Optional Rewards for New Drugs for Developing Countries

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NB: This version of the paper is an early draft. Please check against the most recent version at http://econ.ucalgary.ca/fac-files/ah/drugprizes.htm

Abstract
This paper proposes an optional reward system as a method for stimulating pharmaceutical innovation for diseases endemic to developing countries while also enabling access to the resulting drugs. The essence of the proposal is to offer rewards to drug innovators who relinquish their patent rights, with the reward to be based on the incremental health effects of the innovation in developing countries. The proposal offers the opportunity for innovators to be appropriately rewarded, with free entry into the system ensuring that the rewards will be on a suitable scale. Since the reward system is optional, it must confer a net benefit on drug innovators. The nature of the system also ensures that the rewards will be directed automatically towards innovations with high therapeutic value but which are not profitable to develop under the patent system. The system is scaleable, with greater rewards expected to induce more innovation. The paper presents an economic model to explore how the optional reward system complements the patent system.

1 Introduction
The incentives for research and development into drugs for diseases affecting the poor in developing countries are inadequate. The core, underlying problem is that while research and development of new, safe, and effective drugs is very expensive, sales to sick people in relatively poor countries do not provide a large revenue stream. If drug prices are high, sales are limited to the wealthiest people; setting prices low enough to attract more sales means that there is too small a profit margin to pay for the upfront costs of drug development. The result is that even useful drugs which have been developed with a view to profits in developed country markets are typically priced so high in developing countries that sick people and their governments cannot afford them; and drugs which would have their primary market in developing countries are never developed at all. This paper proposes a solution to these twin problems of access and incentives.

Other proposals have gone partway towards a solution for these urgent problems. Most recently, Kremer and Glennstetter (2004) and the Center for Global Development (2004) have described in detail a plan for “Advanced Purchase Commitments” for

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vaccines, which would commit a global body to pay a fixed subsidy per vaccine delivered for certain diseases, if the vaccine meets pre-specified technical requirements and is priced below some level. This would help to solve both access and incentive problems, but is necessarily limited to products whose technical characteristics can be described in advance, a characteristic which makes it difficult to apply to products which have not yet been developed. Other proposals have attempted to address the incentive problem through special bonuses paid to firms which develop drugs for neglected diseases. GSK has proposed a system of transferable exclusivity, which would allow a firm to extend its patent on a drug for rich countries; Ridley, Grabowski, and Moe (2004) and Moran (2005) have proposed a more modest reward: priority review for a selected rich country drug in exchange for developing a neglected disease drug. These proposals do not address the access problem, but help to increase incentives through creating distortions in markets in developed countries.

This paper’s contribution is the following. First, it develops a simple theoretical model to explore the properties of an optional reward system in which rewards are based on the relative social value of an innovation; and second, it proposes a specific method of identifying the relative social value of a medicine. It would be of particular value in creating incentives for drug R&D for the diseases which are particularly prevalent in developing countries, while also facilitating access. The essence of the proposal is as follows. An international fund pay-out fixed at, say, $1bn per year would be established. Any drug company could obtain a share of this pay-out by open licensing of the patents for a drug in all developing countries. Rewards would be allocated based on the share of total estimated incremental therapeutic benefit of these drugs, during the period that the company maintained relevant patents on the drug in the EU or USA. The international fund, jointly supported through commitments of donor nations and perhaps other donors, would determine the amount to be paid, using information submitted by the companies involved and other sources.

The principle benefits to this scheme are as follows. First, it would create an incentive for R&D for drugs which, though commercially unviable under the current system, would have large incremental therapeutic benefits. Second, the scheme is complementary to the existing patent system, including the agreements on medicines achieved in the Doha round of the TRIPS agreement, as well as other proposals such as the vaccines Advance Purchase Commitment scheme (Kremer and Glennerster, 2004). Third, it would enable drugs to be sold at average production cost to governments and other buyers in developing countries. Fourth, it is scaleable: whatever the size of the fund, it will increase incentives for drug development, and will consistently offer the largest incremental incentives for the drugs with the greatest therapeutic impact but the least commercial value. Fifth, because it is best at rewarding drugs with high therapeutic impact but little commercial value, it is directed particularly at drugs for the poorest people.

1.1 Innovation for neglected disease drugs

Neglected diseases are typically neglected because there are no profits to be made from medicines for them, even if candidate drugs were readily available. The problems involved in trying to make profits in developing country pharmaceutical markets are

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immense and the reasons for this unprofitability are many. Buyers in developing country markets lack the income or wealth to pay much for medicines. Often they are too young, too old, or too sick to have an income sufficient to pay for more than food. Typically they have no insurance, or very limited insurance. At the same time, developing country governments lack the financial resources to pay for expensive drugs. In addition, some countries do not have enough physicians to diagnose, prescribe, or follow up on prescriptions. Pharmacy mark-ups can be very large when prices are unregulated and pharmacies have local monopolies. Supply-chain control may be weak, allowing counterfeit products to capture a significant share of sales, harming both patients and the genuine supplier. Many countries impose heavy import tariffs or other taxes on medicines. And just in case those obstacles were insufficient to make development of drugs for impoverished countries unprofitable, under the 2003 Doha WTO agreements, countries can impose compulsory licenses to allow generic production so that in the event that a really successful therapy is developed, the patentee may never be able to make any meaningful sales at all. So while from the perspective of donors and international agencies, the value of medicines may be high, the patentee may be unable to appropriate very much of the social value of the medicine.

