail.

## THE HIF IS NOT CHARITY FOR THE DEVELOPING WORLD

In the wake of the World Trade Organization's Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement, which has introduced stronger pharmaceutical patent protections into the less developed countries, much greater attention has come to be focused on the deplorable health care situation of the world's poor: the three-quarters of humanity currently unable to afford patented medicines. Many – including some of those who have pushed hardest for or benefited the most from the much-strengthened intellectual property regimes, the United States, Bill Clinton, and Bill Gates, for example – have adopted the cause of improving the health of the world's poor and are directing billions of dollars to it. Many others have developed interesting and promising ideas

about how this can best be done. Is the Health Impact Fund another such idea?

Yes, and no. Yes, because, properly funded, the HIF would make a huge difference to what health care the world's poor have access to. It would have this effect in three main ways. The poor will have immediate access to some new high-impact medicines that would otherwise sell at high, patent-protected prices. The poor will have immediate access to some other high-impact new medicines that would otherwise not have been developed. And the poor will greatly benefit from a newly created motive of pharmaceutical firms: to ensure appropriate use of their products.

No, because the HIF has corresponding benefits also for the affluent. They too will be able to purchase at low prices some new high-impact medicines that would otherwise sell at high prices. This difference will be most obvious to individuals who lack complete drug insurance. But even for people with drug insurance, the lower prices of HIF-registered drugs will result in lower insurance premiums and national health system expenditures.

The affluent will benefit alongside the poor also from the existence of new medicines that would not otherwise have existed. It is likely that, in the short term, these medicines will mostly treat communicable diseases of the developing world. But, so long as these diseases are very poorly controlled there, they pose a substantial danger to all humankind. It is in everyone's interest that the diseases of the poor not be treated with half-measures that lead to drug resistance and new virulent strains, but that they be fully understood and, if possible, eradicated. In the medium to long term, once the "low-hanging fruit" in treatments for tropical diseases has been picked, the HIF is likely to become more focused on supporting innovation for global diseases.

The affluent will also benefit greatly from a realignment of pharmaceutical companies' interests with actual health impact. After all, the interest of affluent people is not in maximizing their medicine consumption as measured in dollars, but to make rational use of medicines toward achieving better health. Pharmaceutical companies have an enormous influence on the practice of health care in afflu-

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ent countries through the diseases they research, the remedies they develop, their influence on the prescription patterns of doctors, and their interactions with national health systems, insurance companies, and legislators. In exerting this influence, these firms are obviously motivated by maximizing their profits. And wouldn't it be good for all – rich and poor alike – if these firms' profits on some of their more important medicines were precisely aligned with the health impact these products actually achieve?

The HIF is not then about affluent people or countries helping poor people or countries, but a crucial addition to the established system governing the development and distribution of medicines. Being optional for innovators, the HIF will initially produce some very important medicines for diseases concentrated among the poor – medicines whose development is not lucrative under the present regime. But in the medium term, the HIF will attract high-impact medicines for global diseases and conditions: those that will make a great difference to the health of rich and poor alike.

With Voltaire one might say that not creating the HIF is worse than a crime, it is a blunder. But we believe that it would be a crime as well. In both rich and poor countries today, poor people—and even people who think they are wealthy enough until they get sick—are unable to purchase the drugs they need because the price is too high. This is not an accident. Patents create monopoly power, which enables the patentee to push prices up as long as the loss in profits from lost sales is smaller than the increase in profits from higher prices. Given the enormous disparities in incomes between and within countries, this means that profit-maximizing companies are forced to deny people access to life-saving medicines in order to meet their obligations to shareholders. That is a hard decision: but if the HIF were created, no one would have to make that decision. Firms would increase their profits by treating more people, rather than the other way around.

An astonishing feature of the HIF is that this realignment of incentives needn't cost more. Wealthy people are already paying for pharmaceutical R&D through the high prices they pay for drugs, or the high insurance premiums and taxes to support gov-

ernment health systems. The HIF reduces the amount consumers pay for drugs through high prices, premiums, and taxes, and takes about the same amount through taxes to be paid on the basis of health impact. Here the HIF takes advantage of the fact that allowing poor people to purchase a drug at marginal cost does not increase the cost to be borne by anyone else. The costs of R&D have to be covered somehow, but obliging firms to cover these costs through high prices that will lead people to die is deeply, morally, wrong. The HIF offers a workable, practical solution to this important moral dilemma.

Intellectual property differs from other property—restricting its use is inefficient as it costs nothing for another person to use it. Thomas Jefferson, America's third president, put it more poetically than modern economists (who refer to “zero marginal costs” and “non-rivalrous consumption”) when he said that knowledge is like a candle, when one candle lights another it does not diminish from the light of the first. Using knowledge to help someone does not prevent that knowledge from helping others. Intellectual property rights, however, enable one person or company to have exclusive control of the use of a particular piece of knowledge, thereby creating monopoly power. Monopolies distort the economy. Restricting the use of medical knowledge not only affects economic efficiency, but also life itself.

Joseph Stiglitz

### HOW THE HEALTH IMPACT FUND WOULD WORK

This section briefly describes how the Health Impact Fund would actually work. A more detailed account of all these aspects is given in chapters 2–5 of this book.

#### Granting Payments

The Health Impact Fund would have a fixed pool of money to pay out annually. Each year, this amount would be disbursed, and each firm would receive a

share of the pool equal to the share of assessed health impact of its registered medicines. When assessing health impact, the HIF would essentially estimate the difference between (1) the actual health status of people who consumed the registered product and (2) the estimated health status of those people, had they not had access to the registered product, or to any other products introduced less than two years before the registered product. (The HIF would also take into account effects due to decreased transmission of communicable diseases.) That is, the HIF will estimate the incremental health impact of each product registered with it, setting the baseline at the set of technologies two years before the registered product became available. This incremental health impact will be estimated each year for ten years during which the firm will be eligible for payments, and in each of those years, the firm will receive a share of the available funds. If agreed by funding partners, the size of the fund could be expanded automatically if the payment per unit of health impact dropped below a predetermined floor.

To be eligible to register a product under the HIF reward scheme, a company must hold a patent (on the product) from one of a set of patent offices specified by the HIF. It can then register its product with the HIF and will then be rewarded on the basis of the product's global health impact in its first ten years following marketing approval. To register a product with the HIF the company would be required to:

1. make a good faith effort to obtain market clearance wherever the product is needed;
2. preauthorize the HIF to seek market clearance for the product wherever the registrant has failed to do so and to subtract the cost of this effort from the registrant's next health impact reward payment;
3. sell the product at a low price, no higher than the long-run marginal cost of production and distribution as determined by the HIF, wherever the product is legal and needed;
4. preauthorize the HIF to sublicense the relevant patents to generic firms who would supply it wherever the registrant fails to provide an adequate supply;
5. provide sales data and other evidence required by the HIF for assessing the product's global health impact during the reward period;
6. pay a yearly fee calculated to cover the costs of health impact assessment; and
7. preauthorize the HIF to sublicense the relevant patents to generic firms following the end of the reward period.

A company could seek preregistration clearance from the HIF to ensure that its product is suitable for HIF registration. Some products might be unsuitable—for example, if a drug were about to become generically available, the HIF would not wish to pay for health impact of a slightly different version of the same product.

## Assessing Health Impact

It would be necessary to summarize the health impact of each product registered with the HIF using a single measure. The standard measure of health impact is the Quality-Adjusted Life Year, or QALY. A drug that extended a person's life by ten healthy years would be recognized as having created ten QALYs. The health impact of a medicine will be considered to have occurred at the time the medicine was consumed; so the entire ten years of extra life would be rewarded even if some of these years fall beyond the end of the medicine's specific reward period. Health impact would be evaluated without regard to wealth or income, and aggregated globally, to assess a drug's total health impact in each year.

Assessing QALYs is difficult, and it would take a great deal of data to be able to make such evaluations credible. The essence of the assessment process involves obtaining evidence on the incremental effect on health of the average consumer of the registered product. When the registered product simply displaces some existing medicine, the analysis is relatively straightforward. But typically a medicine's QALY impact would be more complex, arising from an improved therapeutic profile, from increased use due to a lower price, and from more effective use due to better prescription and patient instruction practices.

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The assessments would be based not only on the kind of information that is commonly available about medicines today. Instead, firms would be required to provide information about their sales directly to the HIF, and would pass on such requirements to their distributors. At the same time, the registrant would have a strong incentive to provide comparative data on its product's effectiveness relative to others, since this would provide evidence for payments from the HIF.

The difficulty of rewarding innovators on the basis of assessed health impact is significant, but the alternative is to reward innovators on the basis of ignorance. The current situation is that insurers—state or private—determine access to drugs for most people in developed countries. They list drugs on their formularies only after doing some kind of assessment regarding the drug's effectiveness and comparing that to its price. The HIF thus requires a judgment to be made on cost-effectiveness similar to that commonly made by insurers today. An important difference is that while most insurers today make their listing decision based on preliminary information from clinical trials about the product's effectiveness, the HIF will rely on data derived from the actual use of the product.<sup>5</sup> In addition, unlike most insurers, its payments are conditional on incremental improvement over alternatives. (Most insurers list new drugs on the formulary if they are no less effective and no more expensive than other similar products.)

Because health impact would be assessed on a global scale, for a variety of types of medicines, a variety of tools would have to be used. Manufacturers would be obliged to submit information about the distribution of their product, or to require distributors to submit such information to the HIF, so that the amount of information about how drugs were being distributed would increase substantially. Random sampling could be used to evaluate how drugs were actually being used in different countries, as well as their effectiveness. The data obtained in this way would be correlated with known global burden of disease measures as a further check. Data from "pragmatic trials" could be combined with data from clinical trials to obtain estimates of the difference between use in ideal settings and use in actual settings.<sup>6</sup>

The Health Impact Fund, as described in chapter 4, would have a substantial department specializing in undertaking continuous evaluation of the health impacts of registered medicines. This would be an expensive feature of the fund. However, not only would this provide the most reasonable way of determining the "reward" for a given drug, it would also create an extremely valuable resource in practical prescribing, since the actual health impact of drugs would be better understood. It would also provide vital data for the promotion of development generally, by poor-country governments, international agencies, NGOs, development aid ministries, etc.

### Funding

The HIF would require substantial government funding, including initial commitments of at least six billion dollars per year. (The net incremental cost to the partner countries would, however, be a fraction of this, since there would be substantial savings from paying low prices on new, patented medicines registered with the HIF.) Partner countries would have to commit to financial support for at least twelve years into the future at any time, so that innovators would have some assurance about the payments they could expect to receive. An ideal structure would involve countries committing a fixed share (perhaps 0.03 percent) of their annual gross national income, so that the HIF would grow in proportion to their economies. Such an approach would also ensure a kind of parity between the contributions of funding partners and lead to a larger scale of funding than any partner would achieve on its own.

It is helpful to put the proposed size of the HIF in the context of annual expenditures on drugs. To do this, let us assume that countries representing one-third of the global product agree to underwrite the HIF. (This one-third target is very easily reached if the HIF is joined either by the United States or else by all or nearly all member states of the European Union.) On this assumption each country would need to contribute 0.03 percent of its gross national income (GNI) in order to reach the minimum \$6 billion Fund size. For affluent countries with GNI per capita of around \$40,000 *per annum*, committing



0.03 percent of GNI would constitute a contribution of \$12 per citizen per year – as compared to average annual per capita expenditure on pharmaceuticals of \$413 in the OECD countries (2005).<sup>7</sup> The actual net cost of the HIF to OECD citizens would be well below \$12 because of the savings they would realize on HIF-registered drugs that, without the HIF, would cost much more. These small net costs are associated with much larger benefits. They would stimulate the development of widely accessible new medicines that greatly reduce morbidity and premature mortality worldwide, would thereby improve global economic performance, and would also reduce dangers from heretofore neglected diseases.

The contributions of funding partners would initially grow over the course of three years to the target level. The reason for having a lower funding level initially is that the number of drugs in the system would initially be smaller, and would increase as more new drugs were registered with the HIF. Contributions would remain at the target level thereafter. If a country were to decide to leave the system as a funding partner, its commitment would require it to continue to contribute over a period of years, though at a declining rate each year. This commitment would be necessary to provide innovators with assurance that after they register their product the HIF will have sufficient funds to meet its obligations.

## Administration and Governance

The administrative structure of the HIF would consist of three main branches: the technical branch, the assessment branch, and the audit branch. The technical branch would determine standards for how health impact was to be assessed, so that there would be consistent expectations across countries and across diseases about data and how it would be interpreted. The assessment branch would apply those standards to the observed data, and assess the health impact of each registered product. The audit branch would check the integrity of this process.

The Board of Directors of the Health Impact Fund would bear ultimate responsibility for overseeing this process. As such, it would need to have the support of the funding partners, and so the composition of

the Board would naturally include representatives of each contributing country, presumably with a voting representation based on their contribution share. It might also be suitable to include other stakeholders on the Board.

## THE HEALTH IMPACT FUND: DIRECTIONS FOR PROGRESS

The Health Impact Fund offers an integrated approach to solving problems of innovation and access to medicines, and along the way addresses many other important issues in pharmaceutical markets, including neglected diseases, counterfeiting, and excessive marketing expenditures. The remainder of the book explains in much more detail how the HIF would work (chs. 2–5) and why it is attractive (chs. 6–9).

Man's mind, once stretched by a new idea,  
never regains its original dimensions.

Oliver Wendell Holmes

This book is a work in progress meant to invite the views and perspectives of the wide variety of stakeholders who would be affected by the implementation of the HIF. Governments, pharmaceutical companies, and citizens should carefully consider this proposal. Their challenges and confirmations, refinements and support will be essential in further progress on the HIF idea.

Ultimately, the HIF can become a reality only if it receives financial support from governments. Since most countries will want to participate only if others share the financial burden, a sensible approach to making progress is for countries to agree to offer financial support conditional on the participation of enough other countries. For example, countries could commit to become founding partners in the Fund at a rate of 0.03 percent of GNI once countries representing one third of global income have made a like commitment.



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### NOTES

1. Over the last five years (July 2003 – July 2008), the Dow Jones Industrial Average has risen by 25%. In contrast, the Pharmaceutical Index (DRG) is down by 4% over the same period.
2. Chirac and Torreele (2006).
3. Pharmaceutical R&D Policy Project (2005, 4).
4. An arbitrageur is a person who takes advantage of price differentials between individual markets.
5. In fact, some insurers have successfully used “no-cure, no-pay” arrangements with drug manufacturers in which the payments to the manufacturer is conditional on the actual success of the product. This obviously requires monitoring similar to the assessment process of the HIF. (See, for example, Moldrup 2005, Hughes, Tunnage, and Yeo 2005.)
6. Roland and Torgerson (1998).
7. OECD (n.d.).

## 2. Reward Mechanism

*The Health Impact Fund pays rewards for registered products over a fixed number of years. The funds paid out in any given year are divided between the registered products in accordance with the health impact each product has achieved in this year. Details about the entry, exit and patent status of products as well as the attribution of health impact are discussed against the background of a variety of design options.*

### INTRODUCTION

The essence of the HIF mechanism is that innovators are rewarded in proportion to the measurable net health impact of their innovations. The HIF would have a predetermined reward fund available for distribution to innovators in any given year. Each year, registrants of eligible innovations would receive payment in proportion to their share of the health impact created by all eligible innovations.

This mechanism creates incentives for innovation that are efficient in the sense of maximizing health impact for a given amount of payments by aligning the interests of the innovator with society's interest in public health. The HIF incorporates Arrow's (1963, p. 964) prescription for "ideal insurance" in which the healthcare provider receives payment "in accordance with the degree of benefit," though it also modifies it, since firms must compete to obtain these payments from the HIF. This competition, together with the fact that the HIF is an option, ensures that the payments made to innovators are fair and reasonable.

There are many ways that the reward mechanism might be specified, and it is difficult to determine which design option is to be preferred in advance of further engagement with stakeholders. To help fix ideas and to provide a more concrete starting point for discussion, we offer a reasonably detailed sketch of one plausible reward mechanism in the next section. We then describe and discuss alternative design options.

Motivation is the art of getting people to do what you want them to do because they want to do it.

Dwight D. Eisenhower

### SKETCH OF A REWARD MECHANISM

Firms can choose to register a drug in the HIF system at any time. Generally, the firm will decide at or before the time of market approval in major markets. The registrant is the firm that owns or has licensed all the patents required to manufacture and sell the product.<sup>1</sup> Registrants of eligible innovations will receive in each of the first ten years following the initial market approval of their product, a payment based on the estimated incremental global health impact of the product as determined by the Health Impact Fund for that year. This payment would be  $S \times F$ , where

$S$  is the estimated Health Impact of that product divided by the sum of the estimated health impacts for all products eligible for reward in that year;

$F$  is the fixed amount of the HIF available for disbursement in that year.

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Payments would in no case exceed a ceiling per Quality-Adjusted Life Year (QALY), the level of which is yet to be determined. (In order to protect registrants, this ceiling could be lowered by the HIF only if prospective innovators are given ten years advance notice.)

Following the ten year payment period, the HIF is entitled to offer royalty-free limited licenses in all jurisdictions, of all patents required to manufacture and sell the product, limited to use in manufacturing and selling the product. This would enable generic competition following the ten year payment period from the HIF.

In some cases, the registrant may face generic competition. When there is such competition, the HIF will include any health impact attributable to sales of generic versions some product when calculating its estimated health impact.

In cases in which the registrant has shown and obtained approval for a new indication of an existing product, *S* will be based on the estimated health impact for that product in its new indication. Such a new indication would be eligible for rewards for five years.

In exchange for these payments, the registrant would be required to supply its product at an administratively determined price in all countries where the product is legal and is needed.

These payments and the relevant conditions are discussed in more detail below.

### Eligible Innovations

Eligible innovations include (1) new drugs that achieve approval in the jurisdictions in which they are sold, and which are protected by patents in at least some set of major patent offices;<sup>2</sup> and (2) new, approved indications for existing drugs when the new indication is patented. If the product is not generically available, the patentee of a new use for an existing product will not be eligible for payments unless it agrees to sell the product at cost, as described below.<sup>3</sup>

The HIF has discretion to refuse to allow registration of medicines that have been previously marketed in a slightly different version, if the older version is generically available or if the HIF expects that it soon will be.

### Obligations of Drug Registrants

Payment by the HIF to a registrant will entail certain obligations on the part of the registrant. To register a product with the HIF, the company is required to:

1. make a good faith effort to obtain market clearance wherever the product is needed;
2. preauthorize the HIF to seek market clearance for the product wherever the registrant has failed to do so and to subtract the cost of this effort from the registrant's next health impact reward payment;
3. sell the product at a low price, no higher than the long-run marginal cost of production and distribution as determined by the HIF, wherever the product is legal and needed; and
4. preauthorize the HIF to sublicense the relevant patents to generic firms who would supply it wherever the registrant fails to provide an adequate supply;
5. provide sales data and other evidence required by the HIF for assessing the product's global health impact during the reward period;
6. pay a yearly registration fee calculated to cover the costs of health impact assessment; and
7. preauthorize the HIF to sublicense the relevant patents to generic firms following the end of the reward period.

A company may seek pre-registration clearance from the HIF to ensure its product's suitability for HIF registration. Some products are unsuitable—for example, if a drug is about to become generically available, the HIF ought not to pay for health impact of a slightly different version of the same product.

### Health Impact

As discussed in more detail in chapters 3 and 4, the Assessment Branch will estimate the incremental health impact of each product or new use globally. The health impact will be estimated each year during the payment period (ten years for new products and five years for new uses), with the health impact understood in terms of the attributed incremental

health impact of the intervention in each year of the payment period, for all approved indications.<sup>4</sup> For interventions that affect the patient only (that is, for non-communicable diseases), the effect would be assessed in terms of the estimated lifetime of the individual. For interventions with externalities (that is, for communicable diseases), the effect will be assessed for the estimated lifetime of the individual who consumed the product, and for a fixed period (for example, ten years) for all other indirectly affected individuals.

The incremental health impact of a given product is defined by the difference between the actual health and a baseline. The baseline is conceived as the expected health level of consumers of the product being assessed, given the set of pharmaceuticals available, their approved indications, and their prices, at the time when the product was first commercially marketed or two years prior to that (with the firm to choose), excluding the new product and any others sold exclusively by the same registrant. The motivation for allowing the baseline to be specified in this manner is that it is frequently the case that firms develop similar drugs at the same time in the wake of some significant clinical or biomechanical advance. If two similar drugs are in simultaneous development, the two-year lag in the baseline will allow both drugs to obtain similar payments per unit.<sup>5</sup>

Thus, at the time that a new product registered with the HIF is introduced, the HIF will essentially take a “snapshot” of the state of care for people whom the product is intended to treat (or, if requested by the registrant, a snapshot of the state of care of such people two years prior to the registration of the drug) and set that as the baseline. Given that there will likely be a fairly small set of drugs introduced to the HIF each year, this approach seems more feasible than trying to keep a constant review of the state of care for all diseases every year.

All innovations developed by the registrant and currently eligible for payments from the HIF will be excluded from the baseline for that registrant. Thus, a firm would find it profitable to introduce incremental improvements on its own products registered with the HIF without the risk of cannibalizing payments. However, if a firm developed a product which

was slightly superior to a different firm’s product, the baseline would include the different firm’s products and in this case, the reward for the incremental improvement would simply be based on the incremental health impact realized.<sup>6</sup>

The fact that a given firm’s products are excluded from the baseline means that it will be more profitable for a single firm to offer two similar products than for two firms to offer the same two products. In turn, this implies that firms may wish to merge to take advantage of this relationship. In a way, this is similar to the fact that firms with similar products in markets without the HIF may wish to merge to prevent costly marketing and price competition between their products, since this undermines the profitability of both firms. Antitrust laws are designed to prevent mergers when they harm consumers by increasing prices. However, with products on the HIF, there would be no price effect on consumers, and only an impact on how much of the HIF payments the merged firms could capture. Thus, antitrust laws would typically fail to stop such mergers. This seems to suggest that the HIF might have to specify that when firms merged, the baselines applicable to their products would not change.

In cases in which there are synergistic effects between two different registered products, each product will receive a supplementary payment. The supplementary payment for each product will be half the normal payment for the estimated synergistic health impact. If only one product is registered with the HIF, and the other is not registered, the product registered with the HIF will be eligible for its entire incremental effect on health, including any synergistic effect. The treatment of synergistic effects is discussed more fully below.

### **The Administered Price**

The HIF will set an administered permissible price range for wholesale sales of all products registered with it, with all sales of the product to be between the permitted maximum and minimum prices. This price range would be determined at that time for the entire payment period, and might be automatically adjusted through the use of an inflation index.<sup>7</sup> The

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administered price range will be listed for each product on the HIF website, so that any buyers can know that the product should be available in that price window, and will therefore be encouraged to report sales outside that range.

The maximum of the administered price window would be set by the HIF at a level intended to mimic average manufacturing and distribution cost, that is, the level at which one would expect generic firms to be able to compete. The minimum of the window would be set at approximately marginal cost of production and distribution, that is, the economically efficient level. In defining this window, the HIF would have to rely at least in part on expert engineering assessments or possibly quotations from contract manufacturers. The registrant would in general always prefer a wider window for pricing. The actual choice of price within the window will depend on the elasticity of demand, the marginal cost of production, and the expected size of the payment made by the HIF per unit sold. In general, the larger the size of the HIF payment per unit and the greater the elasticity, the lower is the profit-maximizing price. In setting the administered price, the HIF must rely at least in part on expert engineering assessments, or possibly quotations from contract manufacturers.

The purpose of setting a *minimum* price is to help reduce the risk that the product is not used appropriately. For example, the registrant might give the product away in hopes of increasing its reward from the HIF through achieving higher volumes of products shipped. At the same time, if the price were too low, patients might be apt to waste the product, potentially causing environmental harm. In cases in which patients are too poor to purchase the product even at marginal cost, and yet the product is essential to the person's health, there is of course a rationale for subsidy. The question is, who should offer the subsidy? Here we think there is a suitable role for a third party such as government or an NGO to purchase the product on behalf of indigent patients.

Registrants would, however, be permitted to contract with wholesalers and distributors to achieve low retail prices for registered products, provided that the retail price did not fall below the minimum.

### A Ceiling on Payments

In order to protect the interests of donors in case of inadequate take-up of the HIF mechanism, the HIF will set a maximum payment per QALY. Determining how high this ceiling should be is beyond the scope of this chapter. However, some sense of the possible range is indicated by the prices that countries have been willing to pay for healthcare improvements in the past. For example, interventions which cost less than \$50,000 to \$100,000 per QALY are often described as being cost-effective (Ubel et al. 2003). At the other end of the spectrum, antiretrovirals that cost \$350–500 per QALY have been considered expensive in a developing country context (Jamison et al. 2006).

When it is possible for pharmaceutical innovators to develop new pharmaceuticals at costs which are much lower than the ceiling price per QALY, we can expect that they will do so and that the actual payment per QALY will in fact be much lower than the ceiling. If pharmaceutical innovators believe that the ceiling is so low that they can always earn more profits outside the HIF, the HIF will find that it has no take-up.<sup>8</sup>

One consideration in setting this ceiling is that it should probably be relatively high because it is paying for innovation only temporarily, while the innovation itself will be available permanently. Thus, assuming continued use of the innovation, the true *average* payment per QALY attributable to the innovation will always be lower than the ceiling.

### Intellectual Property

A key feature of the HIF is that it does not require any substantial changes to the structure of intellectual property or licensing, and largely mimics the structure of the patent monopoly system. Suppose, for example, that a firm requires its own patents plus those of three other parties to market a drug. In the current system, it will have to obtain licenses from the other parties. The same will hold in the HIF system. If a firm develops a new use for an existing product, it will have to make mutually agreeable arrangements with the patentee if the manufacture of the product is

covered by a patent, whether in the HIF system or in the patent monopoly system.

There are, however, several respects in which the structure of the HIF differs from that of the patent monopoly system. First, the incentives to challenge patents will be relatively weak, since generic companies will find themselves competing not against a firm with high prices, but against a firm with low prices. If the registrant sold the product at a price below the generic average cost of manufacture, generic firms would find entering such a market unprofitable until the end of the payment period, at which time the patents would be openly licensed. This approach would thus largely eliminate the wasteful litigation which consumes a great deal of the resources of pharmaceutical companies under the present system.<sup>9</sup>

Second, patentees will be unable to obtain disproportionate increases in profits through evergreening in the HIF. In the current system, small modifications to existing products may extend the monopoly profits. In the HIF system, small modifications are rewarded with small payments. This would diminish incentives for firms to use the patent system strategically.<sup>10</sup>

Third, firms will be able to make use of patents issued for new uses when those new uses are recognized as new indications. At present, patentees are largely unable to capture the benefits of performing clinical trials to demonstrate efficacy and safety of existing (older) medicines for new indications, leading arguably to inefficient use of our pharmaceutical armament. The problem is that a patent for a new use may not allow the firm to exclude other firms from selling the product, since neither the manufacturer nor the pharmacist necessarily knows how the product will be used.<sup>11</sup> However, the HIF reward mechanism does not require exclusion: it only requires the patentee to provide evidence that the existing drug was in fact used for the new indication.

Finally, note that the HIF fixes the period of rewards at ten years for new products and five years for new indications. In the current system, the period of exclusivity tends to vary considerably, depending on how long clinical trials and the approval process takes. Since a drug which has longer clinical trials is not inherently a less valuable drug, the current

system is flawed in this varied period of exclusivity. The HIF system simply offers a reward period of ten years, regardless of the length of patent exclusivity. This may, in some cases, lead firms to choose to use the HIF rather than monopoly pricing, if their expected patent protection under the current system is relatively short. In this respect the HIF provides a superior system of incentives.

### **Cumulative Innovation**

An important feature of innovation is that it is often cumulative. This creates complex patenting and licensing requirements. As discussed above, the HIF essentially leaves all those requirements unchanged. However, it does change the way that cumulative innovation is rewarded, since relatively minor improvements are rewarded with relatively small payments. This should be seen as a positive feature of the HIF system, since limiting payments for small innovations enables larger payments for clinically important innovations.

### **Which Products Would This System Suit?**

An important feature of the HIF reward mechanism is that it provides the largest rewards for those products with the largest health impact. However, since the system is optional, firms will choose to register their product with the HIF only if this leads to earnings higher than those expected from sales at unconstrained prices. Firms will find the HIF system most attractive for products with high health impact but low profitability under the current system. These are likely to include products that can bring substantial health benefits to people who are poor or located in countries where the patent protection is weak. Thus, this system automatically offers the strongest incentives exactly for those products for which monopoly exploitation under the patent system is most inadequate. This set of potential products is likely to be dominated by drugs and vaccines which are targeted primarily at poor, uninsured people, as those products are likely to have large health impact, but low profitability under monopoly pricing.



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I have always believed deeply in the need to offer more protection to weaker victims of globalization; and as diseases cross frontiers—in fact we now speak of the “sovereignty of disease” over that of States—our globalized world response must always remain ultimately focussed on human beings.

Pascal Lamy

An important aspect of the HIF system is that it is global in nature and offers equal rewards for a life saved anywhere in the world. That is quite different from the rewards earned by unconstrained pricing, which tend to be much higher for drugs which are primarily sold in affluent countries than for those primarily sold in poorer countries. Therefore, it is likely that in the near future, the “low-hanging fruit” is likely to consist mainly of treatments for tropical and contagious diseases, which have tremendous health importance but which have so far attracted relatively little investment from pharmaceutical companies. However, especially in the medium to long term a wide range of products and new uses can be expected to benefit from the HIF.

### A Registration Process

It is possible that not every product meeting the registration requirements for the HIF would really be suitable. For example, suppose that a firm has developed and sold an important product at monopoly prices for many years. It expects this product to become generically available in most countries in the near future. It then develops a slightly modified version of the same product, using a different formulation, which it seeks to register with the HIF. The low price of the new HIF-registered product would substantially increase access (compared to the baseline level of access), and the firm would be entitled to substantial payments on this basis, even though low-priced generic versions of the older product would have been launched globally soon after. This is a case in which the HIF clearly should not grant significant payments to the innovator, since the innovation is really not significant, and yet the proposed terms of how payment is to

be determined allow some scope for firms to abuse the system.

To avoid such abuses, the HIF should be granted some discretion in permitting registration of new products. Ideally, firms would seek an early decision from the HIF as to whether it would accept registration of a given new product. In cases in which the new product offered no meaningful expected health impact compared to other products in the firm's portfolio, or where the firm had shown a pattern of abuse of the system, the HIF should be able to advise the firm that its product cannot be registered.

In general, the HIF should be designed to minimize discretion as the amount of payments made for any product (see chapter four for further discussion of this point). However, because of the variety of circumstances the HIF is likely to encounter, and the limited amount of funds it would be able to pay out, it is important to minimize the extent to which unduly rigid rules enable firms to abuse the system and obtain payments for patented products which embody innovations of marginal, if any, value in terms of health impact.

### DESIGN OPTIONS

The mechanism described above is one of several plausible options for designing the reward mechanism of the HIF. In this section we discuss some alternative designs.

#### The “Price” per QALY

The system proposed above makes the “price” per QALY—or the amount which each registrant is rewarded per QALY assessed—endogenous. There are possible alternatives, discussed below, including setting a fixed payment per QALY, or something in between.

There are several useful features of the endogenous price per QALY mechanism. First, it relies on the market to set the price for health impact. It is clear that the HIF administrators cannot know what “price” per QALY is actually required to stimulate meaningful investment in innovation, so that stipulating in advance any particular “price” per QALY

would be arbitrary and counterproductive. If the decision to enter the HIF system is left up to firms, they will rely on their private information about the probability of success of developing a given innovation and the costs of doing so. That is, as in any market setting, the “price” will be determined by the interaction of agents using private information. In addition, because the rate of payment per QALY generated is created in a system in which firms have the option to exploit their patent rights outside the HIF system, the “price” will be within the range which is available in the patent system for a given health impact.<sup>12</sup> Thus, by relying on this market mechanism, the HIF administrators can automatically generate a level of reward per QALY which is consistent with firms’ costs and which is consistent with the expected rewards which are available for other drugs under the patent system.<sup>13</sup> Thus, it is important to recognize that the reward mechanism employed by the HIF is not a regulatory one in which some administrative body determines the reward: it is a competitive one, in which the reward is determined by the measured health impact of each product.

The mechanism employed by the HIF is not a regulatory one in which some administrative body determines the reward: it is a competitive one, in which the reward is determined by the measured health impact of each product.

A second benefit of fixing the total amount of payments per year is that it removes discretion from the HIF regarding how much it should pay out. This is useful, since it is a simple way of committing to investors that the HIF will not try to skimp on the payments made, and of assuring funding partners that the HIF will not over-estimate health impact to increase the total payments made.

Third, by fixing the total amount of payments per year, the funding partners have no uncertainty regarding the extent of their financial obligations.

Finally, the fixed amount of payments means that firms in the system are forced to compete for payments. This in turn implies that there is a benefit to monitoring other firms’ claims about health impacts. Firms with products which had a claim to a substan-

tial proportion of the HIF payments would have the largest incentive to undermine the claims of the other firms—they might do so by providing information to the HIF.

Unfortunately, a system with fixed total payments, and an endogenous amount of reward per QALY, imposes risks on registrants: their payment is dependent on the number of QALYs created by other registered medicines. Registrants would therefore prefer a fixed reward per QALY if it were set high enough. A fixed reward per QALY would eliminate some of the uncertainty inherent in the system described above, in which each firm receives a share of the HIF allocation. Since, all else being equal, firms dislike uncertainty, anything which increases their ability to forecast future profits would be helpful for them.

However, removing risk from registrants only imposes it on funders. If there is a fixed price per QALY, then the funding partners to the HIF must bear the risk of making larger contributions than they expect in case registered drugs create more QALYs than anticipated, in aggregate.

A further option would be to set a guaranteed minimum level of reward per QALY. This would go some way to reducing the risks to innovators, and if the minimum reward per QALY were set sufficiently low, there would be relatively little risk of exceeding the HIF budget. However, it is in exactly those circumstances where the minimum reward was relevant that the budget would be exceeded. The minimum price therefore has similar characteristics as a fixed price, in that it transfers risk from the pharmaceutical innovators to the sponsors of the HIF.

To reduce risks for funding partners and registrants, the HIF could set a fixed reward per QALY and then limit the number of products eligible for payments from the HIF. If the payments on expected health impacts from products already in the HIF system were getting close to the available funds, the HIF would be made unavailable to other products until there was more space in the system. This approach would ensure that existing registrants could count on continued payments at the expected rate per QALY, while firms with products not yet in the system would face much larger risks, since they would be either in or out, and could be out of the system even if (or be-

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cause) they had a product with substantial health impact which could not be rewarded at the established level given the size of the HIF.

An intermediate solution would be to design a risk-sharing arrangement such that the risk of inadequate payments for registrants was balanced with the risk of unexpectedly large obligations for donors. Such a system might involve increasing the total rewards paid out at some predetermined rate if the total QALYs achieved by all registered products exceeded some number.<sup>14</sup> Provided that the schedule of the price per QALY was defined in advance, the price would be endogenous. Such a system could allocate the risks more efficiently between funding partners and registrants, though possibly at some cost in terms of the attractive characteristics of having a fixed reward pool described above. These issues are discussed further in chapter 5.

If firms express concern that a fixed reward pool exposes them to excessive risk, it is perhaps most suitable for governments to address these risks directly through other funding mechanisms, such as direct grants for early-stage research.

### **A Dollar Ceiling on Total Payments per Product**

Given a fixed payout from the HIF each year, firms face the risk that some product may be developed which has such a large impact—for example, a cheap and effective malaria vaccine—that it captures virtually the entire HIF payment stream over the course of many years. While donors to the HIF might be delighted with such an outcome, the risk of this occurring will tend to deter innovators from entering the system. One possible response to this problem is to limit the proportion of the Fund that a single product can capture in any given year. For example, the HIF could limit the total payments for any product in a given year to at most 50 percent of the fund's payout or to a fixed amount. By limiting the payment for a “blockbuster” product, developers of other less therapeutically important products would have greater assurance that they would be adequately rewarded for their innovations.

This approach would reduce risk and encourage entry. Its main drawback would be that incentives for firms to pursue the most important pharmaceutical advances would be weakened.

### **The Duration of the Payment Period**

In the proposal sketched in above, ten years was fixed as the time period for a new product to be rewarded, and five years was proposed for new indications. These durations are somewhat arbitrary. Ten years is intended to replicate roughly the typical period of exclusivity of new products under the patent system, given that the approval process is so lengthy for new pharmaceuticals. The shorter period of five years for new indications is shorter only because it is likely that, in general, it will be considerably less expensive and less risky to show a new indication than to develop a new product (Ashburn and Thor, 2004). In the former case, the product has already been developed and shown to be safe, and all that is required is evidence that the product is effective in the new indication. Either of these periods can be lengthened or shortened.

The length of the HIF payment period is, notably, not as important as the duration of patents under the patent system. The reason is that a shorter period of payment in the HIF will typically result in higher payments per product in each year, as fewer products are eligible for payments in each year. Thus, a shorter period for HIF payments would be compensated by higher payments during each year.<sup>15</sup> Assuming an equal number of products were registered with the HIF each year, the average payments per product would remain the same. (This is not true with the patent system, in which shortening the twenty-year patent duration would cause a significant reduction to the incentives for innovation, since prices would not increase.)

One benefit of extending the payment period is that the HIF requires that the registrant offer a royalty-free license on all patents required for the manufacture and sale of the product, limited to use in manufacturing and selling that product, following the payment period. This is inconvenient, since it introduces a licensing requirement that would be

absent if the payment period were sufficiently long, as eventually all the relevant patents would expire.

The longer the payment period, the stronger the incentives the registrant has to invest in promoting their product. It is well known that it takes several years for new drugs to achieve widespread acceptance, since it takes time for doctors and patients to learn about the effects of the product.

On the other hand, a shorter period reduces the amount of monitoring required by the HIF, thus reducing its costs of administration. A payment period of eight years instead of ten would reduce monitoring costs by twenty percent. A shorter period also increases the amount of payment in the early years, which can be important for investors.

An important feature of the length of the payment period is that it does not depend on patent status. Thus, even if all relevant patents expire in the sixth year of the payment period, the registrant may continue to obtain payments, although in that case generic competitors might make a significant proportion of the sales of the product. However, this means that the HIF would be paying rewards for a product which would have been available at generic prices in any case. This suggests another option: the duration of the payment period could be shortened in cases in which all relevant patents have expired. Since patents are national in character, this would imply that rewards would only be paid in those countries in which a valid patent protected the product. However, this option seems unappealing since then it forces the innovator to apply for patents in *all* countries, including those without a pharmaceutical manufacturing industry. In addition, it would typically be very difficult for the HIF to determine whether patents in various countries would in fact be found valid if they were challenged. Finally, it should be recognized that since the HIF payments are based on incremental health impact of an innovation, it should not really matter whether the duration of the relevant patents is more or less than ten years from the initiation of commercial sales. Unlike the regular implementation of the patent system, the HIF mechanism is designed to reward innovators based on value created.

## Synergistic Effects

The discussion above suggests that, when there are beneficial synergistic effects from two separate medicines eligible for payments from the HIF, the two products should split the benefits of the synergistic impact equally between them for the purpose of determining how large a reward should go to each. There are other possible ways of dividing the synergistic impact. For example, the second firm to develop its product could be awarded all the benefit. Such an arrangement, however, might lead to undesirable delays in the introduction of new products.

In most cases, such synergistic effects would be between one product registered with the HIF, and one or more products or services not registered with the HIF. How the HIF deals with such cases is important and difficult. Suppose there are two perfectly complementary products, *A* and *B*, which together have a given health impact and which individually have no health impact at all. Under the current system, the owners of these two products would in general be motivated to come to an agreement to jointly market the products, and to share the sales proceeds. Suppose instead that product *a* (sold by firm *A*) were registered with the HIF, and *b* (sold by firm *B*) were not. How should the HIF calculate the incremental health impact of *a*? *B* would naturally choose a high price for its product, knowing that *A* would set a low price. *A* would suffer from this, since its profits would be reduced owing to reduced sales (because of the high price of *b*) and hence reduced health impact. *A* might even be willing to pay *B* to reduce the price of *b*.

Consider further an even more troubling possibility. Suppose that *a* and *b* were products that normally would be sold only in rich countries, and that the joint product was not normally be suitable for the HIF. However, given the perfect complementarity between the products, the profit-maximizing strategy would be to charge monopoly prices for *b*, and to obtain supplementary payments from the HIF for *a*. In this case, the profits of *B* would be larger than the profits of *A*. (If the profits of *A* were larger, then this would be a suitable candidate for the HIF to begin with.) To make this strategy work, *B* would therefore most likely have to pay *A*. Such a situation would certainly be

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a concern for the HIF, since it would mean that firms could use the HIF as strictly a supplementary reward for a combination drug which would be priced at a monopoly level. This would defeat the purpose of the HIF and must be avoided. A reasonable rule would be to require that firms which register their products with the HIF be prevented from receiving compensation from other firms. However, payments could flow in the opposite direction, since firms with products registered with the HIF may reasonably wish to lower the prices of other complementary drugs.

Similar concerns arise in cases in which *a* and *b* are owned by the same firm, where drug *a* but not drug *b* is registered with the HIF. In this case, drug *a* would not be credited with any synergies with drug *b*, since it would be assumed that the firm was being fully compensated by high prices for drug *b*. If in fact the firm was not charging high prices for *b*, it would be benefited by registering *b* with the HIF as well. In that case, the firm would obtain the benefit of all synergies between *a* and *b*.

### Voluntary Licensing

Under the system proposed above, the drug registrant retains exclusivity rights in its product, but accepts an administered price in exchange for payments from the HIF. An alternative approach would instead require that the registrant offer a voluntary license with a zero royalty for any generics to produce the product. Assuming a competitive generic drug industry, such licensing would lead to prices roughly equal to the average cost of production and distribution.

There are a number of reasons for preferring a system in which the registrant must forgo only pricing freedom, rather than giving up the exclusivity rights created by the patent.

First, the licensing approach would require registrants to forgo some intellectual property protection, which is not necessary as long as the registrant is willing to sell the product at the administered price. In some cases, the intellectual property arrangements may be complex, and licensing may therefore be difficult. In other cases, the intellectual property may have many applications, and the patentee might prefer not to grant an open license for its use.