These problems, along with others, can create a real barrier to profitability even for medicines which have succeeded in clinical trials. The proposal in this paper can therefore help to address only some of these problems (since to achieve much higher standards of care will take much more time and money).

1.2 Appropriability

Appropriability is the ability of a firm to capture the “surplus” (or value) its innovation creates. The patent system is at heart a system of increasing the appropriability of an innovation. It does this through the grant of an exclusive use of the patented innovation for some period. However, even patentees are generally unable to fully appropriate the surplus in a market. There are a number of reasons why appropriability is incomplete. Other firms can imitate around a patent – in pharmaceuticals, this phenomenon occurs as “me-too” drugs during the term of the patents and generics after patent expiry. In addition, the value of a product varies with each consumer, so that unless firms are able to vary their prices by consumer – to price discriminate perfectly – it will not be possible to capture the entire surplus even in the absence of competitors. Assuming an inability to price discriminate, appropriability will typically be less when the demand curve is more convex to the origin. As Hollis and Flynn (2005) show, such convexity is likely to be relatively high in markets for essential drugs in developing countries because of the nature of the income and wealth distributions. Appropriability may also be low if there are large positive externalities, since consumers pay based on their private value, but the social value may be much greater. In pharmaceutical markets, from the perspective of international donors, the value of saving the life a person may be much higher than the ability of the person to pay – here the appropriability of social value under the patent system may be low, unless the patentee is able to get the international donor to pay for the drug. I discuss this point in greater detail in the following section. There are also positive externalities in cases of drugs for infectious diseases, since an infected person can unintentionally infect others.

Appropriability may also be excessive (greater than one) in the case of me-too drugs which capture profits from an incumbent while adding little in terms of therapeutic
options. (This is essentially the case of entry which is excessive from a social perspective because the “business-stealing effect” dominates the benefits from product diversity, as described by Mankiw and Whinston, 1986.)

Variation in appropriability across products is common in all fields – not just drugs – but pharmaceutical markets do have some special features which may make appropriability a particular concern. In particular, the convexity of the demand curve, the difference between the “market” value of a poor person’s life and the “social” value of a life, and the positive externality of drugs for infectious diseases, could in principle mean that appropriability is a particular concern in pharmaceutical and other medical markets.

1.3 Social Value

Social value in the context of ordinary markets is given by the integral of the demand curve. This may not always be the best measure of social value, since in some cases the demand curve of very poor, sick individuals may be extremely low because of income constraints. From the perspective of potential donors, the value of an individual’s life may be far above his ability to pay. (This explains, for example, why donors give food and assistance at times of famine and other crises.) If the donor could give some money to the individual, then the demand curve might rise. But since transactions costs of identifying poverty-stricken, sick individuals are very high (and because of moral hazard concerns), the donor cannot give money to the individual. Thus the demand curve will be below the social valuation of the product for the individual. In these circumstances, there is an externality from consumption of the product on the potential donor. Thus social value can be much greater than the integral of the market demand. In this paper, the definition of social value is the integral of the market demand curve after incorporating all such relevant externalities.

2 A model of an optional reward scheme

This section presents a simple model whose purpose is to show how an optional reward system relates to the patent system. The model is simplified to have an innovation stage, in which firms invest in research, and then, for research which is (stochastically) successful, a market stage. Each market is characterized by a total possible surplus $S_i$ in case an innovation is made, and a variable $A_i \geq 0$ representing the share of $S_i$ which can be appropriated by the innovator. $S_i$ assumes pricing at marginal cost and includes all relevant externalities. Appropriability varies between markets because of market structure, patentability, patent laws, the shape of demand, social versus private value, and so on. It is not necessary to specify the distribution of markets with respect to expected surplus and appropriability.

The timing of the model is as follows. In stage 1, firms invest in innovating. Firm $j$ will be successful in developing an innovation in market $i$ with probability $n(r_{ij})$, where $n$ is the probability of making a breakthrough in a market, and $r_{ij}$ is the level of research spending in field $i$ by firm $j$. $n'(r_{ij}) > 0$; $n'(0) \geq 0$; $n''(r_{ij}) \leq 0$. The research efforts of firms within a given field, and of the same firm within different fields, are assumed to be

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2 For a helpful analysis of the externalities involved in health care systems generally, see Evans (1984).
independent. After the investments have been made, some investments will be successful in the breakthrough.