Second, in cases where the generic drug industry is not competitive—as is the case in many countries—licensing to generics would fail to achieve the goal of low prices. If competition is ineffective in reducing the price to near cost, registrants would benefit from high prices and still receive reward payments from the HIF. Competition may fail to be effective for a variety of reasons:

- a. Competition can take a long time to push prices down. Generic firms need to ramp up their manufacturing capacity and obtain the approval of regulatory authorities, which can take years.
- b. In many countries, generic competition does not lead to low prices because of other distortions (including insurance) in pharmaceutical markets.
- c. For many products (such as complex biologics and some vaccines), generic versions simply don't exist, or there are very few generics, even when patents do not obstruct entry.
- d. Even if generic competitors have access to patented technologies, they may be significantly disadvantaged if they lack access to unpatented trade secrets or supplies of an essential ingredient.

Thus, generic competition will not always lead to low prices. There are some situations in which generic competition might, however, be more effective in achieving low prices. In particular, generic producers may sometimes have lower costs which are simply not revealed unless competition occurs. On balance, however, direct price control seems like a more effective way of ensuring low prices than open licensing.

Third, the fact that the HIF is optional introduces additional considerations in favor of price control rather than open licensing. If the HIF mandated open licensing rather than price controls, every product for which no generic competition was anticipated even given open licensing of the relevant patents would register for HIF rewards. There are many such products. Many firms producing very expensive biologic drugs, for example, have no generic competitors because of the complexity of the manufacturing process. Since these expensive products would have no generic competition, they could be registered with the HIF and would benefit not only from the usual



high prices, but potentially also from HIF rewards. In this case, much of the money paid out by the HIF would be a supplementary payment for high-priced products, leaving less for rewarding other products.

### Entry/Exit Options

Should firms be permitted to enter or exit the HIF system at any time? One possible design option would allow entry only at the beginning of commercial marketing of the product, without any escape option. However, this would clearly lead to less take-up of the system, particularly for firms which were uncertain of how the HIF would work.

Allowing delayed entry appears attractive, but it is possible that firms with effective patent protection of less than ten years would then exploit their patent rights as long as possible and then switch over to the HIF. This is not a desirable outcome. One possible rule in such cases is to reduce the payment period by some multiple of the length of delay of entry into the HIF system. (The multiple would be a number greater than one.) For example, assuming a multiple of two, if a firm decided to proceed initially outside the HIF system for two years, when it entered the HIF system it would be eligible for payments only for six (ten less two times two) years.<sup>16</sup>

If a firm wished to withdraw its product from the HIF system, it would be permitted to. However, the non-exclusive license of relevant patents, data, and other know-how used for the manufacture and sale of the drug would remain with the HIF, which the HIF could sub-license following the end of the ten-year payment period. Thus, even if a firm withdrew after five years, the HIF could still enable generic competition at the end of ten years. This rule is designed to prevent firms with longer patent protection registering with the HIF, accepting payments, and then withdrawing after nine years and six months to take advantage of extended exclusivity under its patent.

### Interim Payments

Many people have expressed the argument that the risks in pharmaceutical research are so high that the HIF mechanism could be improved by providing

interim payments to innovators upon the achievement of specific technical goals. (For example, the company might be paid an interim payment following successful approval of Stage II clinical trials.) While such interim payments are highly attractive to innovator companies, and may be extremely important in enabling companies to invest in valuable research projects, the HIF should avoid such payments. Governments that wish to sponsor such technical prizes and research grants should continue to do so.

As Peter Drucker (2006, 132) has pointed out, “information-based organizations need concentration on one objective,” which, in the case of the HIF, is accurate measurement of health impact. Research grants or bonuses based on the achievement of specific technical goals are fundamentally not in the mandate of the HIF, which will be more effective if its function is as simple as possible.

### SUMMARY

The reward mechanism of the Health Impact Fund is designed, fundamentally, to make the payments to innovators dependent on the health impact achieved by each registered product. However, it also needs to balance a number of other considerations in pharmaceutical markets, including allocating risk appropriately, minimizing double payment to firms which try to obtain both monopoly prices and payments from the HIF, correctly rewarding registered products which are complementary with other products, and limiting the discretion available to fund administrators.

The HIF is an optional, global pay-for-performance scheme for new medicines. Its design is intended aligns incentives for innovators with the common goal of reducing the global burden of disease. All the innovations it rewards will be cheaply available wherever they are needed. The HIF uses a market mechanism to determine the rate of payment per unit of health impact, letting firms compete for the available reward moneys. This makes the reward rate self-adjusting in a way that assures innovators of an appropriate rate of return and the funding partners of the cost-effectiveness of the HIF itself.



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### NOTES

1. The registrant need not be the innovator but must own or have licensed all the relevant intellectual property.
2. The HIF might require at least one patent issued by a patent office qualified as an International Searching and Examining Authority under the Patent Cooperation Treaty, and could require that the patentee had made an international application, which would be the subject of an international search.
3. If the registrant of a product registered with the HIF registered a new use during the payment period of the product, the registrant may obtain payments based on the old indications as well as the new indication during the initial payment period, and payments based on the new use only (if within the five year period) following the expiration of the initial period. For example, if a firm registered its drug with the HIF for the treatment of heart attacks, and 8 years later received approval for a new indication to treat strokes, it would receive payments based on measured health impact for all approved indications until year 10, and in years 11–13 would receive payments based on the effects of the product for the treatment of strokes only. The registrant will receive payments based on its own sales as well as on sales made by generics during the later period.
4. For clarification, when measuring the health impact of a vaccine given in year 5, the measured health impact would be the estimated decrease in disease burden over the lifetime of the vaccinated individual because of that vaccination in year 5. However, vaccinations given in year 11 would not be eligible for any payment.
5. The two-year baseline lag is somewhat arbitrary. If the baseline lag is too large, (1) it becomes increasingly difficult to assess the state of technology and access at that date, and (2) it may induce imitation. Imitation is not desirable if it does not lead to better health outcomes. On the other hand, if the baseline lag is too short, innovators could be significantly short-changed. For example, suppose that two similar products are introduced to the market on two subsequent days. And suppose that the second product is slightly better and is therefore able to dominate the market. Since the first product obtains small sales, it would obtain only small revenues under any system. In the absence of the baseline lag, the second product would obtain a very small payment per unit, since it would be compared to the first product. Thus, the collective payments would be relatively small. In contrast, with the baseline lag, the second product would be found to have a relatively large health impact, leading to much larger payments.
6. In this case, the later entrant would in effect cannibalize the payments to the first firm, since it would reduce the payments to that firm if it succeeded in capturing some market share for its product. However, the later entrant would likely prefer to exploit its monopoly rights under the patent system, since it would typically receive rather small payments from the HIF if its product was only incrementally better than the first product.
7. Since inflation varies between countries, the inflation index chosen should reflect the countries in which the registrant expected the product to be manufactured.
8. Note that in such a situation the HIF will simply not spend much money.
9. Weak incentives for litigation may also present problems. The HIF should avoid making payments to firms for products not embodying innovations which are significant in improving health outcomes. The registration process discussed in this chapter would be an important screen to prevent abuses of this sort.

10. Note that firms could continue to make use of minor innovations: for example, a minor modification of a product registered with the HIF might be sold outside the HIF at a monopoly price – but it would be competing against the much lower priced similar product registered with the HIF.
11. For example, if a researcher discovered that 500 mg of acetaminophen per day was adequate to stop the progression of Alzheimer's disease, and conducted the clinical trials to show this, she could certainly obtain a patent on this use. However, she would likely be unsuccessful in charging a price for acetaminophen higher than other manufacturers; and she could not stop other firms from selling acetaminophen which might be used in the patented way.
12. Note that while the price per QALY in the HIF is similar to that outside of the HIF, this does not mean that the rewards for a given innovation are the same with and without the HIF. Without the HIF, the reward for a new drug which treats primarily the poor will be low, because the reward is not based on health impact. With the HIF as an option, such a drug would be registered with the HIF, increasing the reward for its development.
13. See Hollis (2007b) for a technical analysis of this point.
14. For example, suppose that the total reward pool was set at \$6bn, provided the QALYs achieved by all registered medicines totaled no more than a pre-determined threshold of 60m. However, the reward pool would automatically increase by  $\sqrt{Q/T}$  (where  $Q$  indicates QALYs achieved and  $T$  indicates the threshold) if  $Q > T$ . Thus, if 80m QALYs were achieved, the total reward pool would increase by about 15% (or by precisely  $\sqrt{80 / 60} - 1$ ) to \$6.9bn. Such an approach leads to increasingly smaller payments per QALY the more the threshold is exceeded. Of course, funding partners would need to agree on a mechanism for increasing their contributions in years in which such excesses occurred.
15. A shorter duration would also suggest a higher ceiling on the payment per QALY.
16. The period of payments cannot generally be dependent on the remaining duration of the patent, since there will usually be a number of patents outstanding in different jurisdictions, all of which may have different expiry dates.



# 3. Health Impact Measurement

*Health impact assessment is at the core of the HIF. This chapter introduces metrics of health impact and a variety of methods for performing assessment. A substantial and well funded assessment branch will be essential for this purpose. The chapter also explores foreseeable difficulties in assessment, and how these can be anticipated in the HIF's design.*

## INTRODUCTION

Measuring the health impact of medicines is an essential task of the HIF. It must be able to make health impact assessments that are reasonably consistent across diseases and countries. We recognize that there is no perfect metric for health or disease and no perfect algorithm for health impact assessment, and that any such assessment will inevitably rely on imperfect data. Perfection, however, is not the relevant standard. What matters is that pharmaceutical firms should have strong new incentives to deliver health improvements – and no strong new incentives to try to capture HIF rewards without health impact. HIF assessment must be sound enough so that the best strategy for firms to capture HIF rewards is to deliver health improvements. With a substantial investment in data collection and analysis, much larger than any national health system's to date, the HIF would be in a position to make its assessments sufficiently consistent and reliable to ensure that payments were allocated fairly between registrants on the basis of health impact, and would thus provide meaningful incentives to innovators to develop products with large health impact.

The HIF is not alone in seeking to measure how drugs affect health. Because of the enormous cost of health care, the measurement of health impact is becoming more important to insurers and especially to governments, which seek to reduce expenditures and to improve health care by relying more systematically on epidemiological evidence. Thus, there has been a

recent flowering of health-technology assessment programs, such as the Canadian Agency for Drugs and Technologies in Health (CADTH), the Swedish Council for Health Technology Assessment (SBU), the German Agency of Health Technology Assessment at the German Institute for Medical Documentation and Information (DAHTA@DIMDI) and similar agencies in other European countries. In the United States, Drug Effectiveness Review Project (DERP) is actively conducting comparative reviews which are being used for formulary decisions. These comparative reviews, however, should not be seen as the standard by which the HIF would assess health impact, as the HIF would review how drugs were used in actual practice in different countries, and would reassess health impact over time as new data became available. Registrants would also have strong incentives to provide data on utilization in order to bolster their case for higher rewards.

Pharmaceutical manufacturers and other health technology companies perceive to an increasing extent the importance of demonstrating that their products are therapeutically effective and therefore worth their high cost. This is leading them to engage more actively in assessing therapeutic effectiveness from an early stage and to incorporate this information in their pricing decisions.

Health impact is already being factored into decisions as to whether drugs should be listed in formularies and made eligible for reimbursement under insurance, and estimates of therapeutic effectiveness are being used to help determine the price points at

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which new products will be sold. It is a natural step from there to make the payment for the product depend on actual health impact. This chapter explains how this might be done.

The plea of impossibility offers itself at every step, in justification of injustice in all its forms.  
Jeremy Bentham

### MEASURES OF HEALTH IMPACT

Since it is necessary to aggregate health impact into a single unit of measurement, the choice of metric is very important. A variety of factors are relevant.<sup>1</sup>

#### Quality-Adjusted Life Years (QALYs)

Arguably, the simplest measure of health is “life years” with each additional year of life saved through a given intervention being given an equal weight. Life-years may not be a satisfactory measure in situations where health is substantially compromised because of a disease, condition, or the medicine itself.

To account for quality differences in health, the standard metric is the QALY or “Quality-Adjusted Life Year.”<sup>2</sup> A QALY is a standardized measure of health impact in which a year in perfect health is given a value of one and a year in poorer health is given a value between zero and one. QALYs account for the fact that a year in good health is worth more to people than a year in poor health. Thus, QALYs can simultaneously capture changes in morbidity and changes in mortality, and combine these into a single metric. In addition, they can be used to measure impacts on different aspects of health in the same scale.

An important part of the QALY metric is that there are weights for different health states. The derivation of how much a given health state should be worth is not trivial, since that fundamentally depends on individual preferences. A common solution to this problem is to use multi-attribute health status classifications whose values have already been evaluated in various populations. There are several widely used systems including the Health Utilities Index and the EQ-5D. These classification systems essentially pro-

vide a standardized way to grade a given health status between zero and one.

Because people generally prefer health gains to occur sooner rather than later, it may be desirable to discount future impacts on health when measuring the health impact of a given medicine. This also requires one to choose a discount rate.

Given the various systems for valuing the future and for ranking different health states, QALYs in different studies are often not directly comparable. Clearly, for the purpose of comparing the health impact of different medicines in different countries, a single metric would have to be chosen for use by the Health Impact Fund.

There has been considerable academic debate over the discount rate, the quality-adjustments, and even the weighting for different ages, and there is no uniquely correct measure of any of these values in the measurement of QALYs. Thus, the HIF would simply have to make some well-informed, public choices, which would form part of the basis of how payments were allocated to the registrants.

#### Disability-Adjusted Life Years (DALYs)

DALYs were developed by the World Health Organization for the purpose of estimating the global burden of disease. DALYs are conceptually similar to QALYs but differ in some significant ways. Most importantly, DALY weights were determined by a group of public health experts, rather than through population-level assessments (see Drummond et al. 2005, 187).

#### Other Approaches

There are other approaches to measuring health impacts of a given intervention, such as Healthy Year Equivalents and Saved-Young-Life Equivalents, which are discussed in Drummond et al. (2005, ch. 6). While these have arguable benefits compared to QALYs, it is important that they are comparable in their approach. They have not, however, been as extensively used as QALYs.

## MEASURING HEALTH IMPACT

In this chapter, we do not prescribe any particular metric; however, the HIF will need to choose one, and for the present we assume that it is QALYs. The HIF then needs to make an estimate of the number of incremental QALYs achieved because of the use of a given medicine globally rather than the baseline technology.<sup>3</sup> This is properly the field of pharmacoepidemiology. Developing such an estimate is obviously challenging and this section examines a number of approaches which can be used.

The problem of determining what a medicine is worth is a familiar one in health insurance. Insurers are required to determine whether a product will be covered, and may have to bargain over the price. If they are to do this, they need to assess the value of the product for health, and in general rely on less comprehensive information about the product's effectiveness than would be available to the HIF. Thus, while the problems of health assessment initially appear overwhelming, it is important to recognize that they are not unique to the HIF system, but are common in insurance markets.

The determination of what medicine works best is also an important clinical question: there has therefore been significant interest in establishing a mechanism to determine what clinical interventions are most effective in what circumstances. The HIF's needs in terms of identifying the health impact of specific drugs are therefore very much aligned with society's interests in learning about what drugs patients should be consuming. The recent report from the Committee on Reviewing Evidence to Identify Highly Effective Clinical Services (Board on Health Care Services, 2008) therefore proposes that the US government should "fund and manage systematic reviews of clinical effectiveness" to enable better health care decision-making. To a large extent, such a program would be over-lapping in its goals and function with the health impact assessment mechanism proposed for the HIF, although of course the mandate for the HIF would be limited to assessment of the drugs actually registered with the HIF compared to the relevant baseline.

The HIF's needs in terms of identifying the health impact of specific drugs are therefore very much aligned with society's interests in learning about what drugs patients should be consuming.

### Crude Aggregation

We begin by considering what it means to estimate health impact. The health impact of medicine "A" can be estimated as

$$(Q_A - Q_B) \frac{n_A}{d}$$

where

$Q_A$  is the average QALY impact of the medicine on each affected patient, as estimated in clinical trials;  $Q_B$  is the average QALY impact of the baseline treatment on each affected patient, as estimated in clinical trials;  $n_A$  is the number of units of the medicine A sold or distributed; and  $d$  is the average number of units per patient.

The aggregation suggested above is extremely crude in various respects and unlikely to provide an accurate estimate of the true health impact of a medicine, as discussed below.

### *Clinical Trials Data Do Not Describe Effectiveness in the Population*

It is well known that efficacy in a clinical trial does not typically reflect actual epidemiological impact (see Revicki and Frank 1999; Oster et al. 1995). There are a number of reasons.

First, trial participants systematically vary from the population. They tend not to have complicating co-morbidities, and they are only included if they exactly meet the characteristics identified in the trial protocol. In addition, physicians may prescribe the product for patients for whom the clinical indications are not very clear, or where the diagnosis is not



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complete. In many developing countries, accurate diagnoses are difficult to obtain owing to a shortage of qualified physicians, and patients may self-medicate, since a prescription from a physician is neither available nor necessary to purchase the medicine.

Second, in a clinical trial, participants are typically motivated or even required to follow the strict trial protocols including taking the medicine at the approved times and frequency. In the population, patients are often non-compliant and fail to follow the prescription accurately. Frequently, patients will skip doses or stop taking the medicine if they feel better or worse.

Third, physicians in a clinical trial tend to be more attentive to their patients and patients are typically monitored weekly.

These differences will generally lead to differences between the estimates of effectiveness from clinical trials and in the general population. Evidently, the problem is confounded if  $(Q_A - Q_B)$  is not estimated directly but through multiple different tests, where drug A is compared to placebo in one trial and the baseline therapy is compared to placebo in a separate trial.

### *Clinical Trials Data on Averages May Not Reflect the Value of Diversity*

For many diseases and conditions, it is difficult for new medicines to show in clinical trials that they are unambiguously better than previous treatments. However, for given individuals, it sometimes appears that one drug may be more effective than another, perhaps because of unobserved differences between patients with similar symptoms. In such situations, clinical trials may fail to demonstrate the true value of having more than one treatment for a condition. That is, in terms of the estimating process above,  $(Q_A - Q_B)$  may be relatively small or even zero as measured in a clinical trial, and yet product A may be more effective for a given individual than the baseline therapy.

### *Incentives for Quantity*

If the number of units actually taken per patient is not known, then the reward, given the measurement

system above, would be based on the number of units distributed, rather than the number consumed appropriately. This would obviously give firms incentives to exaggerate the number of patients actually treated successfully. At the extreme, the manufacturer might collude with a wholesaler to fraudulently claim higher sales volumes than actually occurred – or, more familiarly, firms might use various incentives to aggressively promote their product to physicians, who would then overprescribe the product to patients. In either case, the innovator could obtain a reward for a health impact not realized.

### **Not-so-crude Aggregation**

The discussion above suggests that the HIF should not use naïve aggregation of unit sales times estimated superiority as demonstrated in clinical trials, since this is likely to lead to biased and inconsistent estimates of health impact. However, that does not mean that the approach generally is unworkable.

First, if the HIF is to use data from clinical trials to help establish the degree of superiority of a given medicine over the baseline, it should augment that data with supplementary evidence from observational studies and pragmatic or practical trials which use data from normal clinical practice. It is clear that in many cases such supplementary evidence cannot be available when the product is first commercialized, and that at that time the only data must be from clinical trials. Therefore additional data on ease of compliance, characteristics of possible patients and their similarity to patients in the clinical trial, and evidence on selective superiority of the relevant product, should be provided as early as possible. In due course, epidemiological evidence on the effectiveness of the product in the population should be provided. It could be that payments by the HIF in the first few years could be made partly conditional on observed effectiveness. Since registrants would be paid on the basis of demonstrated health impact, they would have an incentive to try to design data collection systems related to their products which would create information about use and effect.

Second, the HIF should be aware of the incentives for registrants to expand sales volumes to inflate the

estimated impact of the product. To minimize this problem, the HIF should require extensive reporting of sales volumes to it directly from wholesalers, with evidence from wholesalers on which retailers purchased the medicines. This would enable the HIF to conduct audits on how the units were dispensed (as discussed below). Essentially, this is similar to the need for insurance companies to make sure that claimed sales actually took place before payment is made.

Third, the HIF could conduct or require, where feasible, population-level studies to determine the impact of certain products. Such population-level studies are in general likely to be rather expensive, and only relevant for products which are very widely consumed, but in those cases may be particularly important. Mortality data indicating cause of death and other data from hospitals and clinics indicating incidence and prevalence in the population could also be used to assist in identifying the impact of a given therapy.

Fourth, the HIF could use information from the Global Burden of Disease (GBD) project, to help ensure that its estimates across countries were consistent with the measured burden of diseases and conditions. The GBD project, managed by the Institute for Health Metrics and Evaluation, is a major effort to perform a complete systematic assessment of the data on all diseases and injuries, and to produce comprehensive and comparable estimates of the burden of diseases, injuries, and risk factors, around the world.

Finally, it is important to remember that the HIF is intended to be an option, so that in cases where a firm has a product which it believes is effective, but for which the clinical trials and other epidemiological evidence does not show a substantial effect, the firm can exploit its usual rights under the patent system. The HIF is designed to reward products which have high demonstrated health impact.

## THE COST OF HEALTH IMPACT ASSESSMENT

Health impact assessment would be expensive, given the need to assess a variety of medicines globally. There would, of course, be some economies of scale from assessing many medicines at the same time, and efficiencies from assessing the same medicine year

after year. However, a reasonable perspective is that if the HIF had an annual budget of \$6 billion, it could spend about \$600 million on administration and assessment, with the bulk being devoted to assessment. This would make it by far the largest health assessment agency in the world. For comparison's sake, NICE (the UK's National Institute for Clinical Excellence) has a budget of approximately \$50 million. NICE publishes around 25 technology appraisals, 12 clinical guidelines and 60 pieces of interventional procedures guidance each year (NICE 2004). The HIF would have, assuming a stock of about 20 medicines registered at any time, a requirement to evaluate the impact of those medicines around the world, which would be a much more difficult process than that undertaken by NICE. However, there could be considerable external benefits from such an assessment process, including primarily that it would enable better prescribing as the relative therapeutic benefits of different products were better understood.

The HIF would be by far the largest health assessment agency in the world.

A budget of \$600 million, spent on roughly 20 medicines at any given time, yields an average budget per year per drug of \$30 million. How would this be spent? Part would be allocated to evaluating clinical evidence. Current estimates of the cost of trials can be found in Holve and Pittman (2008), who estimate that *head-to-head studies* range in price from approximately \$2.5 million for relatively small studies to \$20 million for large studies. Such studies, of course, would not be conducted every year; some such studies could be performed by the registrants, though the HIF could also commission its own independent studies where needed. *Observational studies* range in cost from \$1.5 million to \$4 million. The HIF would require observational studies in different settings, though not every year, so this could be quite costly. However, it is likely that observational studies would be less expensive in developing countries. *Systematic reviews* of evidence tend to cost up to around \$0.3 million. The HIF would also require a substantial *auditing* function to ensure that the products were be-

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ing distributed and used in ways consistent with the findings of the observational studies. Finally, there would be a significant *overhead* component related to obtaining the functions of the technical branch and other operational branches, which could be shared across products.

Errors using inadequate data are much less than those using no data at all.

Charles Babbage

### FORESEEABLE DIFFICULTIES

#### Location-dependent QALYs

QALYs are essentially meant to be based on the preferences of individuals. It is likely that health preferences and circumstances differ systematically across countries, so that, for example, being confined to a wheelchair may have very different impacts in the Netherlands and in Nepal. However, unless such preferences are accounted for in the QALY system used, the QALY will fail to give proper weights to health states in different countries.

#### Inadequate Data on Drug Use

An important obstacle to estimating the health impact of different medicines is the availability of good data. This is, of course, an obstacle in general to the practice of evidence-based medicine. For example, it is estimated that of the more than two trillion dollars spend on health care in the United States annually, less than one-tenth of one percent is devoted to learning what works best (Institute of Medicine, 2008). There is probably a good case to made for a general increase in expenditures on learning what is effective and when. This, of course, applies particularly to the HIF, which would require better data than is commonly available to make consistent estimates of health impact.

Especially in the poorest countries, it is likely to be very difficult to obtain good-quality data on the distribution and use of drugs, in part because of less well developed information and communications

systems, and in part because in those countries, drug distribution systems tend to be multi-tiered and opaque. In addition, since in the poorest countries physician shortages are endemic, correct diagnosis is less common and many patients purchase drugs directly from local pharmacies or retailers without prescriptions. Adherence to prescription protocols may be spotty. Thus, it is likely that it will be relatively difficult to obtain comprehensive data on health impacts of drugs in such settings.

Here the incentives created by the HIF for firms to monitor data and to promote effective use of their registered medicines, as discussed in chapter 7, not only would help the HIF to assess health impact, but could also be of great value in other health promotion efforts.

The HIF would have to seek out a wide variety of data sources to make the best estimates possible, including confidential information as available. It should also try to obtain input from different sources, including patients, doctors, pharmacists, etc., to enable a comprehensive picture of the use of the registered product.

The problem of inadequate data can lead to a variety of types of errors. Some errors would be random, and would be unlikely to significantly affect the expected payments for a given product. Other errors could arise systematically, with bias between diseases and countries, because of a variety of factors, such as the differing propensity of patients to report health outcomes depending on the illness. Such systematic errors would be more problematic, and would influence firms' willingness to innovate or to register their products with the HIF. A third type of error is more serious: if registrants could systematically misrepresent the health impact of their medicines. The HIF would have to undertake careful auditing of reported data by registrants to minimize the extent to which such misrepresentation influenced the allocation of payments.

#### Differing Interpretations of Incomplete Data

Given that the HIF will make assessments of health impact which will depend on data from a large number of countries, it is certain that data will be incom-

plete in a variety of dimensions, including the estimated therapeutic benefits of a product compared to the baseline per patient, the effectiveness of the drug in the population, the number of units distributed, and extent to which distribution reached persons with relevant indications, and the quality of diagnosis and compliance. All of these will be to varying degrees incomplete in different countries, and this will require sophisticated inference. Based on the assumptions used and the techniques for inference, estimates may differ substantially. Since a ten percent increase in the estimated health impact translates into a roughly ten percent increase in payments from the HIF, firms will have an incentive to make strong claims about the effectiveness of their products. This could lead to disagreements over what share of the HIF disbursement each firm should receive. Thus, the HIF will need to establish a transparent and unbiased methodology developed in conjunction with pharmaceutical firms and governments, *before* it begins actual assessment of health impact. (Again, here it is important to stress that though no single methodology can be ideal in every circumstance, the HIF will have to be clear and transparent about its processes so that innovators can know what to expect if they register their products with the HIF.)

An important consideration is that the HIF has to pay out a fixed sum in a given year, so that the disagreement is fundamentally between the health impact assessments of different companies, with the HIF acting as an arbitrator. Therefore, it will be in the interest of pharmaceutical firms to have a clear and fair methodology established at the beginning.

### **Comparative Clinical Data Failure to Demonstrate Differences**

In order to make appropriate judgments about the effectiveness of one drug compared to another in the population, evidence from clinical trials can be relied on to set some baseline. However, even at the clinical trial level, the data on the superiority of one medicine over another are often unclear. For example, the Comparative Effectiveness Reviews published by the Agency for Healthcare Research and Quality (AHRQ) show that, in a variety of classes of medi-

cines, clinical trial data does not provide a basis to make claims of substantial superiority of one treatment compared to another.

Even with large numbers of trials, it is often impossible to detect significant clinical differences between competing drugs, even when these have different mechanisms of action. This suggests that registrants of new drugs that are similar to existing treatments may find it difficult to claim health impact rewards based on therapeutic superiority. This suggests that most HIF-registrations will be for genuinely novel products that bring substantial incremental benefit to patients. (The HIF would not be an attractive mechanism for products that do not provide significant advantages over pre-existing therapies.) For the HIF to be attractive for novel products with significant health impacts, it will need to be financed adequately. This helps to establish a minimal size for the HIF at several billion dollars per year, since below this level it would not be sufficient to support a portfolio of more than a few important medicines.

### **Surrogate End-points**

A common method for measuring efficacy in drugs is to examine their effect on so-called “surrogate” end-points. The National Institutes of Health define a surrogate endpoint as “a biomarker intended to substitute for a clinical endpoint” (Cohn 2004). For example, the effect of a drug on cholesterol levels has been used to measure efficacy, although the real interest is in the effect of the drug on mortality and morbidity. Surrogate endpoints are used because it is less expensive and much quicker to measure biomarkers, rather than mortality. In cases where there is a strong case that the biomarker is highly correlated with health, its use for the purpose of drug approval may be justified on the basis that patients would otherwise be denied access to a useful drug. However, for the purposes of the HIF, the use of surrogate endpoints clearly raises significant problems since it would be difficult for the HIF to confidently estimate health impact on the basis of such biomarkers.

The question, whatever we spend [on health care], is whether we are getting our money's worth. In general, good information and appropriate incentives are necessary to allocate resources efficiently.

Ben S. Bernanke

### “Excessive” Sales

As mentioned above, firms will have an incentive to exaggerate the number of patients helped and the average health impact on each patient, in order to increase their share of payments from the HIF. The exaggeration of the number of patients may occur in a number of different ways.

First, firms may simply report more sales than actually occurred, possibly in collusion with wholesalers. This would of course be fraudulent and presumably a firm would in these circumstances forfeit any future payments from the HIF on this product.

Second, firms might bribe wholesalers to buy more drugs than they would really want. The proposed mechanism described in chapter 2 suggests that there would be a standard price. However, if a manufacturer offered a bribe of \$2 million to a wholesaler to buy one million pills at the standard price of \$1 each, and then to distribute them at low or possibly negative prices to pharmacies, neither manufacturer nor wholesaler has an incentive to report this activity, which might be hidden through unacknowledged discounts in the price of other drugs. In this case, it becomes harder to identify such collusive activities, without confirming through pharmacy records that the products were sold.

Most insurance companies solve this problem by insuring the consumer directly, so that the manufacturer would need to collude with individual consumers to exaggerate sales, which is generally difficult. However, manufacturers interact with doctors to encourage them to write prescriptions for their products. When these interactions involve payments, subsidies, gifts, etc. to physicians, it may be seen as a form of collusion. In the case of the HIF, it will be necessary to engage in auditing of sales to ensure that pharmacies did actually dispense drugs which were

shipped to them, which in turn makes it essential to obtain records from manufacturers and distributors concerning shipments of HIF-registered products.

### Interacting and substitute treatments

When treatments are not independent of each other—because they are either complements or substitutes—the assessment of health impact is complicated. The HIF could use, in such circumstances, a version of the approach employed by Evans et al (2005).<sup>4</sup> This approach essentially takes account of the interactions between treatments to infer separate effects for each, in a way consistent with the discussion of synergistic effects in chapter 2.

### SUMMARY

It is difficult to conduct uniform and reliable health impact assessments, especially on a global scale and over the full range of medicines. But, with substantial investment into assessment techniques and measurement, these difficulties can be solved to enable health impact assessments that would be sufficiently accurate to create effective new innovation incentives that improve significantly upon those provided by the present system. What is required for the HIF to generate fair, effective incentives is that health impact can be measured in a way that is consistent and predictable across products and countries. Measurement inaccuracies will certainly arise, but provided these are random and not too large, their effect on incentives and on payments to registrants will be small. Ideally, the measurement of health impact should be perfectly accurate, since this would provide the best possible incentives for pharmaceutical innovation. In practice, assessments need only be good enough: to make it profitable for innovators to aim to improve health, to make it unprofitable for them to try to game the system excessively, and to ensure that each registered drug's overall reward – derived from its worldwide impact over the entire reward period – is reasonable given its actual health impact.

**NOTES**

1. For a discussion of measuring health impact in the context of the global burden of disease, see Murray et al. (2002).
2. The following discussion draws heavily on chapter 6 of Drummond et al. (2005).
3. The baseline is the set of pharmaceuticals available two years before the medicine was introduced; see chapter 2.
4. See particularly their Methods Appendix, Boxes C and E.





## 4. Governance and Administration

*The HIF will be governed by a Board of Directors chosen by funding partners, exercising primary responsibility over the Fund. The Board will oversee three branches representing the core functions of the Fund: the Technical Branch, the Assessment Branch, and the Audit Branch. These will, respectively, set the standards for evaluation of health impact (Technical), determine individual products' actual impact (Assessment), and ensure correspondence between standards and evaluations (Audit).*

### INTRODUCTION AND SUMMARY

One important concern about the HIF is that administrative bodies are subject to influence in allocating rewards. Such bodies are liable to intense lobbying by firms with a stake in their decisions, and their officials may be corrupted by bribes or future job prospects. The governance of the HIF must therefore be carefully designed: the formulation of the assessment rules must be kept separate from their application, the assessment rules must be formulated precisely, and the application of the rules must be firmly and transparently guided in ways that leave little room for discretion. To stimulate the most cost-effective research efforts, and thus to be itself cost-effective in terms of promoting global health, the HIF must have a structure conducive to its impartial and effective operation.

### GOVERNANCE

There are many important issues to be resolved concerning the governance of the HIF, including how it should be constituted, the size and composition of its board of directors, the voting mechanism of its board, and the method for selecting its new directors. It is not possible or desirable for us to try to identify a comprehensive and optimal governance mechanism at this stage, but we can identify some of its most important elements and some of the general characteristics it ought to have.

### Composition of the Board of Directors

The Board of Directors will ultimately be responsible for the direction of the HIF and for the annual allocation of payments. It is clear that funding partners should be represented on the board. Because the funding expectations are based on gross national income (GNI), all countries, even the poorest ones, should be able to participate as funding partners. Other possible board members might include public health experts and *ex officio* representatives of the World Health Organization and NGOs that are active in purchasing medicines. Including individuals who do not represent funding partners is problematic since it is unlikely that the funding partners will remain committed to the HIF unless they can exercise a significant amount of control.<sup>1</sup>

An important issue is whether the voting rights should be proportional to the size of contribution by each funding partner. Such an approach gives the greatest voting power to the countries that contribute the most. While this is attractive in some respects, it may lead to domination of the Board by a very small group of directors.

The Global Fund, which is financially supported by relatively wealthy countries, has a board that is effectively split into constituencies. Of twenty voting members, eight represent donors, seven represent developing countries (with a required geographic distribution), and five represent civil society and the private sector, notably including "one representative of an NGO who is a person living with HIV/AIDS or

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from a community living with tuberculosis or malaria.” The board also includes nonvoting members, including a WHO representative, UNAIDS, and one Swiss citizen (presumably to ensure compatibility with Swiss law; Global Fund 2007, 4). In the case of the HIF, this division into constituencies would be artificial, as funding partners are also beneficiaries. It might, however, be appropriate to require a geographical distribution which takes into account the different burdens of disease in different regions.

### Size of the Board of Directors

The size of the board is intimately related to its composition. Larger boards can achieve a broader representation, but can also become more unwieldy.

### Selection of the Board of Directors

Another important issue concerns how members of the board ought to be selected. First, there needs to be a process of determining candidates, which may simply allow each funding partner to nominate one candidate. It might be appropriate for other expert organizations such as the World Health Organization to nominate additional candidates.

The second step is a process of determining which candidates would be named to the Board. One approach is to allow funding partners to have voting rights in electing board members in proportion to their contribution. If regional representation were to be desired, however, there might also need to be a separate process for selecting regional members.

### Board Decision-Making Mechanism

Boards have various mechanisms for making decisions, including simple majorities, supermajority rules, consensus, and other more complex rules.<sup>2</sup> In addition, voting rights might be allocated unevenly across board members to reflect, for example, financial contribution. The core decision problem of the HIF board will be the annual confirmation of estimated health impacts for each drug, since this will effectively determine how much each innovator is to be paid. Evidently, the Board cannot become in-

involved in the details of how much health impact each individual drug delivers. It will have instead to rely on estimates provided by the Assessment Branch, which is described below. Thus, the Board will exercise control more through its choice of personnel appointed to the Assessment Branch and other administrative branches of the HIF and through general oversight and internal policy making, than by involvement in detailed assessment of individual drugs. Given, however, the requirement to approve annual payments, and given that there will likely be some degree of disagreement between Board members, a consensus requirement for decisions seems problematic as it would likely create roadblocks and provide excessive veto power to individual members.

### The Board's Role in Funding Partner Relationships

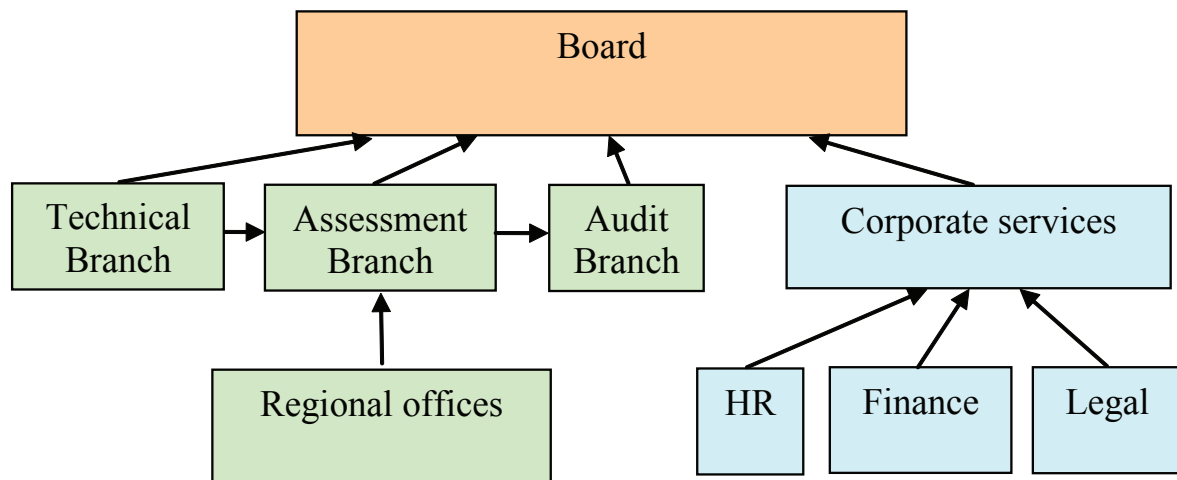
The Board will also have an important role not only in ensuring that the interests of various stakeholders are represented in the decisions and activity of the HIF, but in representing the HIF to funding partners and other stakeholders. For example, as the HIF demonstrates its effectiveness, it will perhaps wish to increase the size of its annual rewards. At that stage, the Board will be responsible for raising additional funding in a responsible manner.

One problem facing the HIF is ensuring that the financial commitments of funding partners are actually fulfilled, and therefore members of the Board will require support at the highest political levels. The fact that the HIF will be dependent on such commitments, and must be perceived to be credible for it to stimulate research investment, makes it essential that the Board members have the experience and authority necessary to represent the HIF to funding partners.

## ADMINISTRATION

The HIF would need several administrative branches, including legal, financial, human resources, and other typical corporate functions. In this section, we discuss three critical divisions which would be unique to the HIF: a Technical Branch, an Assessment Branch,

Figure 1: Administrative Structure



and an Audit Branch. The Technical Branch would set the standards for how health impact would be assessed; the Assessment Branch would undertake the actual assessment following the protocol established by the Technical Branch; and the Audit Branch would monitor adherence to these protocols and the accuracy of the data reported to the Assessment Branch. The division into three branches reflects an ambition to ensure that there is a transparent, fair, and consistent process for estimating health impact.

The administrative structure of the HIF is summarized in Figure 1. The Board assumes overall responsibility for the administration of the Fund, reporting to funding partners. The health impact assessment framework is determined by the Technical Branch; this is used by the Assessment Branch in determining assessed health impact for each product on a global basis. The Audit Branch confirms the accuracy of the Assessment Branch's analyses. This enables the Board to determine the payment to each registrant. The HIF would also require other corporate services as shown. Arrows show information flow.

### Health Impact Technical Branch

The Technical Branch would be responsible for designing assessment tools for use in evaluating the health impact of participating firms' interventions. This branch would not actually perform assessments, but would provide guidelines so that assessment procedures are technically sound, consistent, fair, and

predictable for registrants. Such guidelines are especially important because it is not possible for one individual, or even one team, to conduct all assessments for all drugs in all countries. Consistency of assessment across different drugs in different countries must then be achieved through clear standards that are followed in each assessment exercise. The Technical Branch will formulate such common standards by which all assessments will be performed.

The assessments to be undertaken would be similar to those performed by other expert committees for national insurers. Though these techniques are admittedly contentious and difficult, they have a track record with which many pharmaceutical innovators are already familiar, as noted in chapter 3. There are many useful sources on assessing interventions, and the Technical Branch would not be required to invent entirely new techniques. Rather, it would select the techniques appropriate for the particular purposes of the HIF and adapt them as necessary.<sup>3</sup>

The staffing requirements of this branch would be determined in part by how large the Fund is, and how many different types of drugs enter the system. The personnel required would include epidemiologists, health economists, and statisticians. They would require an understanding of the kinds of data which are available or can be collected in different countries, the kinds of data which are available through clinical trials and actual practice, and how these data vary by disease. The Technical Branch would set up protocols for health impact assessments at the initiation of the

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Fund, and would continue to modify and refine these protocols in light of experience.

### Health Impact Assessment Branch

The Assessment Branch would apply the guidelines established by the Technical Branch to the actual data for each product in each country. Each year, the Assessment Branch would receive submissions from all firms having products in the system.<sup>4</sup> It would also solicit reports from governments, other relevant users such as insurers and NGOs, wholesalers, pharmacies, competitors, and other interested parties. Using this data and the theoretical framework developed by the Technical Branch, the Assessment Branch would estimate the health impact of each product.

The work of the Assessment Branch will be difficult, since data on health impacts are likely to vary meaningfully between countries and between diseases in terms of accuracy, reliability, and comprehensiveness. For example, if data is available for only two percent of patients who used a drug in one country, but for forty percent of patients in another country, the accuracy of the estimate in the second country is likely to be higher. The Assessment Branch would have to rely on guidelines from the Technical Branch on how to evaluate such different data; but it would also have to rely on its own judgment, since these guidelines or policies cannot be made so detailed as to provide clear guidance on all difficult choices that it will encounter in practice.

The Assessment Branch would constitute the core of the administrative functions of the HIF. It would require personnel with expertise in epidemiology, public health, statistics, and health economics.

It would be required of the Assessment Branch that it publish its recommendations and provide detailed reasons for them, including how the Branch established the quality of evidence. This transparency would lend credibility to the system, and allow other firms to make meaningful predictions about how their products would be treated in the future. Such a transparent process is commonly followed by courts and regulatory bodies all over the world.

The Assessment Branch would be required to use the best available data to estimate health impacts,

within the guidelines specified by the Technical Branch. The honesty and integrity of the Assessment Branch is an important component of the entire system. If this Branch were not viewed as unbiased in its estimates, it could lead firms to spend more on efforts trying to influence its decisions rather than trying to reduce the burden of disease. This motivates both the creation of the Technical Branch, to reduce discretion in assessments, and the creation of the Audit Branch, to ensure that the assessments do in fact follow the guidelines. Note that by separating the actual performance of assessment from the establishment of guidelines concerning how assessments are to be performed, there would be a substantial reduction in discretion exercised in each assessment. Reducing discretion has costs, of course, and will sometimes lead mechanically to assessments that appear not to reflect the “true” situation. By reducing discretion, however, transparency is enhanced and the complexity of the assessment process is reduced, as is the opportunity for lobbying and rent-seeking by firms. Evidently, the staff of the HIF would have to satisfy strict conflict-of-interest guidelines.

By reducing discretion, transparency is enhanced and the complexity of the assessment process is reduced, as is the opportunity for lobbying by firms.

Assessment is clearly expensive and would require a significant investment of time and resources. Thus, it would be undesirable for the Assessment Branch to perform assessments on drugs with only small health impacts since the assessment costs could even exceed the health impact reward. The HIF will avoid this problem by charging an annual fee reflecting the costs of assessment to registrants, since this will deter the participation of drugs with relatively small health impact.

To help ensure fairness, there would have to be an appeal mechanism, and firms would be very likely to appeal the decisions of the Board in some cases. To the extent that the Board did not wish to be overwhelmed by such appeals, it would probably be appropriate for the costs of appeals to be borne by the

appellant (to be refunded should the appeal result in a substantial revision in the applicant's favor). This would ensure that only meritorious appeals were actually likely to be pursued; it would also ensure that scarce HIF assessment resources were not absorbed in the appeals process, since the appellant would be responsible for funding the appeal.

### Health Impact Audit Branch

The Audit Branch would have the core function of ensuring that the recommendations of the Assessment Branch complied with the guidelines established by the Technical Branch. The audits would help to ensure that the recommendations of the Assessment Branch were unbiased and consistent across countries and drugs. The Audit Branch would of course report directly to the Board and would publish results of its findings annually.<sup>5</sup>

Such an auditing function could be performed by in-house staff, by outside experts, or both. For example, audits could be performed by independent consultants trained to evaluate health or social impact in similar contexts. Specific audits would be assigned to multiple stakeholders: academic and research institutions, and private sector partners identified through a standard request-for-proposals process.

Specific audits would be focused on evaluating a particular assessment to confirm reporting and evaluation conducted by the Assessment Branch. The frequency and level of stratification of such audits depends on system resources. Sampling techniques and new technologies for conducting such surveys (including, for example, new electronic medical record systems in parts of Africa), could substantially reduce the burden of this auditing.

One possible aid to the audit process is that firms participating in the HIF system would have an incentive to provide information about how *other* firms might have exaggerated their claims, since by reducing the payment to these other firms, each firm might increase its own payments. This kind of assistance would not only increase the amount of information available to the auditors, but would also enable it to understand how firms might exaggerate or even try to defraud the HIF.

The Audit Branch might also perform more general audits designed to evaluate the overall performance of the HIF. General audits would assess the system's capacity to generate health impact with a given level of funding, as compared with similar options available (for example, Advanced Market Commitments, direct research grants, and other initiatives discussed in chapter nine). This loosely follows the "Best Available Charitable Option" assessment framework used by the Acumen Fund.<sup>6</sup>

### EXPENSE OF ADMINISTRATION

It is evident that performing annual health impact assessments on a variety of drugs on a global scale would be very expensive—perhaps absorbing ten percent of the annual budget of the fund. In a way, this is comparable to the administrative expenses of insurance companies, which devote substantial resources to avoiding moral hazard and fraud on the part of policyholders. The HIF is similar in many respects to a drug insurer that makes payments to drug sellers based on the estimated health impact of their products rather than on some negotiated price. While an insurance company controls its payout by monitoring drug usage, the HIF would control its payout by monitoring health impact (which, to a large extent, is determined by use).

The administrative expenses of the HIF would, however, offer some distinct benefits. The first is that they would enable the HIF to create highly desirable incentives for valuable innovation that are well aligned with public health needs. The second is that the expense of assessment would enable much better information about the medical value of different medicines in different situations. This would in turn allow for more informed treatment decisions, and hence better health.

### NOTES

1. Related issues are discussed by Ngaire Woods (2000) in terms of the Board and executive of the IMF and the World Bank, which face considerable problems created by their global mandate and membership but effective financial



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- control by a smaller group of countries.
2. The GAVI Alliance operates on a presumption of consensus (e.g. consensus is strongly preferred), but falls on majority vote if necessary. The GAVI Fund, the separate entity which controls financial operations, operates on majority voting. The Global Fund has a complex supermajoritarian voting principle. To take action not based on consensus requires a two-thirds majority of both the group of eight donors and the group of developing countries and NGOs. Either group can thus block action.
  3. Examples of organizations which are required to make similar kinds of assessments include the Global Fund, NICE in the UK, CDR in Canada, and the Global Burden of Disease Project.
  4. It is likely that abbreviated assessments might be possible in some cases in some years, where the nature of the disease and the sales of the product were relatively constant.
  5. The Audit Branch could be in part modeled after the Global Fund's Technical Evaluation Reference Group, which functions independently from the Fund's operations and grant approval process and reports directly to the Board.
  6. For more on the Acumen Fund's approach, see <http://www.acumenfund.org/investments/investment-performance.html>

# 5. Financing the Health Impact Fund

*The Health Impact Fund will require substantial funding to benefit from economies of scale in its operation and long-term commitments from funding partners to assure investors of future revenue streams. The level of annual funding should be set at a level which benefits from economies of scale in measurement and administration and allows at least two new drugs per year. A mechanism for setting relative contributions across funding partners is suggested. Risk-sharing between funding partners and HIF registrants may give stronger incentives for innovation and participation.*

## INTRODUCTION

Core funding for the HIF will be provided by states which agree to become funding partners. A small number of states can commence the HIF while allowing other states to join the agreement at any time. By joining the HIF, a state undertakes a pre-structured commitment that matches the commitments undertaken by the other contributing states. Whether they are funding partners or not, states can, alongside other non-state contributors, make unstructured payments into the HIF at any time, as will be further described below.

The specifics of the pre-structured commitment that funding partners undertake match the details of the reward mechanism described in Chapter 2. Chief among these specifics are the following.

## THE COMMITMENT TERM OF THE FUNDING PARTNERS

The commitment term should at least equal the length of time during which HIF-registered products are rewarded. A somewhat longer period is desirable so that potential innovators have advance notice with regard to the funds that will be available during the reward period. Since the bulk of R&D expenses are incurred in the final few years before market clearance (clinical trials), a commitment of two years beyond the reward period should be sufficient to satisfy this requirement. Thus, with a reward period of 10

years, the commitment term of the funding partners should be specified at about 12 years.

## ANNUAL CONTRIBUTIONS BY THE FUNDING PARTNERS

The annual financial contributions to the HIF by the funding partners would ideally be proportioned to their ability to pay. It may be best to fix these obligations in terms of states' gross national incomes (GNIs) in the current or preceding year. Thus, if one member state's GNI is 3.7 times that of another, the contribution assigned to the former would be 3.7 times that assigned to the latter. There are three main advantages to this simple approach. First, the contributions of the various countries are automatically adjusted in a way that tracks their shifting fortunes — fast-growing countries automatically assume a larger share while countries declining income find their burden alleviated. Second, this method pre-empts protracted struggles over contributions such as those that have occurred within the United Nations.

Third, allocating financial obligations in this way facilitates the gradual scaling up of the Fund on the basis of income shares (discussed below), since each country would be assured that its contributions will be matched by a corresponding increase in the contributions of all other member states. This way, any country providing  $1/n$  of the HIF's core funding will understand that each additional dollar it agrees to contribute will raise the money the HIF has available to promote global health by  $n$  dollars – or by even

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more thanks to economies of scale achievable in the HIF's administration. If contribution increases were left to ad hoc negotiations, by contrast, then each additional dollar a country agreed to contribute would add only this one dollar to the coffers of the HIF. This mechanism also eliminates uncertainty related to exchange and inflation rates, as each partner's contribution is denominated in its own currency.

It may be argued that the contribution schedule should be progressive with respect to income per capita, so that more affluent countries would contribute a higher proportion of their GNI than poorer countries. But such progressivity would make the HIF a much harder "sell" in the more affluent countries. And poor countries are already favored to some extent insofar as they contribute less on a per capita basis even while the health of their citizens is given equal weight. It is also important that the HIF should reflect, and be seen to reflect, a genuine commitment by all the funding partners who maintain it. The large avoidable excess of morbidity and premature mortality in this world is not just a problem of the poor countries, whose people bear most of this burden, nor just a problem of the affluent countries which will bear much of the financial costs of the HIF. Rather, it is a common global problem, and all countries ought to contribute to its solution in accordance with their means.

For the very poorest countries, the cost of HIF membership may be a serious deterrent. These countries might simply decline to join and then enjoy the benefits of the scheme without sharing its cost. It would be highly desirable, however, for these countries to be full partners in supporting the HIF and in making it work. Though they contain 37 percent of the world's population, the 53 countries the World Bank currently lists as "low-income" account for only 1.3 percent of global income. Their partner contributions to the HIF would therefore be quite low – around \$30,000 to \$200,000 per million population – and, if needed, could easily be subsidized by wealthier states or other donors.

### THE HIF BUDGET

As the large costs of developing a new medicine require correspondingly large incentives and as the

costs of administration and health impact assessment should not be excessive relative to the reward payments, a reasonable minimum funding level for the HIF is around \$6 billion or roughly 0.01 percent of global income. This amount can be compared with the 5-year budget of PEPFAR recently announced at around \$10bn per year, and funded only by the United States. \$6bn is easily affordable if countries accounting for one third of global income were willing to join the partnership, as each partner country would then need to commit only 0.03 percent of its GNI. This initial commitment rate might be lower (assuming wider participation in the partnership) or it might be higher (assuming smaller participation). The following discussion assumes a 0.03-percent initial commitment rate for purposes of illustration.

A reasonable minimum funding level for the HIF is around \$6 billion or roughly 0.01 percent of global income.

The \$6-billion budget is justified by a goal of enabling the HIF to maintain a reasonable portfolio of drugs. It should maintain at least 20 registered drugs at a time, implying that on average two new drugs are registered each year. A portfolio of 20 drugs with an average of two new drugs per year would mean that the rates of payment per QALY would be reasonably smoothed over time, since each product would share the payout with 19 other products. Ensuring some degree of predictability over time with respect to the expected payment per QALY is desirable in order to mitigate the risks involved in registering a product with the HIF.

With 20 drugs being rewarded at any given time, a HIF with \$6 billion annually would have \$300 million available per drug per year. Assuming that the production costs of HIF-registered drugs are covered by the selling price agreed at registration, this \$300 million would need to cover three kinds of expenses. The largest of these arises from the need to recoup the R&D costs of the company as amortized over the 10-year reward period. DiMasi, Hansen and Grabowski (2003) claim that, taking account of the risk of failure, pharmaceutical companies must spend

about \$0.8 billion on R&D for each drug they bring to the point of marketing approval. They also assert that pharmaceutical firms work with a real discount rate of 11 percent. (This rate is used to inflate R&D expenses incurred before marketing approval and also to deflate the recovery of such expenses through earnings occurring after marketing approval. Thus, a \$90 expense incurred a year before marketing approval is considered to be equivalent to \$100 at the time of marketing approval.) Based on these two assumptions, HIF-registered products must obtain payments averaging \$170 million per year, over ten years (starting at the end of the first year), merely to offset average R&D costs of \$1-billion.

This leaves \$130 million per drug per year. This amount must offset the company's selling, general and administrative (SG&A) expenses, including the cost of required submissions to the HIF demonstrating health impact. While SG&A costs for HIF-registered drugs might be lower than those for high-priced drugs under patent, these costs of selling a drug worldwide would still be substantial. Those \$130 million per drug must also compensate the firm for the expenses incurred by the HIF for administration and global health impact assessment. Such assessment expenses would be largely or wholly covered by registration fees paid by registrants to the HIF. Still, registrants must be able to cover these fees out of the rewards they receive from the HIF; and so it is appropriate here to include these costs which, with 20 registered drugs, would likewise be substantial. (Recall that the registrant's costs of production are covered by the price that it charges for the drug.)

A firm could earn greater profits (over and above those implied in the assumed 11-percent real discount rate) with a HIF-registered product if it succeeded in developing an effective product for less than a billion dollars, in reducing its SG&A costs, or in capturing a larger than 1/20 share of annual HIF reward payments. However, on average, a budget of \$6 billion appears to create a payout large enough to support approximately two new drugs a year. If the average costs of R&D and/or SG&A are in fact lower than here assumed, then a budget of \$6 billion might over time end up supporting more than two drugs a year. If average costs are higher, this budget would over time

end up supporting fewer. A recent analysis purportedly by a "Big Pharma" company estimated the cost of developing a new drug for a neglected tropical disease to be in the range of \$300m, which is well below the DiMasi *et al* estimates, possibly because there are low-hanging fruit to be plucked, or possibly because the cost of clinical trials in developing countries are likely to be considerably below those used in the DiMasi *et al* analysis (McCaughan 2008).

A further consideration supporting a \$6-billion minimum annual allocation to the HIF appeals to the cost of performing credible health impact assessments. There are likely substantial economies of scale to be realized by increasing the number of registered medicines under assessment. For example, the costs of developing an appropriate methodology, which is the function of the Technical Branch described in Chapter 4, is independent of the number of drugs being assessed. Similarly, assessments in different countries may be performed more efficiently when there are more medicines under review.

Given such substantial economies of scale, a poorly funded HIF would face a dilemma. If it performed credible global health impact assessments, then the cost of these assessments would become excessive relative to the net health impact rewards the HIF pays out on their basis. Yet, if it limited assessment costs to some reasonable proportion of total reward payments, then the assessments could become unreliable and even subject to manipulation.

A HIF budget of \$6 billion would suffice to avoid this dilemma as the costs of assessment and administration could be kept around a reasonable 10 percent of the HIF's annual budget and still be large enough, at \$600 million annually, to support a credible operation.

In sum, then, \$6 billion annually seems a reasonable minimum. Were the HIF to be funded at a level substantially below \$6 billion, then it would not generate a smooth and adequate flow of new high-impact medications and would also have to devote too much of its funding to administration and assessment expenses.

Looking above this minimum, there is no "optimal" budget for the HIF. The larger it is, the more drugs it could sustain in its portfolio, and the larger

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the incentive effects it would have on R&D. However, there appear to be benefits from having a larger portfolio of drugs, both in terms of increasing predictability about rates of payment for firms, and in terms of exploiting economies of scale in assessment. An appealing feature of the HIF is that, as it grows larger, it will tend to displace drugs from high pricing, leading to savings for patients and insurers. Thus, the net costs of increasing the budget are likely to be far less than the increase in the budget. (This point is discussed further in Chapter 8.)

A simple example can illustrate the point. Suppose the developer of an important new medicine could – charging a patent-protected high price – sell annually 7 million packages to affluent patients at \$50 each and thereby earn \$315 million (\$45 per package) over production costs. Suppose further that, were the same medicine sold worldwide at cost, it would serve a much larger patient population. In this scenario, affluent patients stand to gain \$315 million (\$45 on 7 million packages) annually from at-cost pricing. If the HIF, by offering the prospect of a \$315 million annual reward, induced the firm to register its product, the net cost to the public would therefore be much lower. The HIF might pay out \$315 million in taxpayers' money, but affluent patients (or their national health systems and insurance companies) would save \$315 million. Therefore, it would effectively cost the public nothing to include the four-fifths of humanity who cannot now afford patented medicines. If the increased production runs enabled by higher sales volumes reduced the cost of production, the net cost to the affluent would be negative. In addition, there would be worldwide gains in productivity due to the reduced burden of disease as well as the prospect of eradicating some communicable diseases (which now proliferate among those too poor to be promising targets for pharmaceutical sales).

### COMMENCEMENT OF FUNDING

As it takes several years to develop new medicines and bring them to market, the HIF need not be funded at full strength from the beginning. Nonetheless, the phase-in should be fairly rapid because companies are likely to have some recently patented

and also some partially developed products that they would want to register soon after the HIF's commencement. Too slow a phase-in is also undesirable if it signifies lack of commitment to potential registrants. The dollar-per-QALY ceiling (discussed in Chapter 2) insures against overpayment should early uptake be poor. And reward funds unspent in an early year – or indeed in any year – could simply be rolled over into the subsequent 10 years. In this way, no money would be wasted if the aggregate health impact achieved by all registered medicines in some year were insufficient to exhaust reward funds available.

A reasonable phase-in schedule might call for the funding partners to contribute one-half of their standing contribution in the first year and three-quarters in the second year of the HIF's operation. At an initial commitment rate of 0.03 percent, each initial funding partner would then contribute 0.015 percent in the first year, 0.0225 percent in the second year, and 0.03 percent in the third and subsequent years.

Other countries may be invited to join the HIF in later years on the same phase-in terms. This seems reasonable in light of the fact that any money they contribute in their first two years as funding partners could not have been counted on by the registrants who are rewarded in these two years.

### LEAVING THE FUNDING PARTNERSHIP

Countries joining the HIF at inception might be uncertain to some extent about how well it will work. They will be more likely to join if there is an exit option. But if countries were allowed to exit the HIF at any time, its failure would be assured as innovators would not take seriously the opportunity to register their products without reasonable assurance of the envisioned rewards.

This dilemma can be resolved by including the option of a phased withdrawal. Countries would have the option to withdraw from the partnership by winding down their commitment at the rate of 10% per year, following an announcement period of 2 years. Thus, if a country had a commitment of 0.03% of GNI annually to the HIF, and wished to

withdraw, it would be required under the terms of the agreement to contribute this amount for the next two years, and then an amount declining by 0.003% of GNI a year over the following ten years, after which its commitment would be zero. During the ten-year drawdown period, the amount committed by that country would be segregated, and paid only on the basis of health impact by products that were registered with the HIF before the drawdown period commenced.

## SHARING THE COST OF THE HIF BUDGET

The suggested minimum amount of \$6 billion per annum is quite small for states — not much more than the annual development assistance provided by the Netherlands, for example. Even affluent countries with low population number — Australia, Switzerland, Norway — could fund such a commitment by themselves. But, in light of the goal that the HIF should gradually be expanded, early buy-in by many states is much to be preferred.

Global income is currently nearly \$60 trillion. Thus, if all countries were to join the HIF, each of them would need to contribute 0.01 percent of its GNI in order to reach the minimum \$6 billion per annum. With countries representing half of global income participating, each funding partner would need to commit 0.02 percent of its GNI to reach the minimum \$6 billion per annum. And with countries representing one third of the global product as funding partners, the corresponding contribution percentage would be 0.03. This one-third target is very easily reached if the HIF is joined either by the United States or else by all or nearly all member states of the European Union.

One can put the cost of the HIF in perspective by comparing its initial annual cost of \$6 billion to global spending on pharmaceuticals which, in 2008, is expected to be about \$735 billion. Given population growth — as discussed in Appendix B — global expenditures on pharmaceuticals seems likely to continue to rise. Total health-care spending is much larger still, around 10–15 percent of GNI in affluent countries — \$2,000 billion in the US alone. And, as

discussed above, the cost of the HIF would not be incremental spending on medicines, but would often merely change the way a pharmaceutical innovation is paid for.

Assuming the HIF works well, the contribution percentage could gradually be increased, and funding would, of course, also increase through real GNI growth in the partner countries as well as through the accession of new funding partners.

## COPING WITH UNCERTAINTY

The HIF is to reward pharmaceutical innovators each year in proportion to the health impact their registered medicines have achieved in this year. This requires relating a fixed amount of money to a varying health impact (which we here express in terms of QALYs). A simple solution is to divide each year the available funds over the registered pharmaceuticals in proportion to their health impact in this year. This solution has various advantages outlined in chapter 2, in particular that no dollar-amount per QALY needs to be specified in advance. A scheme structured in this way will lead innovators to adjust the supply of rewardable pharmaceutical innovation through decisions about whether or not to undertake potential research efforts, and through decisions about whether to register a new medicine with the HIF.

If the aggregate health impact of all registered medicines is small in any year, the HIF is protected against excessive pay-outs through the dollar-per-QALY ceiling already discussed. But there is an inverse problem: what if the global health impact achieved by all registered medicines is very large in a given year? This prospect is very agreeable, of course, from the standpoint of global health. But this prospect might also reduce the attractiveness of the HIF to innovators, deterring potential research efforts and making firms less willing to register their products with the HIF.

One possible solution to this problem is insurance. The Health Impact Fund could negotiate an insurance contract that would commit a consortium of insurance companies to guaranteeing a minimum dollar-per-QALY rate in exchange for a fixed premium. Or individual companies could negotiate such



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insurance contracts for their HIF-registered products. A drawback of this solution is that, in light of the considerable uncertainty involved at least in the early years, the premiums would be high and thus would reduce substantially the net rewards received by registered innovators, with detrimental effects on incentives. In addition, there are problems of moral hazard which render insurance probably infeasible since, with insurance, the HIF would be perceived to have no incentive to control the amount of QALYs attributed to the registered products.

Another solution to the problem of inadequate rewards would be for the HIF to underwrite a minimum \$-per-QALY rate by tapping into funds assigned to future years. But allowing the HIF to run such deficits would reduce committed funds available for future pay-outs and would thereby — rather than solve the problem of reduced incentives — shift this problem into future years.

A third solution would be to transfer some of the uncertainty from pharmaceutical innovators to the funding partners. Obviously, both sets of actors are averse to financial uncertainty in their relations with the HIF. Pharmaceutical innovators have a strong interest in predictable rewards, such as a fixed payment per QALY assessed. They already face great uncertainties relating to research, testing, patenting, obtaining market clearance, and marketing of a new medicine. The funding partners contributing to the HIF, on the other hand, have a strong interest in predictable outlays, specified perhaps as a proportion of GNI as suggested above. They will be less willing to make a 12-year commitment to an international scheme the more uncertainty there is about how much this commitment will cost.

Likely neither by the funding partners nor by innovative firms, the uncertainty nonetheless has to be borne by someone, and the more one set of actors is shielded from it, the more must be imposed on the other set of actors.

There are three reasons for imposing some of the uncertainty on the funding partners. First, countries are generally better able than companies to absorb financial risk and uncertainty. This is especially true with respect to small- and medium-sized companies, including those located in developing countries

— companies that account for a large proportion of pharmaceutical innovation and whose innovative efforts the HIF is intended to encourage. But it is true even for the very largest of pharmaceutical companies, because the HIF payments they receive could constitute a significant fraction of their profits. While HIF payments might initially constitute about one percent (and eventually much more) of Pfizer's \$50 billion in annual revenues, state contributions to the Health Impact Fund would be only a small fraction of one percent of the government budget of each partner country. Therefore, it is easier for states to cope with a cost overrun than it is for pharmaceutical firms to cope with a corresponding shortfall.

Second, there is an important asymmetry: insofar as uncertainty is imposed on innovators, and things go badly for them because the collective health impact of all registered medicines is unexpectedly large, such innovators suffer an unmitigated loss of anticipated reward revenue. By contrast, insofar as uncertainty is imposed on countries and things go badly for them because the collective health impact of all registered medicines is unexpectedly large, such states suffer a mitigated loss: they are required to make a supplemental payment to the HIF, but they also benefit from a larger than expected decline in the burden of disease, from larger than expected cost savings on patented medicines, and from larger than expected economic gains from better global public health.

Third, insofar as uncertainty is imposed on companies, they will factor an extra risk premium into their decision making. This will cause them prudently to forgo some research efforts of more marginal expected profitability, and the HIF will then achieve less health impact for its \$6 billion annual cost than would be the case if less uncertainty were imposed on companies. This in turn is undesirable for the funding partners which, by absorbing more of the uncertainty, could make the fund more cost-effective.

Powerful as these considerations are, they do not show that governments should shoulder all of the uncertainty by agreeing to a rigid dollar-per-QALY floor. Such a rigid reward mechanism would lose a desirable informational feature discussed in Chapter 2, namely that a scheme under which the dollar-per-QALY rate varies inversely with supply provides

valuable information about the cost of innovation on a per-QALY basis and thereby allows the member states to reach better-informed decisions about how to structure and how richly to fund the HIF. These advantages can be preserved through sharing of uncertainty between governments and registered innovators, as discussed in Chapter 2.

The decision as to whether member states are willing to accept a commitment that involves the risk of paying somewhat more than expected is ultimately a political one. There are, however, some advantages that could be realized if the commitment of states to the HIF were sufficiently flexible to help mitigate the uncertainties faced by innovators. However, there are also other, less open-ended ways to mitigate such uncertainties, including by making contributions to early-stage research.

## EXPANDING THE HIF OVER TIME

An important aspect of the HIF is that, if successful, it can be expanded, enabling ever more products to be registered. Growth in the size of the HIF can occur in various ways.

One dimension of growth is firmly locked in: as partner states enjoy real growth in GNI, their contributions to the HIF increase apace.

A second dimension of growth is the accession of additional countries as funding partners. This could be a very substantial source of growth if (as we assumed) countries accounting for two-thirds of global income initially opted not to join. Such accessions might easily double the size of the HIF from \$6 billion to \$12 billion or more annually.

A third dimension of growth is an increase in the contribution percentage. (In order to reassure potential innovators, the contribution percentage cannot be decreased except in the special case of departing partners as described above.) The funding partners have an opportunity to observe the HIF in operation and, in particular, to learn at the end of each year the reward rate of dollars per QALY for that year. If the reward rate is near the maximum, then there is little urgency in raising the contribution percentage. If the reward rate is much lower — signalling that the HIF is producing particularly good value for the money

invested in it — then this could serve as a signal to expand the HIF's size. The terms of the HIF might be written so that low payments per QALY in any given year would trigger official consideration of an increase in the contribution percentage for subsequent years. The decision about whether to increase the percentage, and by how much, would obviously be made by the funding partners. Here it seems reasonable to weight the votes of the larger contributors more heavily (though perhaps not quite in proportion to their contribution) and to require a substantial supermajority of these weighted votes for any increase to become effective. Such a conservative structure also has the advantage of making it easier for states to agree to join the HIF in the first place.

A fourth way in which annual HIF pools can increase over time is through sponsors other than member states. The HIF should invite such other potential sponsors large or small, to contribute as well: foundations, corporations, and individuals, for example, and also governmental and non-governmental organizations, non-member states, and sub-national governments. Such additional sponsors can make a similar 12-year rolling commitment. Or, alternatively, they may make a one-time contribution. Such casual contributions could be collected into an endowment in order further to stabilize expectations that funding will continue to be available long-term and perhaps also to smooth out fluctuations in the reward rate. Over time, a pattern of casual funding may emerge and strengthen the innovation incentives. Nonetheless, the funding partners' reliable long-term commitments for a 12-year period are crucial for the success of the scheme. And sponsors — especially states — should therefore be strongly urged to join the Health Impact Fund as full funding partners rather than to remain outside as casual sponsors.

A fifth, less significant way in which annual HIF payments may increase over time is through a reduction in the HIF's net operating expenses. These expenses consist — simplifying slightly — of fixed costs, incurred regardless of the number of registered products, and variable costs, rising somewhat less steeply than number of registered products. The variable costs should be estimated in advance and charged to the registrants as user fees (thereby dis-

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couraging the registration of low-impact medicines whose assessment would be disproportionately costly). As the HIF grows, its assessment expenses per registered medicine will fall. This will result in higher net gains (reward payments minus registration fees) for registrants and will therefore strengthen the incentives the HIF provides.

### CONCLUSION

The last four chapters have given a detailed sketch of how the Health Impact Fund might work. The point of this sketch was to show that the HIF is possible, along the lines here suggested. Attentive readers will have found things to disagree with. Such disagreements are welcome as they will make it possible to improve the specification of the HIF and of the arguments in its favor. The viability of the HIF does not

depend on each and every detail of our description. We invite constructive critique that is mindful of the urgency of the problem and of the great promise of the solution we have outlined.

Having described the HIF, we will proceed in the next four chapters to present the most important arguments in its favor. We will show how the HIF can be justified in moral and specifically in human rights terms, how it is uniquely capable of reducing the last-mile problem of delivering minimally adequate health care to the world's poorest populations, how it relates to a simple reliance on the patent system, and how it stacks up against alternative ideas for improving global public health.

# 6. A Moral Argument for Creating the Health Impact Fund

*Is it morally permissible to impose strong patent protections where doing so prices important new medicines out of the reach of many poor people? We argue that doing so is not permissible and in fact a human rights violation. To become human rights compliant, the global patent regime must be complemented by an enduring institutional mechanism that effectively incentivises the development and distribution of high-impact medicines that meet the health needs of poor people and are accessible to them. The Health Impact Fund is designed to be such as complement. At the end of the chapter, we discuss and refute three popular arguments claiming that no such complement is needed because high prices for vital patented medicines, backed by the legal suppression of cheaper generic substitutes, does no injustice to poor people.*

## INTRODUCTION

One important aspect of globalization is the increasingly dense and consequential regime of global rules that govern and shape interactions everywhere. Covering trade, investment, loans, patents, copyrights, trademarks, labour standards, environmental protection, use of seabed resources and much else, these rules – structuring and enabling, permitting and constraining – have a profound impact on the lives of human beings and on the ecology of our planet. It is therefore important to think carefully, in moral terms, about their design.

With the 1994 adoption of the TRIPS (Trade-Related Aspects of Intellectual Property Rights) Agreement, the most important rules governing the development and sale of medicines have been shifted from the national to the global level. States implement the rules of the Agreement through national legislation and enforcement, but in doing so they are tightly constrained by its terms. In particular, they are required to offer 20-year patents for a wide range of innovations, and pharmaceutical innovations such as drugs and vaccines in particular.

The introduction of strong pharmaceutical patent protection into the less developed countries has been characterized by many as an unmitigated disaster. Our assessment differs in two respects. First,

we recognize that patents can play a positive role in meeting the health needs of people in the future, both poor and rich, by incentivizing pharmaceutical research, and so the introduction of stronger patent rights in developing countries may be particularly important with respect to tropical diseases; so the disaster is a mitigated one. Second, we believe that it is neither morally necessary nor politically realistic to roll back TRIPS in the domain of pharmaceuticals. The preceding arrangements were by no means ideal; and the structural problem of the status quo can be solved through an institutional complement, the Health Impact Fund, which is specifically designed to resolve problems in pharmaceutical markets. The crucial moral issue is then not the presence or absence of strong pharmaceutical patent protection, but rather the presence or absence of (something like) the Health Impact Fund.

## ASSESSING THE STATUS QUO THROUGH FOCUSED COMPARISONS WITH ALTERNATIVE OPTIONS

Freshly globalized through the TRIPS Agreement, the current regime governing the development and distribution of new medicines — “the Status Quo” or “SQ” — is often defended through a focused com-

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parison with alternative possibilities. One such defence imagines what the world would be like (holding all else fixed) without the practice of rewarding pharmaceutical innovations through patents. In such a world, nearly all the innovative pharmaceutical research currently undertaken by privately owned firms would be absent. The reason is that such research efforts, even if successful, would foreseeably result in economic losses to the innovating company as its competitors — unconstrained by patents — would copy or retro-engineer its invention and would then compete the price of the medicine down close to the long-run marginal cost of production. Since it is better to have the option of buying commercially developed expensive medicines than to lack this option, a system of patent rewards is clearly better than no rewards at all.

It would be wonderful if we could make the newest drugs affordable for anyone who needs them and keep the lifesaving research going. But cut prices and you cut profits. Cut profits and you cut research and development. Cut research and you slow new drug innovation. You may get cheaper and more widely available drugs in the short term, but you'll also get worse drugs in the long term, and risk ending the greatest era in research in memory.... Slap on de facto price controls, squeeze profits to get more short-term access for more people – and you'll have one sure result. Investment for research will dry up, innovation will slow down and the great gains of the last decade will recede into history.

Andrew Sullivan

This comparison would sustain a compelling defense of SQ, if there were only these two options available. But this is not so, and the argument is then based on a false dichotomy. It's not much of a defense of how things are to show that they could be even worse. The justifiability of SQ turns not on whether there is any option that is worse, but on whether there is any option that is appreciably better. Exploring this latter question requires creativity and an open mind. One must loosen one's attachment to the status quo and then try to develop promising alternatives into

their best possible form. Only if we have tried this in a serious and sustained manner and have failed again and again can we morally accept SQ with the great burdens it places on poor people.

One commonly proposed alternative to SQ is the "Pre-TRIPS" regime that preceded it: a regime under which states were free to decide separately, each on the basis of its own interests, what rewards, if any, to offer for pharmaceutical innovation. Let us examine this comparison.

### COMPARING SQ TO THE PRE-TRIPS REGIME

The main argument for favoring SQ over Pre-TRIPS is that the former stimulates the development of medicines that otherwise would not have existed. When pharmaceutical companies can obtain 20-year patents in less developed countries and can, thanks to such market exclusivity, sell their medicines there with high mark-ups, they will take such potential profits into account when deciding about potential research efforts. To be sure, only a minority of the population of the less developed countries can afford to buy patented medicines. Still, eventually such poor people will also benefit. Once the relevant patents expire, they may have access at generic prices to medicines that would never have been developed without the extension of strong intellectual property rights into the less developed countries.

It is too early for success stories of this kind. Most of the less developed countries were required to institute the TRIPS-mandated product patent rules by 1 January 2005, and certain "least developed" countries still have until 1 January 2016. So the new incentives may well have spawned some of the recent or current research efforts, but no medicine resulting from such efforts has yet become generically available. Patents applied for after 1 January 2005 will not expire until 2025 at the earliest.

In the long run, however, SQ is likely to bring substantial benefits compared to the alternative of no patent protection in developing countries. These will be most obvious in the domain of so-called type 3 diseases, defined as ones that occur exclusively or overwhelming in poor countries. These diseases have long

been neglected as unprofitable by firms involved in pharmaceutical research. But such firms may well become more interested in such diseases when the availability of patents in less developed countries allows them to collect high mark-ups there on drugs sold to affluent patients, government agencies, and NGOs.

With regard to any new medicine for a type 2 or type 1 disease it will probably always be difficult to know whether it owes its existence to the TRIPS-expanded intellectual property protections. Still, it is likely that the inclusion of the less developed countries — which expands the potential market for patented medicines by adding some 500 million affluent people to the 1000 million residents of the high-income countries<sup>1</sup> — will accelerate the pace of pharmaceutical innovation in the domains of type 2 and type 1 diseases as well. Again, access to such TRIPS-inspired new medicines will initially be confined to the most affluent quarter of humanity. But eventually, when such medicines come off patent, much larger numbers of poor people will also be able to benefit from their existence.

These important advantages of SQ must be balanced against the advantages of its predecessor. Before the TRIPS Agreement was adopted, most of the less developed countries had weak intellectual property protections or none at all, which enabled them to produce or import cheap generic versions of advanced medicines that were patented and thus much more expensive in the affluent countries. Relative to Pre-TRIPS, SQ thus imposes a serious loss on the poorer three quarters of the human population by pricing out of their reach new medicines that otherwise they could have obtained at generic prices either through their own efforts or with the help of friends, relatives, NGOs, or governmental or intergovernmental agencies.<sup>2</sup>

Which of the two regimes is morally preferable? It is evident that SQ is preferable for the population of the affluent countries who gain access, on familiar terms, to additional medicines that would not have existed without the added market demand for patented medicines which now is anticipated from the less developed countries.

The comparison is more complex in the case of the affluent minority in these less developed coun-

tries. They are better off insofar as they can now buy — albeit initially at high prices — some new medicines that would not have existed without the TRIPS Agreement. They are worse off insofar as they must now pay much more for new medicines that would have existed even without the TRIPS Agreement. It seems plausible that, for this group as well, the gains in terms of health and survival outweigh the financial losses.

The most difficult comparison is that from the standpoint of the poor in less developed countries, who cannot afford to buy new medicines at monopoly prices. The standpoint of this group ought to be accorded great moral weight, since it constitutes about three quarters of the human population and also has the most at stake. The extension, through the TRIPS Agreement, of strong intellectual property rights into the less developed countries, burdens the poor in those countries by causing to be priced out of their reach all the new medicines that would otherwise have been available to them at generic prices. Yet, this extension of intellectual property rights may possibly also benefit the poor of the future, if the additional incentives it provides lead to the development of important medicines that would not otherwise have existed. To be sure, poor people will not be able to afford such an additional medicine during its initial period under patent. But they may benefit from purchases made on their behalf by aid agencies and governments, and there will come a time when the relevant patents will have expired and these medicines will be available at generic prices. This latter benefit could begin to materialize in 2025.

It is clear that the magnitude of these burdens and benefits is enormous. Under SQ, millions are unable to afford new medicines during their early years under patent protection and the exclusion of these people from access to advanced medicines will exact a heavy toll of disease and death for the indefinite future. Yet millions of poor people may survive or be healthy in the future thanks to the generic availability of medicines that would not have existed but for the additional incentives introduced by the TRIPS Agreement.

A clean-cut theoretical solution to this dilemma invokes the difference in the time at which the bur-



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dens and benefits materialize. Strengthened intellectual property protections in the less developed countries burden the poor immediately by pricing vital medicines out of their reach. Yet, such protections may benefit only future poor people, starting in 2025, when patents on medicines that owe their existence to such protections expire. Appealing to this time difference, one might then propose to resolve the dilemma in favor of Pre-TRIPS on the ground that it is morally impermissible to cause severe harms, including death, to poor people now for the sake of protecting millions of poor people from similarly severe harms later on. Many endorse such a principled stance. Yet, one can not be satisfied with such an outcome in view of all the harm that stimulating new drug development could avert from so many future lives.

It may seem as though compulsory licenses — as envisioned in the TRIPS Agreement and reaffirmed in the 2001 Doha Declaration — are a practical solution to this dilemma. By issuing a compulsory license, a government can force down the price of a patented invention by compelling the patent holder to license it to other producers for a set percentage (typically below 10 percent) of the latter's sales revenues. Yet, compulsory licenses cannot fully solve the dilemma because, insofar as governments actually use them to improve access by the poor to patented medicines, compulsory licenses weaken the innovation incentives that were supposed to result from the extension of strong intellectual property rights into the less developed countries. Pharmaceutical companies will understandably discount any such incentive if they are uncertain whether and to what extent they will actually be allowed to reap the financial reward from inventing a new medicine.

We believe that there is far better practical solution to the dilemma. The Health Impact Fund, added to the status quo, would strengthen pharmaceutical innovation incentives while reliably avoiding high mark-ups that obstruct access by poor patients to new medicines.

### COMPARING SQ TO SQ+HIF

The world's governments can now, while retaining the TRIPS Agreement and its benefits, take an important

step toward freeing the poorer three-quarters of humanity from imprisonment in a cycle of mutually reinforcing poverty and ill health, while also benefiting the fourth quarter — those who are relatively wealthy. Most governments are unable single-handedly to create the HIF. But its creation requires nothing like unanimity. Many of the richer states could create it on their own. And every state, no matter how small or how poor, can publicly declare its commitment to start or join a partnership of countries ready to underwrite the HIF.

The third [of the four freedoms] is freedom from want, which, translated into world terms, means economic understandings which will secure to every nation a healthy peacetime life for its inhabitants — everywhere in the world.

Franklin D. Roosevelt

This is then the central moral question we pose: Given the available option of adding the HIF to the existing global patent regime, is it morally permissible to continue SQ? Is it morally permissible for any state to reject the HIF in favour of the status quo?

Answering this question requires discussing what difference creation of the HIF would make and then assessing this difference in moral terms. We discharge the former task in the present section and the latter in the next.

The most important consequences of creating the HIF can be brought under three headings: Innovation, Price, and Last Mile.

### Innovation

The HIF would mitigate the long-standing problem of incentivizing the development of new medicines that would have large health impacts but small profits under SQ — because of impoverished markets, for instance, or because of inadequate protection from competition (as in the case of new uses). With the HIF in place, all diseases that substantially aggravate the global burden of disease would come to be among the most lucrative research opportunities, as discussed in Chapter 8. Without losing any of their

present opportunities to cater to the health needs of the affluent, pharmaceutical companies would have additional opportunities to develop new medicines against heretofore neglected diseases, and they would be incentivized to do so with an eye to prioritizing the diseases they can fight most cost-effectively. The notion of cost-effectiveness relevant here relates a familiar notion of cost to a rather unfamiliar notion of benefit. Costs comprise the large fixed costs of bringing a new medicine to market (research, patenting, testing, and obtaining regulatory approval) plus the variable costs of production, distribution, and marketing. Benefit is the assessed global health impact attributable to the new medicine. Given similar costs across the various plausible target diseases, firms will concentrate on researching the diseases against which the largest health impact can be achieved. These will include HIV/AIDS, tuberculosis, malaria, and various other tropical diseases discussed in Appendix A, in regard to which the present arsenal of pharmaceutical interventions is woefully inadequate.

### Price

HIF-registered medicines will be available worldwide at very low prices, usually even below prices currently charged for comparable generic medicines. HIF registrants will be obliged by contract to sell their products everywhere near cost (see Chapter 2) and will, in the case of the most therapeutically effective products, have an incentive to choose the lowest permissible price.<sup>3</sup> Some such cheap HIF-registered medicines would not have existed but for the HIF. But there will be other cheap registered medicines that could have been profitably developed even without the HIF. In these latter cases, the innovating firm could choose high prices to exploit the market exclusivity to which it is entitled during the life of its relevant patents. But the firm chooses to register its product with the HIF nonetheless because it expects to make more money by foregoing high prices in favor of health impact rewards. In such cases, the HIF does not bring the medicine into existence, but still makes a huge difference to its price in the years it is patented. Products priced by a profit maximizing monopolist will always be marked up to the point where

some cannot afford them. When economic inequalities are large (as they are today), a large majority may find such products priced beyond their reach. When the products are important new medicines, the harm caused by such access problems to this excluded majority can be staggering. As the more high-impact drugs would come to be registered with the HIF, this majority would no longer be excluded by high prices from using those drugs.