An innovation leads to the exploitation of a given market in the second stage and some of the social value from each innovation can be appropriated for some given period, after which generic competitors arrive and no further profits can be expected by the innovator. If two or more firms are successful in innovating in the same field, they will each be able to appropriate only a fraction of social surplus. Thus private gross profits (after marginal costs of supply, but without considering research spending) are given by \( \pi = A_i S_i \). Note that \( A_i \) may be greater than 1. For example, consider an innovation which largely duplicates an existing technology and therefore adds little social value; if it captures some market share from the incumbent, its profits may represent an appropriation of social value greater than one.

Some caveats are appropriate. Both \( S_i \) and \( A_i \) will in general depend on research spending in all markets, since there may be complementarity or substitutability between innovations, but these effects are, on an expected basis, likely to be rather small, and I ignore them. I also assume, for the purpose of making the notation more transparent, that \( n(\bullet) \) is the same for all fields; however, in practice one would expect it to be different for each firm and field. This assumption is innocuous, however, since what is really important is the relationship between \( n' \) and \( S_{ij} \). Thus the variable \( S_{ij} \) can be thought of as having undergone a suitable normalization in this paper.

In the following sections, I compare three different systems for inducing innovation.

2.1 The baseline: R&D under the patent system

Research spending is determined by equating the expected marginal private benefits and the marginal private costs of \( r: n'(\bar{r}_{ij}) \bar{A}_i \bar{S}_i = 1 \), where the bar above a variable denotes its expected value. This equation implicitly defines the privately optimal amount of research in each field. Investment will be made only in fields for which \( n'(0) > \frac{1}{\bar{A}_i \bar{S}_i} \). Evidently, social surplus and appropriability are both important in determining research investment. As Figure 1 shows, research investment will be attracted only to fields in which both \( \bar{A}_i \) and \( \bar{S}_i \) are sufficiently high.

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3 However, note that each field has its own probability function: it is likely that spending in some fields will be more productive for all firms.
Figure 1
Innovation under the patent system

Notes: The shaded area indicates markets in which investment into innovation is profitable. This is only in markets in which both social value and appropriability are high.

2.2 R&D under a mandatory reward system
Now consider, as an alternative to the existing market with patents, a reward system as discussed in Hollis (2005). In this market, innovators must offer an open license for their innovations, and government rewards them with a share of a fixed fund $R$, based on the social surplus actually generated. The open license means that the innovator will not generally make significant profits from selling the product: the innovator’s profits are derived from the reward. I discuss below a method for identifying the social surplus of an innovation without reference to its price; for now, however, we will simply assume this to be possible. The share $\frac{S_{ij}}{\sum_j \sum_i S_{ij}}$ of the reward which each firm receives for any given innovation is equal to its share of the total surplus generated by all firms in all fields in which research investment was successful. For a given fixed reward fund $R$, investment will occur up to the point where the expected marginal profit from the reward equals the marginal cost of investment. Assuming that any firm’s share of total rewards is relatively small, this implies $n'(r_{ij}) R \frac{S_{ij}}{\sum_j \sum_i S_{ij}} = 1$, implicitly identifying the privately optimal amount of investment $r_{ij}$. The marginal market which will induce investment under the
reward system is determined by \( n'(0)R \sum_{i} \sum_{j} S_{ij} = 1 \). Note that the research spending is optimally allocated, given the total rewards available, in the sense that research is directed to the fields which have the highest expected social value per dollar of research investment. In addition, fields in which an innovation would have greater social value will receive higher research investment. Figure 2 shows the set of markets in which there would be an investment in innovation: notably, \( A \) is irrelevant in the mandatory reward system.

**Figure 2**

Innovation under a mandatory reward system

Notes: The shaded area indicates markets in which investment into innovation is profitable under the mandatory reward system. Only social value matters in this case.

There are two key differences between the patent and mandatory reward systems, offering trade-offs in multiple dimensions. First, while fields with high \( S \) and high \( A \) will induce research spending in both systems, the fields with high \( S \) but low \( A \) will be developed only in the reward system. Thus there is, from a social perspective, a better allocation of research spending in the reward system. However, by choosing \( R \), government determines the total amount of spending on research: this amount may be better or worse than under the patent system. It is widely believed that the patent system creates inadequate incentives for innovation, since the innovator is unable to fully appropriate social surplus. Thus if the reward system led to less (or much more) research than the patent system, that could be undesirable.
The second key difference between the systems is that in the patent system, monopoly pricing creates deadweight losses – that is to say, some people may not purchase the product even though their valuation of the product is above the marginal cost of production. The reward system allows for competitive production, which implies pricing at approximately average production cost, and a large reduction in deadweight losses. However, government rewards need to be financed, which implies deadweight losses through the tax system. Generally, deadweight losses are likely to be less in the tax system because the burden of taxation is spread more evenly across different commodities and income.

A third key difference is that in the reward system, the government needs to use some non-price method for determining the social value of an innovation, while in the patent system this occurs automatically through prices. Generally, it is believed that market prices are likely to be relatively efficient at sorting out relative social values, since markets effectively incorporate unobservable individual preferences. Pharmaceutical markets, however, may not work very well because of significant informational problems, externalities, and market power, as discussed in Hollis (2005). In these circumstances, it is possible that a non-price determination of social value may be preferable; section 4 below discusses this comparison at greater length.

3 An optional reward system

Now consider a third case in which the patent system is available and the reward system is offered as an option, where accepting the reward entails offering an open license of the patent. Given the presence of the patent system, not all innovations with high social value will be offered into the reward system. Those with high appropriability may prefer to exploit the patent. To understand the effect of an optional reward, we must first determine whether a firm with an innovation will choose to accept the reward or to exploit the patent.

We begin by defining the total social surplus of innovations rewarded by the fund as \( \Omega^R = \sum_j \sum_i S_{ij}^R \), where \( S_{ij}^R \) is the social surplus from an innovation which the patentee has offered into the reward system. A firm will choose to exploit the patent only if \( \frac{R S_{ij}^R}{\Omega^R} < A_i S_{ij} \), which implies a vertical iso-profit frontier between the patent system and the reward system at \( A^R = \frac{R}{\Omega^R} \). Along this iso-profit frontier \( A^R \), the appropriability of project \( i \) under the patent system is equal to the effective appropriation by the firm of social surplus through the reward payment.

The lowest value market which will induce investment under the reward system is determined by \( S^\min = \frac{\Omega^R}{n'(0)R} \). Consider the intersection of \( S^\min \) and the locus of \( (A_i, S_i) \) which is exactly sufficient to induce investment under the patent system \( A_i S_i = -\frac{1}{n'(0)} \). At the intersection, \( A_i = \frac{R}{\Omega^R} \). Notice that this is at \( A^R \).
This characterization allows us to draw a diagram of how the optional reward system interacts with the patent system, as shown in Figure 3. Fields with parameters in the darker shaded area will have some investment into research, and if successful innovations arise, the firms will choose the reward system for those innovations. Note that the innovations which are induced by the reward system are those with high social value and low appropriability. In fields above the curved locus $A_iS_i = \frac{1}{n'(0)}$ and to the right of $A^R$, investment in innovation is rewarded through the patent system. Fields below $A_iS_i = \frac{1}{n'(0)}$ and $S^{\text{min}}$ will not attract research investment.

Figure 3
Innovation under an optional reward system

Notes: The dark shaded area indicates markets in which investment into innovation is induced by the optional reward system, while the light shaded area indicates markets in which the patent system is preferred by innovators. The substitution between the patent system and the reward system is relatively small unless the reward system has very large rewards. The optional reward system induces investment into markets with high social value but which are unprofitable because of low appropriability.

It is noteworthy that the overlap between the reward system and the patent system is relatively small, if the $R$ is not extremely large. Innovations with high $S$ and high $A$ will continue to use the patent system, since the effective appropriation of social surplus under
the reward system is competed downwards by projects which have low appropriability under the patent system. Those projects which have relatively high appropriability under the patent system will always do better using that system, so that the reward system will complement, rather than substitute for, the patent system. This in turn implies that the reward system will, through the choices of firms, automatically reward firms which have projects with relatively low appropriability under the patent system, and relatively high social value. Thus the incentives to invest created by the reward system are focused on possible innovations which are of the greatest social value and which would not be developed under the patent system. From the perspective of governments which would fund a reward system, this should be a very attractive proposition.

Another interesting feature of the optional reward system is that it obviates the need to worry about how much to pay for a given innovation: rewards are determined by the share of social surplus created by the given innovation. At the same time, however, on average the rewards paid are guaranteed not to be excessive. This is because by construction the appropriation of social surplus through the reward system is equal to $A^R$, which is within the level of appropriability that the patent system allows.

In addition, it is not necessary to know exactly how large total rewards should be. The size of the rewards should be large enough to justify the cost of obtaining information on social surplus, and not so large as to eliminate use of the patent system. If all firms are choosing the reward system over exercising their patent rights, that implies that rewards are entirely substituting for the patent system and indicates that the reward may be encouraging too much research. (It is not necessarily inducing too much; since we don’t know the appropriate amount of research investment in the economy, it is hard to say. However, we would know that the reward system was inducing research on projects which would not have had sufficiently high social surplus as to be induced by the patent system.) What is more, the amount of the reward is flexible upwards over time; no firm would be hurt by an increase in the amount of the reward. However, a commitment of a minimum amount is required for some period of time going forward; a firm which invests in research on the basis of a reward in the future requires and deserves some assurance that the reward will be there. If the reward system did not offer a guarantee of continuing payments far out into the future, the incentives for undertaking research into fields with low appropriability would be very limited.