### Last Mile

Poor people's access to vital medicines is currently obstructed by various obstacles other than price, such as lack of local availability of a medicine, lack of available knowledge and information about diseases and their remedies, and gross negligence, incompetence and corruption in the health systems of many poor countries (as discussed in Chapter 7). Many governments of less developed countries have shown themselves unable or unwilling to address these obstacles. Inability is often a matter of lack of resources as when a poor country's government lacks the funds to train and retain local doctors and nurses. Unwillingness is typically due to a lack of democratic accountability which allows rulers to stay in power and prosper even while the poorer segments of their country's population is decimated by malnutrition and disease. HIF-registrants are much better positioned than the very poor themselves to compensate for such government failures. Incentivized to make their registered medicine competently available to as many poor patients as they can cost-effectively reach, such registrants will — perhaps in collaboration with one another — provide knowledge, information, expertise, training and funds to help maintain basic health infrastructure where it can be profitable for them to do so. Such registrants may also bring the pressure of publicity to bear on governments that obstruct health improvements for their poor citizens. To be sure, these are tasks that other governments, media, NGOs and private citizens could also perform. But more effort is clearly needed, and profit-oriented companies can make an important contribution.

These benefits in terms of innovation, price, and “the last mile” accrue not only to the poor in less de-

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veloped countries. All people benefit when pharmaceutical firms organize themselves for optimal health impact: when their innovations target the most burdensome diseases and when they market their products for optimum disease reduction and not merely for sales. And low prices for advanced medicines will have a large impact on poor people in the United States no less than in Haiti, because high prices deter the poor everywhere from purchasing medicine. Even in countries with publicly financed universal health insurance coverage, high prices may lead to certain products being excluded from formularies, so that even those who never bear any out-of-pocket costs for pharmaceuticals may suffer from a lack of access because of high pricing. And the HIF would of course greatly reduce the cost of medicines even for the affluent who currently pay — directly or else through taxes or insurance premiums — the lion's share of all costs for pharmaceutical research. Taking account of these savings, the net cost of the HIF even to the affluent would be only a fraction of the nominal cost they would bear through the tax system.

Considering together how the addition of the HIF to SQ would affect the various groups, it may seem evident that the benefits outweigh the cost. But some of the more affluent populations may not be moved by such considerations. They might say: "Let us take for granted that the HIF is feasible and would work as intended. It is then surely morally better for there to be a strong HIF rather than none, and morally better, for our countries to offer to participate in such a Fund rather than to decline. But it does not follow from this that our countries are morally required to support the HIF — no more than it follows from the fact that it would be morally better if a rich woman gave half her assets to charity that she has a moral obligation to do so. It is morally permissible for each government to make this decision on the basis of the interests of its own citizens. If the costs of the HIF to us are larger than its benefits to us, then our governments may permissibly decline to participate even if this decision leaves large disease burdens in other countries unalleviated. And we suspect that, indeed, the HIF's benefits for us will be small if many of the additional medicines the HIF would induce are for tropical diseases from which we have little to fear. We will gain,

to be sure, from low prices of some medicines that would otherwise be sold with high mark-ups. But these savings may not be large enough to justify the contribution we would be making to the HIF."

This nationalist standpoint is widespread. It can be addressed in two ways. One way involves arguing that creating the HIF would actually improve the situation of the affluent relative to SQ. They too would benefit from refocusing the innovation and marketing priorities of pharmaceutical companies from sales toward health impact. They too would benefit from the availability of cheap HIF-registered medicines that would otherwise be sold at high prices under patent protection. They too would benefit from a serious attack by the pharmaceutical industry on the diseases whose harm can be reduced most cost-effectively. Such a sustained offensive with new HIF-registered medicines would better protect the affluent from these most dangerous diseases and their possible mutations by greatly enhancing our knowledge about these diseases and also of course by reducing their prevalence. The affluent would also benefit, finally, from HIF-induced expansion of the pharmaceutical industry in their countries and from the global increase in economic productivity due to better health worldwide. The creation of the HIF can be beneficial (relative to SQ) for all relevant groups because it is a much more efficient way of paying health gains achieved by innovative medicines.

The present chapter addresses the nationalist standpoint in a different way: by challenging its legitimacy in this case. Here we assume for the sake of the argument that the HIF would, relative to SQ, cost some group of affluent people more than it would benefit them. We then argue that these people would still not be entitled to insist on SQ because SQ imposes morally unacceptable burdens on poor people. These burdens are shown to be reasonably avoidable by the availability of SQ+HIF as a feasible option; and the continuation of SQ is then morally impermissible. This does not mean that the affluent, or anyone, are morally required to support the HIF, for there may be other ways of averting the unjust burdens SQ imposes. We discuss such other ways in chapter 9. We argue there that other reform ideas and initiatives, though good and helpful, are neither

systemic nor as cost-effective as the HIF would be. The HIF offers certain distinct advantages: it operates globally (which dilutes its costs but not its benefits); it potentially applies to all diseases and pharmaceutical remedies (offering a large space in which firms can optimize cost/benefit); it addresses both innovation and access; it uses the power of competition to control costs; and it operates into the indefinite future (hence taking full advantage of long-term incentive effects). If the HIF is indeed the most cost-effective solution, then the self-interested affluent have prudential reasons to endorse the HIF as the (for themselves) most advantageous permissible regime.

If SQ is impermissible, then modifying it, even at some net cost to some affluent people, is not charity — no more than it would be charity for the rich woman to give up assets that do not belong to her. The woman's insistence that she is entitled to retain possession of her wealth can be challenged by showing that this wealth is not legitimately hers. Analogously, any insistence by the affluent that they are entitled to maintain SQ can be challenged by showing that SQ is grievously unjust. This challenge proceeds by way of appeal to human rights.

## HUMAN RIGHTS AS A GLOBALLY SHARABLE MINIMAL STANDARD OF INSTITUTIONAL ASSESSMENT

The moral argument for creating the HIF would be greatly helped if it could be shown that SQ is unjust. But showing this would seem to presuppose a widely shared conception of global justice. There is no such conception widely endorsed across regions and cultures. We seek to overcome this lack through a two stage argument.

The first stage (the present section and the next) builds on the realization that, while an international consensus on global justice is lacking, it is also not the case that there is agreement on nothing at all. There is a widespread and enduring consensus on one basic element of a conception of justice, namely on the high moral priority of certain fundamental human rights. To be sure, human rights constitute very minimal requirements, and most would reject the view that anything that does not violate human rights is

therefore permissible. By adopting a human rights standard, we do not endorse this view but merely commit ourselves to the converse: anything that does violate human rights is therefore impermissible.

I am quite certain that my way of justifying belief in the rights of man and the ideal of liberty, equality, and fraternity is the only way with a firm foundation in truth. This does not prevent me from being in agreement on these practical convictions with people who are certain that their way of justifying them, entirely different from mine or opposed to mine ... is equally the only way founded upon truth.

Jacques Maritain

The second stage of the argument (the last three sections of the chapter) shows that the answer delivered by a human rights assessment cannot be overturned by other morally relevant considerations. We can display some work on this second stage here, in an exemplary way. But we cannot, of course, work through all the moral considerations that could be claimed to be alive in some country or culture in order to show that none of them generates reasons that would undermine or override our human-rights argument for creating the HIF.

Human rights have come to be understood as entailing counterpart duties to *respect*, *protect*, and *fulfill*.<sup>4</sup> It would not be difficult to show, to those who share this understanding, that adding the HIF to SQ would be a great advance in terms of protecting and fulfilling human rights — especially social and economic human rights as formulated, for example, in the 1966 International Covenant on Social, Economic and Cultural Rights which expands upon Article 25 of the 1948 Universal Declaration of Human Rights:

Everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care.

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Many people in the affluent countries claim, however, that they and their countries do not have such “positive” duties to protect and fulfill. These people recognize human rights only in the narrow sense where the only duties these rights entail are duties to respect, that is, duties not actively to violate human rights. We do not endorse this view. But in order to present as broadly-based an argument as possible, we work with this narrow understanding of human rights throughout.

So understood, human rights constrain how agents — principally governments, but also corporations, military units, rebel groups and other organized collective agents — may treat human beings. The human-rights violating treatment in question may involve direct action: as when a government terrorizes opposition candidates and voters, or tortures prisoners. In other cases, human-rights violating treatment is built into social rules, as when discriminatory burdens are imposed by law on certain minorities, or when a government policy systematically deprives some group of its livelihood. Cases of this latter sort are the ones that interest us here (the question before us concerns the choice between alternative rules governing the development and distribution of new medicines). In such cases, it is in the first instance the rules or policies that violate human rights. But in the final analysis these violations are committed by those who formulate, interpret, and enforce these rules and policies and by those in whose behalf the former are acting.

There is another dimension in which human rights can be given a wider or narrower understanding. The demand that social rules must be human-rights compliant is often interpreted to entail that human rights require their own juridification: that a state realizes a particular human right only if it incorporates this right explicitly into its basic law or constitution. So interpreted, the demand has been rejected by many, most prominently by appeal to “Asian values.” This rejection involves the thought that human rights promote individualism or even egoism, lead persons to view themselves as Westerners — as atomized, autonomous, secular, and self-interested individuals ready to insist on their rights no matter what the cost may be to others or to society at large.

Once again, we do not endorse this rejection. Yet, in order to present as broadly-based an argument as possible, we appeal here to human rights in a narrower, more widely sharable sense. This sense can be explicated as follows: There are various basic goods that are essential to a minimally worthwhile human life. All human beings ought to have secure access to these goods. Insofar as is reasonably possible, social rules should then be so designed that the human beings subjected to them have secure access to these essentials. This is what human rights require. The assertion that there is a human right to a minimally adequate food supply entails then that, insofar as reasonably possible, social rules must be formulated so that all human beings have secure access to a minimally adequate food supply. This assertion does not entail that human beings must have a legal right to a minimally adequate food supply. If a state is so organized that its citizens have secure access to food even without a legal right thereto, then this state is fully compliant with the human right as we understand it.

This understanding of human rights is not subject to the usual critique based on “Asian values”. Rather, it accommodates this critique by accepting its central point: that human rights leave each state free to decide how to achieve secure access to their objects. Some societies may choose to do this through legal rights and legal institutions; others may do this through a communal ethos of virtue and solidarity. So long as people really have secure access to the objects of their human rights, both models, and others as well, are fully human-rights compliant in the narrow sense we invoke.

### **THE APPLICABILITY OF HUMAN RIGHTS TO SUPRANATIONAL REGIMES**

The development and sale of medicines worldwide is governed by certain national and international rules centring around the TRIPS Agreement. Do these rules as they currently operate in the real world (SQ) violate human rights?

Some may want to reject this question as ill-posed. While national laws can violate human rights, they hold, international rules and treaties cannot in



principle do so. But this is not a plausible objection. Imagine a few states that have made it legally permissible to assault those who join a union. Such a law is a clear-cut violation of the human right to life, liberty and security of person. This human rights violation does not disappear when the relevant states conclude an international agreement that commits them to the offensive legislation. On the contrary, the fact that they have made this agreement can only heighten their responsibility. With the agreement, each state assumes some responsibility for the human rights violation built into the legal system of the other treaty members even while it remains fully responsible for the human-rights-violating character of its own national legislation. If a state is violating human rights by imposing a rule or scheme of rules domestically, then binding that state to this imposition through a treaty makes the other treaty members complicit in the violation. Human rights then constrain international laws and agreements no less than they constrain national laws and policies.

This conclusion is firmly endorsed in Article 28 of the Universal Declaration of Human Rights:

Everyone is entitled to a social and international order in which the rights and freedoms set forth in this Declaration can be fully realized.

Again, we use the doubly narrow understanding of human rights in interpreting this Article. It then requires that any national and international order must be shaped so that it does not deprive human beings subjected to it of secure access to the objects of their human rights. In a world of sovereign states, it may not be possible to design international institutional arrangements that effectively guarantee secure access. For this reason, it makes sense to require merely that the international order must be such that secure access can be fully realized. The international order must not obstruct the realization of human rights. It must not, for instance, undermine either the capacity or the willingness of national governments fully to realize human rights. A design of the international order fails to be human-rights compliant insofar as it foreseeably gives rise to an avoidably large number of

governments that lack either the means or the motivation to realize human rights.

Today, most human beings lack secure access to their human rights. In particular, many of them lack secure access to the medicines they need. Often, these medicines are known and available, but nonetheless not accessible to the poor on account of their high price. There are generic producers willing and able to manufacture these medicines and to sell them at much lower prices. But these firms are legally barred from doing this by patents that their governments are issuing in accordance with their commitment under the TRIPS Agreement. This Agreement blocks mutually advantageous sales of life-saving medicines at low prices. By blocking such sales, it causes the deaths of many poor people and deprives many more of a standard of living that is adequate for their health. (The very high mark-ups on patented medicines may render inadequate an income that would be adequate if the needed medicine were available at a lower price.) SQ is violating the human rights of

Everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care.

Everyone is entitled to a social and international order in which the rights and freedoms set forth in this Declaration can be fully realized.

Universal Declaration of Human Rights

poor people worldwide by undermining their secure access to health and survival.

This conclusion can be disputed by appeal to the benefits of SQ. Here the most significant benefit, which can also be cast in human rights terms, is the future availability of important medicines that would not have existed if strong patent protections had not been extended into the less developed countries. This benefit can be appealed to by pharmaceutical companies, which can say: "If we did not fully exploit our patent privileges, we would not have the money to undertake many of the research projects we are now engaged in. And there would then be fewer important medicines coming off patent in the future, fewer good medicines that will protect poor people in the



future. Some poor people suffer and die now because of the high prices we charge under patent protection. But more poor people will be saved in the future, after expiration of the patents that enabled us to finance the innovation. And the cost is necessary for realizing the greater gain: we simply cannot develop new medicines that future poor people will be able to obtain at generic prices unless we keep raising money by charging high prices for medicines still under patent protection.”

While pharmaceutical companies can plausibly make this argument, governments defending the status quo can not. To be sure, these governments can point to the benefit of additional new medicines that, thanks to TRIPS, will become generically available starting in 2025. And they can claim that this benefit will outweigh the burden of high prices that will exclude the poor from advanced medicines in their first ten years or so. But such governments can not say that they had to impose this burden in order to secure that benefit. The SQ+HIF option makes it possible to achieve for future people access to important additional medicines at low generic prices without preventing poor people from buying these medicines cheaply in their early years on the market. It is certainly not morally permissible to violate the human rights to life and health of millions of people in order to secure a benefit that can be secured without inflicting such harms.

This concludes the human rights argument. Appealing to human rights that governments themselves have repeatedly recognized as binding constraints, this argument shows that the HIF is required as a complement to the status quo for the sake of realizing the human rights of the global poor. Under the existing international order, these human rights are not realized as the poorer half of the world's people lack secure access to a standard of living adequate for their health and well-being. One factor preventing their secure access is the suppression of the trade in generic versions of important new medicines. The possibility of adding the HIF to this order shows that much of the present human rights deficit is avoidable. Maintaining SQ without the HIF constitutes a massive violation of the human rights of the global poor. So long as there will be poor people in this

world – whether in poor or rich countries – who are unable to obtain expensive medicines still under patent, SQ will gravely harm, and kill, many of them. By continuing to impose and enforce SQ nonetheless, governments would be violating the human rights of these innocent people.

## **APPEAL TO THE POOR BEING DOOMED ANYWAY**

The next three sections consider and refute three popular replies aiming to defeat the human rights argument. Some have argued that high prices are not the real reason why so many poor people are excluded from advanced medicines. Most of those who cannot get access to patented medicines would still lack access even if these medicines were not patented in their country. This is so because the health systems in many poor countries are in very bad condition, making it highly unlikely that the right medicine would be prescribed, dispensed, and consumed, and also because many of these patients are so poor that they would find it difficult or impossible to buy the needed medicine even at the generic price. That this is so is made evident by the fact that poor people often lack access even to the cheap off-patent medicines they need. Introducing into the less developed countries high pharmaceutical prices protected by much strengthened patent protections is therefore doing little harm. It is not substantially worsening the situation of poor people who are in any case doomed to suffer, without health care, whatever diseases they may get.

These claims are true for some, but not all, patients. The much lower prices typical of generic medicines would make a great difference to many, most obviously to the poorer people in the more affluent countries. And even in the poorest countries, low prices of high-impact medicines would greatly magnify the capacities of government health systems, of international organizations such as UNICEF, of NGOs and of various initiatives such as PEPFAR, GAVI, and GFATM. The resources of all these agents and agencies — woefully insufficient to meet the huge health needs of the global poor — would stretch much farther if they could substitute generic

versions for the patented medicines they now often are obliged to purchase.

Moreover, the argument is morally troubling. Its central thought is that a barrier that prevents people from protecting themselves is acceptable — that is, may be interposed and need not be removed — so long as there is another barrier that is also preventing them. The problem with this idea is that it symmetrically justifies — and thereby helps perpetuate — both barriers: “if each of two barriers is sufficient to prevent a person from saving her life, then there is nothing wrong with either barrier.” Or, for the sequential case here at issue: “there is nothing wrong with erecting another barrier excluding the poor from access to vital new medicines when this barrier adds little to the harm done by already existing barriers.” This is a very strange morality indeed. According to it, a barrier that is objectionable on account of the harm it inflicts becomes unobjectionable in the presence of a second barrier that has the same effect.

An obvious alternative to this bizarre idea is that no such barrier is acceptable, and that governments ought to remove all of them, or at least those that are their responsibility. The governments of affluent countries, in particular, should not impose asymmetrical global trading arrangements that prevent many poor populations from participating in global economic growth and thereby reaching minimally adequate levels of income and wealth. They should not pressure or induce the governments of poor countries to collect monopoly rents for their pharmaceutical companies from poor populations chafing under heavy disease burdens. And they should allow poor countries to build effective health systems rather than raid these countries for doctors and nurses who were trained there at great cost to the local population that urgently needs their services. The HIF is designed to meet these obligations by helping to remove the institutional barriers that stand between poor people and the medical care they need. The HIF makes new medicines available to everyone at cost and it also provides incentives to the registrants of such medicines to promote their effective use.

To sum up, the first response to the human rights argument fails on three counts. First, it is factually incorrect that high prices for patented medicines

make no difference to the health situation of patients worldwide. Second, it is not morally permissible gravely to harm other people so long as they would suffer a similar harm in any case. A barrier that prevents people from obtaining life-saving medicine from willing generic suppliers is not acceptable merely because there is another barrier that does the same job. Third, that other, last-mile barrier, which all-too-often excludes poor people even from cheap generic medicines, is likewise an avoidable effect of institutional arrangements and, like the price barrier, would be greatly reduced by the HIF.

### **APPEAL TO *VOLENTI NON FIT INIURIA***

Moral criticisms of the current global pharmaceutical patent regime (SQ), and of other international rules deemed unfavorable to the poor, are often rejected as inconsistent with a proper recognition of the sovereignty of states. All states governed by the requirements of TRIPS have freely signed up to these requirements, with no HIF on the horizon at that time, and any complaint on their behalf against SQ is thereby preempted. As that venerable Latin precept has it: *volenti non fit iniuria* — no injustice is being done to those who consent.

A customary retort to the *volenti* defense points to the highly unequal bargaining power and expertise of the national delegations that negotiated the WTO Treaty. Most countries were excluded from the drafting of the Treaty (the so-called Green Room negotiations) and many of them lacked the expertise to evaluate the extremely long and complex treaty text they were then offered: “Poor countries are also hobbled by a lack of know-how. Many had little understanding of what they signed up to in the Uruguay Round. That ignorance is now costing them dear.”<sup>5</sup> With regard to many less developed (and even a number of affluent) countries, there are then serious questions about whether the consent they gave was free and well-informed.

Even if a state’s consent to SQ was well-informed and freely given, it is still problematic to appeal to such consent in order to rebut the charge that SQ violates human rights. This is so, because human

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rights are rights of individual human beings, and SQ received the consent of governments. Not all governments are democratically elected or responsive to the interests of the people they rule. Among the signatories of the TRIPS Agreement were, for instance, the Nigerian government headed by Sani Abacha, the SLORC military junta of Myanmar, the Indonesian government headed by Suharto, Zimbabwe's government headed by Mugabe, and the Zairean government headed by Mobuto Sese Seko. As this list illustrates, many of the consenting governments ruled by force and did not represent, or show much concern for, the will or interests of the people they ruled. Insofar as they gave free and informed consent, it was driven by their own personal interests and therefore not indicative of the consent of their compatriots. It makes no sense then to contend that a regime cannot possibly be violating the human rights of citizens of Zimbabwe because Mugabe consented to this regime. Those who manage to acquire and hold power in a country, by whatever means, do not thereby become entitled to waive the human rights of the people they subject to their rule.

A further problem is that the appeal to consent is supposed to justify imposition of the regime upon people who were children or unborn at the time the consent was given. Thus, even if every single adult citizen of every participating country had given free and informed consent to the TRIPS Agreement at its adoption in 1994, these consenters could not thereby have waived the human rights of their children. Nor could they have waived the human rights of all the people born in these countries since that time — today's children, who are bearing a disproportional share of the global burden of disease (more than half the avoidable deaths each year are of children under age 5).

Finally, on the predominant understanding of human rights, these rights are inalienable. This means that they cannot be waived or relinquished at all. One main rationale for such inalienability is the need to protect people against losing their human rights protection through fraud, blackmail, manipulation, threats or inducements. If human rights are indeed inalienable, then the appeal to consent cannot un-

dermine in even a single case the charge that SQ violates human rights.

We have raised four mutually independent objections to the idea that an appeal to consent can shield SQ from the challenge that it violates the human rights of those whom it deprives of access to vital medicines at competitive prices. If even one of these objections is valid, then the appeal to consent fails so to shield the regime.

### THE LIBERTARIAN APPEAL TO PROPERTY RIGHTS

Another way of rejecting the human rights argument is rooted in the libertarian moral tradition which goes back to John Locke and is characterized by the endorsement of strong rights to freedom and property. This tradition supports a powerful rejoinder to the human rights argument — a rejoinder that resonates in current debates about the TRIPS Agreement and finds much sympathy especially in Anglophone countries. This rejoinder endorses and invokes the narrow understanding of human rights according to which the only duties these rights entail are duties to respect human rights, that is, duties not actively to violate such rights. It then points out that property owners who refuse to share their wealth — including their medicines — with poor people are not human rights violators, even when their refusal foreseeably causes human rights to go unfulfilled. Such property owners are not actively harming the poor, but merely failing to help them.

The rejoinder then adds as a further claim that human rights to life and health do not impose duties to develop, or to fund the development of, new medicines that others need for health or survival. Affluent people are entitled to pay for the development only of medicines they need themselves while declining to pay for the development of medicines needed by the poor. When affluent people do this, they are merely failing to fulfill human rights, not violating them. The following two subsections unpack and refute these two claims of the libertarian rejoinder.

## Denying the Poor Access to Generic Medicines

Property owners are entitled not to share what they own even with poor people whose human rights will remain unfulfilled as a result. To be meaningful, this entitlement must include the entitlement actively to defend their property against those who would take it (even for the sake of fulfilling human rights). Owners are entitled to protect their property against theft, with walls, doors, and locks — and even with force if need be. Such protection of property must often be active, as when an owner physically prevents poor people from stealing his food. Still, such an owner does not violate human rights, because he is merely blocking interference from others, not interfering with them. He is merely protecting his right not to help.

If owners are entitled to protect their property, then they are also entitled to authorize others to do so — for example, the police. And the police are then entitled actively to prevent attempts to steal even when such attempts aim to fulfill human rights. In this way, the creation and enforcement of legal property rights can be defended: such a regime for protecting property should not count as violating human rights even if, as a result of its suppression of theft, human rights remain unfulfilled.

The last step in the rejection of the human rights argument posits that what holds for physical property also holds for intellectual property: a system of rules that defends intellectual property should not count as violating human rights even if, as a result of the suppression of theft, human rights remain unfulfilled. SQ is precisely such a system. It suppresses the trade in generic versions of new medicines and may thereby cause the death of poor patients who cannot gain access to the medicine they need because of its high, patent-protected price. This suppression of theft is, however, no violation of human rights, but merely a failure to fulfill human rights by redistributing the wealth of shareholders in pharmaceutical companies or by leaving their property unprotected.

The TRIPS Agreement gave pharmaceutical innovators rights they did not have before: rights to strong 20-year patent protection in the less developed WTO member countries. The creation of these

new property rights cannot be defended by appeal to these same property rights. Such a defense would be arguing in a circle. The defense can succeed only if it justifies the creation and enforcement of legal property rights by appeal to independently existing moral or natural property rights. It is only because innovators have a moral right to the fruits of their creative efforts that it is permissible to use legal rights and enforcement to defend their possession of these fruits even when such defense leads to misery and death of innocent people.

To see how the libertarian argument presupposes such moral or natural property rights, suppose a government passes and enforces a new law that makes one man the owner of all unowned water. As people run out of water, its price shoots up, and soon there is only one person from whom water can legally be bought or received. The rich buy what they need from this man, and the poor suffer and die. Clearly, the law in this story is grossly unjust. Libertarian thinkers would join in its rejection because that law cannot be justified as protecting the man's legitimate property rights. When the law came into being, this man had no special claim to the water not owned by others and hence no claim to exclude others from it.

A contrasting scenario, and one that libertarians would approve, is one where the government passes and enforces a law that recognizes those who plant and harvest food as the owners of this food, so that one can acquire food grown by others only by buying (or receiving) it from them. People who run out of food buy more from others if they can but, if they lack the money to do so, they suffer and die. In this case the law arguably does not violate human rights because it merely defends antecedently legitimate property rights. Perhaps human rights would be better fulfilled if those without money and food were free to help themselves to food grown by others. But the suppression of such acquisitions counts as merely a failure to fulfill human rights, not as an active violation — on the libertarian assumption that the growers of food are entitled to it and entitled to withhold it from others even before the law is passed.

The philosopher Robert Nozick has explicitly extended this line of thought to justify excluding poor people from medicines. He imagines a medical re-

searcher who invents new medicines that greatly improve people's health and functioning. No one else knows how to make these drugs. In a situation like this, the researcher is entitled to withhold the medicine from others, even if their lives are at stake. To explain this entitlement, Nozick writes: "A medical researcher ... does not worsen the situation of others by depriving them of whatever he has appropriated. The others easily can possess the same materials he appropriated; the researcher's appropriation or purchase of chemicals didn't make those chemicals scarce in a way so as to violate the Lockean proviso" (Nozick 1974, 181). The Lockean proviso here alludes to a principle Nozick adapts from John Locke. This principle allows people to acquire natural resources — by appropriation or through gift or exchange — provided they leave "enough and as good" for others. Each person's acquisition of raw materials must be consistent with a like acquisition by others. Pharmaceutical production easily fulfils this condition for most drugs.

To be sure, by keeping all the medicine to himself, Nozick's researcher is not leaving enough and as good medicine to them. But he is not required to do so, because this medicine is his own product and would not exist but for his labour. By producing this medicine just for himself, the researcher is not taking anything away from others. He is merely failing to let them participate in his invention by sharing with them either his medicine or his knowledge. By declining to help them, the medical researcher is acting within his rights; and a legal system cannot be faulted for recognizing and protecting these rights.

Suppose next that Nozick's medical researcher is willing to share with others — at a price. Because he is the only one who knows how to make the medicine and because this medicine is highly useful, affluent people are willing to pay a high price. The medical researcher therefore charges a high price, reckoning that he will make more money by selling dear to a few than by selling more cheaply to many. Nozick affirms, once more, that the medical researcher is within his rights to act in this way. It is his medicine to keep or to sell as he pleases.

Committed to a human-rights perspective, one might disagree with Nozick that property rights

trump even the right to life. One might say that, when lives are at stake, society may confiscate the researcher's medicine and even compel him to make more or to share his knowledge. We do not dispute that a convincing response along these lines can be constructed and that this response can be extended into a formidable challenge to the libertarian defence of SQ. Here we formulate, however, a different and more broadly based response that, for the sake of the argument, accepts the libertarian endorsement of strong property rights that entitle the medical researcher to act as he does. We accept this not because we agree with it, but because we can make a more effective response to libertarians by showing them that even their own signature commitments do not support the current regime against the human rights critique.

The current global pharmaceutical patent regime (SQ) is different from Nozick's story in one respect that is very important within the libertarian frame of thought. In the real world, innovators assert not merely physical property rights in tokens of materials they produce, but so-called intellectual property rights in abstract types of such materials as well. We will show that, far from supporting intellectual property rights, libertarian thinking is in fact inconsistent with them.

Consider a simple example. Once upon a time, a clever woman took a piece of her wood and shaped it into a wheel. She then attached this wheel to a large basket and, with this primitive wheelbarrow, greatly eased her agricultural labour. Seeing her invention at work, others were eager to have such wheelbarrows as well. The inventor can make additional wheelbarrows for sale, of course. But she will find it hard to charge exorbitant prices, because people can just make their own wheelbarrows or pay someone other than the inventor to produce them. In contrast to Nozick's imagined medical researcher, the wheelbarrow inventor cannot commercialize her invention without spreading the knowledge of how to make it. (And this, of course, is the actual situation with regard to medicines today: what one company develops and tests at great cost, another firm can cheaply re-engineer.)

Suppose the inventor of the wheelbarrow now has the bright idea to claim ownership not merely of any



wheelbarrows she herself constructs, but of the very type wheelbarrow. She is setting forth this idea not as a proposal for the consideration of all, but rather asserts it as a natural right. Just as all persons have a natural, pre-institutional right not to be murdered (and perhaps to own the food they have grown), so all persons have a natural, pre-institutional right to “intellectual property” in their inventions — regardless of others’ consent.

If there is such a natural right, independent of any and all human laws and conventions, then our inventor has veto powers over the making and using of wheelbarrows by other persons anywhere. And anyone intending to make or acquire a wheelbarrow is then required to bargain with her for her authorization. The same is true for medicines. One might say that the TRIPS Agreement did not give rise to new constraints on the production, sale and use of medicines but merely (partially) recognized natural constraints that existed all along and incorporated these constraints into the international legal framework. There is a sense in which the adoption, implementation and enforcement of this Agreement takes something away from generic manufacturers and also from the poor patients who were benefiting from the availability of generic medicines at competitive market prices. But what it takes away was never, morally speaking, theirs to begin with. Even in the absence of patents, it would be wrong for generic manufacturers to produce a cheap supply for poor patients without the innovator’s authorization. What the TRIPS Agreement takes away, then, is the opportunity to commit moral crimes — theft, counterfeiting, piracy — crimes whose legal recognition and suppression has finally been extended to nearly all countries around the world.

But is there really such a natural right of inventors not to have their inventions copied without their authorization? Within a libertarian frame of thought, such a natural right is deeply puzzling. Before the invention, all were free to build wheelbarrows with their own hands, wood and reed, without anyone’s permission. Yet as soon as someone actually does this, the freedom of the others supposedly disappears — displaced by the need to bargain with the inventor for her permission. Why should anyone, by doing

something creative with her stuff, be able unilaterally to limit what all the rest can do with their stuff? Why should one person be able unilaterally to impose new constraints on your conduct and property?

The woman can answer that your erstwhile freedom to make wheelbarrows was not worth much in advance of her invention. And she can add that, even with the encumbrance she insists upon, her invention still makes you better off than you would otherwise be by giving you the new option of making a wheelbarrow after buying her authorization.

This answer has a certain plausibility — but not within a libertarian frame of thought. Libertarianism is focused on the values of freedom, property, and consent. It cannot permit someone to impose an exchange upon you, no matter how beneficial this exchange may be for you. So the innovator has no right, without your permission, to deprive you of something even if she gives you something much more valuable in return. No matter how great a benefit she may have foisted upon you, she is not entitled to divest you, without your consent, of your freedom to make wheels and wheelbarrows with your own hands and materials. As Nozick forcefully insists, even the voluntary acceptance of benefits that were conferred on the express understanding of reciprocation does not create any obligations to reciprocate.<sup>6</sup>

Libertarianism is the philosophical tradition most friendly to natural property rights, taking them to be absolute constraints on the design of social institutions. Even if countless lives could be saved by taxing every affluent citizen a dime a year, doing so would still be morally intolerable — or so Nozick asserted. This status of rights to freedom and property as absolute constraints is inconsistent with “intellectual” property rights which would permit people unilaterally to place new limits on the freedom of others and (in particular) on what they may do with their property. The fact that others have invented a new dance or dish or gadget or medicine gives them no right to restrict what you may legitimately do with your body and property. So long as you have violated no rights in learning about the invention and have not contracted otherwise, you are within your rights when you try to copy their dance (with a willing partner) or try to reproduce their dish, gadget or medicine



from materials you legitimately own. Others may keep their invention secret from you, of course. And they can try to share it only with those who promise not to share it farther. But if someone who has made no such promise chances upon the invention, she is free to try to reproduce it.

The discussion of the libertarian challenge leads then to a surprising conclusion. Libertarian thought does not merely fail to vindicate intellectual property rights but actually condemns them. From a libertarian point of view, the enforcement of intellectual property rights is expropriation which, as others keep inventing things, increasingly limits what you may do with your property. Far from supporting a natural right to intellectual property that could override the freedom to reproduce the inventions of others, the libertarian tradition defeats such a right and vindicates the rights of generic producers and their customers. They may transact with each other on mutually acceptable terms provided only that they are not bound by any voluntary contract to refrain from such activity. Restricting their activities through the imposition of intellectual property rights violates their natural rights to do with their property as they wish.

We do not endorse libertarian thinking and the priority it gives to property rights. Rather, we think that human laws and conventions should be designed and reformed in light of a broader range of human needs and interests among which those recognised in the main human rights documents are of greatest weight. On this view, the question of intellectual property rights should be treated instrumentally. Intellectual property rights should be instituted and fine-tuned, maintained or abolished so as best to realize human rights (and other human needs and interests). We support intellectual property rights as embedded in SQ+HIF because we believe that they would serve important human ends better than any feasible alternative (including abolition of all intellectual property rights).

Some defenders of intellectual property rights share this instrumental view. With them we must examine the empirical facts in order to ascertain in what contexts such rights do more harm than good, in what contexts they can be helpful, and how they should best be specified and embedded in the con-

texts in which they are helpful. Other defenders of intellectual property rights insist that such rights are natural rights and therefore must be instituted everywhere regardless of consequences. This kind of thinking resembles and appeals to the libertarian tradition. But, on closer inspection, it can find no home there. Libertarianism indeed rejects the instrumental perspective. But it pre-empts the question of intellectual property rights in the opposite direction: the ordinary physical property rights that libertarians hold sacrosanct are inconsistent with any powers on the part of others unilaterally to place limits on how a person may use her own body and property. According to libertarianism properly understood, the thieves and pirates are not those who reproduce an invention without permission, but those who use state power to suppress owners' free use of their property in order to extort payments from such owners.

### **Neglecting the Diseases of the Poor**

Very poor people cannot obtain basic necessities while rich people have vastly more than they need. Libertarians do not find this problematic as such. They would argue that affluent people are entitled to use what they own as they see fit, and that it would be wrong for the state, or anyone else, to compel them to give some of their assets to the poor.

A highly uneven distribution of income and wealth can influence the priorities of pharmaceutical research. If those interested in anti-hair loss products are disposed to pay much more than those in need of a medicine against Chagas disease, then profit-oriented pharmaceutical companies will target hair loss in preference to Chagas. In this way, diseases concentrated among the poor come to be systematically neglected.

Again, libertarians do not find this wrong in principle. And they do find it morally unacceptable to take money from the rich in order to support research into the diseases of the poor even when such research would lead to medicines that poor people need for their health and survival. Owners have rights in the full use and enjoyment of their property; they must not harm others, but they are not required to help them.

In responding to this challenge, we again accept, for the sake of the argument, these central libertarian commitments in order to formulate a response that may convince those who find themselves in sympathy with libertarian sentiments.

The present setting of research priorities would be supported by overridingly strong property rights if the existing distribution of these rights had a morally sound pedigree of the sort libertarian theorists envisage. But without such a pedigree, the existing huge economic inequalities in *de facto* ownership have little or no justificatory force. Imagine for a moment a human world whose economic distribution resembles ours, but whose inhabitants have just sprung into existence. In this fictional world, the more powerful impose on the rest an institutional order that reserves for themselves the vast majority of wealth, thereby leaving a non-consenting three-quarters of humankind with insecure access to the most basic necessities. Libertarian thought does nothing to legitimate the economic advantages of the rich in this world. Their greater possessions are founded on mere assertion backed by power.

Are existing property rights in our world well founded? Consider the present highly unequal global economic distribution discussed in Appendix A. Which factors determine who ends up where in this economic hierarchy? It turns out that citizenship and income class at birth determine about 80 percent people's economic position,<sup>7</sup> which is hardly surprising given that gross national incomes per capita vary between \$100 and \$60,000. Libertarians would not find such great international differences disturbing if these had accumulated, say, through different work habits compounding over generations. But the huge inequalities in our world did not accumulate in such a benign way. The social starting positions of the poor and of the affluent have emerged from a single historical process that was pervaded by massive, grievous wrongs. The present circumstances of the global poor are significantly shaped by a dramatic period of conquest and colonization, with severe oppression, enslavement, even genocide, through which the native institutions and cultures were destroyed or severely traumatized. The present circumstances of the affluent are shaped by the same historical pro-

cess. Some of the countries that give their citizens a great headstart today owe their very existence to genocide and ethnic cleansing. These undeniable historical facts undermine the libertarian thought that existing holdings have a moral standing that exempts them from claims based on human rights.

The historical crimes just mentioned play no role in the human rights argument we have formulated. Rather, they undermine one particular objection to this argument. The human rights argument is forward-looking. Whatever human history may have been like, we should now structure national and international rules — including those governing the development and distribution of new medicines — so that at least human rights (and perhaps important other human needs) are fulfilled insofar as this is reasonably possible. When rules are known to be associated with an enduring massive human rights deficit that is avoidable through an adjustment of these rules, then it is unjust — a violation of human rights — to maintain the former. In particular, it would be a violation of human rights to insist on the perpetuation of SQ when the alternative of SQ+HIF is known to be available.

The libertarian objection to this argument is that such a human rights fulfilling regime requires resources and that these resources are simply not morally available. The needed resources are owned by people or nations who are entitled to refuse to contribute them to solving others' problems. Affluent countries are free to contribute to the HIF if they like, but they are equally free, morally, to retain what they own — even when their doing so will leave human rights massively unfulfilled.

Our response to the objection is that, even if it is indeed always permissible to refuse to contribute to the fulfilment of human rights by sharing what one legitimately owns, the actual history of existing holdings does not confer upon them, according to libertarian principles, the moral standing that the objection requires. Given the actual history, affluent people and nations cannot have the kind of confidence in the full legitimacy of their holdings that would entitle them to decline to contribute a tiny fraction of one percent of their income toward making our newly globalized pharmaceutical patent regime much more respon-

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sive to the health needs of poor people worldwide, whose starting position makes them victims of the same unjust past that gives the affluent such vastly superior starting positions.

These last three sections have refuted some popular objections to the human rights argument in some detail. We could go on refuting less prominent objections for many more pages – a great deal of human inventiveness is expended on rationalizing the advantages of the most affluent. Leaving this task to future work, we conclude by reiterating that the human rights argument is straightforward. Its central point is that we must not continue to uphold a pharmaceutical innovation regime that is known to be associated with a massive human rights deficit if this deficit is reasonably avoidable through a feasible modification. The next three chapters show that creating the HIF is a feasible modification that would avoid (depending on the amount of its funding) at least a substantial part of this human rights deficit. Continuing the status quo despite this available alternative violates the human rights of those whose access to vital medicines it jeopardizes.

### NOTES

1. See Appendix A for details about the global distribution of income and wealth.
2. “When India signed the World Trade Organization’s agreement on intellectual property in 1994, it was required to institute patents on products by Jan. 1, 2005. These rules have little to do with free trade and more to do with the lobbying power of the American and European pharmaceutical industries. India’s government has issued rules that will effectively end the copycat industry for newer drugs. For the world’s poor, this will be a double hit — cutting off the supply of affordable medicines and removing the generic competition that drives down the cost of brand-name drugs.” Editorial “India’s Choice,” *New York Times*, January 18, 2005.
3. The condition for wishing to choose a lower price is given by  $c < p$ , where  $Q$  is the quantity consumed,  $R$  is the average HIF payment per unit sold,  $p$  is the price at which the medicine is sold, and  $c$  is the marginal cost per unit. If this condition holds at the price floor stipulated by the HIF, the price will be set at that floor.
4. This idea goes back to Shue (1980), and was refined in Alston and Tomaševski (1984) and Eide, Eide, Goonatilake, and Gussow, (1984), esp. 169-74. This account then found its way into Article 15 of General Comment 12 ([www.unhchr.ch/tbs/doc.nsf/0/3d02758c707031d58025677f003b73b9?OpenDocument](http://www.unhchr.ch/tbs/doc.nsf/0/3d02758c707031d58025677f003b73b9?OpenDocument)), adopted by the UN Committee on Economic, Social and Cultural Rights in 1999, which reads as follows: “The right to adequate food, like any other human right, imposes three types or levels of obligations on States parties: the obligations to respect, to protect and to fulfil. In turn, the obligation to fulfil incorporates both an obligation to facilitate and an obligation to provide. The obligation to respect existing access to adequate food requires States parties not to take any measures that result in preventing such access. The obligation to protect requires measures by the State to ensure that enterprises or individuals do not deprive individuals of their access to adequate food. The obligation to fulfil (facilitate) means the State must pro-actively engage in activities intended to strengthen people’s access to and utilization of resources and means to ensure their livelihood, including food security. Finally, whenever an individual or group is unable, for reasons beyond their control, to enjoy the right to adequate food by the means at their disposal, States have the obligation to fulfil (provide) that right directly. This obligation also applies for persons who are victims of natural or other disasters.”
5. “White Man’s Shame,” *The Economist*, September 25, 1999, p. 89.
6. Nozick endorses this central commitment of libertarian thought, for example, in the context of his critique of H.L.A. Hart’s principle of

fair play: “Suppose some of the people in your neighbourhood (there are 364 other adults) have found a public address system and decide to institute a system of public entertainment. They post a list of names, one for each day, yours among them. On his assigned day (one can easily switch days) a person is to run the public address system, play records over it, give news bulletins, tell amusing stories he has heard, and so on. After 138 days on which each person has done his part, your day arrives” (Nozick 1974, 93). Nozick concludes about this case that, however much you may have enjoyed the efforts of the others, you are under no obligation whatever to staff the public address system.