Since the reward system is a complement to – rather than a substitute for – the patent system, it increases overall investment into research. Consider other ways of increasing research, such as extending patent life, transferable intellectual property rights, or priority review vouchers. Those approaches increase the appropriability of a given investment, in effect shifting all markets (but not the lines) to the right in Figure 1. This would encourage research investment, but the net impact on consumers is uncertain, as they would benefit from more innovation, but at greater cost. The increase in incentives to undertake research extends through the entire area above (and just outside) the curved locus $A_i S_i = \frac{1}{n'(0)}$, including those areas of innovation which have high social surplus and high appropriability under the patent system. Thus firms which are developing very profitable products will be rewarded even more. Consider how this compares to increasing the incentives for research through an optional prize system. New research
expenditures are targeted to the area above $S^{\text{min}}$ and to the left of $A_i S_i = \frac{1}{n'(0)}$, i.e. at research with high social value but low appropriability. There is no excess payment to any such innovation, since the effective rate of appropriation is $A^r$. And deadweight losses are relatively small since they arise from the general tax system instead of from high prices on individual products.

4 How to make rewards depend on relative social value

While the attractions of a prize system, in which prizes are based on social value, over the patent system have been recognized by others (notably Gallini and Scotchmer, 2001; Abramovicz, 2003; and Shavell and van Ypersele, 2001), what has been lacking is a methodology for implementing it. There have been two general classes of methods for determining prizes or rewards. First, some proposals or actual prizes have identified a specific target which would be rewarded with a prize of a certain dollar value. For example, the “Ansari X prize” of $10m was offered for the first privately funded orbital vehicle which could make two trips within two weeks. Kremer and Glennstetter (2004) have proposed a purchase commitment fund for vaccines, in which vaccines meeting certain pre-specified technical and price requirements would be eligible to receive a subsidy per vaccine delivered. The practical objection to these kinds of prizes is that it must be possible to specify in advance the technical requirements to be met by the innovation. This makes it difficult to offer rewards for innovations which do not completely meet the prize requirements, but which may be very valuable. It also makes it very difficult to reward innovations whose technical requirements cannot be easily described in advance, a common problem for innovations which have not yet been developed.

The second general class of solution is to use the market to provide evidence on the private value of the innovation, and then to reward the patentee based on this evidence, while requiring the patent to be freely licensed. Kremer (1998) and Guell and Fischbaum (1995) suggest different versions of such a patent “buy-out” system. There are two important problems with this sort of payment scheme. First, it introduces no additional incentive for innovation, since the prize simply replaces the profits earned from the patent. (Thus, in terms of drugs in developing countries, this eases only the access problem but not the incentive problem.) Second, such an approach will typically encounter all kinds of difficulties in determining how much to pay for a given innovation. Under these proposals, it is not possible to rely on a relative measure of value: it is necessary instead to know the dollar amount that is to be paid directly.

In this paper, I propose a third class of rewards, based on relative social value without reference to private valuations and without specifying technical characteristics in advance, where the relative social value of a drug is measured by its impact on health outcomes. Most national health insurance agencies use a system of measuring whether pharmaceuticals offer “value for money” which of course implies that they are able to make some measurement of value. The standard measure of value in pharmaceuticals is identifiable impacts on health outcomes. From the perspective of donors such as international aid agencies which are funding health interventions, of course, impacts on health outcomes is in any case much more likely to be the thing which they are concerned about. A measure of value which relies on prices will typically give greater weight to the
welfare of the rich over that of the poor, which is hardly consonant with the objectives of an aid agency.

A useful measure of health outcomes would however, have to be meaningful across different health interventions. Fortunately, there are a number of such measures: so-called Quality-Adjusted Life Years (QALYs) are the most commonly used. QALYs represent a way of comparing effects of medical interventions across different patients and diseases. While not a perfect measure of health outcomes, QALYs or similar measures are arguably the best available measure, if one is interested in aggregating and comparing health effects of different medicines. In particular, QALYs need not be a worse proxy for social value than prices.

Using QALYs in this way is difficult, but not impossible. The first problem is that it would be necessary to have reasonable numbers about how many people were taking a given patented medicine. So this implies a better system of reporting than now exists in many developing countries. Such information could arise from evidence on prescriptions and from sales.

Another important requirement for the proposed system to be effective is that it has to be possible to make reasonably good assessments of the QALY impact of a drug. There are two key components to this. First, one must be able to assess the impact of a drug on health outcomes. This can be problematic, since different individuals respond differently to identical treatments, and it is sometimes difficult to identify what effect is attributable to the treatment and what effect is due to some other feature of a patient’s condition. However, every drug approved by the FDA must show efficacy, and the demonstration of efficacy essentially requires the observer to measure the health effects attributable to the drug. Therefore, this aspect of determining pharmaceutical value is in fact already performed universally. The second part of the analysis is to transform these health outcomes into QALYs, or a similar measure such as DALYs (Disability-adjusted life years), HUIs (Health Utility Index), or even a willingness to pay index. Essentially, this requires making judgements about the relative value of additional years of life against health levels and quality of life. Different individuals have widely varying willingness to trade-off various health outcomes, so attempting to standardize the weighting of health outcomes is not straightforward. Hedonic estimates have been

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4 Consider, for example, what would happen if a hospital in a wealthy part of Johannesburg were compared against a hospital in Soweto. If the only measurement were how much patients were willing to pay for the services rendered, it would turn out that for a given treatment, the hospital in Johannesburg gave much more valuable services. But why should the life and health of a rich person be of greater value than the life and health of a poor person? From the perspective of the market, the answer is simply given by willingness and ability to pay. But from the perspective of an outside observer – a donor living in Germany, for example – there is no obvious reason to favor one over the other, and the QALY measurement of social value seems much more appropriate.