7. Branko Milanovic: “Global Inequality of Opportunity”, Development Research Group, World Bank.



# 7. The Last Mile Problem

*Getting drugs to patients and ensuring their effective use represents a major challenge, especially in poor countries. High prices can make a drug unaffordable to all but the wealthiest patients. Defective transport and storage systems can make a drug unavailable to many population groups. Lack of trained and motivated medical practitioners can lead to poor diagnosis and dispensing practices. Poverty and lack of understanding can lead to weak adherence by patients to treatment regimes. The HIF will directly address the problem of high prices and give HIF registrants strong incentives to support initiatives to reduce non-price barriers to access and rational use.*

## WHAT IS THE LAST MILE PROBLEM?

The last mile problem refers to the challenge of ensuring that available medicines of good quality are (1) accessible to and (2) correctly used by the people who need them. A global system for pharmaceuticals such as the HIF needs to address this point carefully, since a large proportion of the global population lives in areas in which the last mile problem is acute.

### Accessibility

As highlighted throughout this book, one main barrier to access to available drugs is price. When manufacturers' prices are lower, then the prices consumers are charged through both public and private distribution systems will also be lower. Affordable manufacturers' prices are therefore crucial to improved access.

But manufacturers' prices are not the sole determinant of the cost to the consumer. Import duties, port clearance charges, inspection fees, pharmacy board fees, central and regional government taxes, storage and transportation costs, and wholesale and retail mark-ups add substantially to the manufacturers' price.<sup>1</sup> These supplementary costs are not always passed on to the consumer in their entirety, since the state or the nonprofit sector may provide subsidies to consumers. But in this case the financial burdens placed on the state or the nonprofit sector are increased by high prices. Even where supplementary costs are only par-

tially passed on to consumers, they can significantly affect the affordability of essential medicines.

Price, while crucial, is not the only determinant of access. In many low-income countries, weak health infrastructure significantly limits the extent to which essential drugs are accessible. For example, Ministries of Health are often reluctant to distribute drugs to hospitals and health clinics if they believe these facilities lack the trained and motivated medical staff or the physical assets needed to ensure that the drugs are properly stored, prescribed and dispensed.<sup>2</sup> Alternatively, a Ministry of Health's administrative systems may be such that it is not able to manage the efficient distribution of the drugs that are available to it, resulting in shortages, particularly in less accessible parts of the country. Weaknesses in transportation systems and drug management practices can also result in spoilage, thereby compromising the quality of available drugs.<sup>3</sup> On the demand side, weak infrastructure often imposes significant costs and time burdens on poor people in need of health treatment. For example, patients may have long distances to travel, and in many countries, "informal payments" or bribes are required to obtain access to subsidized medicines (Lewis, 2007).

### Rational Use<sup>4</sup>

The second main element of the last mile problem is the failure to use correctly the drugs to which patients do have access. The WHO estimates that worldwide



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50 percent of all medicines are prescribed, dispensed, or sold incorrectly, and that about half of all patients do not take medicines as directed (WHO 2004b, 75). This incorrect use exacts a huge toll in increased morbidity and mortality, in addition to the toll exacted by lack of access. Estimates suggest that between 60 and 90 percent of household health expenditure in developing countries is on medicines (DFID 2006, 1). Poor prescribing and dispensing practices, and weak adherence by patients to treatment requirements, means that much of this spending brings little in the way of health benefits. It can actually be harmful, increasing the likelihood that certain diseases will develop resistance to the drugs that are used to treat them.<sup>5</sup> These problems occur not only in developing, but also developed countries.

If you don't have compliance, you might as well not have the medicine. There also has to be follow-up and testing.

Bill Clinton

Common types of incorrect medicine use include (WHO 2004b, 76):

- use of too many types of medicines per patient (polypharmacy);
- prescription of antimicrobials in inadequate dosage or for inadequate periods or the prescription of antibiotics for non-bacterial infections (the WHO estimates that around two-thirds of all antibiotics worldwide are sold without prescription);
- use of injections where oral formulations would be better, increasing the transmission of hepatitis, HIV/AIDS and other blood-borne diseases;
- failure to prescribe in accordance with clinical guidelines (survey data show that between 1990 and 2004 only around 40 percent of primary care level patients in Africa, Asia, and Latin America were treated in accordance with clinical guidelines for a number of common conditions, with no improvement over this period; WHO 2006c, 2); and
- inappropriate self-medication, often of prescription-only drugs.

A key cause of incorrect use is the lack of suitably qualified medical personnel available to developing country health systems. Recent figures show that the number of health workers per 1,000 people was only 2.3 in Africa and 4.3 in South & East Asia, compared to 18.9 and 24.8 in Europe and the Americas respectively.<sup>6</sup> Moreover, many developing-country health workers are poorly trained and paid and are not given adequate administrative support. This in turn contributes to low morale and a high incidence of absenteeism. This problem is especially acute in rural and remote areas. Health facilities that are understaffed or staffed by inadequately trained or motivated workers are very poorly placed to meet the requirements of rational drug use (Das, Hammer, and Leonard 2008). The WHO estimates that 57 countries suffer critical shortfalls of doctors, nurses, and midwives that prevent these countries from meeting even the most basic standards of health care (WHO 2006d, 5, 11–12).

This human-resource crisis is complicated by the fact that in many low-income countries staff salaries take up an inordinately large share of the health budget, leaving insufficient funds for non-staff requirements such as vaccines, essential drugs, diagnostic tools and infrastructure maintenance. Public sector health payrolls are often poorly administered, and phenomena such as so-called ghost workers (people who are on payrolls but do not provide the relevant services) result in significant inefficiencies. Resource-constrained countries are confronted with the need to reduce the share of the wage bill in their health budgets while increasing the number and quality of health professionals, particularly in poorer areas. In many cases, greater efficiency in the use of existing resources, while necessary, will not be sufficient to remedy these problems entirely. There is no escaping the need for significantly larger amounts of resources to be made available to developing country health sectors.<sup>7</sup>

While public sector and not-for-profit private providers are key parts of the health sector in most low-income countries, the for-profit private sector—particularly in the form of private drug outlets—is often the first point of call for large parts of the populations of these countries when they fall sick. In Cambodia, for example, it is estimated that more than 70

percent of the population first approach private drug sellers when they fall sick, and that 75 percent of legal antimalarials are sold through the private sector. In Senegal, four private wholesalers linked to pharmacies and chemists represent nearly 65 percent of all sales of antimalarials (Institute of Medicine 2004, 40–41).<sup>8</sup> Worldwide, an increasing share of health care is being delivered through the private sector (WHO 2006c, 4).

Especially in low-income countries, governments often regulate private-sector drug outlets poorly. Even where suitable regulations and licensing procedures exist, the supervisory and enforcement support needed to ensure compliance is often lacking. Coupled with poor training of staff in private drug outlets, these regulatory, supervisory and enforcement shortcomings result in poor diagnosis and dispensing practices, and subsequently in the sale of unnecessary or contra-indicated drugs or incomplete courses of medication. This wastes resources, compromises successful treatment, and can lead to adverse patient reactions and the development of drug-resistant disease forms. The incentives that private sellers have to maximize sales regardless of clinical requirements add to the likelihood of incorrect use. These incentives are present not only in the private sector, but apply where the prescribing and dispensing functions are combined, as is sometimes the case in some public health facilities in low-income countries. This point notwithstanding, survey data available to the WHO show that, in developing and transition countries, the use of medicines is significantly worse in the private than in the public sector (WHO 2006c, 4).<sup>9</sup>

Even where drugs are correctly prescribed, they are often sold in inappropriate packaging, with inadequate instructions for patient use, or both. This creates serious problems when patients are illiterate or ill-informed about the implications of not taking medication as directed. This is particularly problematic with respect to medicines whose partial completion is often sufficient to relieve symptoms. The result is a serious problem with patient adherence to the requirements of their drug treatment. Drug prices are also a factor in lack of patient adherence to treatment regimens. Poor patients may purchase

insufficient amounts of the medicine, in an attempt to economize.

A 2006 WHO report suggests that, unless effective action is taken, the problem of incorrect drug use is likely to get worse. This is so for two reasons. First, an increasing share of health care worldwide is being provided through the private sector. In developing countries and countries in transition to a market economy, provision through the private sector is likely to result in a higher incidence of incorrect drug use than provision through the public sector, which is important given the prominence of private drug sellers as a first point of call. Second, many large-scale initiatives to treat diseases of major public health importance, such as malaria, HIV/AIDS, and tuberculosis, concentrate primarily on access and give insufficient attention to the problem of irrational use (WHO 2006c, 4).

Irrational use also occurs in developed countries. As Avorn (2004) notes, there is a paucity of reliable clinical trials comparing the risks and benefits of different medicines, and at the same time, pharmaceutical companies' marketing muscle sometimes leads to poor prescribing choices by clinicians.

### **Pharmaceutical Companies, the Current Patent System, and the Last Mile Problem**

Under present arrangements, pharmaceutical companies have little incentive to do anything about the last mile problem, particularly in poor countries where this problem is most acute. Typically drug manufacturers sell their products to public health authorities or private wholesalers well removed from consumers of the product, and do so at a price designed to maximize profits.<sup>10</sup> Nonprice factors associated with the accessibility of their product and issues relating to its correct prescription and use are matters that manufacturers have little incentive to address, for two interrelated reasons. First, these problems are complex and difficult to address in many developing countries. And, second, the financial gains pharmaceutical companies might reap from helping to resolve such problems—higher sales volumes flowing from wider accessibility and better outcomes—are, under

current remuneration arrangements, uncertain and likely to be small. (In fact, correct and effective use of a medicine may *reduce* demand for it).

It might be argued that pharmaceutical companies should not be given a role in tackling the last mile problem because they are ill-equipped to deal with it, especially with respect to issues such as systemic problems in the health systems of low-income countries. That pharmaceutical companies are poorly equipped to deal with such issues is true but unsurprising, given the lack of incentives that they currently have to address them. The important question is whether such companies could help solve the last mile problem if they were provided with a very different set of incentives.

### **PHARMACEUTICAL COMPANIES, THE HEALTH IMPACT FUND, AND THE LAST MILE PROBLEM**

Rewarding pharmaceutical companies on the basis of their product's health impact changes their relationship to the last mile problem in a fundamental way. Far from having no interest in this problem, Health Impact Fund registrants would have a strong incentive to address it, since their profits are based on their product's health impact. How will companies respond to the last mile problem with respect to the drugs they have registered with the HIF?

Rewarding pharmaceutical companies on the basis of their product's health impact changes their relationship to the last mile problem in a fundamental way.

#### **Lack of Access: Price and Nonprice Factors**

Consider first lack of access due to unaffordability. As detailed elsewhere in this book, HIF registrants will be required to sell their product worldwide within a price window ranging between the average and marginal cost of production and distribution as determined by the HIF. Furthermore, registrants will have strong incentives to try to reduce wholesale and retail

mark-ups on their products, and to use their lobbying power with politicians to ensure that taxes and other government charges are kept to a minimum. It is therefore reasonable to expect that the retail prices of HIF-rewarded medicines will be within the reach of a very large proportion of those who need them.

The incentives of suppliers of HIF-registered medicines are quite different from those of suppliers of patented medicines outside the HIF. HIF-registered drugs sell at very low prices and are more likely to have many highly price-sensitive customers. A small addition to the retail price can deter a large number of patients at a significant cost to the registrant in terms of reduced payments from the HIF. Thus, retail mark-ups and taxes, which both increase the price to the patient, may substantially reduce the registrant's profits. As a result, HIF registrants will be strongly motivated to lobby for reduced taxes and also to monitor and try to restrict retail mark-ups. These incentives are much weaker for suppliers of patented medicines not registered with the HIF. Such medicines sell at much higher prices, where variations in mark-ups and taxes typically have smaller effects on the number of patients buying the product. And their suppliers will therefore not be as interested in controlling mark-ups and taxes.

What about lack of access caused by nonprice factors? Take the case where a country's health ministry is unwilling to purchase a particular drug, or willing to purchase it only in relatively small amounts, because it considers that the necessary medical and logistical support to administer the drug effectively does not exist in parts of the health system, or because the ministry's drug distribution system is not up to the task of distributing the drug effectively. How would the HIF registrant respond? At present, developing country governments, supported by aid donors, are directing large amounts of time and money to strengthening public health systems, including procurement and distribution systems. Much of this work is being done through so-called Sector Wide Approaches (SWAs) and similar sector-focused programs, in which donors work with governments to develop a comprehensive health-sector budget, providing a framework within which government and donor funds are prioritized, disbursed, and ac-

counted for. If systemic shortcomings in the health sector were adversely affecting the widespread accessibility of its HIF-registered drug, a pharmaceutical company might well be prepared to provide financial and other support to a SWAp designed to address these problems, though the company would understandably be focused on issues relating to the distribution of its own product.

It should be emphasized that the kind of support here envisaged would in no way represent the outsourcing of responsibility for a country's health system to pharmaceutical companies. Clearly, governments should take primary responsibility for public health systems. But just as bilateral and multilateral aid donors can participate in SWAps without absolving home governments of their responsibilities, private companies could play a constructive supporting role as well. It might be objected that pharmaceutical companies with substantial resources at their disposal and with big financial rewards at stake might skew the implementation of a SWAp in their own favor, potentially undermining the process of priority setting which the SWAp is designed to facilitate. Such dangers would doubtless exist, but the composition of a SWAp, which normally includes a number of major donors as well as the home government, would act as a strong countervailing force.

The involvement in a SWAp of a commercial company with a specific and relatively narrow area of interest might also bring significant advantages. SWAps and similar initiatives are sometimes criticized on the grounds that, insofar as they involve cooperation between a several agencies directed at the achievement of broadly-specified goals, they lack the individualized accountability needed for success. It is a short step, the argument goes, from everyone being responsible for everything to no one being responsible for anything at all (Birdsall 2007, 2; Easterly 2006, 14–15). A pharmaceutical company continually questioning how the work being undertaken through the SWAp is overcoming obstacles to the competent use of its drug—obstacles that are likely to be endemic and therefore relevant to essential medicines generally—could play a constructive role in keeping SWAp members focused on the need to undertake rigorous priority-setting for health-sector

expenditure and to support this with practical, solution-oriented programs. Insofar as the HIF, by tying reward to health impact, aligns the financial interests of HIF-rewarded companies and the health interests of relevant population groups, such companies could strengthen the accountability of the health system to patients by forcefully representing their interests within SWAps and similar programs.

While SWAps are designed to incorporate all major players in the health sector, they typically are more representative of the public than the private sector. They rarely include private for-profit drug retailers, for example, even though these outlets often play a major role in the distribution and sale of vital drugs in low-income countries. Manufacturers of HIF-rewarded drugs would therefore have strong incentives to ensure that private distribution systems were as efficient as possible in getting their drugs to private outlets.

In addition, the incentives that companies would have to ensure good handling, diagnostic, dispensing, and labeling practices in relation to their drugs would in turn lead them to support improved public regulatory and supervisory systems, because the alternative of developing and running alternative systems themselves, or contracting them out to private sector agencies, would not be cost-effective. In other words, HIF registrants would be motivated to support the development of an effective public regulatory system.

The following section discusses in greater detail the incentives that drug manufacturers would have to address rational use issues.

## **HIF-rewarded Companies and Rational Use**

Rewarding pharmaceutical companies on the basis of the health impact of their products clearly gives these companies a pressing interest in how their drugs are actually used. In order to promote a drug's health impact, a company will want all those who need the drug to have timely access to it in the right amounts, will want the quality of the drug to be good, and will want the drug to be used properly by patients. HIF

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registrants would have strong incentives to work toward achieving these conditions.

Rewarding pharmaceutical companies on the basis of health impact gives these companies a pressing interest in how their drugs are actually used.

There are a variety of measures that are being or could be taken through the public sector to encourage rational use of essential drugs. These include:<sup>11</sup>

- the establishment of a national body to develop an essential medicines use policy;
- the development of a national essential medicines list;
- the preparation of clinical guidelines for treatment of specific diseases;
- the preparation of standard operating procedures to govern pharmaceutical management tasks relating to specific drug treatments;
- the establishment of drug and therapeutics committees in hospitals and health clinics;
- continuing in-service medical education;
- strengthening regulation, supervision, audit and feedback mechanisms, including pharmacovigilance systems;
- improving public education about medicines and their use; and
- providing sufficient funds to facilitate the availability of medicines and suitably qualified and motivated staff.

While several countries have implemented or are implementing some of these policies, data from the period between 1999 and 2003 shows that a significant number of countries fail to make use of many of the options available to them. Of member states reporting to the WHO:

less than 60% had monitored the use of medicines in the previous two years; about 50% had undertaken a public-education program on use of medicines in the previous two years; about 40%

supported independent, continuing medical education for prescribers and had established a medicines information centre; 30% to 40% had drug and therapeutic committees in most hospitals and regions; in about 60% clinical guidelines had been updated in the previous five years; just over 70% had a national essential medicines list but only 30% used this list for insurance reimbursement; and only 60% to 70% trained their prescribers in the essential medicines concept, pharmacotherapy, rational prescribing and the application of clinical guidelines. (WHO 2006c, 4)

While these measures are of broad scope, and have impacts beyond the distribution and use of any particular drug, a HIF registrant might support one or more of them directly or use its influence to advocate for their introduction or expansion by relevant governments. We have already suggested that a strengthened regulatory and supervisory system is something that would interest an HIF registrant, and a pharmaceutical company may well be able to mobilize the resources needed to make a significant difference to the reach and performance of these systems. Registrants might also be willing and able to provide financial resources—which in other circumstances might be directed to marketing—to improve the pay and conditions of health workers in those areas of the system that suffer from acute human resource shortages, to improve pre-service or in-service training of front-line health care workers, or both, to the extent that such expenses supported the increase in the use of their products leading to higher payments from the HIF.<sup>12</sup> Registrants might find it attractive to provide funding for consumer education campaigns.

It is worth considering that pharmaceutical manufacturers provide services to encourage rational use in developed countries, because the high prices they charge make it worthwhile for them to do so. They have large numbers of sales representatives whose job it is to provide clinicians with relevant informa-



tion on their products. They support pharmacies in providing supplementary information to patients, and they engage in very expensive patient education campaigns. To be sure, much of the current marketing to doctors and patients is designed not so much to inform as to persuade (this is especially true when competing firms offer similar products in a given therapeutic class). However, some current marketing is informative and valuable. Because the HIF is designed to provide large rewards only to first-in-class medicines, with small rewards for follow-on products, the extent of competitive marketing is likely to be small, but firms will still have incentives to engage in informative promotional activities.

Promotional activities by pharmaceutical firms to doctors and patients have been widely criticized. Firms whose only reward is a high price, regardless of the therapeutic outcome, have an incentive to encourage as much use as possible of their product, and this had led to promotional spending that has not been useful and may even have been harmful to patients. Whether a drug is actually indicated for a patient does not affect the profit earned by a monopolist. It should be recognized that the incentives for HIF registrants will be somewhat different from those of nonregistrants in two significant ways.

First, the HIF only offers high rewards per unit for products that have a high impact per unit. Thus, the motivation to increase sales will be strongest for those products which are really therapeutically important, not those with the highest price. The incentive to sell products that are less therapeutically effective than older alternatives will be very low, since the HIF payments for such products will also be very low.

Second, the HIF will assess health impact, including how the product is used in practice. If sampling of prescribing practice—whether through private drug retailers or government clinics—shows that the drug is being sold inappropriately, the HIF will take that into account in determining the health impact of the medicine, and the assessed health impact will fall, rather than rise, because of such sales. To be sure, the HIF will not be able to measure health impact perfectly, and there will evidently be challenges as firms attempt to expand sales volumes inappropriately. But overall it is important to recognize that

some of the less attractive outcomes of pharmaceutical promotion will be avoided for HIF-registered drugs because the reward is based on health impact, not simply on price times volume. These benefits of better-aligned incentives with respect to pharmaceutical promotion apply equally to developing and developed countries.

There is a range of issues relating to improved drug use where additional research is needed (see ICIUM 2004). HIF registrants can be expected to have a strong interest in supporting efforts aimed at: identifying key factors that prevent the acquisition of knowledge about appropriate use of medicines leading to changed behavior on the part health care workers and patients; determining how information on poor-quality drugs can best be communicated to the general public; identifying which strategies are most effective in encouraging health care providers in both the public and private sectors to adhere to standard treatment guidelines; developing simple tests that can be used by community health workers, dispensers or drug sellers to detect counterfeit drugs; and identifying how best to conduct improved drug use information, education and communication campaigns for consumers.<sup>13</sup>

A number of initiatives have already been undertaken that seek to improve the way in which private drug retailers in low income countries do business. HIF registrants could well improve compliance with the correct use of their drugs by helping to scale-up such initiatives. The fact that these initiatives exist and are having a positive impact means that HIF registrants would not have to start from scratch. Replication (with due attention to the specifics of local conditions), scaling-up, and promoting sustainability would be the main challenges they would face. These are undoubtedly significant challenges, but developing new initiatives from scratch would be more difficult still.

One example of a private-sector focused program is the accredited drug dispensing outlet (ADDO) program in Tanzania (Mbwasii et al 2005). The goal of this program is to improve access to essential drugs and other pharmaceutical services in rural and peri-urban areas where there are few if any registered pharmacies. Nonpharmacy drug shops are the



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most numerous outlets for essential drugs in Tanzania, but they often fail to meet minimum standards. A program of accreditation by the Tanzanian Food and Drug Agency was introduced to encourage these retailers to improve standards concerning products, premises and staffing. Key program elements included: (1) training courses for dispensers and owners; (2) incentives for owners, including legal approval to sell a limited range of prescription drugs, a marketing campaign financed by the program, access to microfinance and links to health financing schemes; and (3) a regulatory system using local government officials trained and deputized as officials of the drug regulatory authority to ensure compliance with regulatory requirements. An evaluation of the program found that it had significantly improved access to essential drugs and encouraged better use of these drugs by consumers. It is noteworthy that this program, while targeting private drug sellers, is strongly linked to the public sector through the regulatory system.

Instead of accreditation, Ghana has trialled a franchise model to improve the performance of licensed chemical sellers (LCS), the first-line providers of medicines in 60 percent of medicine sales (Mensah 2005). Poor dispensing practices of LCSs were common due to a combination of inadequate technical knowledge and the distorting effect of the profit motive. With technical support from the US nonprofit health consultancy Management Sciences for Health, the Ghana Social Marketing Foundation established a franchisor to build the capacity of existing LCSs to enhance access to quality essential medicines. Franchisees operate under the name of CAREshops, and receive training and supervision to produce a uniformly high quality of service. Advocates claim that the CAREshop franchise has improved both the accessibility of essential drugs and the quality of pharmaceutical care and services that franchisees provide their customers.

Similar initiatives have been undertaken in Kenya (Ombogo 2005). Child and Family Wellness Shops (CFWS) operate under a tightly controlled license and focus on a short list of infectious diseases referred to as “treatable killers,” such as malaria, respiratory infections, diarrhoea, TB, and worms. They also treat opportunistic infections associated with AIDS.

CFWS outlets may only stock and prescribe medicines purchased from the franchisor, which includes in its formulary only those treatments that have been approved by the Kenyan Ministry of Health. There is an approved price list to which CFWSs must adhere. CFWSs are increasing their focus on prevention through the aggressive promotion of bed nets, vaccination, and condoms.

It is possible to make significant gains in access and correct usage of vital medicines by supporting small enterprises that are already in the business of selling drugs.

Initiatives such as these suggest that it is possible to make significant gains in access and correct usage of vital medicines in low income countries by supporting small enterprises that are already in the business of selling drugs. The resources that pharmaceutical companies have at their disposal could have a major impact on the reach of these organizations and on the quality and amount of training and other support provided to their owners and staff, at least in relation to HIF-registered medicines. The involvement of pharmaceutical companies could also help to address two of the key problems with initiatives of this kind, namely how to sustain them over time and how to scale them up effectively. HIF registrants with an ongoing interest in the health impact of their products would have strong incentives to ensure that improvements in dispensing and related practices did not disappear as initial enthusiasm for them wanes.

Skeptics might argue that pharmaceutical companies would use their substantial resources to encourage private outlets to maximize the sale of their drugs, even when sales were harmful to patients. But, so long as reward is determined by health impact, such conduct would be counter-productive. Provided the HIF is able to measure health impact effectively, drug companies would not be rewarded for sales of their product to those who derive no benefit from it. They would therefore have no incentive to pressure retailers to maximize sales of their product. But they would have incentives to ensure that retailers make sound judgments about where their products were

likely to be beneficial, as well as to dispense their products and explain use requirements to customers in a way that increases the likelihood that they will be used correctly. They would also have incentives to find ways of encouraging consumers to use their products as directed, and to support the development of systems to monitor use.

These initiatives could be further strengthened, for example by introducing treatment registers to record basic patient information (age and gender), diagnoses made and drugs and dosages given. It has been shown that, with proper incentives, private retailers can be relied upon to acquire this information. Relatively simple computer-based analysis of this information can identify problems such as use of third- rather than first-line treatments of malaria, poor handling of diarrhoea through high usage of antibiotics or low usage of oral rehydration salts (Chalker 2005). Again, while pharmaceutical companies seeking HIF rewards would be focused on monitoring the use of their particular drugs (where the use of their drugs would be counter-productive, their concern would be that these drugs not be used), they may well find that the best means to do this is to support the establishment of systems that are able to monitor drug use.

## CONCLUSION

Neither the current patent system nor other methods of incentivizing the development of new drugs, such as prizes and limited Advance Market Commitments, will provide pharmaceutical companies with adequate incentives to ensure that the drugs they produce are (1) accessible to all those who stand to benefit from them, and (2) used by consumers to good effect (defined not merely in terms of effect on the patient but also on the broader human population). These factors of accessibility and rational use constitute the last mile problem, which is a severe impediment to reducing the burden of disease, particularly (but by no means exclusively) in low-income countries. While significant efforts are underway to tackle last mile issues in both the public and private sectors of developing countries, there is little evidence of

major successes, although a number of smaller-scale initiatives have shown promise.

By tying reward to health impact, the Health Impact Fund gives participating pharmaceutical companies strong incentives to address last mile issues. HIF registrants will be required to sell their products at a price determined by the HIF, and they will have incentives to use their financial and lobbying power to keep taxes and other charges and mark-ups that increase prices throughout the distribution chain to a minimum.

Ensuring that available drugs are used correctly is a more complex problem, since it involves difficult systemic challenges. Properly trained and motivated front-line health workers must be in place in sufficient numbers to be reachable by patients. These workers must be supported by sound management and administrative systems and be subject to effective regulatory and supervisory mechanisms. While HIF registrants will not be able to fix all of these systems, they will have incentives to address weaknesses particularly relating to their registered drugs, and it is likely that some of the resulting administrative improvements will apply to other drugs as well.

HIF registrants will be incentivized to maximize the health impact of their drugs and will find it profitable to engage in activities that increase correct uses, and reduce incorrect uses, of their products. HIF-rewarded companies can thus be expected to bring their considerable energies and resources to bear on some of the most difficult problems besetting the health systems of developing countries. This injection of energy from the private sector toward solving these problems may be just what is needed to enhance the efforts already underway.

In developed countries, where the last mile problems are less severe, HIF registrants will be motivated to increase the awareness of their products among physicians and patients to ensure appropriate prescribing and use.

## NOTES

1. HAI (2004, 35–6) and HAI (2005, 26) indicate that mark-ups in the order of 100 percent, and sometimes substantially higher, are not uncommon. Detailed survey results on the components of retail prices of medicines in a number of developing countries are available at <http://www.haiweb.org/medicineprices/surveys.php>.
2. In 2006, the WHO drew attention to a global shortfall of 4.3 million health workers, with the worst shortages in the poorest countries. The Global Health Worker Alliance (GHWA) was launched at that time to tackle this issue. A GHWA taskforce has recently estimated that an additional \$2.6 billion a year is needed in Africa alone to train an additional 1.5 million health workers over a ten-year period. Documents detailing the scale of the health worker problem and proposed solutions are available at <http://www.ghwa.org/>.
3. UN Millennium Project (2005, 5–6) identifies inadequate national commitment to health care and inadequate human resources for health as two of the four primary reasons for lack of access to existing medicines in developing countries (the other two reasons it gives are inadequate financial resources from the international community and poorly coordinated international aid).
4. The earliest definition of rational use, formulated by the 1985 Conference of Experts on the Rational Use of Drugs held in Nairobi, included low cost to the consumer as a defining feature. Our discussion of the last mile problem includes cost primarily as a determinant of accessibility, although we acknowledge that cost can affect rational use by reducing the likelihood of poor patients completing full courses of medication.
5. The WHO identifies inappropriate prescribing and use as the primary cause of the growing resistance to antimicrobial medicines, which is a major challenge to public health around the world. This is exemplified by chloroquine resistance, which is now established in 81 of the 92 countries where malaria is endemic, necessitating the use of higher-cost second- and third-line treatments (WHO 2004b, 75, 87–8). Das, Hammer, and Leonard (2008) argue that, while access to health care in many low-income countries has improved, the quality of medical treatment, a function of both the competence of medical practitioners and the effort they expend on diagnosis, is exceedingly low, particularly for poor patients.
6. GHWA (2008b, 6) identifies a “massive shortfall in the production of health workers” as the key to the problem, compounded by other factors such as the impact of HIV/AIDS on the health workforce, international migration, poor wages and working conditions and political instability. “If all the doctors trained in Ethiopia in the last 30 years were still working in the country, there would be about one doctor per 10,000 population. In the United Kingdom, there is one doctor for about every 450 people.” Eyal and Hurst (2008) contend that the “brain drain” of doctors and other health workers from poor to rich countries is a major contributing factor and suggest ways of reducing it. Clemens and Pettersson (2008) argue that data on African doctors do not support this thesis.
7. The Global Health Workforce Alliance (GHWA 2008a, 5; 2008b, 3) calls on the World Bank, regional development banks, the IMF, and domestic finance ministries to show greater flexibility and initiative in finding ways to enable developing countries to increase health expenditure significantly without violating necessary macroeconomic disciplines. It also calls on relevant Ministries of Health to create the conditions for increased health spending by developing evidence-based and carefully costed health workforce plans. CGD (2007) and IMF (2007) discuss in detail the impact of IMF programs on health spending in poor countries.

- McKinley (2005) argues that larger levels of foreign aid need not, as is often feared, lead to domestic inflation or higher real exchange rates. Aid can be used effectively to increase domestic public investment and real resource transfers from abroad, although the increasing practice of using aid to build foreign currency reserves reduces the latter benefit. Ooms and Hammonds (2008) argue for more foreign aid to finance the “core content of the right to health.” They claim that providing this aid within a framework of rights and duties under international law—for which, they argue, there is substantial warrant—rather than as discretionary spending by well-off nations would mitigate the risk of it contributing to a new form of colonialism.
8. The situation differs in Zambia, where it is estimated that up to 70% of people seeking malaria treatment first go to the public sector healthcare providers (Institute of Medicine 2004, 36). This is indicative of the variability across developing countries in the mix of public and private healthcare service providers and drug retailers.
  9. The private and public sectors referred to here include not just medical practitioners but all those involved in dispensing medicines.
  10. Particularly for drugs treating high profile diseases such as HIV/AIDS, negative publicity generated by drug companies charging high prices in low-income countries can change this equation and give the companies an incentive to concern themselves with the impact of price on accessibility. Publicity about nonprice issues affecting access and irrational use is much less likely to change the incentives facing drug companies.
  11. These points are based largely on a list of core policies to promote rational drug use proposed by WHO (2004b, 88). For a discussion of standard operating procedures for ART, see Thuo and Wachira (2005). Pharmacovigilance is the detection, assessment and prevention of adverse drug reactions (see WHO 2004b, 89).
  12. Data contained in Das, Hammer, and Leonard (2008, 25–6) suggest that increasing the training that doctors receive does not necessarily lead to significant improvement in the quality of the care they provide. However, they refer (2008, 27) to the finding of Barber and Gertler (2007) that empowering women to demand better health care from their doctors can lead to a significant increase in effort and therefore in the quality of care.
  13. It is possible that the marketing skills of a pharmaceutical company, usually employed solely to promote its product, could have a major impact if put to the task of providing nonpromotional information about the importance of adhering to treatment guidelines.



# 8. An Economic Analysis of Patents and the Health Impact Fund

*Patents are an effective mechanism to stimulate innovation, but lead to a number of economic inefficiencies – most importantly, “deadweight losses” caused by high prices, and sub-optimal innovation investment decisions. The HIF can rectify some of these inefficiencies for registered drugs, while offering increased opportunities for pharmaceutical innovators. The HIF’s reward mechanism ensures that the rewards are not excessive, and the new funding required is likely to be very modest.*

## INTRODUCTION

The patent system is a mechanism for incentivizing innovation: essentially, it allows firms to exclude others from the use of an innovation so that the patentee can capture more of the benefits created. It is a robust, but imperfect, system which has served society well. This chapter discusses both the merits and failings of this system, particularly with respect to pharmaceuticals. It shows how the Health Impact Fund addresses many of the failings, not by eliminating patents, but by building on them, and offering innovators a new way of using patent exclusivity to earn profits.

## PATENTS

### Description of the Patent System

A patent is a special privilege conferred by a government. It entitles the patent owner to use the legal system to stop unauthorized use of an innovation disclosed in the patent, typically for a period of 20 years. The patent system is designed to provide a reward for inventions that are made public, and it does so by temporarily preventing any competition relying on the patented innovation. In pharmaceuticals, patents are particularly important, since competition with generic products tends to be fierce and the cost of product research and development (R&D) very large relative to the cost of production.<sup>1</sup> In a free market system without patents (and other rewards for innovation), pharmaceutical firms would be unable to

earn enough from their inventions to recover their R&D outlays and would therefore be unwilling to invest in the development of new medicines.

The existing pharmaceutical Patent System is defined primarily by the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement, signed at the end of the Uruguay Round of WTO negotiations in 1995. This agreement governs nearly all aspects of intellectual property in international trade. TRIPS requires all WTO member states to adhere to strict patent protection laws for patented pharmaceuticals; at least 20 years of market exclusivity are guaranteed. The patent system, while still defined in domestic law and enforced in each country by its government, has now become effectively internationalized through the TRIPS agreement. Prior to TRIPS, different countries had different patent laws, which often reflected their level of development and the social goals that patent laws were thought necessary to achieve. Developed countries typically had the broadest and most restrictive patent laws, providing strong protection for monopoly manufacturing and sale of a wide range of patented products.

Poor countries’ access to cheap generic versions of patented medicines ended in 2005, when the 10-year compliance window for TRIPS came to a close in all but the so-called least developed countries. WTO members were required to bring their domestic patent laws up to the standards of TRIPS, effectively universalizing the strong patent protection favored in developed countries. The provisions of this treaty have been supplemented, as part of bilateral trade



agreements, by bilateral “TRIPS-plus” measures that further strengthen the protection of pharmaceutical patents, sometimes extending monopolies beyond 20 years through “data protection”.<sup>2</sup>

Until quite recently, patent laws were much less generous to innovators in most developed countries. Despite this, even very poor developing countries have signed on to TRIPS at the same level of patent protection as is granted in the most developed countries. It is clear that relatively poor small countries have little to gain directly from this. They could have continued to free ride on the innovation incentives created in the rest of the world, which are not meaningfully strengthened by the addition of their own domestic patents, and would thereby have spared their populations the high prices domestic patents enable. So it was presumably the promise of greater access to Western markets that motivated these countries to accept intellectual property protections that are substantially higher than those the most industrialized countries had just a few decades ago.

### Strengths of the Patent System

The patent system – as a means of inducing innovation – has a number of very attractive properties. First, all the risk of R&D is left with the firm that tries to develop an innovation. Thus, if a firm makes a poor choice of how to invest its money – in a drug which is ineffective or unsafe or for some other reason unprofitable – it does so at no cost to the public. Second, the party that typically has the most information about the prospects for successfully developing a product or process is the one that makes the investment decision. This allocation of responsibility for investment decisions decreases the likelihood that resources will be squandered on projects that are unlikely to come to fruition or are unimportant to consumers. Scotchmer (2004, p.38) notes that the decentralization of investment decisions is key to the patent system because ideas for innovations are widely distributed among firms and inventors, and no central authority can know about all these different ideas. Third, under the patent system rewards for successful development of innovations are positively correlated with consumers’ valuations of the innova-

tion, since the larger the aggregate demand for the product, the greater the valuation of the product embodying the innovation and the larger the innovator’s profits. Thus, firms have stronger incentives to invest into research (a) the less it costs, (b) the more likely it is to lead to a patentable innovation, and (c) the more highly the public is likely to value this innovation. Finally, the patent is limited in duration and thus the invention disclosed in the patent will eventually become freely available for use by the public.

### Weaknesses of the Patent System

#### *Lack of Access*

The most obvious objection to the patent system is that the high prices it enables inhibit access for some consumers who are able and willing to pay for the product at prices higher than the average cost of production, yet are unable or unwilling to pay the higher price enabled by the patent. The patent system thus creates economic inefficiencies, known as deadweight losses. In pharmaceutical markets, deadweight losses are likely to be enormous, particularly in countries where drug insurance is not widely available.<sup>3</sup> This inefficiency means that many patients go untreated and the patentee fails to benefit from potentially profitable sales. This enormous waste comes primarily through limiting sales to the poor in developing countries, who are not able to purchase essential medicines.<sup>4</sup>

One response to the problem of high prices, which limit access for poor consumers especially in less developed countries, is a strategy of differential pricing. Thus some firms, such as Glaxo, have a policy of charging high prices in the wealthiest countries, lower prices in medium income countries, and at-cost prices in the poorest countries. However, such price discrimination is not universally used, for a variety of reasons. First, there are substantial higher-income markets in many poor countries, and the profit-maximizing pricing strategy within the country itself may be to charge high prices (Flynn *et al*, 2008). Second, charging different prices in different countries can lead to parallel imports between countries – the importation of inexpensive drugs from

poor countries into rich countries – which results in some loss to the patentee of sales at high prices in the richer countries. Finally, there is a web of price-referencing schemes between countries, many of which refer to foreign prices in setting domestic reimbursement levels. Thus while a differential pricing strategy seems at first glance to benefit both innovators and consumers, the fact that innovators have not universally set prices in different countries at levels which reflect incomes indicates that firms do not typically consider this strategy to be beneficial to them.<sup>5</sup>

High prices also lead to deadweight losses in wealthy countries, as consumers without complete insurance choose not to purchase prescribed medicines, or as insurers decide not to reimburse certain medicines. For example, in the United States, many insurance plans require co-payments of between 20% and 33% on “Tier 4” drugs. When drugs are priced in the thousands of dollars, this can impose severe financial hardship on patients, resulting in their not following the prescribed therapy. In countries with government-sponsored drug insurance programs, some expensive drugs are simply not being listed on the formulary as eligible for reimbursement. Such deadweight losses are inevitable given substantially different willingness to pay across payers, because the patentee maximizes profits by setting a price which excludes some potential buyers.

### *Counterfeiting*

A second problem that results in part from the high prices of patented pharmaceuticals is the profitability of counterfeiting. According to a recent World Health Organization study, “counterfeits are deliberately and fraudulently mislabeled with respect to identity or source. Counterfeiting occurs both with branded and generic products and counterfeit medicines may include products with the correct ingredients but fake packaging, with the wrong ingredients, without active ingredients or with insufficient active ingredients.”<sup>6</sup> The proportion of drugs which are counterfeit is unknown, though estimates range from approximately 1% in developed countries to well over 10% in developing countries.<sup>7</sup> (Sometimes infringing generics which are correctly labeled but

infringing are described as counterfeits, and in fact the incentives to infringe are similar to the incentives to counterfeit.)

Counterfeit drugs that are fraudulently mislabeled as to their source, but that are faithful copies of the original, cost the innovator lost revenues. In this case, counterfeits are essentially a form of theft from the innovator, and reduce the incentive to innovate. More troublingly, many counterfeit drugs simply do not contain the listed ingredients in the listed amount, and some do not contain these ingredients at all. This not only harms the innovator by taking away market share; it also damages the reputation of the branded product that is being counterfeited. Counterfeit medicines also harm patients when they do not contain the listed ingredients, contain them in the wrong concentration, or contain other toxic substances.

When counterfeits contain less than the correct amount of the active ingredient they may also increase drug resistance. For example, a recent study of malaria drugs sold in the most severely affected parts of Africa showed that over a third of all drugs tested did not contain the advertised amounts of the ingredients (Bate et al. 2008). 42% of tested products claiming to be artemisinin monotherapies were found to not meet “international standards” for active pharmaceutical ingredient content. The use of artemisinin monotherapies – especially in partial doses – is likely to lead to parasitic resistance to the extremely effective artemisinin combination therapies which are now recommended by WHO.

### *Innovation*

Perhaps the greatest weakness of the patent system is that it fails to induce the most efficient set of innovations. We consider two aspects of efficiency: “internal” efficiency refers to how well resources are allocated over all possible R&D projects; and “external” efficiency refers to how well resources are allocated between R&D and other activities. Given any amount to be invested into innovative activities, internal efficiency is attained when the benefit to society of investing another dollar into any given innovation project is equalized across all projects with

positive funding, and when the benefit from projects that receive no funding is below that of projects that do receive funding. External efficiency is achieved when the marginal benefit to society from increasing R&D spending is equal to the marginal benefit from investing in other activities.

Perhaps the greatest weakness of the patent system is that it fails to induce the most efficient set of innovations.

An important point in the definitions of efficiency above is that the social benefit should be equal to the social cost at the margin. However, under the patent system, innovative companies generally consider only their private benefit when making investment decisions. Therefore, the patent system gives firms research incentives that are distorted from what would be socially optimal. In particular, these incentives are too weak for most areas of research and biased in specific ways described below.