5 And again, note that the current patent monopoly system already suffers from this sort of problem. Many consumers who try a drug do not in fact benefit from it, but the patentee earns profits nonetheless. Other patients must benefit immensely, but pay the same as those who are, perhaps, harmed by the drug.

6 In fact, much efficacy testing compares new drugs to placebos, which is not quite the same as showing efficacy compared to existing treatments. However, in principle the requirements for comparing against a placebo and against another treatment are the same.

7 One of the key problems in the use of QALYs and DALYs is to avoid the inference that the life of a disabled person is worth less than the life of a person without disabilities.
extensively used to value disabilities and compromised health status in terms of QALYs, but this is not an exact science.

QALYs have been recommended as the standard measure of healthcare outcomes by a task force of experts organized by the U.S. Public Health Service (Gold et al, 1996). Similarly, the OMB has recently been encouraging a greater use of cost-effectiveness analysis (using QALYs, DALYs, willingness-to-pay indices, etc.) in all regulatory decision-making by US government departments. So the US government is already basing decisions – at least in part – on QALY-type analysis, an indication that it has found a fairly high level of acceptance both inside and outside government. There is very extensive experience with evaluating QALYs related to drug treatments, since a large number of governments and other insurers all over the world use such an approach to determine inclusion of drugs on formularies, but this does not mean that the approach has been perfected, by any means. Drug companies have also used QALY-type analysis themselves in order to demonstrate economic effectiveness of treatments (Davidoff, 2001). Indeed, to the extent that organizations funding the reward proposed above are interested in rewarding pharmaceutical innovations based on their health effects, this is the obvious and direct measure to use.

Krupnick (2004) provides an up-to-date summary of issues related to QALYs and similar measurements. For an analysis of the theoretical validity of QALYs, see Doctor et al. (2004). A recent OECD study by Dickson, Hurst, and Jacobzone (2003) offers a guardedly positive analysis of the use of pharmaco-economic analysis, concluding that it is a “useful decision-making tool” but that there are difficulties relating to the quality of assessments, shortages of qualified staff, off-label use of drugs, and biased studies.

Many types of pharmaceuticals, such as psychotherapeutic drugs, present another difficult class to value in terms of QALYs. However, it is important to recognize that the difficulties faced would be no worse than the problems the patent system currently faces in determining optimal pricing or investment into R&D for such drugs. Indeed, the kinds of uncertainties are exactly the same as those present in current insurance markets, which have struggled with questions of what drugs they should cover. Given the optional nature of this system, and assuming some prediction of QALY impact could be given before the innovator committed a drug into the reward system, the problems related to determining how large a QALY impact a drug should have seem of secondary importance.

It is well known that QALYs have all kinds of drawbacks: they cannot be perfectly measured, and there are many problems with evaluating QALYs. (For example, is a healthy life year of life worth the same when the person is 15 as when the person is 75?) However, relying on the price system exclusively for value is probably even more problematic. Suppose that the characteristic of pharmaceuticals that consumers principally value is their effect on health. Then consumer willingness to pay must be based on their limited information about the health effects of a given medicine. But where do consumers (and their doctors) obtain information the effectiveness of prescription medicines? It arises mainly from studies which measure health effects, and which is summarized in terms of QALYs.

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Prescription medicines are characterized by economists as either “credence goods” or “experience goods” and consumers are unable to determine in advance whether the product will work for them, and may even be unable to tell after taking the medicine whether it worked or not. Generally, medicines are only effective and safe in a probabilistic sense: there will typically be some patients for whom a given medicine works well, which is why large-scale trials are generally necessary. The information from experience of a given medicine is useful, but probably not a better guide to prescribing than the information revealed in the large scale trials which is summarized in QALY-type analyses. In this sense, prices depend on QALY-type information, and so the information revealed by prices is a signal of QALY information. Thus, an argument that QALY information is of inadequate quality to provide reliable signals about the value of innovation is probably also revealing the same problem in the price system. QALYs by themselves do not indicate how large a dollar payment should be paid for innovation. However, by construction in the optional reward system, only the relative impact on health effects is required to be known.

5 The Mechanism

When a drug was approved for use in a country and the patent owner agreed to enter the reward scheme, it would be registered by a firm, normally by the owner of related patents required in the production of the drug. An International Pharmaceutical Innovation Fund (IPIF) would make payments to registrants, and in exchange for such payments, registrants agree to grant zero-priced licenses for all listed patents when used to sell the drug in a developing country. The payments would be annual during the period in which the registrant’s drugs were patented. Rewards might also be paid for court verdicts of invalidity or non-infringement which allowed for generic production without a compulsory license, as discussed in the appendix (S. 8). The purpose of this section is to outline how the fund should determine the reward for a given innovation.