*Patent duration.* There are limits on the duration of the patent. The limitation on duration reduces the incentives to invest in innovations that will have substantial impact more than twenty years into the future. In the pharmaceutical industry, this means that the patent system does little to incentivize basic research, and creates sub-optimal incentives for other research as well. Thus in general the incentives for R&D are reduced below what would be optimal and are skewed particularly towards innovations with benefits that can be realized within twenty years.

There are some specific problems relating to patent duration for pharmaceuticals. For many pharmaceutical products, the effective period of protection granted by the patent system is much closer to ten years, since the clinical trials and the regulatory approval process may take many years. This means that the incentives created by the patent system are particularly strong for those drugs whose clinical trials are likely to be relatively short, since for them the period of effective protection will be relatively long. This structure also gives firms strong incentives to try to speed through clinical trials.<sup>8</sup>

In addition, there are important classes of products – such as anti-infectives – where it makes sense to reserve new drugs to treat only those bacterial or viral infections that do not respond to the older therapies. Such an approach is sensible since it reduces the probability of resistance to the newer drugs. However, it means that the newest drugs may obtain very small sales volumes during the period of patent protection.

*Patent scope.* Limits on the scope of the patent often allow other firms to invent around the patent. (Inventing around is a strategy of mimicking the patented discovery without actually infringing any of the claims in the patent.) For example, once one company shows that some molecule is useful in addressing some particular health problem, other companies will begin to search for related molecules that work in a similar way. When they succeed, the firm that did the pioneering research will find its profits much reduced (DiMasi and Paquette 2004). This loss to the pioneering innovator is aggravated by the aggressive marketing that pharmaceutical firms undertake in order to persuade doctors to prescribe one medicine rather than another.<sup>9</sup> Reducing what the patentee can earn from its monopoly, limits on patent scope discourage socially valuable innovations and bias research investment away from products that, if invented, would be easier to imitate.

*Inability to perfectly price discriminate.* Incentives to invest in R&D are further distorted by the fact that patentees cannot charge different prices to different customers – they cannot find out what each potential buyer is maximally willing to pay and also cannot prevent secondary trading among consumers. Charging one uniform price, the patentee does not appropriate the full social value of its innovation. Much of this social value is captured by the customers who are willing to pay more than the uniform price. And some potential social value is lost entirely as the patentee cannot realize mutually beneficial exchanges with customers who are willing and able to pay more than marginal cost but less than the uniform price. Economists measure this loss in currency units: if a patient cannot afford to pay the uniform price but could have paid \$15 while the patentee's marginal cost is \$10, then there is a \$5 loss in social value from

the unrealized exchange. This calculation leaves out the human cost: the misery and perhaps premature death this exchange would have averted.

The inability to charge different prices to different customers based on their willingness to pay has two important implications: incentives to invest in R&D are (a) weaker than would be socially optimal and (b) biased towards innovations from which the patentee can, at the profit-maximizing price, capture a larger proportion of the total surplus.

It seems possible that the inability to price discriminate has stronger implications in developing countries where there is no drug insurance. In wealthier countries with near-universal insurance, almost all consumers are served, and insurance performs the role of ensuring that low-income consumers are not priced out of the market. In developing countries without insurance, many patients who are ready to pay more than marginal cost are unable to afford the product. As a result, no sales are made to these patients, and a large part of the innovation's potential value is lost to the world and, of course, to the patentee. As a result of this inability to price discriminate, innovators' incentives are reduced compared to the social optimum; and in respect of pharmaceuticals, the incentives are especially reduced for the development of products that insurance companies may decide not to cover.

*Externalities.* The patentee may be unable to capture the benefits created by a drug which has significant externalities. Drugs and vaccines for contagious diseases are an important example of this problem, as, in addition to benefiting the user, they also benefit many others by reducing their probability of infection. Thus, the private valuation of the purchaser will be below the social value of the product. This leads to suboptimal incentives to develop products, such as vaccines and anti-infectives, which have positive externalities.

*Incomplete enforcement and non-patentability.* The patentee may not be able to prevent use by consumers of patented innovations, when there is no mechanism for stopping infringement. For example, a firm which discovers a new use for an existing generically available drug could obtain a patent on the new use, but might be unable to prevent competing manufac-

turers from selling the product, since at the point of sale there is no infringement of the patent. Consumers who used the product in the new use would be infringing, but the patentee might be unable to use the law to prevent this.<sup>10</sup> In such a case, the patent system would be of little value to the innovator because the mechanisms for preventing infringement are limited.

A related problem occurs when the enforcement mechanisms in a country are inadequate to prevent counterfeiting or competition from infringing products. This generally reduces incentives to undertake investment in innovations for which the patent system offers limited or ineffectual protection from infringement. With respect to pharmaceuticals for developing countries, since counterfeit products are so widespread, it can be anticipated that the incentives to develop drugs specifically for neglected diseases are meaningfully reduced by the prospect of competition from counterfeit products.

Enforcement may be completely unavailable for certain molecules with predictable functioning, since the non-obviousness standard under patent law renders those molecules unpatentable.

Enforcement may be completely unavailable for certain molecules with predictable functioning, since the non-obviousness standard under patent law renders those molecules unpatentable. As Roin (2008) observes, the non-obviousness requirement "denies patent protection to the drugs that appear most likely to succeed at the time they are invented and that have expected beneficial properties; i.e., the drugs that appear most promising in early research." This rule can therefore discourage investment into exactly the pharmaceutical research projects which have the highest probability of success.

*Cost of application and enforcement.* Protecting the patent is costly. A patent is not a guarantee of no infringement, but rather allows the patentee to sue for infringement, and then, if successful in court, to obtain a court order requiring the cessation of infringement. The costs of applying for the patent and then enforcing the patent may be very substantial, reduc-

ing the reward to innovation. A recent study by Besen and Meurer (2008) shows that the costs related to patent litigation are not only very substantial but for some classes of patents exceed the average value realized by patenting. However, for pharmaceuticals in particular, costs related to enforcement are smaller than the value realized. Nevertheless, the prospect of litigation discourages some socially valuable innovative activities and also biases innovation toward products for which litigation costs are expected to consume a smaller proportion of future earnings.

*Racing and duplicative investment.* Another important problem with the present patent regime is that firms engage in excessive, duplicative investment. In some cases, discoveries in basic science create opportunities for commercializable innovations which multiple firms invest in. The firms may then end up duplicating one another's research, which is clearly wasteful. Or they may pursue very similar drugs, which is also wasteful because an additional research effort adds very little to the probability of success and an additional drug very little to the medical arsenal.

A separate, but related, problem is that firms may "race" to be first, incurring waste by trying to accelerate their discovery so as to be able to be the first to submit their innovation to the patent office. While generally it is better if a given innovation is made earlier, rather than later, accelerating an innovation may be wasteful when the amount spent to accelerate the patent is greater than the incremental benefit of having the discovery earlier.

*Summary.* Like other economic instruments, the patent system brings benefits but is incomplete and imperfect. By itself, the patent system is likely to lead to predictable biases in the allocation of research investment, with some areas receiving too much and others too little. Other instruments may be needed to address these limitations.

### *Inefficient Production*

Patentees may be hesitant to sub-contract production to low-cost generic producers, because of the threat of diversion of some product by the contract producer. This may lead to inefficient production

methods, since the patentee may not have the lowest cost technology and also may lack economies of scope in production.

### *Essential Medicines and the Valuation of Life*

An important problem in the patent mechanism arises specifically with respect to the case of essential medicines. The patent system generally rewards innovators through the profits that can be achieved because of the exclusive exploitation of the patented innovation. Suppose for a moment that all the technical problems discussed above had been resolved, so that the incentive for innovation was exactly proportional to the economic value of the innovation as expressed in the aggregate demand curve. There would still be an important problem in the case of essential medicines. The incentive to invest in R&D related to the diseases of the poor would still be relatively small because the poor are, by virtue of their poverty, unable to pay much even to save their lives.

The standard economic valuation of a good is what a person is willing to pay for it. If person A is willing to pay only \$10 for any good, it follows that the good is not worth more than \$10 for that person. If person B is willing to pay \$20 for exactly the same good, and there is only one unit available, then it appears to be "efficient" to allocate the good to B. If A had the good, then he would generally be willing to sell it to be for a price above \$10, and B would be willing to pay a price below \$20.

Now suppose that the good is a pill which will extend either person's life by a year. A is willing to pay his entire wealth, \$10, for the pill, and B is also willing to pay his entire wealth, \$20. How should the pill be allocated? Here, our usual intuition, derived from expressed willingness to trade, fails us. Neither A nor B may be willing to give up the pill for any amount of money, and their "valuation" of the pill might be infinite. Given their wealth, third-party C who owns the pill will price it at \$20 and sell it to B. However, neither \$20 nor \$10 necessarily reflects the true value of the pill to buyers (i.e. what they would be willing to sell it for) – instead it reflects what the seller can get for it.



It is useful to turn to the economic literature on the value of a statistical life for clarification of this point. Viscusi (1993, p. 1942) argues that “The appropriate measure of the value of life from the standpoint of government policy is society’s willingness to pay for the risk reduction, which is the same benefit formulation in all policy evaluation contexts.” The implication is that richer people have higher “value of life,” since they are willing to pay more. And indeed, Viscusi (2003) based on a study of value-of-life estimates from different countries, suggests that the income elasticity of the value of a statistical life is around 0.5-0.6, so that as one’s income increases, so does the willingness to pay for reductions in risk.

It is important to understand how these studies are framed. Workers accept higher risk of death in certain jobs in order to be paid more. In other circumstances, travelers accept higher risk of death in order to travel at lower cost. Similarly, surveys show worker willingness to accept higher rates of death in order to be paid more. Thus, the trade-offs facing workers in these circumstances relate to willingness to exchange greater probability of early death for more available money for spending today. From the perspective of government, designing programs which reduce the probability of death for citizens, such studies provide the correct measure of how much to spend on such programs, since government need not spend more to save a person’s life than the individual is willing to spend.

Thus, we arrive at the conclusion that, if poor workers are willing to accept a given risk of death for a smaller increase in income, it must be the case either that (a) poor people assign a lower value to their life; (b) the marginal utility of income for a poor person is higher; or (c) both (a) and (b). Both of these, from the perspective of government policy, imply that the government should spend less to reduce risks to poor people, since there are more effective ways of increasing the utility of the poor (such as income transfers).

However, in the case of a person who is sick with a disease which will kill him, if the person does not spend his money on a treatment, he will simply die and the money will be useless to him (aside from as a bequest). The trade-off of getting more money today

in exchange for an earlier death does not occur in this situation. That is, there is no benefit in this case from accepting the earlier death. Therefore the willingness to pay should be infinite, although the ability to pay may not be.

How does this relate to economic value of saving a person’s life? What it suggests is that the willingness of a person to pay for a life-saving drug may not be well reflected by ability to pay. While on average poor people may be willing to take a given risk for a lower compensating payment, this need not indicate that they value their life less than that of a wealthy person; but it may only indicate that the marginal utility of income is higher for them. It does not mean, intrinsically, that the value of a poor person’s life is less than that of a wealthy person. Therefore, when the patent system values an innovation according to the amount that a person is willing to pay, it is using a mechanism which applies generally in cases where willingness to pay is meaningful. When “ability to pay” constrains the willingness to pay, the standard tools for valuing innovation apply poorly.

The patent system creates a reward for innovation which is based on how much people are willing and able to pay for a given medicine, and as such it is intrinsically biased against innovations which are principally consumed by poor people.

### Waste

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Aside from the failure of patent system to incentivize the most efficient set of possible innovations, it also induces considerable waste. In particular, it is well known that drug companies invest enormous sums of money in marketing, which is used to increase sales of one drug at the expense of another.



Thus, marketing and administration expenses are by a wide margin the largest single expense in drug company income statements. The outgoing CEO of Glaxo complained about this in a recent article, noting that “In 2006 the top seven pharmaceutical companies spent twice as much on SG&A (about 33% of revenues) as on R&D (about 16% of revenues)” (Garnier 2008, 71). While some marketing is valuable – that is, when it informs physicians and consumers about the benefits of the product – much of it is clearly more about transferring sales than improving the health of patients. The marketing efforts even extend into clinical trials, many of which have more value as marketing instruments than as scientific experiments (Angell 2004, ch. 9).

There is also considerable waste in the set of research projects chosen under the patent system, since firms tend to develop “me-too” drugs which imitate other successful drugs. While having multiple drugs in a therapeutic category can certainly be beneficial, there is reason to think that in some cases there may be too large an incentive to undertake research on products which do little or nothing to increase patient health.

There is also much waste in the patent litigation which inevitably arises out of the patent system. Because extending a monopoly can be enormously profitable, firms engage in all kinds of legal maneuvers, which generic firms must respond to. This results in enormous costs, none of which are beneficial for patients.

### Summary

The previous sections have shown that there are a number of problems with the patent system as an incentive mechanism for innovation. Not only are there problems in the patent system which apply in any field, but there are also reasons to think that the incentives to address the disease burden of the poor may fail to fully reflect the value of the health impact achievable.

*Synergy for diseases of poverty.* One of the striking features of the weaknesses of the patent system is the extent to which these weaknesses seem to apply with particular force to the situation of drugs for

Type II and Type III diseases (those which are largely or almost entirely present only in developing countries). If the value of human life is reflected in the prices which people are willing and able to pay for drugs, then of course drugs which are primarily sold to the poor must be of less commercial interest. But the poor are less appealing commercial targets for other reasons too, as discussed in Chapter 7. The distribution systems in poor countries are often less well developed; and the accompanying health systems required for diagnosis also less extensive, so that there would be less profit to be made from selling to the poor, even if they could pay the same prices for the drugs. Typically, there is relatively weak enforcement of patent rights in poorer countries, which makes it harder for innovators to earn profits in poor countries. In many poor countries, counterfeiting is especially widespread. In addition, in poorer countries, consumers generally lack drug insurance, which makes the inability to price discriminate a more significant problem. Finally, many Type II and Type III diseases are infectious, so that there are significant positive externalities from treatments. This means that the sum of private valuations for drugs for those diseases will be lower than their social value. Collectively, these problems mean that innovating for the diseases of the poor is much less profitable than it is socially valuable, and profits from patent monopolies are likely to present insufficiently large rewards to motivate the kind of investment into innovation which is desirable.

### THE HEALTH IMPACT FUND AND ITS RELATIONSHIP TO PATENTS

This chapter has described both strengths and weaknesses of the patent system as mechanism for incentivizing innovation. How does the HIF perform as an incentive system, and how does it fit with the patent system? In considering the HIF, it is important to recall that it is intended to be an optional, supplementary mechanism, and it therefore does not carry the entire weight of responsibility for innovation on its shoulders – what it needs to be is efficient in its own right, and to fill in the gaps in the existing systems.

## Similarities to the Patent System

Like the patent system, the HIF puts risks on the innovating firm; it allocates the decision to invest in innovation with the party that has the most information; and it is able to effectively decentralize investment decisions. The HIF mechanism thus shares these strengths of the patent system.

## Differences from the Patent System

### *Improved Access*

Unlike the patent system, the HIF is designed to maximize access for all drugs registered with the Fund. With this solution, no mutually beneficial exchanges remain unrealized and deadweight loss is eliminated. Some people will still be too poor to buy medicines even at HIF prices, but this problem is dramatically reduced because the number of patients unable to afford the medicine is much smaller.

Not only will low prices increase access and eliminate deadweight loss, but access will also be enhanced by the efforts of the registrant. As discussed in Chapter 7 there is a “last mile” problem of getting pharmaceuticals to patients, a problem that is particularly acute in developing countries. Given that the payments are based on health impact, however, the HIF registrant will be motivated to invest in marketing and distribution to maximize its profits from sales of the drug, even in situations where the ability of the final consumer to pay for the product is quite small. In this respect, the HIF mechanism is superior to the patent system by itself, given that the weak ability to pay of poor patients may fail to incentivize the requisite investments to turn basic innovations into widely marketed products in poorer countries.

### *Reduced Counterfeiting*

Because HIF-registered drugs will be cheaper, there will be less incentive to counterfeit them. Under the current system, either the drug is patented, with high prices, or not patented, with low prices. When patented, the incentives for counterfeiting are high, although the amount of counterfeiting may be lim-

ited by the efforts of the patentee to stop counterfeits. Once the product has been made available for generic production, the incentive to counterfeit becomes weaker, but no firm has a significant interest in patrolling the market to prevent counterfeits. While a drug is registered with the HIF, however, the incentives to counterfeit it will be weak, and the interest of the registrant in preventing counterfeits is strong.<sup>11</sup>

### *Consistent Duration*

In the HIF mechanism, the reward period starts at the time of commercial marketing of the product, rather than long before, as with the patent system. This reduces the incentive to rush clinical trials. At the same time, it evens out the reward across products: those with shorter clinical trials, and hence longer periods of exclusivity under the patent system, are not advantaged.

### *Reduced Imitation Despite Limited Patent Scope*

As discussed above, an important problem in the patent system is the limited nature of patent scope: a patent can prevent only those imitations that fall within the specific claims of the patent. This limits the ability of the innovator to capture the benefits created by the innovation and may lead to a pace of innovation that is substantially slower than would be socially desirable. The HIF does not prevent imitation either, but the profits to be earned from imitating under the HIF are extremely small. In particular, for an imitative product which only replaces sales by the first firm, but does not increase health impact, the HIF offers no reward at all. In this respect, the HIF provides superior incentives.<sup>12</sup>

### *Compensating the Registrant for Innovation and Production Separately*

Recall that a significant problem for patentees is that they are unable to appropriate the full value of their innovation when potential customers differ in the price each is maximally ready to pay. Such differences may arise either because of different preferences and incomes, or because the health impact differs predict-

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ably across individuals. Given any price above marginal cost, the monopolist is sacrificing some profits because of lost sales, and sacrificing other profits from failing to charge a higher price to those consumers who buy at prices lower than they would be willing to pay. The HIF resolves this problem by establishing a low price approximately equal to marginal cost, and then rewarding patentees based on the health impact their innovations create. If this health impact differs among individuals, reward payments will reflect the average, rather than the marginal impact. In the jargon of economics, the HIF uses a two-part tariff to reward the innovator: marginal cost pricing is used to allocate the good efficiently, and direct payments from the HIF to pay for the innovation. Because the reward payments are not tied to the price per unit, the reward can be proportional to the social benefit of the innovation.

### *Externalities*

The HIF rewards innovators not on the basis of the assumed benefit to the user of the innovation, but on the basis of the actual global health benefit. In this way, population benefits, such as reduced risk from infection, are incorporated into the reward calculations and therefore also into the research strategies of innovator companies. The current reward system is irrational in this regard, biasing pharmaceutical firms to discount the global threat posed by local infectious diseases that are not treated. Following the explosive international growth of SARS, of the spread of avian flu, and even of HIV/AIDS, there is an increasing appreciation that everyone is at risk when infectious diseases in far-away places are not treated and controlled effectively (Gostin 2007). It is in everyone's interest, then, that the incentives to pharmaceutical innovators be designed so that the impact of medicines on non-users is taken into consideration. The incentives created by the HIF meet this condition. The incentives created by the current patent system do not.

The underfunding of disease control remains one of the greatest acts of moral irresponsibility and political shortsightedness in the world today.

Jeffrey Sachs

### *Incomplete Enforcement*

As discussed above, the institutional enforcement of the patent system is problematic in many countries. For example, in some countries infringement by generic firms is not preventable through the court system in a timely manner. This problem currently reduces the profits and distorts the incentives of pharmaceutical innovators. But it would have no such effect on HIF registered innovators. The very low prices of their products would deter generic competition. And even if an infringing generic were sold in competition with the registrant's patented product, the registrant would suffer no serious loss because it would still be entitled to health impact payments on the competitor's product.

Similarly, in cases where the innovator has an invention, but the patent system is incapable of preventing infringement, as could occur when the innovation is the development of a new use for an existing generically available drug, the HIF can offer payments based on the innovation. Since the payment mechanism is not based on exclusivity but on health impact, the HIF's ability to reward such innovations is more robust. The patent system normally requires the firm to be able to exclude others from the use of an innovation for the patentee to benefit from it; under the HIF, however, exclusion is not required. In cases where exclusion is not feasible or its enforcement overly costly the HIF is a particularly attractive supplement to the patent system.

### *Reduced Racing and Duplicative Investment*

Because the HIF relies on the patent system to establish ownership rights to the stream of payments, the HIF is also subject to the problem of racing. However, unlike the patent system the HIF does not so strongly encourage duplicative investment into close imitations, because – absent incremental therapeutic benefit – it would not reward such innovations except when they increase access. (There is an exception to this, as discussed in Chapter 3, since the baseline for determining the incremental health impact of a new drug is set two years before the approval of that drug. In those cases, the HIF does not discourage duplica-

tive investment any more than would the patent system on its own.)

### **Waste**

Because of the reduction in imitative competition, with its excessive marketing, and in duplicative investment, the HIF is likely to lead to much less waste than the patent system.

### **Increased Market Orientation**

When compared to the patent system the HIF may seem to be more bureaucratic and less market-oriented, since the payment to the registrant is dependent on a determination by the Assessment Branch of the health impact of the product. But this is a false impression. In fact, outside the HIF, in most health systems, the decision concerning the reward to the innovator is made by the bureaucracy inside the insurance system, which decides whether or not to admit a given product to its formulary, based on the price. This implies that the insurer – in many countries a government agency – must make some administrative determination as to how much it is willing to pay for a given drug. This process is intrinsically more bureaucratic in nature than the competitive mechanism employed by the HIF.

The HIF is less bureaucratic, and more market-oriented, in its determination of the reward for an innovation, than the free market, which is dominated by the administrative determinations of insurers.

It is true that HIF must engage in a great deal more monitoring of sales and performance of registered drugs than do ordinary insurers, since the rewards may change from year to year, based on the known characteristics of the product and its sales volumes. But this is a strength, rather than a drawback: consistent and impartial monitoring of the impact various drugs actually have on human health provides information that is extremely valuable as a guide in future prescribing decisions.

## **The Relationship Between HIF Payments and Monopoly Rewards**

A critical feature of the HIF is that it is supplementary to the patent system and optional. This means that patentees will only register their product with the HIF when they anticipate that they will profit more through the HIF than they would through charging unconstrained prices. For some types of innovations, the HIF will be a natural choice. For example, for patented new uses of older generics there may be no alternative. Similarly, innovators seeking to develop drugs for treating serious diseases that primarily affect the very poor will likely find the HIF to be much more attractive than the patent system. Thus, because it is optional, the HIF expands the opportunities for pharmaceutical innovators to earn profits.

A second important implication of the fact that the HIF is an optional supplement to the patent system is that it ensures that funding partners obtain value for money. It is easy to show why this is so. All products registered with the HIF receive the same payment per QALY. Products which are sold at monopoly prices produce fewer QALYs than if they were sold at marginal cost. Thus, any products outside the HIF must expect to earn a significantly higher net profit per QALY, since otherwise they would be registered with the HIF (where they would earn a lower rate per QALY on a higher number of QALYs). Thus, products registered with the HIF will provide greater value (in terms of QALYs generated per dollar paid) than non-registered products. A mathematical proof of this point is provided in the Technical Appendix to this chapter.

## **The Allocation of the Cost of Innovation**

Given that the HIF is paying innovators directly, it needs to be financed somehow. It may seem obvious that the citizens of the partner countries will have to foot this bill. But in fact, the incremental expense to them is likely to be rather small.

To see why, consider how drug innovation is currently funded: buyers pay high prices for drugs under patent. Of course, in most developed countries, the buyers don't personally pay the entire price. In fact,

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in most OECD countries, the government's share of drug expenditures is over 60% (OECD, 2007).<sup>13</sup> The remainder is paid for mostly through employer-financed health insurance plans, and to a lesser extent, through co-payments by patients. In the United States, the share of pharmaceutical expenditures paid for by patients out-of-pocket is approximately 20% (CMS, 2007, Table 11), with government paying for 35%, and private insurance (mostly employment-based) paying for 45%. Employment-based insurance is essentially a tax on workers, as employers must offer lower wages because each worker adds additional insurance expenses. As economists have pointed out, when employers finance health insurance, the effect is similar to a regressive "payroll tax" which falls indiscriminately on low- and high-income employees (Summers, 1989). The net effect is that in most countries, patients pay for almost all drug costs through actual taxes or through reductions in wages equivalent to payroll taxes.

Thus, to the extent that the HIF pays for drugs which would have been developed in any case and consumed in wealthy as well as poorer countries, the net cost to citizens of wealthy countries is likely to be about the same, and the way that it is financed is also very similar – in both cases, the cost of the medicine is being financed through taxes and tax-like instruments. What is different is that high prices are not the mechanism used to transfer money from the government/insurer; instead there is a direct payment from the government. The national shares of drug costs are also likely to be similar, as at present more affluent countries are paying an overwhelming share of drug costs, as shown in Appendix B. However, with approximately the same amount of funding from approximately the same sources, the HIF enables much more widespread access to such drugs.

To the extent that the HIF pays for drugs or new uses which would not have been developed without the HIF, there is an additional cost to taxpayers. But this additional cost brings into existence additional high-impact medicines cheaply available wherever needed, plus the associated medical knowledge and know-how. Citizens pay for reduced mortality and morbidity worldwide and for reduced risk from diseases that, without the HIF, would have remained

unresearched. As shown in the previous section, the HIF mechanism also ensures that the rate of payment for these new medicines is lower than the payment per unit of health impact for medicines not registered with the HIF. Last but not least, the taxpayers funding the HIF also benefit from the positive externalities that better health worldwide brings for global economic performance.

## SUMMARY

The patent system has an impressive record of supporting successful research and development. As a stand-alone mechanism, however, it has some very serious limitations that clearly demonstrate the need for complementary mechanisms. The Health Impact Fund holds great promise as just such a mechanism. The next chapter further examines the HIF in comparison to alternative complements that have been proposed toward better supporting pharmaceutical R&D than the patent system can on its own.

## TECHNICAL APPENDIX

The HIF's mechanism ensures its payment per unit of health impact is lower than the net revenue per unit of health impact paid for medicines which are not registered with the HIF. A simple mathematic proof of this assertion is provided here.

Assume  $I$  medicines indexed over  $i$  are developed, with a fixed cost of development which is sunk. Each has a specific constant marginal cost  $c_i$ .

At the time of market approval, the firm can choose either HIF or monopoly pricing.

Firms outside the HIF set the profit maximizing price  $p_i$  for that drug, yielding net revenue  $(p_i - c_i)q_i(p_i)$ , where  $q_i(p_i)$  is the number of units sold at price  $p_i$ .

Each unit sold of the drug yields some health impact  $h_i$ .

The net revenue earned by the firm per unit of health impact for drug  $i$  is therefore the ratio

$$\frac{p_i - c_i}{h_i}$$



All drugs registered in the HIF are sold at a price of  $c_i < p_i$  which results in sales volume  $q_i(c_i) > q_i(p_i)$ .

The patentee receives a payment directly from the HIF, equal to  $\bar{p}$  per unit of health impact. Thus its net revenue per unit of health impact is  $\bar{p}$  implying a payment of  $\bar{p} h_i$  per unit of the drug. The net revenue of firm  $i$  if it registers its product with the HIF is therefore  $\bar{p} h_i q_i(c_i)$ .

Any firm that could earn more profits outside the HIF would choose to be outside the HIF. This implies  $\bar{p} h_i q_i(c_i) < (p_i - c_i) q_i(p_i)$  for all firms outside the HIF. This inequality can be re-written as

$$\bar{p} < \frac{p_i - c_i}{h_i} \frac{q_i(p_i)}{q_i(c_i)}.$$

The left-hand side of this inequality is the net revenue earned by the firm per unit of health impact for a product registered in the HIF. The right-hand side shows the net revenue earned by the firm per unit of health impact for a product not in the HIF, times the ratio

$$\frac{q_i(p_i)}{q_i(c_i)}.$$

This ratio is less than one, implying that the net payment per unit of health impact offered by the HIF is less than the net revenue earned by the firm per unit of health impact for any product outside the HIF. Given that the net revenue per unit of health impact is the same for all products inside the HIF, it follows that the HIF's payment per unit of health impact is lower than the net revenue per unit of health impact for medicines which are (by choice) not registered with the HIF.

## NOTES

1. Estimates for the average cost of R&D per new drug approved for sale range between \$200m and \$1.3bn, which includes the cost of essential clinical trials as well as the cost of failed efforts (compounds that are explored but do not come to market). See DiMasi and Grabowski (2007) for high-end estimates.
2. An important part of the process of pharmaceutical innovation is performing clinical trials to demonstrate safety and efficacy of the drug. Generic companies usually rely on the data from these trials as the basis for approval of their bio-equivalent generic drugs. Many countries now grant "data protection" of 5-10 years to the firm which performed the trials, preventing any generic company from obtaining marketing approval for their products on the basis of the trial data during that time. The period of data protection is frequently synchronous with the patent protection, though in some cases it may increase the period of effective protection from generic competition.
3. However, even in countries with drug insurance, the insurer must undertake some rationing to keep prices (and costs to the insurer) down.
4. Compliance may also be affected by high prices. If consumers are unable to afford to purchase the entire prescribed amount, the effect may be an increase in drug-resistant organisms.
5. It is not reasonable to expect for-profit drug companies to systematically lower prices in developing countries on the basis of altruism. While in some cases companies may have lowered prices in poor countries at a cost to their profitability, this would not be consistent with their responsibilities to shareholders if undertaken on a broad scale, and it is not fair to impose such requirements on the pharmaceutical industry (which is developing drugs that will some day be generically available at low prices) when other industries (which do nothing for poor people) have no such expectations placed on them.
6. World Health Organization, "Counterfeit Medicines" Fact Sheet number 275, November 2006. Available at <http://www.who.int/mediacentre/factsheets/fs275/en/print.html>
7. For a discussion of the unreliability of data on



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counterfeit medicines, see Outtersson and Smith (2006).

8. While it is good for products to become available earlier, the incentives for pharmaceutical firms to accelerate clinical trials may be too strong. Extending the clinical trial by a month to obtain more data does not merely delay the reward period by a month, it shortens it by a month.
9. Pharmaceutical firms are well known to invest enormous sums in their marketing. As a recent article by the CEO of Glaxo pointed out, in 2006 the top seven pharmaceutical firms spent twice as much on SG&A (sales, general and administrative expenses) as on research (Garnier 2008).
10. The difficulty with stopping infringement in such cases is that typically the patentee prevents infringement by stopping the manufacture and sale of the infringing good. However, in the case described above, the patentee would need to observe each consumer using the product, which would make it impossible to police.
11. Note that the HIF is unlikely to make any payments to the registrant for counterfeit drugs, since those drugs would tend not to be captured in any assessment of how many units had been sold.
12. Note that in the patent system imitation tends to benefit consumers through increased competition leading to lower prices competition, which may lead to price reductions for consumers. In the HIF system, competition is not required to generate price reductions.
13. Within the OECD, Mexico has a relatively low share of government expenditure on drugs (compared to total expenditure). However, the government share is likely to rise with incomes.

## 9. Alternative and Complementary Solutions

*The Health Impact Fund is only one of a number of alternative proposals which have been suggested as a solution to the problems inherent in the use of the patent system as the sole incentive mechanism for innovation in pharmaceutical markets. Direct research funding support – especially through private-public partnerships – has an important role to play. Other proposals – differential pricing, AMCs, compulsory licensing, priority review vouchers, patent pools and prize funds – all have merits, and are compared with the Health Impact Fund in this chapter.*

### INTRODUCTION

The previous chapter outlined various problems with using monopoly pricing to incentivise research and development. It also highlighted ways in which systems of monopoly pricing have contributed to the lack of access to certain patented medicines, especially in developing countries. This chapter surveys some complements and alternatives to systems of monopoly pricing and evaluates them based on their potential to increase access, stimulate innovation, work efficiently and generate political support. The point of the discussion is to examine how the Health Impact Fund stacks up against other reforms and reform ideas.

### GOVERNMENTAL AND NON-GOVERNMENTAL DIRECT PURCHASES

An important means to increasing access to essential medicines, while also potentially stimulating innovation, is government purchasing of medicines. The larger the budget for medicines, the more medicines can be purchased, and the more profits innovators can earn. In the United States, for example, the Medicare Part D provisions, which insure medicines for seniors, not only increase access for patients, but also boost the sales of pharmaceutical companies, and thus gives them incentives to develop new medicines relevant to this group.

Direct funding for purchasing drugs for developing countries has similar effects. The very successful US PEPFAR (President's Emergency Plan for AIDS Relief) program has recently been extended and increased in scale to allow for spending up to \$48bn on anti-retroviral therapies and other HIV/AIDS programs over five years. Given the increasing need for expensive second-line therapies, additional funding is likely to be necessary to continue to finance purchases of drugs for indigent people with HIV/AIDS. Many other countries have programs to subsidize purchases of pharmaceuticals for their own citizens and for foreigners. Inter-governmental efforts have also been made, such as the WHO/UNAIDS "3 by 5" initiative.

Direct purchasing programs are extremely valuable, but they are also limited and problematic in various respects. First, they are often susceptible to political influence that can distort funding priorities. For example, political considerations resulted in the requirement that at least one third of PEPFAR funds must be used for abstinence-only educational programs (Stolberg 2008). Political considerations may also influence the choice of diseases for which treatments are funded, the products which are purchased, and the countries to which products are supplied.

Second, these purchasing programs are often *ad hoc* and therefore subject to rapid change. The philanthropists and affluent country governments funding such programs may withdraw their support or alter their spending priorities at any time. These efforts

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do not therefore provide reliable long-term access to essential medicines.

Third, purchasing programs such as PEPFAR, like insurance programs generally, may handicap themselves by encouraging higher prices for patented medicines. If a profit-maximizing firm has a patented medicine that is the treatment of choice against some given disease, this firm will raise the price of its product when a new buyer appears who is disposed to purchase large quantities even at high prices. (The new buyer affects the aggregate demand curve and thereby the optimal monopoly price.) This problem is not severe when there are several competing drugs in one therapeutic class. Often, however, patented drugs face little competition; and the benefit from increased funding may then be largely offset by price increases. A particularly undesirable outcome would be if the *anticipation* of such a large buyer with deep pockets resulted in high prices.

While a funding initiative offset by price increases may make little difference to access, it does boost corporate profits. Such a boost would be good if it strengthened innovation incentives; but it is unlikely to do so. Existing research efforts cannot be restructured to fit new funding initiatives because pharmaceutical research takes many years to produce a marketable product. And new research efforts cannot be tailored to future funding initiatives whose magnitude and direction are unpredictable. Still, pharmaceutical firms will maintain higher R&D spending when they expect occasional windfalls from new funding initiatives. Though they cannot predict which drugs will benefit, they can assume that many drugs they could develop have a chance to be favored or a chance to attract new funding.

The HIF has several clear advantages over direct support for the purchase of medicines. First, the HIF is designed according to general principles that strictly tie its payments to global health impact as assessed in terms of a single metric. It cannot favor any particular disease or innovator or country, and thus is, as far as possible, free of political influence.

Second, as expressed by the long-term commitments of its funding partners, the HIF is designed as an enduring institution. As such, it will provide stable and reliable innovation incentives. Innovators

contemplating some specific research project can know that the HIF will still be accepting registrations by the time the research (if it succeeds) produces a marketable new medicine.

The HIF harnesses competition in a way that ensures cost-effectiveness and protects patients.

Third, the HIF harnesses competition in a way that ensures cost-effectiveness and protects patients. Recall that direct purchases by larger buyers are likely to drive up the prices of patented drugs unless there is serious competition in their therapeutic class. The HIF will not suffer from this problem, because it constrains the prices of registered medicines. And it will not suffer from the analogous problem of funding increases driving up the reward rate per QALY, because the HIF creates competition between all products, regardless of their therapeutic class. In response to a funding increase, any new medicine that otherwise would have been a little more profitable outside the HIF than inside can be registered or be switched over. And these extra registrations will keep the dollar-per-QALY rate very nearly where it would have been without the funding increase.

### DRUG PRICE REDUCTION EFFORTS

Various attempts have been made by Governments, NGOs and pharmaceutical companies to lower drug prices for patients in developing countries, thereby increasing access. Such efforts include bulk buying to exert more bargaining power, differential pricing, and compulsory licensing. Despite the obvious short-term improvements they produce in access, such programs do nothing to stimulate innovation, and may even deter it.

#### Differential Pricing

Differential pricing involves selling the same treatments at different prices in different markets, depending on relative ability to pay. Differential pricing is often put forward as a plausible mechanism

for making patented pharmaceuticals available to developing countries at affordable prices. Widespread implementation of differential pricing would, in certain respects, reconstruct the pharmaceutical market prior to TRIPS, when loose international patent protection forced pharmaceutical companies to sell drugs at lower prices to poorer markets or face generic competition. But once the implementation of TRIPS has eliminated the threat of generic competition, differential pricing would require some additional mechanism to encourage patent holders to sell their drugs at reduced prices.

Systems of differential pricing can guard against some of the deadweight losses caused by the patent system. However, and as discussed in the previous chapter, pharmaceutical companies are understandably concerned about the scope for parallel imports as well as indirect impacts on pricing in affluent countries through comparison, and have therefore not systematically charged lower prices in developing countries.

Further, differential pricing does not incentivize innovation into new medicines for diseases that predominantly afflict developing countries. A very positive overall evaluation of differential pricing notes that even under optimal conditions, in which there are strong barriers to parallel imports and external referencing and confidential price agreements, differential pricing would be an effective long-term strategy only if confined to drugs with a substantial market in affluent countries (Danzon and Towse 2003).

## Compulsory Licensing

Compulsory licensing is a mechanism for enabling competitive production of a patented product by mandating a license at a set royalty rate for a patented innovation, and is in effect an overturning of the normal patent right to the exclusive use of the claimed invention. By issuing a compulsory license, a government authorizes the production and marketing of a cheaper generic version of a patented medicine on condition that the authorized generic firm pays a small license fee to the patent holder. Such a license, and even the mere threat of one, will typically cause the price of the relevant medicine to fall substantially in the relevant country. In Canada, compulsory

licensing applied to pharmaceutical patents from 1923 until 1993. Thailand and Brazil have recently imposed compulsory licenses on a number of medicines. Compulsory licensing was expressly envisaged in the TRIPS Agreement and again prominently endorsed in the 2001 Doha Declaration, which stated that “the TRIPS agreement does not and should not prevent members from taking measures to protect public health” (WTO 2001). Since Doha, compulsory licensing has become popular among many NGOs, who see it as an effective mechanism for improving access to essential medicines. However, compulsory licensing has important limitations.

First, the scope for increasing access to existing medicines is limited. Compulsory licensing is normally only allowed for domestic consumption. This does not help the many countries that lack domestic generic drug manufacturing capacity, which include almost all developing countries other than Brazil, India, and China. According to a 2003 WTO General Council decision, exceptions exist for issuing compulsory licenses to countries lacking domestic production capacity, but the cost of the compulsory license must be borne by the exporting country (WTO 2003). Even when the will to export under a compulsory license exists, the process is often so complex and “riddled with restrictions, safeguards, practical hurdles, and red tape that it is unworkable” (Johnston and Wasunna 2007, S18).<sup>1</sup>

Second, the use of compulsory licenses is limited by the fierce opposition of the pharmaceutical industry, which has attempted to suppress the use of compulsory licenses or to confine it narrowly to cases of acute crisis. For this reason, developing countries are often reluctant or uncertain about whether to engage in compulsory licensing, lest they provoke political retaliation.

Third, while systems of compulsory licensing may provide an expedient solution to short-term health problems, they discourage investment in R&D for diseases whose remedies may become targets for compulsory licenses. The welcome relief from the problem of high prices compulsory licenses bring thus aggravates the neglect of diseases concentrated among the poor. Pharmaceutical companies spend less on the quest for vital medicines — especially ones

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needed mainly by the poor — when the uncertainties of development, testing, and regulatory approval are compounded by the additional unpredictability of whether and to what extent successful innovators will be allowed to recoup their investments through undisturbed use of their monopoly pricing powers. Compulsory licensing may thereby even exacerbate the health crisis facing developing countries over the medium and long terms (Pogge 2008b, 240).

### **Bulk Buying to Lower Prices**

An interesting strategy which has been widely trumpeted is bulk buying of drugs. The Clinton Foundation has focused its HIV/AIDS campaign on achieving price reductions through bulk buying contracts. If these contracts resulted in a decrease in the cost of producing drugs, then bulk buying could yield gains to all parties. However, it is more likely that costs will remain the same, so that the effect of the price reductions is to reduce the buyers' costs and the sellers' profits. Bulk purchasing may be able to achieve such price reductions through exercising market power owing to a stronger position in negotiating with sellers. This approach, however, is similar in its effects to compulsory licensing, since it will lower profits and thereby reduce innovation incentives.<sup>2</sup>

The proposals discussed in this section can, at best, address effectively only one of the problems with the existing pharmaceutical patent system - that of high prices. And they address this problem in a way that will aggravate other problems faced by the same populations: the lack of incentives to research their specific diseases and to help overcome their last-mile problems. Alternatives to the above mentioned programs can be broadly divided into two types: push programs, in which innovators are provided with funding to undertake particular research, and pull programs, in which a reward of some kind is offered for the achievement of some valued innovation.

### **PATENT POOLS**

A new mechanism to assist with lowering drug prices in specific countries is the patent pool approach recently espoused by Unitaid. What makes this ap-

proach particularly interesting is that it could also result in a reduction in transactions costs which could benefit patentees too. A patent pool is a portfolio of patents related to a particular technology and held by companies, universities, and government institutions. The patents would be made available under a non-exclusive license to manufacturers and distributors, and the pool operated through the auspices of a licensing agency. The licensing of patents to the pool is to be done on a voluntary basis with royalties paid, and there could be geographic limits on the license. The appeal of this approach is particularly for formulations which may require patents from multiple firms, since the pool would substantially reduce the transactions costs of dealing with separate patentees. Unitaid has initially suggested a focus on patents relating to pediatric anti-retrovirals and new combination products.