Payments from the IPIF would be made based on the proportion of points attributable to a drug. Each patented drug in the reward system would be given points reflecting the gain in average therapeutic value less costs of treatment over that of the next best pre-existing treatment, for all units of the drug consumed in developing countries in a given year. Therapeutic value is determined by multiplying the incremental QALYs generated by the drug by the dollar value of a QALY. (In determining the next best pre-existing treatment, the IPIF should exclude patented medicines registered by the same firm and medicines relying on the same patented innovations as the medicine under consideration.)

In other words, the IPIF agency will determine the net benefit of a drug, and then compare it to the net benefit of the next most effective pre-existing therapy, and award points based on the improvement. These points would be awarded to the registrant for each year in which the registrant’s patents would, in the absence of compulsory licensing, be sufficient to prevent other firms from producing bio-equivalent products. Evaluation would be undertaken annually or as needed, based on the available information about a

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9 It is possible that a registrant might not own all the required patents, in which case registration would require the registrant to obtain a license to the patents from the patentee.

10 In the US, HR 417, the Medical Innovation Prize Act of 2005, suggests that firms should be eligible for rewards for ten years from the time the medicine is introduced.
Encouraging Pharmaceutical Innovation for Developing Countries

Each registrant would obtain a payment equal to the total reward fund multiplied by its share of the total points allocated. The total amount available to be paid should be fixed, with the share of the payment to each registrant being determined by its share of points. The registrant would obtain points for every sale of its drug, no matter who produced or sold the product, so that the reward is really for the innovation, clinical testing, and marketing of the drug. In principal, the innovator need not produce or sell the drug at all, though it would have an incentive to market the drug so as to increase the volume of sales on which it could earn points. In many cases, drugs are given for a variety of different conditions, and so the therapeutic value, as well as the next best therapies, would be different for different conditions. This implies that it would be useful to obtain evidence from prescribing doctors on what conditions drugs were prescribed for, through random sampling of doctors.

Since any drug that entered the reward system could be generically produced, prices should be expected to fall to approximately average production cost, which in the case of most pharmaceuticals is close to marginal cost. This would enable more widespread access than drugs that chose to use the patent system. Innovators would continue to have some incentives to promote their drugs, in order to increase the number of units sold, since rewards are linked under the mechanism to total sales.

6 Discussion

This section briefly discusses a number of issues regarding the proposal.

6.1 Predetermination of the QALY Value of an Innovation

It might be possible to determine the QALY value in advance of the decision to enter the optional reward system, subject to modification during the period of the patent, as new information came to light about the effectiveness, safety, and use of the drug. This would enable the innovator to make an informed decision about whether to enter the reward system: if the offered QALY value was too low, the firm would always have the opportunity to introduce its drug into the market as a patented drug without the benefit of any rewards.

6.2 Measurement of quantities

A more pressing problem is that of measuring how many units of a drug had been consumed. The problem is that in many developing countries, the system of controls on recording how many units of a drug have been prescribed or sold at the retail level is incomplete, and only estimates are likely to be available. A firm which was receiving a reward per pill consumed have an incentive to over-estimate the number of pills sold or consumed. While this is indeed a problem, it is not that dissimilar to the problems of

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11 Annual analysis would be useful mainly in cases where the therapeutic benefit of a product is not fully understood when it is introduced.
12 This would be particularly important for some drugs which have extensive off-label uses (uses for which the FDA has not approved the product). There are claims that up to half of all prescriptions are written for off-label uses. “How Drug Directory Helps Raise Tab for Medicaid and Insurers”, Wall Street Journal Oct. 23, 2003. IMS Health already conducts in the US a survey of this sort entitled the “National Disease and Therapeutic Index.”
counterfeiting already so common in developing countries. However, a major pharmaceutical company which was found to have engaged in intentionally exaggerated the number of pills sold in order to increase its reward could at least be punished.

6.3 Reversibility
A decision to enter the reward system would have to be irreversible, since once a drug was in the reward system, generic manufacturers would start producing it. If the patentee could simply pull the drug back out, it would impose unreasonable set-up costs on the generic manufacturers. This uncertainty would lead to less than the optimal amount of generic entry. However, there seems no reason why a firm could not start off by using the patent system, and then enter the reward system later, provided there was still some time left in its patent.

6.4 What would it cost?
One of the attractive features of this approach is that it is scaleable. In general, it will attract drugs which have high social surplus but low appropriability. These are the drugs which can make the most from the rewards and the least (given their social value) from the patent system. Therefore annual rewards could be $500m or $5bn – in either case they would add incrementally to the incentives for research into drugs for diseases that affect developing countries.

6.5 Should the fund pay rewards for all drugs?
Drug companies have substantial rewards for drugs which treat conditions common in rich countries. It is unlikely that the proposed system could add much of an incentive for research into such drugs, even if they were widely used in developing countries. On the other hand, incentives to perform research on diseases common mainly in developing countries, such as tuberculosis, chagas, and malaria, are obviously very inadequate. Therefore, to make the most of the additional incentives, it might be useful, at least if the total available reward was relatively small, to limit the payment of rewards to drugs relevant to a list of pre-specified diseases which were endemic in developing countries but not in developed countries. Limiting the list would require some arbitrary distinctions, but this need not be a problem as long as the list is clear in advance.