### **PUSH MECHANISMS**

Most existing efforts to incentivize innovation for neglected diseases and to provide affordable access to the resulting drugs fall in the category of push mechanisms. Push mechanisms reduce the cost of research by providing some or all of the funding for R&D directly. The most common kind of push program is a research grant, where researchers are paid by governments or other funding sources for research on a topic thought to be socially valuable. Overall, the amount of publicly subsidized or supported R&D in the US is roughly equal to the amount of private R&D (Baker 2004, 12).<sup>3</sup>

A second common form of push funding involves public-private partnerships (PPPs), in which public or non-profit institutions collaborate with private firms. There are currently 60-80 PPPs in the global health field. Examples include the International AIDS Vaccine Initiative, the Medicines for Malaria Venture, the Global Alliance for Tuberculosis Drug Development, and the Drugs for Neglected Diseases Initiative (Johnston and Wasunna 2007, S26).

### **Strengths of Direct Funding**

Governments and foundations (and their partners in PPPs) can use direct support for research that pat-

ents cannot incentivize. If the funding agency is well informed about the quality of projects, then direct support can be a cost-effective mechanism for obtaining desired research. If the funding agency has an interest in supporting research in an area perceived to be of great importance, it can directly pay for that research. (In contrast, the patent/HIF system is by its nature a market-based mechanism in which private interest dictates the direction of research investment.) This, of course, enables granting agencies and PPPs to focus resources on research related to high-priority and neglected therapeutic areas.

A second important strength of direct funding is potentially superior information about alternatives. When a firm with an idea for an innovation is deciding whether to proceed with investing into research and development into this idea, it only knows about a limited set of possibilities. For example, it may be unaware that another firm is developing a parallel idea or superior innovation, until the patents are actually published. This can clearly lead to wasteful duplication of efforts as well as expenditures on inferior innovations.

In contrast, when investment decisions are centralized through a granting agency, the agency can know about the entire set of ideas which have been proposed to it. If the proposals convey sufficient information to make good decisions, the agency can direct funding towards proposals with the greatest expected value. While under the patent/HIF system the decision about funding is made by a party that is very likely to have the best information about its specific proposal but perhaps little information about alternatives, funding decisions in a centralized system of grants will typically be made with less information about each specific proposal but more information about alternatives. In a sense, research grants resemble a system of central command and control over research investment, while the HIF mechanism more closely resembles a market in that decisions are made by agents on the basis of their private information.

Research grants resemble a system of central command and control over research investment, while the HIF mechanism resembles a market in that decisions are made by agents on the basis of their private information.

## Weaknesses of Direct Funding

### *Incomplete Information*

Direct funding is, as discussed above, likely to be efficient when the funding agency has good information about the costs of research, the probability that such research will result in valuable innovation, and the expected value of the innovation should it be successfully developed. However, funding agencies are likely only to have reliable information about the costs of research, while the probability of success is much more difficult to estimate. Granting agencies, in order to minimize their risks, tend to rely heavily on the past research record of the investigator – in general, only those investigators who have been successful in the past will be supported in the future. While this encourages investigators to put forward projects which they anticipate will be successful, the information available to the funding agency about the specific proposal is still inferior to the information about the project that is available to the researcher. In addition, rules in many research grant competitions do not allow the granting agency to selectively request more information – instead, the applicant may simply be required to submit a single application.

In some cases, funding agencies support research by for-profit companies, and here the willingness of a for-profit company to share the research cost does provide some assurance that the (better informed) company really believes in the value of the research project. However, in these cases the funding agency does not know whether its contribution is in fact necessary to support the project, or whether it is simply providing a subsidy to the firm to undertake research that it would have undertaken anyway.

### *Weak Incentives for Efficient Allocation*

In addition to incomplete information on the part of granting agencies, the financial incentives for employees of funding agencies to choose the “best” projects are relatively weak, since they personally cannot profit. In many contests, the funding agency asks academic volunteers to assess the quality of proposals. Evidently, the incentives of assessors are in



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part likely to be swayed by what they find of interest personally, perhaps because of a relationship to their own research interests or because of familiarity with the applicants. Research targets can be influenced by political factors, so that research is not necessarily targeted toward innovations that will have the greatest health impact (Baker 2004, 13). The selection of funding recipients is also open to political manipulation and bias. Even when funding recipients are chosen with the best intentions, due to information asymmetries between donors and innovators donors may not be able accurately to determine which projects are most likely to lead to successful innovations (Hollis 2007a, 78-79; Johnston and Wasunna 2007, S26; Pogge 2008b, 242).

The problem of assessment is exacerbated by the incentives of potential grant recipients to overstate the amount of progress they have made in order to attract more resources to their projects. Since the costs of R&D are covered regardless of the success of the research and because grants are an essential source of revenue, push programs encourage potential innovators to continue research into projects that have a high likelihood of failure, causing enormous waste (Schwartz and Hsu 2007, 26). This makes it difficult for the funding agency to sort out which projects are the most valuable. In contrast to for-profit companies, which are exposed to the discipline of the market when they fall short in the development of valuable products, governmental and non-governmental granting agencies have much weaker incentives to avoid and cull projects with low prospects of success.

### *Incomplete Mechanism for Bench to Bedside*

Innovators who have received a research grant have relatively weak financial incentives to finish the research and turn it into a commercializable innovation, since they cannot usually profit substantially from this. (This is not to say that such researchers have no incentives to succeed in their research: but a commercial firm is motivated by desire for success in the same way and by the desire for profits. Since the prospect of financial gain appears to be a very powerful motivating force, it is of course desirable to harness it to the greatest extent possible.)

This problem is emphasized by Kieff (2001) who notes that simple patent buy-outs (i.e. purchases of the patent right by government) might not lead to the accompanying investments required to generate full impact from a given innovation. The problem is that it is not sufficient merely to invent a new drug and obtain patents. Following the invention, an enormous investment in clinical trials is required before market approval can be granted. Even after market approval, continued clinical trials are often important for demonstrating relative effectiveness. If no one has a commercial incentive to undertake these expensive trials, they will not occur. Similarly, once the product has been commercialized, the patentee will normally invest in marketing to physicians even if the product has no close competitors, in order to educate physicians about its properties. Without such promotional activities, prescribing volumes would tend to be lower, and the health impact of the product smaller.

For pharmaceuticals in the developing world, the lack of incentive to distribute medicines might be a particularly acute problem. This is often due to the challenges involved in the final stages of the distribution of medicines, known as the “last mile” described in Chapter 7. The final distribution mechanisms for drugs influence whether they are appropriately prescribed, whether patients receive them on time and in sufficient freshness and quantity, and whether they are properly administered to achieve full effectiveness.

### *Access Hindered by Patents Even When Research Funded by Grants*

Funding agencies have financed many important innovative drugs, which have nevertheless been patented and then priced as if they had never benefited from public funding. Public funding is irrelevant at the time the drug is being sold, since all funding costs are sunk and cannot affect decisions about pricing. Thus, unless the funding agency, as a condition for the funding, requires the firm to set a low price for the resulting product, or requires some licensing, the public funding will affect only the innovation decision, but not reduce the deadweight loss arising from monopoly prices. Of course, outside funding may

help in these cases to reduce the cost of research, thus enabling research that would not have been profitable without the subsidy. (But, as noted above, grantee incentives to conceal information make it very difficult for funding agencies to direct their subsidies to research projects that would not have proceeded without such a subsidy.)

There is thus an important dilemma faced in the case of direct funding for drugs for relatively poor patients. If high prices are charged, access is limited. But if low prices are charged, commercial incentives to invest in distribution are weakened. The HIF effectively addresses this problem because it provides a substantial reward for effective distribution without obstructing access through high prices.

### *Direct Funding May Be Unstable*

Finally, push programs may lack stability over the long-term. Publicly funded grant programs and grants must be frequently re-approved, and are often terminated. Philanthropic support for research may dissolve as sponsors' priorities change. Since direct funding subsidizes pre-determined research targets, financial support will shift together with the interests and sympathies of funders. Such shifts are especially disruptive in the domain of pharmaceuticals where the time from conception to public use of an innovation is especially long. Especially in this domain, potential innovators require a reliable source of financial support.

## **PULL MECHANISMS**

Pull mechanisms are designed to incentivize innovation by rewarding successful innovators through enhanced profits or some other form of reward for the achievement of a socially valuable product. The existing patent system is itself an example of a pull mechanism, which promises a market monopoly for patented medicines. Though the patent system is flawed in some respects, it has proven effective at stimulating innovation for markets that can afford monopoly pricing. As described in Chapter 8, however, the patent system is less effective in certain circumstances, where either great need does not mani-

fest itself in strong market demand at high prices or where patents do not allow potential innovators to capture enough of the surplus their innovation would create to justify their investment.

Publicly funded pull programs are a significant departure from the way in which innovation has traditionally been incentivized, and therefore such programs are often met with skepticism by governments and potential innovators alike. However, given the poor record of existing programs, there is strong reason to seek a better alternative. Pull programs will be successful only if they meet at least these two important conditions. First, the basis for eligibility for rewards must be clearly specified far in advance, so that potential innovators understand the goal they are working towards. Second, the size of the reward must be sufficiently large to incentivize innovation, even given the risk of failure.

A main advantage of pull mechanisms is that they do not pay for failed research, thus encouraging innovators to work quickly and cost-effectively toward the successful development of new treatments (Pogge 2008b, 241; Hollis 2006, 128). Pull mechanisms are also able to overcome the informational asymmetries of push mechanisms by taking advantage of the internal assessment of potential innovators. Firms which believe that they stand a good chance of being the first to achieve the research goal would undertake the R&D, while those that feel they are not likely to succeed will not make such investments.

Pull mechanisms impose significant risks on firms, especially in pharmaceutical markets where it can easily take ten years or longer to bring a successful innovation to market. Firms responding to pull mechanisms face two main risks: their research efforts may fail because they are unable to develop a new treatment, and they may fail because some other innovator is able to develop such a treatment more quickly. For this reason, the size of the reward must be considerably larger than what each firm expects to spend on its effort to capture this reward. However, removing this risk from firms through financing research directly simply imposes the same risks on the public which is supporting the research grant or subsidy.

Although publicly funded pull programs are a relatively new idea, they have the potential to gain

broad political support from taxpayers and pharmaceutical firms alike. Pull mechanisms can align the interests of profit-seeking innovators with those of society, which seeks efficient pharmaceutical innovation and affordable medicines. By relying primarily on private risk, competition and entrepreneurial innovation, pull mechanisms replicate some of the advantages of the market system. Because they reward only successful innovation and can stipulate the conditions for rewards (including the sale price of the drug) in advance, well-designed pull mechanisms can help increase access to medicines and incentivize innovation for neglected diseases.

### **Medical Research and Development Treaty**

The Medical Research and Development Treaty was proposed by the Consumer Project on Technology in 2005 (Love 2005). The purpose of the treaty is to create a “new global framework for supporting medical research and development that is based on equitable sharing of the costs of research and development, incentives to invest in useful research and development in the areas of need and public interest, and which recognizes human rights and the goal of sharing in the benefits of scientific advancement” (Love 2005, 2). The treaty proposal was submitted to the WHO in February 2005 with the signatures of over 160 researchers, NGOs, politicians, government officials, and other stakeholders.

Under the terms of this treaty, member states agree to support qualified medical research and development, including the development of pharmaceuticals. A committee of representatives from member states would be responsible for determining qualified medical research targets, including vaccine development, neglected diseases, and global infectious diseases. Countries would be free to choose how to spend their required contributions to qualified medical research, though there will be specified minimum contributions to those targets identified as priorities by the committee. State contributions would be proportional to per capita national income, so that the burdens of supporting R&D are distributed equitably. Since these contributions to R&D are

made domestically, they can come in the form of tax credits, direct funding, or product purchasing.

This proposal combines push and pull mechanisms by leaving the form of R&D funding to the discretion of member states. The treaty has potential to resolve problems related to high prices and neglected diseases. By firmly establishing long term commitments to funding, the treaty would provide a stable and reliable source of funding for R&D.

While it is a valuable and interesting proposal, the Medical Research and Development Treaty has some drawbacks. One significant concern about this treaty is that its terms allow too much flexibility in funding allocations. Such flexibility would enable governments to make resource allocations based on domestic political interests, rather than global health needs.

### **Priority Review Vouchers (PRVs)**

PRVs were initially proposed by Ridley, Grabowski, and Moe in 2006 (Ridley et al. 2006). The proposal caught the attention of US legislators, and under the sponsorship of Senator Sam Brownback (R-KS) it was included as the Elimination of Neglected Diseases Amendment in the FDA Amendments Act, which was signed into law on September 27, 2007 (Food and Drug Administration Amendments Act of 2007). Under this scheme, a pharmaceutical company that obtains approval for a drug or vaccine for a specified neglected disease would receive a voucher for priority FDA review of another pharmaceutical. By expediting the FDA review process, the voucher could reduce the time required to gain FDA approval of the second drug by up to one year. The additional profit that a pharmaceutical innovator could earn from this additional year of market exclusivity is estimated at more than \$300 million for a blockbuster drug (Ridley et al. 2006, 315). Vouchers can also be sold to other firms. In either case, the increased revenues from the voucher would offset the R&D costs of the development of the drug targeted to a neglected disease.

As a pure pull mechanism, the PRV is attractive. It does not pay for unsuccessful research. Even the costs associated with expedited FDA review would be paid by the innovator, and would likely consti-

tute only a very small fraction of the resulting profits from a quicker review. The plan can therefore be implemented at no additional cost to consumers or taxpayers. Further, by choosing a broad list of targeted diseases, PRVs would allow innovators to determine which drugs to pursue based on an internal evaluation of the likelihood of success.

While the PRV mechanism has yet to be tested in practice, there are a number of reasons why it is unlikely that it could constitute a complete solution to innovation and access in pharmaceutical markets. First, it is not clear that priority review is really costless. As Ridley, Grabowski and Moe point out, priority review can accelerate approval of new medicines by as much as a year. This could result in three possible outcomes: (a) a lower quality review, with potentially higher risks to patients; (b) the same quality review, but with other medicines being delayed because resources were transferred; or (c) the same quality review, without other medicines being delayed, because the innovator pays a supplementary fee for priority review. Of these three possible outcomes, the first is unattractive since it implies that there may be substantial hidden costs of unknown size. The second is also problematic, as drugs of greater potential health value might be unnecessarily delayed. The third appears to be the outcome envisioned by the bill's sponsors. However, if the reason for slower reviews is lack of resources in the FDA, it appears that the option of paying for a quick review should be available in any case.

Second, it is questionable whether the reward of a priority review voucher is proportional to the value of the neglected disease drug. A new drug for a neglected disease, inferior to treatments which are currently available, could still be approved as safe and effective. Such a product would have little or no health impact, but could result in the award of a PRV worth as much as \$300m. Arguably, the reason the patent system has been effective is because the reward for an invention is roughly proportional to the benefit obtained by consumers. A system in which there is a fixed prize for any innovation, no matter how unimportant, is evidently susceptible to abuse and likely to lead to significant inefficiencies.

Finally, there is little reason to believe that once drugs eligible for reward under the PRV scheme re-

ceive market approval from the FDA, they will be widely accessible to the global poor. The original voucher proposal included a stipulation that innovators forgo patent rights for neglected disease drugs in order to receive vouchers (Ridley et al. 2006, 312). Unfortunately, this condition is not included in the version that was actually implemented. Thus the Act does not ensure that any innovative medicines that are used to claim a PRV will actually be available at affordable prices to the majority of those who need them. It is also important to note that the condition for receiving the reward of the PRV is the achievement of market approval for a neglected disease drug, and not any actual positive health impact of the drug. For this reason PRVs do not address the last mile problem.

However, PRVs can claim one important advantage: they have been passed into law. Though the health impact of PRVs is uncertain and focused only on neglected diseases, the political achievement is highly significant. PRVs were able to assemble broad support by appealing to the interests of all stakeholders, including political leaders, pharmaceutical companies, and global health advocates, allowing the proposal to be implemented in remarkably little time. In this respect PRVs serve as an important example for future reform efforts.

### **Medical Innovation Prize Act of 2007**

This bill, introduced in the US Senate by independent Senator Bernie Sanders, proposes a non-voluntary replacement for the existing monopoly patent system that would eliminate market exclusivity for patented products in favor of a government fund that would reward innovators for the health impact of their patented innovations.<sup>4</sup> It is intended to impact the domestic US pharmaceutical market exclusively. The legislation establishes a Medical Innovation Prize Fund that would incentivize research into new medicines that improve health outcomes, especially in essential areas, and would expand access to new medicines by separating rewards for innovation from monopoly pricing. Patents would no longer serve to guarantee market exclusivity, but would instead be used only to determine eligibility for reward

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funds. Patent holders would be immediately forced to allow the open use and production of the patented innovations, and the patentee would be rewarded by the government according to the positive health impact of the innovation, much as in the Health Impact Fund. The distribution of prize payments to innovators would be made by a panel consisting of government officials and representatives of stakeholder groups according to the criteria of the incremental therapeutic benefit of a drug and access improvement as compared to the baseline of existing drugs and the degree to which the drug meets health priorities including global infectious diseases, neglected diseases, and rare diseases and conditions.

This proposal achieves a number of important advantages, going far beyond any of the other proposals considered here to address both problems of access and innovation. The prize fund would entirely replace the market monopolies granted by patents to new medicines, completely separating prices from drug valuation. The requirement that all patented medicines be immediately available for generic production is intended to allow prices to drop to the marginal cost of production, increasing access. The proposal also contains provisions for special payments to be made for drugs treating neglected diseases.

Despite these important advantages over the current patent system, the Medical Innovation Prize Act is problematic in some respects. The fact that it is a mandatory, comprehensive system for all pharmaceuticals, not just for those products which opt in, means that its implementation requires a substantial re-organization of the entire pharmaceutical industry, which is unlikely to be politically feasible. At the same time, its comprehensive approach would create problems for innovators developing drugs with relatively small measured health impact but which patients were willing to pay for. In such cases, a willing exchange between innovator and patient could be blocked, since the Act would require only small payments to the innovator, inadequate to incentivize the innovation. There are also questions regarding whether the act would be compliant with the TRIPS agreement.

The HIF has several important advantages over the scheme envisioned in the Sanders bill. The HIF does not aspire to be a comprehensive, mandatory

system. Rather, it would provide an additional option that firms could choose selectively for products with large health impact but small profitability under the existing patent scheme. This makes it more attractive to pharmaceutical companies and to significant numbers of affluent patients and therefore easier to implement and to sustain. In addition, by allowing firms to maintain their exclusivity rights – but not freedom of pricing – for products registered with the HIF, the HIF has an advantage in creating fewer problems related to licensing. Finally, the HIF is clearly compliant with the TRIPS Agreement.

### **Advance Market Commitments (AMCs)**

AMCs are designed to incentivize commercial development of vaccines through the provision of a commitment by sponsors to partially or fully purchase new vaccines that meet certain predetermined requirements (Center for Global Development (CGD) 2005; Kremer and Glennerster 2004). To qualify for the AMC, the new vaccine would have to meet predetermined technical specifications relating to the effectiveness of the vaccine established by a committee. The same committee would also determine which vaccines are to be targeted for AMCs. Targeted vaccines might include those for HIV, tuberculosis and malaria. A “pilot” AMC of \$1.5bn – funded by Italy, the UK, Canada, Russia, Norway, and the Gates Foundation – has been set up for pneumococcal disease, a major cause of pneumonia and meningitis among the poor. An AMC would guarantee a predetermined price per treatment by supplementing the market price up to a certain number of treatments, on the condition that the treatments are sold at a fixed, affordable price. In this manner, the AMC would incentivize drug companies to scale up production and distribution of their new vaccines.

As a pull mechanism, the AMC achieves some advantages in terms of efficiency. The AMC would not pay for failed research, and innovators would have a strong incentive to work quickly toward bringing an effective vaccine to market. The AMC is structured to encourage the firm to sell its product at low prices, thus reducing deadweight losses.



Because AMCs supplement and are consistent with the existing patent system and create new sources of revenue for pharmaceutical companies, they have received substantial political support.

AMCs are likely to be very effective for speeding the distribution of some new vaccines in developing countries. However, they are limited in what they can achieve for several reasons. First, AMCs need to specify in considerable detail the conditions that a successful vaccine must meet (Farlow et al. 2005). Proponents of AMCs recognize this, noting that an AMC “must specify the desired research outputs beforehand, and coming up with the right specification and eligibility requirements may be difficult” (Kremer and Glennerster 2004, 64-65). The Center for Global Development has noted that even the most minimal specification must include the disease that the vaccine prevents, the effectiveness of the vaccine, the side effects of the vaccine, and the ease with which it can be effectively distributed and administered (CGD 2005, 44). This essentially means that AMCs cannot be designed until the product’s characteristics are reasonably well known. An AMC may then be a suitable mechanism for incentivizing only late-stage development of a medicine and its distribution at low prices. That AMCs are limited in what they can achieve is not a criticism, but is a function of their being designed to achieve a particular function.

One possible objection to AMCs is that they must rely on a non-market system for deciding how much to award for a particular product. The Pilot AMC for pneumococcal vaccines has been accused of paying a large sum of money for a vaccine that is already in late-stage development and would have been commercialized with or without the AMC. To the extent that the AMC is designed so that multiple firms may compete to obtain the available funding, this problem is however somewhat mitigated.

The HIF can be seen as a kind of “comprehensive” AMC which addresses effectively the problems encountered by more limited AMCs. Instead of specifying a technical requirement, the HIF specifies that what will be rewarded is measured health impact. This means that any new product – vaccine or drug – can qualify, permitting firms more flexibility and allowing the HIF to incentivize even early stage drug

development. In addition, by setting a fixed fund for which firms compete, the HIF does not need to decide how much to pay for each medicine – instead firms compete for the available funds.

The HIF can be seen as a “comprehensive” AMC which addresses effectively the problems encountered by more limited AMCs.

## CONCLUSION

No single complement to the current global pharmaceutical patent regime can solve or compensate all of its problems. However, relative to the other proposals reviewed here, the HIF offers a number of advantages. In particular, it is the only reform that is structured to use a market mechanism to set the reward for innovation; it is comprehensive; and it is feasible. Even with the HIF in place, grant funding for basic research and innovation incentives for orphan diseases will still be needed. But the HIF offers an opportunity greatly to improve global health in an economically and morally attractive way.

## NOTES

1. One notable example of this protracted and inefficient process is the case of the combination AIDS therapy ApoTriAvir, which was exported to Rwanda under compulsory license by the Canadian firm Apotex according to the terms of Canada’s Access to Medicines Regime Program, discussed in detail in Rimmer (2008).
2. One recent proposal for a “Multilateral Treaty on Health Technology Cost-Effectiveness Assessment and Competitive Tender” may be able to overcome some of the problems discussed here (Faunce and Nasu 2008).
3. For an extended discussion of the inefficiency of push mechanisms compared to pull mechanisms, see Schwartz and Hsu (2007).



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4. S.2210. An earlier version, H.R. 417, was introduced in the US House of Representatives in 2005 when Senator Sanders was a member of that chamber.

# 10. The Health Impact Fund: A Cost-effective, Feasible Plan for Improving Human Health Worldwide

## THE NEED FOR CHANGE

At present, the development of new medicines is driven by the reward of temporary market exclusivity. When a new medicine is protected from generic competition, its profit-maximizing price inevitably prevents a large proportion of the world's population – including many in affluent countries – from purchasing it. As a result of this system of incentives, people suffer and die needlessly and R&D is focused on those medicines from which investors can make the most money, rather than on those that would lead to the greatest improvements in human health.

We can clearly do better – but there are also some very difficult problems to be resolved. How do we maintain incentives for innovation if prices are low? And how do we encourage innovators to work on projects that will improve health, rather than merely those that lead to profitable sales? Plausible solutions to these problems can take advantage of the international patent system, but must be more responsive to the health needs of the poor.

We propose the Health Impact Fund as the most sensible solution that comprehensively addresses the problems. Financed by governments, the HIF would offer patentees the option to forgo monopoly pricing in exchange for a reward based on the global health impact of their new medicine. By registering a patented medicine with the HIF, a company would agree to sell it globally at cost. In exchange, the company would receive, for a fixed time, payments based on

the product's assessed global health impact. The arrangement would be optional and it wouldn't diminish patent rights.

The HIF has the potential to be an institution that benefits everyone: patients, rich and poor alike, along with their caregivers; pharmaceutical companies and their shareholders; and taxpayers.

## HOW THE HEALTH IMPACT FUND WORKS FOR PATIENTS

The HIF increases the incentives to invest in developing medicines that have high health impact. It directs research toward the medicines that can do the most good. It can also reward the development of new products, and the discovery of new uses for existing products, which the patent system alone can't stimulate because of inadequate protection from imitation. All patients, rich and poor, would benefit from refocusing the innovation and marketing priorities of pharmaceutical companies toward health impact.

Any new medicines and new uses of existing medicines registered for health impact rewards would be available everywhere at marginal cost from the start. Many patients – especially in poor countries, but increasingly in wealthy ones too – are unable to afford the best treatment because it is too expensive. Even if fully insured, patients often lack access to medicines because their insurer deems them too expensive to reimburse. The HIF simply and directly solves this problem for registered drugs by setting their prices at marginal cost.

## HOW THE HEALTH IMPACT FUND WORKS FOR PHARMACEUTICAL COMPANIES

Most proposals for increasing access to medicines would reduce the profits of pharmaceutical companies and hence their ability to fund research. The HIF, however, leaves the existing options of pharmaceutical firms untouched. It merely gives them the opportunity to make additional profits by developing new high-impact medicines that would be unprofitable or less profitable under monopoly pricing. Selling such registered medicines at cost, firms won't be forced to defend a policy of charging high prices to poor people and they won't be pressured to make charitable donations. With HIF-registered medicines they can instead "do well by doing good": bring real benefit to patients in a profitable way. Research scientists of these firms will be encouraged to focus on addressing the most important diseases, not merely those that can support high prices.

We will spare no effort to free our fellow men, women and children from the abject and dehumanizing conditions of extreme poverty, to which more than a billion of them are currently subjected. We are committed to making the right to development a reality for everyone and to freeing the entire human race from want.

United Nations Millennium Declaration

## HOW THE HEALTH IMPACT FUND WORKS FOR TAXPAYERS

The HIF will be supported mainly by governments, which are supported by the taxes they collect. Taxpayers want value for their money, and the HIF provides exactly that. Because the HIF is a more efficient way of incentivizing the pharmaceutical R&D we all want, total expenditures on medicines need not increase. However, if they do, the reason is that new medicines that would not have existed without the HIF are being developed. The HIF mechanism is designed to ensure that taxpayers always obtain value for money in the sense that any product regis-

tered with the HIF will have a lower cost for a given amount of health impact than products outside the HIF. Taxpayers may also benefit from a reduction in risks of pandemics and other health problems that easily cross national borders.

## WHY FOR PHARMACEUTICALS? AND WHY NOW?

The patent system is a very general mechanism for stimulating innovation in many fields. Applied to pharmaceuticals, it works poorly. This is so because pharmaceuticals are a very special case in at least these three respects. First, medicines are exceptionally important products of great consequence for well-being and even survival. Second, users typically do not have the information and power to make a rational decision about which product, if any, to consume. Third, the widespread use of insurance in the more affluent countries distorts the prices of patented medicines worldwide. To address these three special challenges, we propose creating a complement to the patent system that takes advantage of a fourth respect in which pharmaceuticals are special: their value to human beings can be summarized in a single measure – health impact – that is morally far more plausible than readiness to pay. Tailor-made for the special case of pharmaceuticals, the Health Impact Fund complements the patent system to correct for its defects in this area of innovation.

Readers may be wondering why, if the Health Impact Fund would work so well, it hasn't been proposed before now. There are two answers. First, the problem of price barriers to access to new medicines is growing rapidly given the development of global health systems, the implementation of the TRIPS agreement, and the worldwide escalation in pharmaceutical prices. The HIV/AIDS pandemic further underlines the importance of pharmaceutical treatment, and the terrible consequence of high prices of essential medicines. Second, the technology for measuring health impact has been developing over the last twenty years or so, and is only now in widespread use. Thus, along with growing political interest in implementing a mechanism such as the Health Impact Fund, we now also have the technical capability to do so.

## THE PATH FORWARD

For the HIF to become a reality, our proposal will need to be studied, challenged, refined, and considered from every angle. We have made a start on formulating the HIF – but we need help from a wide range of stakeholders – innovative companies, governments, insurance companies, epidemiologists, NGOs, lawyers, economists, doctors, and many others too – to push forward with the ideas presented here and to strengthen our proposal. We therefore encourage you to contact us at [www.incentivesfor-globalhealth.org](http://www.incentivesfor-globalhealth.org) if you have comments or ideas on this proposal.

It is also necessary that governments – supported by their citizens and with the collaboration of pharmaceutical firms – begin making commitments to support the HIF, once they are satisfied of the merits of the proposal. We hope to convince governments, one by one, to commit to supporting the HIF financially if enough other countries do so as well.

The Health Impact Fund is a fair and cost-effective way of stimulating research and development of high-impact pharmaceuticals. It would make advanced medicines available to all at competitive prices, while at the same time offering ample rewards for innovators.



# Appendix A: Poverty, Global Health, and Essential Medicines

*Due to the mutually reinforcing effects of poverty and ill-health, developing countries suffer from a disproportionate share of the global burden of disease. Around six million people die every year from AIDS, tuberculosis, and malaria alone, even though these diseases are treatable and preventable. The prevalence of these diseases illustrates the role that lack of access to medicines plays as both a cause and symptom of weak health systems. Pharmaceutical innovation driven by patents alone fails to incentivize the creation and distribution of treatments for diseases that are widespread in developing countries. The Health Impact Fund will disproportionately benefit these countries, contributing to an end to the cycle of poverty and disease.*

## INTRODUCTION

While the Health Impact Fund is a global mechanism that will require low pricing all over the world for registered medicines, it will have a particularly large impact on the poor, who do not have drug insurance. This appendix therefore examines in some detail the problem of access to medicines for poor people—its scope and its importance.

Some 18 million human beings die each year from diseases we can prevent, cure, or treat. This is equivalent to 50,000 avoidable deaths per day, or one-third of all human deaths.<sup>1</sup> Hundreds of millions more suffer grievously from these diseases, while the lives of additional hundreds of millions are shattered by severe illnesses or premature deaths in their families.<sup>2</sup> This huge incidence of avoidable mortality and morbidity occurs primarily in poor countries and especially among their poorest inhabitants, who continue to suffer from many of the communicable diseases that have been virtually eliminated in the rich world. This disease burden puts great strains on poor countries, communities, and families, helping to perpetuate their poverty, which in turn contributes to their members' ill health. As discussed in chapter 6, this situation is morally untenable.

## INCOME POVERTY AND HEALTH

### The Scale of Global Income Poverty

In 2004, some 970 million people, around 15 percent of the world's population, were living below the extreme poverty line of \$1 a day (more strictly defined, \$392.88 annually) in 1993 Purchasing Power Parity (PPP) terms (Chen and Ravallion 2007, 16579).<sup>3</sup> Furthermore, those living below this very low poverty line fell on average around 28 percent below it. Their average annual purchasing power therefore corresponded to approximately \$420 in the US in 2008 dollars.<sup>4</sup>

These are the poorest of the poor. The World Bank also uses a somewhat less miserly poverty line, namely \$2 dollar a day, or an annual amount of \$785.76 PPP 1993. The Bank's data show that around 40 percent of the world's population, or over 2.5 billion people, lived in income poverty so defined in 2004,<sup>5</sup> with this population falling on average 41 percent below this higher line.<sup>6</sup> Individuals in this much larger group could buy, on average, about as much in 2004 as could be bought in the US in 2008 for \$690.



### The Effects of Global Income Poverty on Health

The effects of such extreme income poverty are foreseeable and extensively documented. It is estimated that around 13 percent of all human beings (830 million) are chronically undernourished, 17 percent (1.1 billion) lack access to safe water, and 41 percent (2.6 billion) lack access to basic sanitation (UNDP 2006, 174, 33). About 31 percent (2 billion) lack access to crucial drugs and 25 percent (1.6 billion) lack electricity (Fogarty n.d., IEA 2002). Some 780 million adults are illiterate (UNESCO 2006), and 14 percent of children aged between five and 17 (218 million) are child laborers, more than half in hazardous work (ILO 2006, 6).

Worldwide, diseases related to poverty, including communicable, maternal, perinatal, and nutrition-related diseases, comprise over 50 percent of the burden of disease in low-income countries, nearly ten times their relative burden in developed countries (WHO 2006b, 3). If the developed world had its proportional share of poverty-related deaths (one-third of all deaths), severe poverty would kill some 16,000 Americans and 26,000 citizens of the European Union each week.

The cycle of mutually reinforcing poverty and disease besetting low income countries, and particularly the poorer communities in these countries, could be broken by significantly reducing severe poverty. But it is also possible to make substantial progress against the global burden of disease more directly by improving health care in developing countries.

Poverty does not merely render poor people more vulnerable to disease, but also makes it less likely that they can obtain medical treatment for the diseases they contract. This is because in poor countries medical care is rarely available for free, and poor people are typically unable to buy either the care needed by themselves or their families or the insurance policies that would guarantee them such care. The price of health care in poor countries therefore also plays a crucial role in explaining the catastrophic health situation among the global poor.

### The Effects of Global Economic Inequality on Health

The following table presents the wealth and annual-income distributions of years 2000 and 2002, respectively, converted into US dollars at then current exchange rates. The figures give the per capita wealth and annual income for each decile. In 2000, owning property worth \$1,299 per person would have put a given household at the median of the global distribution: with half of humanity above and half below. In 2002, the median annual income per person was \$326.<sup>7</sup>

*Table 1: Global Wealth and Income Distributions*

	Wealth per capita, 2000, US\$	Household income per capita, 2002, US\$
Percentiles 1-5		57
First decile	61	70
Second decile	183	109
Third decile	407	148
Fourth decile	611	199
Fifth decile	1018	274
Sixth decile	1,629	410
Seventh decile	2,851	669
Eighth decile	5,702	1,198
Ninth decile	17,920	5,005
Tenth decile	173,300	19,497
Top percentile	812,700	48,400
Top percentile US only	4,810,000	397,000
Global average	20,368	2,758
Global median	1,299	326

Source: Sales data: CIPIH 2006, p. 15.

Reading these figures, we should bear in mind that the goods needed to meet basic needs are cheaper in poor countries—usually by a factor of three to five. Even after accounting for this difference in purchasing power for a given amount of income, it is evident that large segments of humanity are extremely poor. Spending \$5 on a course of treatment involves a serious sacrifice of other urgently needed goods even for people at the median. And, by definition, half of humanity has an income below the median, many of them far below.

Severe and widespread poverty like this has always existed. But it has never been so easily avoidable. The poorest *half* receive 2.9 percent of all household income worldwide, and 1.1 percent of all household wealth. In 2000, the bottom half had a wealth shortfall from the median that amounted to only 2.4 percent of the wealth in the top decile alone. And in 2002, the bottom half had an income shortfall from the median that amounted to merely 4.3 percent of the income in the top decile alone.

Access to an available medical treatment is a function of two factors: the price of the treatment in question and the money a patient's household can devote to purchasing this treatment. The discussion above has already described how extremely limited the financial resources of many poor households are. The other factor, the price of medical treatments, is normally determined by the cost of providing such treatments. These costs are often much lower in poor countries because it costs less there to build and maintain medical facilities, to pay doctors and nurses, and so on. A very important exception to this rule are medicines, on which households in developing countries are estimated to expend between 60 and 90 percent of their total health expenditures (DFID 2006, 1). Especially advanced medicines still under patent protection can be extremely expensive relative to a poor household's financial resources.

High prices for advanced medicines are often presented as related to the very high cost of researching and developing new medicines. This high R&D cost provides a general explanation of why many diseases concentrated among the poor have been neglected in pharmaceutical research: commercial pharmaceutical enterprises will research and develop only those drugs whose global sales they foresee to be profitable enough to cover research and development expenses plus some reasonable rate of profit on the funds invested. Other research efforts will simply not be undertaken. We discuss this topic further in the section "The Disease Burden in Developing Countries" below.

Once a new medicine has in fact been patented and brought to market, the pricing strategy of the patent holder is unrelated to its costs for research and development. The latter are what economists call *sunk costs*, now in the past. The objective of the com-

pany now is quite simply to maximize its profits over the term of the patent. We can illustrate this with the example of Lipitor, a blockbuster drug sold by Pfizer. This drug cost perhaps a few hundred million dollars to bring to market, but it currently earns the company around \$13 billion each year. Pfizer could lower the price of the drug considerably and still make a handsome profit on it. But why would the company do this? Its objective is to make money for its shareholders, and it will seek to design its global pricing strategy for Lipitor so as to maximize its profits defined as sales revenues minus ongoing variable costs for manufacturing, marketing, distribution, and the like.

The problems inherent in using patents as the incentives of choice for eliciting pharmaceutical innovation are very substantially aggravated by an extremely unequal economic distribution.

When setting a global pricing strategy for a patented medicine, a firm would ideally like to differentiate among its potential customers, charging each customer the most she or he is willing and able to pay (so long as this price results in a profitable sale, in other words, exceeds the long-run marginal cost). Now the optimal price for a patented drug depends on the demand curve, and this demand curve, in turn, depends on the distribution of willingness to pay among potential customers worldwide. As it happens, this distribution is extremely unequal. And the optimal global pricing strategy for most patented medicines is then to choose the highest price acceptable to national health systems, insurance companies, and potential patients in the affluent countries. At this price, the medicine will be bought, as needed, by the one billion people in the affluent countries and another roughly 400 million people in the developing world – altogether about one quarter of the human population. Any substantial broadening of the potential customer base would require substantial price reductions that, by greatly reducing the profit margin, would lose more in potential profits than they would gain (through sales to additional patients).

The problems inherent in using patents as the incentives of choice for eliciting pharmaceutical inno-

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vation described in chapter 8 are very substantially aggravated by the fact that, in our world, this mechanism operates in the context of an extremely unequal economic distribution.

### THE DISEASE BURDEN IN DEVELOPING COUNTRIES

Due to the mutually reinforcing effects of poverty and ill-health, developing countries suffer from a disproportionate share of the global burden of disease. This disease burden contributes to, and is exacerbated by, weak health infrastructure, including very low numbers of medical professionals in some areas, inadequate training, poor incentives and support systems for the medical professionals that are available, and inadequate health facilities, as well as limited transport, water, and sanitation infrastructure and weak educational systems. The lack of availability of medicines for diseases that predominantly afflict the developing world compounds these problems. Currently, developing countries account for more than 80 percent of the world's population but for only around 10 percent of global pharmaceutical sales (WHO 2006b, 15). The lack of market demand from developing countries leads inevitably to weak incentives for research and development into diseases which particularly afflict the poor. And to this is added the problem that even when medicines are developed, they are often priced out of the reach of most patients in developing countries. These are problems which the HIF can help to rectify.

### Case Studies

Around six million people die every year from just three preventable and treatable infectious diseases—AIDS, tuberculosis, and malaria. A brief discussion of these conditions and of some other tropical diseases (malaria is classified as a tropical disease) illustrates the devastating impact of weak health systems in the developing world, of which the lack of urgently needed medicines—due to the medicines being either too expensive, not available in drug outlets serving the poor, or simply not having been invented—is both a cause and a symptom.

### HIV/AIDS

According to the United Nations Programme on HIV/AIDS (UNAIDS), during 2007, 33.2 million people were estimated to be living with HIV worldwide, 2.5 million people were newly infected with HIV and 2.1 million people were killed by AIDS. “Every day, over 6800 persons become infected with HIV and over 5700 persons die from AIDS, mostly because of inadequate access to HIV prevention and treatment services” (UNAIDS 2007b, 1, 4). Around 95 percent of persons living with HIV/AIDS reside in low- and middle-income countries (UNAIDS 2007a, 1). Over two-thirds of those infected with HIV/AIDS live in sub-Saharan Africa, including 90 percent of infected children, while 76 percent of deaths from AIDS in 2007 occurred in sub-Saharan Africa. Adult HIV prevalence reaches, and sometimes exceeds, 30 percent in parts of southern Africa. AIDS remains a leading cause of mortality, and the leading infectious cause of mortality, worldwide and the primary cause of death in sub-Saharan Africa, which continues to bear a hugely disproportionate share of the HIV/AIDS disease burden (UNAIDS 2007b, 6–7).

A large proportion of those living with HIV/AIDS in developing countries do not have access to treatment due to the high cost of anti-retroviral medicines and poor health infrastructure. At the beginning of this decade, it was estimated that only five percent of those in need received AIDS medication. A number of governmental, intergovernmental and non-governmental efforts have been undertaken to improve the provision of retroviral medication to developing countries, including the WHO's 3 by 5 initiative, the US President's Emergency Plan for AIDS Relief (PEPFAR), and Global Fund and Clinton Foundation HIV/AIDS programs. Despite these efforts, most recent estimates are that nearly 70 percent of the approximately 9.7 million people in need of anti-retroviral therapy had not received it by the end of 2007 (WHO 2008a). In best-case scenarios, anti-retroviral medication costs around \$100–500 for a year of treatment, but it often costs much more (MSF 2007, 6). Drugs priced even at the lower end of this cost range are well beyond the reach of the poorer half of the human population. Many of the people cur-

rently being treated with antiretrovirals will benefit from being switched to second-line, patented drugs, which often cost in the thousands of dollars per year per patient. The high cost of these drugs may make such a switch to preferred medicines impossible not only for poor patients to pay for privately, but will also stretch the budgets of donation programs.

### *Tuberculosis*<sup>8</sup>

It is estimated that tuberculosis (TB) killed one billion people during the past two centuries. Though TB cures have existed since the middle of the 20th century, and though TB medication is relatively inexpensive, TB remains the second leading infectious cause of mortality worldwide, killing 1.7 million people yearly. One-third of the world's population is infected with the latent form of the disease, and 5 to 10 percent of these are expected to develop active illness at some point in their lives. There are almost nine million new active cases each year and approximately 15 million persons are living with active TB at any one time.

The WHO declared TB a global health emergency in 1993. Though TB rates had been steadily declining in developed countries since the early 1800s, the disease started to make a come-back during the 1980s, largely as a result of HIV/AIDS (which promotes susceptibility to TB) and the growing problem of drug resistance. New York City spent over \$1 billion fighting an epidemic of multi-drug-resistant TB (MDR-TB) that plagued the city's prisons, hospitals, and homeless shelters during the 1980s and 1990s.