6.6 Bureaucratic/Political Control of the IPIF
Putting a large reward system in the hands of a bureaucracy is fraught with risks. Experience with regulated industries suggests that bureaucracies are liable to collude with regulated firms (“regulatory capture”); political interference leads to questionable decision-making; and government agencies may lack well-defined objectives and cost-saving incentives, leading to bureaucratic inefficiency. It is possible to mitigate some of these problems, but not, perhaps, to avoid them altogether.

In order to lessen the risks of “regulatory capture”, the IPIF should be of a fixed amount. Each firm could put forward its best case of how many points it should be awarded, and perhaps even present evidence to show why other firms should get less. The fixed total payout of the IPIF would lead to a zero-sum game so that firms would compete to obtain points. In these circumstances, collusion seems more difficult to sustain, although direct bribes by individual firms to IPIF employees could always be a

There would also need to be a substantial investment in analysis of health outcomes and health economics by an “International Pharmaceutical Innovation Fund Agency” to enable a reasonable allocation of points. With hundreds of significant drugs under patent at any given time, substantial resources could be required for determining QALYs and costs for all these medicines.

7 Summary
This paper has proposed an optional reward fund for pharmaceutical innovations for developing countries. The proposal offers a way to reward firms which develop valuable innovations while preserving access to the medicines by the poor. The optional nature of the proposal means that innovations which have very high market value will continue to use the patent system; but drugs which are of high therapeutic value but relatively low market value will be highly rewarded. The system thus rewards exactly the sort of innovations which at the moment are most desired but for which research incentives are lacking. The rewards would need to be funded – perhaps by governments in developed countries and charitable institutions – but offer a novel way to create incentives while preserving access. The nature of the rewards, for which firms would compete, means that rewards would be adequate, but not excessive.

This paper is only the first effort at considering this sort of system, and much more work remains to be done. Some obvious questions include the following. How large should total rewards be? Would the system face excessive costs of evaluating therapeutic benefits? How could the system be gamed? What would be the effect of limiting rewards to only some (presumably neglected) diseases? Which countries should be included, and should a life year in each country be valued the same? What would be required to ensure a reasonable estimate of volume of drugs produced? Where should patents be registered?
8 Appendix
This appendix shows the exact formulation for determining the number of points to be awarded for each patented medicine in the reward system.

1. The points allocated to medicine A in any year in which it had patent exclusivity for the medicine should be $\sum_i \left[ (vQALY_i^A - c_i^A) - (vQALY_i^B - c_i^B) \right] q_i$, where $i$ indicates the different possible conditions treated by a drug, $q_i^A$ indicates the amount of medicine A sold to treat condition $i$, $v$ is the standardized “value” of one QALY, $QALY_i^A$ is the average therapeutic benefit (in terms of QALYs) of a single unit of drug A when used for condition $i$, and $c_i^A$ is the per-pill treatment cost using medicine A (including the price of the medicine). $QALY_i^B$ and $c_i^B$ are the corresponding therapeutic benefit and cost of the most effective pre-existing treatment not using medicine A, for each condition $i$. All conditions for which the drug is prescribed should be included in this calculation, including off-label uses.

2. A person who was able to show in court the invalidity or unenforceability of all remaining patents on a drug should be rewarded with a share (say 10%) of the previous year’s reward for that drug.

IPIF payments of type (1) should be repayable by the registrant in cases in which a court determined that the registrant’s patents were invalid or insufficient to block generic competition in the absence of a compulsory license, with repayment retroactive to the date on which the registrant contested the claims of invalidity. Such repayment is necessary in order to discourage firms from filing speculative patent claims or opposing invalidity claims in court when there is little expectation that a finding of validity will be made.

Category (2) awards are necessary to provide an incentive for firms to eliminate invalid or unenforceable patents. Under the current system, generic firms have an incentive to discover invalid or incomplete patents because the first generic firm to obtain FDA approval to market obtains a 6-month generic exclusivity period in the US. Under the proposed system, any person would have an incentive to discover invalid patents, or non-infringing processes. Discovery of invalid patents and non-infringing processes would free up resources in the IPIF to pay for genuine advances in drugs. At the same time, however, it is important to ensure that the mechanism used would not encourage excessive, frivolous litigation in the hope of a favorable settlement. There is no reason to think that the proposed system would lead to more or less litigation, if the reward for discovering invalid patents were approximately the same as today.

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13 It is important to preserve incentives to demonstrate invalidity since the IPIF agency would then not have to have the expertise to determine patent validity.

14 The current system already suffers from a great deal of patent litigation. There is no reason to think that the proposed system would lead to more or less litigation, if the reward for discovering invalid patents were approximately the same as today.
9 References