TB had all along remained a major problem in developing countries, which account for 95 percent of TB cases and 98 percent of TB deaths. This is largely due to lack of access to medication and the fact that the spread of TB is fostered by the poor nutrition, overcrowding and lack of sanitation and hygiene associated with poverty. The TB problem in poor countries has been exacerbated in recent decades by HIV/AIDS. The overall TB burden is highest in Asia, but the highest prevalence rates occur in sub-Saharan Africa.

In 1995 only 23 percent of those in need worldwide had access to WHO's recommended TB treat-

ment regimen. Treatment access increased to 56 percent by 1998 and 62 percent at the end of 2007. Although ordinary TB can be cured with a six-month course of medication costing only \$10–20, even this is commonly unaffordable for those who need treatment. Lack of affordability of TB medication is partly responsible for the problem of drug resistance, which is facilitated by people starting but not completing courses of treatment. This occurs in poor countries when patients cannot afford to continue medication, or cannot afford time off work or travel costs to clinics.

TB drug resistance levels are now higher than ever. MDR-TB is defined as TB resistant to at least two "first-line" TB medications. MDR-TB is usually curable, but treatment takes two years and is 100 times more expensive than standard treatment. The "second-line" medications used to treat MDR-TB are also both more toxic and less effective than first-line medications. In 2006 the WHO and the US Centers for Disease Control and Prevention announced the emergence and spread of "extreme" or "extensively" drug-resistant TB—XDR-TB. XDR-TB is defined as TB resistant to two first-line medications and two or three second-line medications. It has been found in every region and in a total of 45 countries, with only 30 percent to 40 percent of patients surviving. Though new drugs are needed to treat it, no new TB drugs have been developed since the 1960s and none can realistically be expected to become available before 2015.

A 2007 case of suspected XDR-TB led to the first imposition of federal isolation/quarantine restrictions in the US since 1963, and XDR-TB patients sometimes face prison-like conditions in South Africa. Despite the Millennium Development Goal of reducing the incidence of major diseases including TB, the disease continues to kill 1.7 million people annually (WHO 2006b, 8).

### *Malaria*

Malaria kills over one million people, mostly children, every year, despite the fact that the current recommended and highly effective treatment for falciparum malaria, the most deadly variety, costs only

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\$1–2 per course. Like AIDS and TB, the heaviest burden of malaria is felt in developing countries, with 80 to 90 percent of malaria deaths occurring in sub-Saharan Africa (Selgelid 2007b, 73). Those who survive may suffer brain damage, learning disorders, and incapacitating weakness and lethargy later in life. The WHO observed in 2006 that “today, 58% of malaria cases occur in the poorest 20% of the world’s population, a greater proportion than that of any other disease of major public health importance in developing countries – and among poor people, the hardest hit by far are sick children and pregnant women” (WHO 2006b, 4). In addition to those one million deaths per year, there are between 350 and 500 million clinical episodes of malaria annually, again suffered mainly by poor people without health insurance (WHO 2005,intro.).

While many existing malaria drugs are effective and relatively inexpensive, the scale of malaria morbidity and mortality indicates that they are failing to reach those who need them, due to a combination of cost and poor health infrastructure. Until relatively recently, while it was widely acknowledged that new malaria drugs and diagnostics, including a vaccine, were needed, little R&D was devoted to this goal, undoubtedly because the extremely poor victims of malaria have little economic power and do not represent an appealing target for most drug companies. Grants from the Bill and Melinda Gates Foundation—one to establish the PATH Malaria Vaccine Initiative in 1999, another in 2004 to support research into the development of a semi-synthetic form of artemisinin, a key ingredient in first-line malaria treatments, to supplement the current botanical source—are partially redressing this situation, although it remains to be seen what impact these initiatives will have (PATH n.d.; Connor 2008).

### *Tropical and Parasitic Diseases*

Tropical diseases, most of which are parasitic infections, are almost exclusively confined to the poor. As a result, little has been done to develop appropriate drugs. Of the 1,556 new drugs approved for commercial sale from 1975–2004, only 18—just over one percent—were for neglected tropical diseases (Chirac

and Torreele 2006, 1560; Trouiller et al. 2002, 2189). In addition to malaria, these diseases include Chagas’ disease, Helminthic infections, human African trypanosomiasis, leishmaniasis, and schistosomiasis.

Spread by a sand fly, leishmaniasis is common in India and Sudan. Each year 1.5 million people develop cutaneous leishmaniasis and 500,000 the more serious visceral variant (CDC). Chagas’ disease, another potentially lethal infection, is common in South America, where in 2000 it was estimated that 16 to 18 million people were infected (WHO 2000, 10). In Sub-Saharan Africa, about 60 million people are estimated to be at risk of human African trypanosomiasis, better known as sleeping sickness, of whom “only 3 to 4 million . . . are under surveillance, with regular examination and access to a health center” (WHO 2001). Other common parasitic afflictions that continue to plague the poor are schistosomiasis, lymphatic filariasis and onchocerciasis (river blindness). Pharmaceutical research into these conditions, to the limited extent that it exists, is undertaken primarily by product-development partnerships largely dependent on philanthropic funds. While welcome, these partnerships will only go a small way towards redressing the longstanding neglect of R&D for diseases primarily affecting the developing world (Chirac and Torreele 2006, 1561).

## CONCLUSION

A vicious circle of poverty and ill-health afflicts many parts of the developing world. Measures directed at both the poverty and the health dimensions of the problem are needed. Major elements of the health problem are the high price of existing medicines and the lack of medicines that tackle some of the biggest sources of mortality and morbidity afflicting poor countries. As argued elsewhere in this book, the HIF could make a major contribution to solving (especially the second of) these problems by incentivizing new research on diseases which exact a large human health toll and encouraging innovators to distribute the fruits of their research at low prices.

However, high prices and lack of relevant essential-medicine R&D are by no means the only problems besetting the health sectors of poor countries.



Many developing countries are confronting major systemic problems in their healthcare sectors, with weak budgetary and administrative processes resulting in underfunding and/or poorly prioritized spending, leading in turn to shortfalls of trained and motivated health professionals, run-down facilities, poor administrative support and oversight and weak outreach, particularly in less accessible areas. These failings can constitute the “last mile problem,” which if not overcome means that medicines fail to meet patient needs even where they are available to Ministries of Health or other suppliers within a country. The HIF’s unique potential to address this problem is described in chapter 7.<sup>9</sup>

## NOTES

1. In 2002, there were just over 57 million human deaths. The main causes that are highly correlated with poverty were (with death tolls in thousands): diarrhea (1,798) and malnutrition (485), perinatal (2,462) and maternal conditions (510), childhood diseases (1,124—mainly measles), tuberculosis (1,566), malaria (1,272), meningitis (173), hepatitis (157), tropical diseases (129), respiratory infections (3,963—mainly pneumonia), HIV/AIDS (2,777) and sexually transmitted diseases (180). See WHO (2004, 120–5).
2. Such morbidity is due to the conditions listed in note 1 as well as other communicable diseases, including dengue fever, leprosy, trypanosomiasis (sleeping sickness and Chagas’ disease), onchocerciasis (river blindness), leishmaniasis, Buruli ulcer, lymphatic filariasis, and schistosomiasis (bilharzia). See Gwatkin and Guillot (2000).
3. \$1 PPP 1993 is the equivalent of the purchasing power that US\$1 had in the United States in 1993.
4. The World Bank’s poverty database PovcalNet ([www.iresearch.worldbank.org/PovcalNet/jsp/index.jsp](http://www.iresearch.worldbank.org/PovcalNet/jsp/index.jsp), accessed June 4, 2008) enables the user to duplicate the Bank’s poverty estimates as well as to produce estimates based on different assumptions. Aggregating over the set of all low- and middle-income countries gives a ‘dollar a day’ poverty headcount for 2004 of 17.75% and a poverty gap (the mean distance below the poverty line as a proportion of the poverty line) of 5.02%. These figures mean that, if the burden of extreme poverty had been spread over all people in the developing world, it would have amounted to a 5% average shortfall from the dollar-a-day line in 2004. But since this burden was in fact concentrated on the 17.75% of the total developing country population living in extreme poverty (the non-poor are counted as having a zero poverty gap), it amounted to a 28% average shortfall for the members of this group. The inflation calculator available at the US Bureau of Labor Statistics website ([www.bls.gov/cpi/home.htm](http://www.bls.gov/cpi/home.htm), accessed June 4, 2008) shows \$392.88 in 1993 dollars to be equivalent to \$584 in 2008 dollars. 72% (100% – 28%) of \$584 is \$420.
5. PovcalNet, <http://iresearch.worldbank.org/PovcalNet/jsp/index.jsp>, (accessed June 4, 2008) gives a 2004 poverty headcount using this poverty line of 46.75% of the population of developing countries and a poverty gap of 19.3%.
6. This is arrived at by dividing the 19.3% poverty gap by the 46.75% headcount (see note 4 above).
7. Global wealth data from Davies et al. (2006). Global income data were kindly supplied by Branko Milanovic of the World Bank. The wealth figure for the top percent of US households is calculated from Kennickell (2003, tab. 10 [year 2001]). The income figure for the top percent of US households is from Saez and Piketty (2003), as updated in “Tables and Figures Updated to 2006 in Excel Format,” March 2008, <http://elsa.berkeley.edu/~saez/>, tab. A6, cell D95 (accessed August 1, 2008), and dividing by average size of tax unit.



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8. This section draws on Selgelid (2008), primarily 10–13.
9. Mercurio (2006, 3) argues that the problems of inadequate health systems are so acute and pose such pressing problems in many parts of the world that in these regions “the impact of patents on public health is moot.” As chapter 7 shows, the HIF, while designed primarily to respond to weaknesses in the existing patent system, has the potential to help address the broader problems in developing country health systems to which Mercurio refers. See also the section “Appeal to the Poor Being Doomed Anyway” in chapter 6 for a discussion of the no-impact argument.

# Appendix B: Pharmaceutical Markets and Innovation

*While North America, Europe and Japan currently account for the bulk of pharmaceutical expenditures, rapidly ageing populations in the emerging markets of Asia could provide important new targets for pharmaceutical companies. However, these populations will lack the buying power of OECD members for the foreseeable future. The Health Impact Fund will enable manufacturers to take advantage of the enormous opportunities for profit this demographic shift brings, while benefiting patients. This Appendix also explores the importance of insurance in pharmaceutical markets, as well as the international rules governing the administration of patents.*

## INTRODUCTION

This appendix provides background material on pharmaceutical markets. Section 2 discusses the distribution of pharmaceutical expenditures globally, as well as their absolute size, and considers how income growth and changes in demography may change this distribution. Section 3 examines the importance of insurance in pharmaceutical markets. Section 4 examines the intersection of pharmaceutical innovation and patents.

## GLOBAL PHARMACEUTICAL MARKETS

Pharmaceuticals are becoming an increasingly important part of health care around the world. Drugs, when properly used, not only improve health but reduce other health care costs, and it seems likely that the trend to increased use of pharmaceutical treatments will continue.

While drugs have become more important for health, expenditures have also risen very substantially, with global expenditures on pharmaceuticals in 2007 estimated at over \$700bn, or approximately one percent of global income. Table 1 shows regional expenditures on drugs in 2005. The data shows ex-manufacturer prices; the final price to payers is considerably greater owing to the costs of pharmacy. The table also shows the global share of population

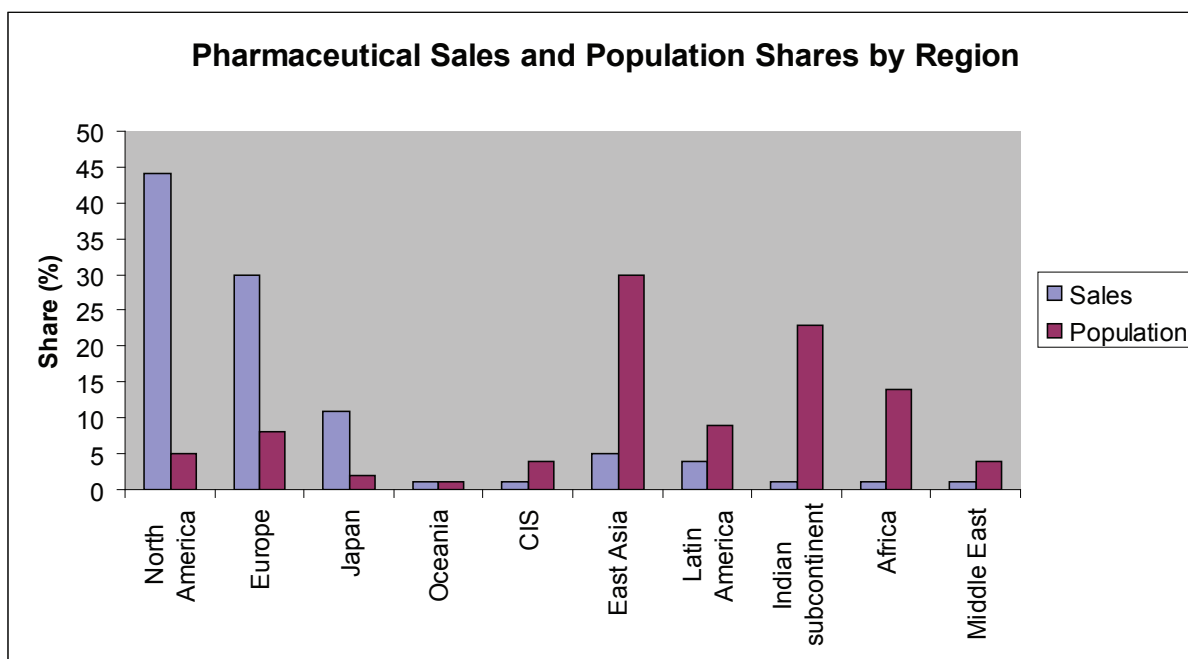
in each region in 2005. These data are represented graphically in Figure 1.

**Table 1: World Pharmaceutical Market by Region in 2005 (Ex-manufacturer prices)**

Region	Sales (\$bn)	Global share of sales (%)	Global share of population (%)
North America	268.8	44	5
Europe	180.4	30	8
Japan	69.3	11	2
Oceania	7.7	1	1
Commonwealth of Independent States	5.0	1	4
East Asia	28.8	5	30
Latin America	26.6	4	9
Indian subcontinent	7.2	1	23
Africa	6.7	1	14
Middle East	4.9	1	4
World	605.5	100	100

*Source: Sales data: CIPPIH 2006, p. 15. Population data extracted from Source: Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat, World Population Prospects: The 2006 Revision, <http://esa.un.org/unpp>, last accessed July 25 2008. (There may be imperfect matching of regions between sales and population, as the sales data does not disclose region boundaries.)*

Figure 1: World Pharmaceutical Market by Region in 2005



What is most striking about these data is the extent to which expenditures are dominated by North America, Europe and Japan, which collectively have 15% of the global population and 85% of pharmaceutical expenditures. This helps explain the interest pharmaceutical innovators have shown in addressing principally diseases prevalent in those areas.

What also appears clearly is that the emerging markets of Asia – and especially India and China – represent enormous commercial opportunities for pharmaceutical companies as populations age. A key feature for pharmaceutical markets in developing countries is the extraordinary growth in the proportion of the population over 50. In developed countries, pharmaceutical expenditures per person tend to rise with age. For example, Morgan (2006) shows that pharmaceutical expenditures in Canada rise by approximately 3.5% per year of age between the ages of 35 and 65. Pharmaceutical demand in developing countries is likely to be similar, and this implies that the rapid increase in the average age, and especially in the proportion of the population over 50, is likely to yield enormous increases in pharmaceutical demand.

China offers a good example of a population which is rapidly aging. Figure 2a shows the population distribution in 2008; Figure 2b shows the ex-

pected distribution in 2020. It is clear that there will be substantial growth in the population in older age ranges. The US Census Bureau figures shown here predict an increase of 45% to 455m in the number of people aged over 50 in just twelve years. A similar transition is occurring in India, where the population aged 50 and over is expected to rise 52% to 274m by 2020. The predicted increase in the population aged over 50 in the US and France, in contrast, is predicted to be approximately 25% and 17%, respectively.

Given this demographic shift in population age, demand for – and the potential impacts on health of – pharmaceuticals in the emerging markets such as India and China will unquestionably grow at a rapid annual rate for many years. For the HIF, the growth in the target population of older people who have a modest ability to pay for pharmaceuticals implies that there will be very substantial opportunities for new drugs which treat global diseases. Since incomes in developing countries will not rise to European levels for many years, drug companies will miss out on huge opportunities if drugs are priced to maximize profits from OECD sales only. The HIF will offer a way for drug companies to profit from the large populations in need of pharmaceuticals.

Figure 2a: Population Distribution of China in 2008

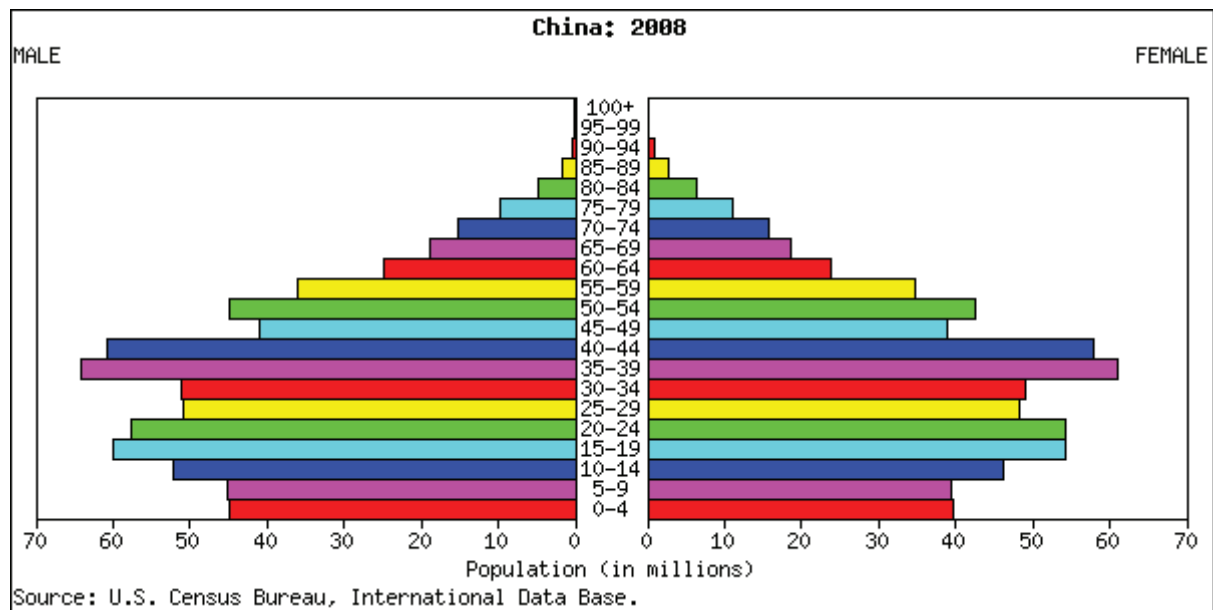
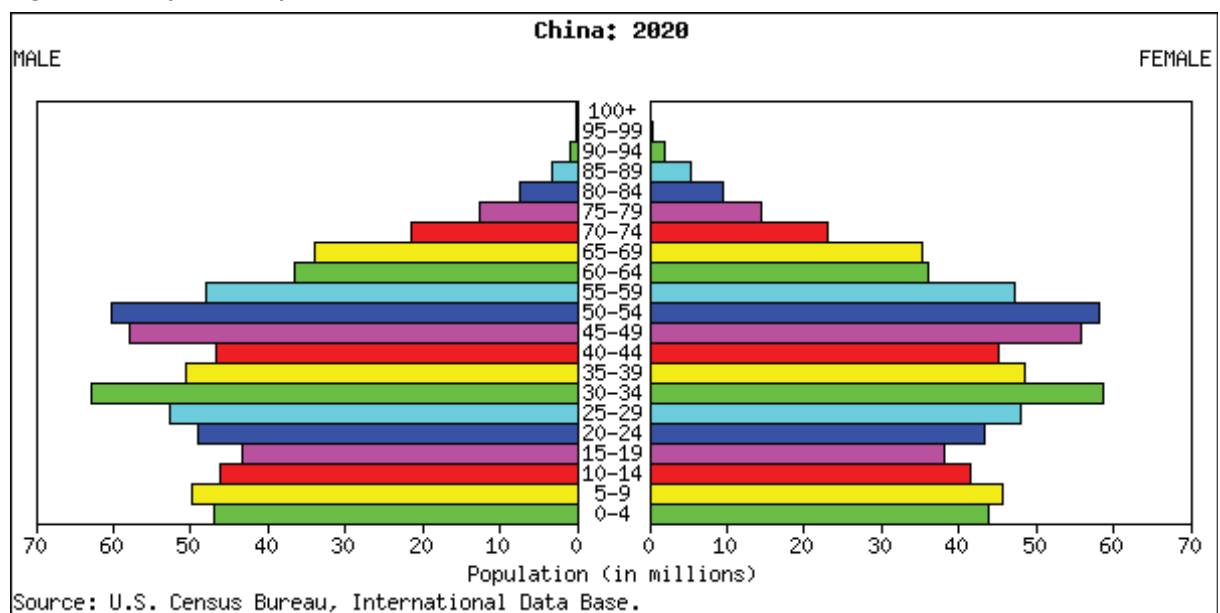


Figure 2b: Projected Population Distribution of China in 2020



## INSURANCE AND PRICING

Pharmaceutical markets are highly complex, and have many peculiar characteristics. In most developed countries – and for over 90% of total sales dollars as shown in Table 1 – patients rely on physicians to prescribe the pharmaceuticals they consume. Most patients in developed countries do not pay the full cost of the drug consumed, but rely (at least partly)

on insurance. Thus, one party chooses, another pays, and a third consumes, which makes pharmaceutical markets extremely unusual. This is not a market like that for automobiles, in which the consumer assesses the characteristics and prices of different cars, purchases a car, and then drives it. Thus, the simple assumption that what works in other markets should work in pharmaceuticals is likely to lead to mistaken policy conclusions.

The fact that prescribing is done by an expert is very important in pharmaceutical markets. First, it means that pharmaceutical firms tend to market their products primarily to physicians, since physicians are in effect the gateway to sales. Second, it means that the individual choosing the drug is in most cases completely insensitive to its price.

Patients, in many cases, are also insensitive to price, since they are fully or at least partially insured. This insensitivity is compounded by an inability to prescribe for oneself, either because of laws or because of uncertainty as to which product (if any) is the most suitable.

Insurers, therefore, cannot rely on patients or doctors to act as a controlling factor on drug prices. Instead, the insurer must try to control drug prices through bargaining over inclusion of the drug in the formulary. When a drug is too expensive, relative to its effect on health, the insurer may exclude the drug from reimbursement, which tends to lead to very low sales volumes, and may harm the patients who are therefore unable to benefit from the product.

Many countries in which the dominant insurer is government impose some form of price controls to achieve low prices without exclusion. The price controls have been based on a variety of factors, including drug company profits, and prices charged for the same product in other countries, or similar products in the same country. In many countries, cost-effectiveness analysis is applied explicitly in the coverage decision.

Using cost-effectiveness analysis as a tool to control the pricing of new drugs is problematic, since it encourages firms to price their product up to the limit of what the insurer deems to be cost-effective.

It is helpful to compare standard cost-effectiveness analysis to the HIF. First, the HIF only undertakes effectiveness analysis, and does not need to set any artificial thresholds to determine whether a given price meets that threshold. Second, rather than firms raising their price to the level at which the insurer is only just willing to include the product in its formulary, firms compete to obtain payments. Third, drugs registered with the HIF do not need to be rationed, or restricted on the basis of price, since the price to the patient is low and the cost to the HIF of having

another unit sold is zero, given a fixed reward fund. Fourth, the HIF has an approach to paying for innovation which focuses on incremental health impact, not total health impact, compared to no treatment at all. This means that “me too” or “follow-on” drugs which offer little therapeutic benefit obtain small payments from the HIF.

## INNOVATION AND PATENTS

### The Cost of Developing a New Drug

The costs of developing new drugs are enormous, not least because drugs require very expensive clinical testing before marketing approval can be granted. This section briefly reviews the process of drug development and the costs associated with it.

Identifying possible candidate new drugs for the diagnosis, prevention and treatment of disease often requires that hundreds or possibly thousands of compounds are made and tested before one is found that shows clear promise of producing desired results. The process might involve a series of test-tube experiments (assays) in which compounds are added one at a time to enzymes, cell cultures or cellular substances grown in a laboratory, with the goal of identifying which additions show important effects. Naturally occurring compounds such as fungi, viruses and molds can also be tested to determine whether they have a desirable effect on the target molecule. Computers can be used to simulate a chemical compound and design chemical structures that might work against it. And vast libraries of compounds have been built up that can be ‘mined’ through high-throughput screening for leads on potentially useful molecules.

Once a promising compound is identified, a period of rigorous chemical and pharmacological testing follows to identify possible toxicity to bodily organs and how the product is absorbed and metabolized by the body. Data from these tests are required by government regulatory agencies such as the US Food and Drug Administration (FDA), which must be satisfied that the drug (termed at this stage an ‘investigational new drug’ by the FDA) is reasonably safe before approving it for human use in initial, small-scale clinical studies. In the discussion below, the process

of regulatory approval in the United States is referred to. However, this process is similar to that in other developed countries.

It should be noted that not all pharmaceutical patent applications are for new drugs in the strict sense of the word (New Molecular Entities or NMEs). Applications for the approval of non-NMEs are common (around two-thirds of drugs approved by the FDA are non-NMEs) and typically involve alterations to the original drug to produce new desirable features relating to dosage or means of administration (CBO 2006, 2; GAO 2006, 8). FDA approvals for NMEs increased significantly over the 1980s and peaked in the mid 1990s, reaching a high of 53 in 1996. In the following years the number fell back, with only 20 NMEs approved in 2005. Approvals for so-called priority NMEs (the subset of NMEs that the FDA considers to offer a “significant therapeutic or public health advance”) have not shown a clear upward or downward trend over the last 20 years, moving largely in a range between five and eighteen annually (CBO 2006, 11-12).

Once approval is given for a new drug to be used on human subjects, three phases of clinical trials must be undertaken.<sup>1</sup> Phase 1 trials involve the initial introduction of the new drug into humans. These trials are closely monitored and usually involve healthy volunteer subjects. Phase 1 studies are designed to determine the metabolic and pharmacologic actions of the drug in humans, any side effects associated with increasing doses, and if possible early evidence on effectiveness. During this phase sufficient information should be gathered about the drug’s pharmacokinetics (what the body does to the drug) and pharmacodynamics (what the drug does to the body) to facilitate the design of well-controlled, scientifically-valid Phase 2 studies. Phase 1 studies normally involve from 20 to 80 subjects.

Phase 2 studies are designed to obtain preliminary data on the effectiveness of the drug for a particular disease in patients with the disease. This phase of testing also helps to determine any common short-term side effects and risks associated with the drug. Phase 2 studies are typically well controlled (they involve comparisons with control groups involving, for example, treatment with a placebo, no treatment,

or treatment with a known effective therapy), closely monitored and conducted in a relatively small number of patients, usually several hundred.

Phase 3 involves expanded controlled and uncontrolled trials. This phase is undertaken after preliminary evidence suggesting that the drug is effective has been obtained in Phase 2. Phase 3 trials are intended to gather additional information about the effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug. Phase 3 studies are also designed to provide an adequate basis for extrapolating the results of the studies to the general population and transmitting that information in so-called physician labeling, a primary means of providing critical information about drugs to practitioners (regulatory agencies such as the FDA review and approve the physician labeling initially proposed by manufacturers). Phase 3 studies usually include several hundred to several thousand people.

The FDA has provisions allowing promising new drugs (termed treatment investigational new drugs) to be used to treat desperately ill patients as early as possible in the drug development process. It has a specialized accelerated development and review program to speed up the development of drugs that promise significant benefit over existing therapies for life-threatening illnesses. It has a parallel track which allows patients prevented by their AIDS conditions from participating in controlled clinical trials to receive investigational drugs shown in preliminary studies to be promising.

Once the Phase 3 trials are complete, an application for approval to market the drug is filed with the relevant regulatory authority. The review process typically involves the reviewer attempting to confirm the applicant’s conclusions that the drug is safe and effective for its proposed use. It may involve a reanalysis or an extension of the analyses performed by the applicant. The review usually involves pharmacologists and toxicologists, physicians (to synthesize the results of toxicological, pharmacological and clinical reviews), chemists (to ensure that compounds are reproducible and stable; if a compound either can’t be reproduced or is unstable the validity of the clinical testing is brought into serious question); and statisticians (to evaluate the statistical relevance of the data



submitted in the application). Other areas of expertise are called in as required. The approval process may also involve inspection of the applicant's manufacturing facilities and clinical trial sites. It is only when this process is complete and approval is given that the applicant is able to market the new drug. Regulatory agencies typically undertake post-market surveillance, in which they reassess risks based on the analysis of new data gathered after the drug has come to market.

At each stage of the discovery and development process significant attrition occurs, with only a tiny proportion of compounds that begin the journey finding their way onto the market. According to the industry organization Pharmaceutical Research and Manufacturers of America (PhRMA), 10,000 compounds initially investigated might lead to 250 compounds receiving sustained preclinical testing. Only five of these will make it to the clinical testing stage, and only one of these will receive marketing approval (quoted in US Government Accountability Office: New Drug Development, November 2006). PhRMA suggests that the discovery of a new drug and the preclinical phase typically takes around 6.5 years, the clinical trials a further 7 years and the regulatory body's review process 1.5 years (GAO 2006, 8).

This lengthy process is costly, although exactly how costly is a matter for debate. DiMasi, Hansen and Grabowski (2003) suggest an average development cost per drug of at least \$800 million, but this has been questioned. Critics argue that the DiMasi figure is based on 'self-originating new chemical entities' (NMEs created entirely in-house by the drug company), the most expensive class of new drugs. It also includes the expense of using money for drug research rather than other investments (the opportunity cost of capital), while not including the tax deductions that companies ordinarily obtain for R&D. The US Government's Office of Technology Assessment found that, after subtracting tax deductions and the opportunity cost of capital, the cash outlay in 1990 dollars for the development of a NME was \$65.5 million (CPIH 2006, 17; Congress Watch 2001).

One of the important developments now occurring in pharmaceutical innovation is out-sourcing of research and of clinical trials. With increased glo-

balization of R&D, there are likely to be considerable cost savings. However, the extent to which those savings are realizable will in part depend on the development of suitable regulatory controls over clinical trials in developing countries.

## **Patents and the Discovery and Development of New Drugs**

A patent is a form of property right. It is a creation of government whereby a patent owner is given the right to apply to the legal system to stop unauthorized use of the innovation disclosed in the patent, typically for a period of 20 years. The patent system is designed to provide a reward for inventions which are made public, and it does so by temporarily preventing any competition relying on the patented innovation. Patents are particularly important in the pharmaceutical industry, since competition with generic products tends to be fierce and the costs of product research and development relatively high. In a purely free market system firms would be unable to recoup any investment in research and development, and would therefore not invest in it.

In the case of new drugs a patent application is usually entered when a promising compound has been identified and is ready to be subjected to pre-clinical testing. A patent application needs to demonstrate that the product (or process) for which the patent is sought represents a significant innovation. This requires a detailed examination of the field ('prior art') to support the claim to innovation.

Patents have a number of functions. By granting protection from competition for a specified time and therefore increasing the likely returns to a given product/process, they create incentives for investment. By giving agents in the development process property rights in particular aspects of their work they take on a transactional function, whereby the trading of these rights is facilitated, primarily through licensing agreements. Patents have a disclosure function, in that they require the patentee to make publicly available all relevant technical information about the patented product or process. Patents can also serve a signaling function by demonstrating a firm's innovative capabilities and thereby encouraging invest-

ment in the firm. This signaling function is especially important for start-up companies in fields such as biotechnology, which rely on protected intellectual capital to raise funding (CIPIH 2006, 20-1).

While all these functions are important, it is the incentive function that receives most attention. An important aspect the HIF is that it enhances the incentive function, while not harming these other aspects of the patent system.

### **Impact of Patent Law on Drug Discovery/Development Process**

Changes in patent law have had a significant impact on the development of the pharmaceutical and related industries. A US Supreme Court case in 1980, *Diamond v. Chakrabarty*, confirmed the patentability of genetic inventions. This decision was vital to the development of the biotechnology industry by investing property rights, and therefore potential commercial value, in knowledge in 'upstream' genetic technologies. The biotechnology industry has subsequently become a major contributor to research and development in biomedicine. Patents have also been important in facilitating the interchange of knowledge between institutions and disciplines, increasingly important in pharmaceutical research, through systems of licensing and contracts based on intellectual property rights (CIPIH 2006, 39-40).

The US Bayh-Dole Act of 1980 was another development with important ramifications for the pharmaceutical industry. To encourage the development and application of university-based research, this Act permitted universities to take out patents on inventions that arose from publicly-funded research (CIPIH, 40). A rapid growth of patenting in universities has followed, resulting in universities and public institutions becoming significant players in patenting and licensing in, among other fields, biomedical research and development.

According to the 'linear model' of scientific research, innovation is grounded in basic research which is motivated purely by the quest for knowledge, without commercial or industrial objectives (CIPIH, 33). This knowledge, according to the model, is largely paid for through the public purse in universi-

ties and research institutes, and is then readily available to (primarily) commercial interests to be turned into marketable products. However, closer examination suggests that basic science, applied research and product development are far more interdependent than this linear model suggests, with priorities for research often influenced by views about where opportunities for solving specific human problems lie (CIPIH, 34). The work of Louis Pasteur is a compelling historical example, with fundamental discoveries in microbiology and immunology resulting from Pasteur's desire to solve pressing medical problems.

Universities and publicly-funded research institutions have always played a role in applied research, often in partnership with the private sector. But changes in patent law have increased this role and encouraged the further involvement of universities in applied research. In many cases university scientists receive a share of licensing revenues which patents make possible, and many have played a role in establishing new companies to exploit the research conducted in their universities. The lines between basic (upstream) and applied (downstream) research have become increasingly blurred, as have the lines between the roles of universities, research institutes and commercial companies in pharmaceutical innovation (CIPIH 2006, 40).

### **Patenting: Scale and Trends**

In 2005 about 1.6 million patent applications were filed in patent offices around the world (WIPO 2007, 10). Five patent offices accounted for 77 percent of the patents filed. The Japanese Patent Office and the United States Patent and Trademark Office were the two largest in terms of filings, followed by the Chinese Patent Office, the Korean Intellectual Property Office and the European Patent Office (WIPO 2007, 12). The World Intellectual Property Organization's (WIPO) patent databases, which stretch back to the 19th century, show acceleration in the use of patents beginning in the 1960s. Since 1995 the average annual increase in total patent filings has been around 4.7 percent (WIPO 2007, 10). Pharmaceutical patenting forms a significant part of patenting activity, with pharmaceuticals and cosmetics the third fastest

growing field in 2006 in terms of international patent applications published under the Patent Cooperation Treaty (WIPO 2007, 30).

### The Internationalization of Patents

Patent laws are issued by national governments. They should therefore be expected to reflect national needs and priorities. For poor countries, cost-benefit considerations would seem to weigh against patents. The high prices of patented products represent a clear cost (in the case of pharmaceuticals, not just a financial cost but a human cost in increased mortality and morbidity), while the lack of research capacity significantly limits the ability of these countries to benefit from the incentives that patents offer. The balance is different in rich countries with substantial research capacities, and it is unsurprising that it is in these countries that patent systems have received most support and been most developed.

The existing pharmaceutical patent system is defined primarily by the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement, signed at the end of the Uruguay Round of the World Trade Organization (WTO) negotiations in 1995. This agreement governs nearly all aspects of intellectual property in international trade. TRIPS requires all WTO member states to maintain strict patent protection laws for patented pharmaceuticals, with a guarantee of at least 20 years of market exclusivity. The patent system, while still defined in domestic law and enforced in each national jurisdiction by its government, has now become effectively internationalized through the TRIPS agreement. Prior to TRIPS, different countries had different patent laws, which often reflected their level of development and the social goals that patent laws were thought necessary to achieve. Developed countries typically had the most restrictive patent laws, providing strong protection for monopoly manufacturing and sale of patented products.

Access to cheap generic versions of patented medicines ended in 2005 for most poor countries when the 10-year compliance window for TRIPS came to a close in all but the so-called least developed countries. WTO members were required to bring their domestic patent laws up to the standards of TRIPS,

effectively universalizing the strong patent protection favored in developed countries. TRIPS did contain a number of flexibilities – for example, it enabled countries to exclude from patentability therapeutic methods for the treatment of humans and new indications of known products which amount to a therapeutic method, and allowed patented products to be licensed for cheaper sale on various grounds (CIPHI 2006, 21-2). However, TRIPS provisions have in some cases been supplemented by bilateral “TRIPS-plus” measures as part of bilateral trade agreements that further strengthen the protection of pharmaceutical patents, sometimes extending monopolies beyond 20 years through “data protection”.<sup>2</sup>

Until quite recently, patent laws were much less generous to innovators in most developed countries than is now the case. It is therefore striking that even the poorest developing countries have been pressured to sign on to TRIPS at the same level of patent protection as that given in the most developed countries. It is clear that relatively poor small countries have little to gain directly from TRIPS, since they can gain little from domestic patents. Such countries can, of course, simply free ride on the innovation incentives created in the rest of the world, to which their own domestic patents would add only negligibly. However, their domestic consumers are harmed by the high domestic prices that patents enable. Developing countries have agreed to a standard of protection of ideas that is high even when compared to the level of patent laws which existed in developed countries only thirty years ago.

The TRIPS process has led to a significant degree of harmonization of substantive patent law. At the same time much has been done to harmonize patent administration, through greater cooperation between national patent offices and greater integration of countries into the Patent Cooperation Treaty.

### Patent Cooperation Treaty

The Patent Cooperation Treaty, which has 139 Contracting States, is a procedural treaty that allows an applicant to make one international application that designates countries that are members of the treaty as targets of a national application in that country.

(Applicants can exclude particular member countries if they wish.) While the PCT allows a so-called international application, this leads to national patents in the designated countries, not to one international patent.

Under the PCT, an international application has to be the subject of an international search, which lists so-called prior art (all existing similar developments or inventions) relevant to the patentability of the applicant's invention. An international search must be carried out by a patent office that has been appointed an International Searching Authority (ISA) under the Treaty. Along with the search report the ISA also provides a preliminary written opinion on the novelty, inventiveness and industrial applicability of the invention and thus on its patentability. Applicants under the PCT also have the option of requesting an international preliminary examination, which provides a more detailed analysis of the application. This examination is carried out by an International Preliminary Examination Authority (IPEA; all International Searching Authorities are IPEAs). A favorable IPEA report can lead to expedited passage through a national patent examination.

Most applicants with global patenting strategies begin the process by establishing a priority date in a major national office and then move to the PCT. The national filing gives them a period of 12 months under the Paris Convention for the Protection of Industrial Property in which to file a PCT application. From that filing applicants have a further 18 months before the international application turns into a bundle of national applications. Essentially applicants can therefore defer national entry for 30 months or so. Deferral of national entry is a common goal of PCT applicants since it allows them time to gather more information about the commercial desirability of moving to the national phase of the patent application process, and also enables them to defer the costs associated with that process (WIPO 2001). Companies from industries with long product development and marketing lead times, like the pharmaceutical industry, find advantage in delay, while those with relatively short lead times, such as information technology, may prefer to move quickly to grant. Both options are possible under the PCT.

While companies can use a number of different patenting routes to obtain a national patent, the PCT route has become the single most important one for most companies: it is a very important route for pharmaceutical companies.

Most national patent offices are part of the PCT system in that they function as receiving offices for PCT applications. However, only a few offices meet the standards needed to function as International Searching and Preliminary Examining Authorities in the PCT system.

### Cost of Patenting

Obtaining effective patent protection is enormously costly, in part because relevant patents may be filed in a variety of countries. Part of the difficulty is that pharmaceutical innovators are commercially motivated to file patents on as many aspects of a drug as possible, in order to protect their exclusivity for as long as possible. A recent report claims:

Scores of lawyers at both pharmaceutical and medical device companies now submit documents of 50,000 pages or more, in order to prevent the copying of not only the product but also the process. The submissions have to be made in all the companies' major markets and countries where generic manufacture and patent-busting is rife. The total cost of the exercise can reach US\$100m per product. [Deloitte 2005, p. 6]

Costs at this level represent about one tenth of the average cost of R&D for a new product. Therefore any mechanism which could reduce the costs of obtaining patent protection could be of immense value. The internationalization of patent administration may reduce costs over time by streamlining the examination work needed in each national jurisdiction. But the HIF may also have significant cost reduction implications, by allowing the innovator to choose not to patent in every country.

## SUMMARY

Pharmaceutical markets are complex and difficult. International differences in diseases, incomes, and demography make innovation and access problematic under our existing systems. Insurance for pharmaceuticals distorts incentives of buyers and sellers. And patents are complicated and their application to pharmaceuticals problematic because they are a general mechanism applied to a very unusual market.

The Health Impact Fund has the potential to address these problems very successfully, because its mechanism is specifically designed for pharmaceutical markets. And because it treats all human lives as of equal value, it is able to address international inequities in a morally appealing way.

## NOTES

1. The following discussion of the regulatory pathway for new drugs is based largely on CDER.
2. An important part of pharmaceutical innovation is the performance of clinical trials to demonstrate the safety and efficacy of the drug. Generic companies usually rely on the data from these trials as the basis for approval of their bio-equivalent generic drugs. Many countries now grant “data protection” of 5-10 years to the firm which performed the trials, preventing any generic company from obtaining marketing approval for their products on the basis of the trial data during that time. The period of data protection is frequently synchronous with the patent protection, though in some cases it may increase the period of effective protection from generic competition.

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## **The Health Impact Fund: A Pay-for-Performance Option for New Drugs**

The Health Impact Fund is a carefully conceived mechanism for improving global health. It rewards pharmaceutical innovators on the basis of measured health effects of medicines and vaccines they choose to register with the fund, in exchange for selling their product everywhere at cost. Patients all over the world get access at prices they can afford. And governments sponsoring this innovative fund are assured that their money is well spent.

This book lays out how the Health Impact Fund could work, and why it is needed.

**Incentives for Global Health** is a non-profit organization created by an international and interdisciplinary group of scholars and practitioners to promote the Health Impact Fund and other market-based solutions to public health problems.