An Efficient Reward System for Pharmaceutical Innovation

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Draft – updated 28.06.2004 – most recent version at http://econ.ucalgary.ca/hollis.htm

1. Introduction

The global system of drug development and marketing is broken. Research spending is misdirected into products which add little therapeutic value to the medicine chest; and high prices for patented drugs are preventing access to life-saving drugs and distorting international trade. These worldwide problems – which are of immense importance – are results of the way the patent system is implemented, but they are not inevitable. In this paper, I describe an alternative implementation of the patent system to reward innovation and to provide medicines at their cost of production. The key to unblock the impasse of high drug prices is to reward drug innovators based on the therapeutic value their products create through a central Pharmaceutical Innovation Fund. Depending on the size of the fund, incentives for pharmaceutical innovation could be made larger or smaller than at present, but a fund with annual rewards on the scale of $100bn a year would likely provide more and better directed incentives for effective pharmaceutical innovation than exists under the current system. The incremental cost to governments of such a scheme would be relatively small – if anything – since they would save so much on pharmaceutical purchases. And because therapeutic benefits of drugs can be well identified using standard techniques, it is possible to make rewards proportional to therapeutic benefits in a predictable, meaningful way. In this paper, I describe how to implement such a system.

The proposed approach is not intended to be a replacement for the patent system. It maintains the patent system but establishes a different system of rewards based on patents. In the existing implementation of patents, government involvement in the market is through preventing other firms from using the patented innovation, but there are no direct government payments for innovation. Governments also intervene in pharmaceutical markets in most countries through price controls. In the proposed system, government would not be involved in the market at all, but it would retrospectively determine the therapeutic benefit of an innovation in order to make a payment to the innovator. So it should not be assumed that the proposed system somehow involves "more government" than the existing system, which depends on very substantial intrusions into competitive markets. Nor, to re-emphasize the point, is the proposed system in any way getting rid of the patent system. It simply replaces the old patent reward (the right to profits obtained through exclusive use of the innovation) with a new

type of patent reward (a payment based on the incremental therapeutic benefit of the product).

Many other proposals have been made for prizes and rewards to be used in place of patent monopolies, but the current proposal is much more limited in its ambitions, as it applies only to pharmaceuticals. There is a reason for this: the purpose of pharmaceuticals is to improve human health outcomes. Within this single area, there exists a widely used technique for measuring value known as Quality Adjusted Life Years, or QALYs. This measure can be used to roughly aggregate health effects of medicines across individuals with different levels of health. The use of QALYs thus enables a comparison to be made between the therapeutic benefits of different drugs in a standardized way. Such a comparison is much more difficult for other types of products – are cars or computers move valuable? – because in the absence of market prices we lack a standard measure of value across such commodities. Health outcomes can also be tricky – is a "lifestyle" drug treating 10000 people more valuable than a cancer drug treating 100? – but insurance programs all over the world have been undertaking such comparisons systematically for many years now using QALYs and other similar approaches. The implementation of the QALY technique in deciding which pharmaceuticals to fund in a number of jurisdictions around the world has been highly successful, and it offers strong encouragement for a broader application of QALYs to determining how much to reward pharmaceutical innovations.[2] There are problems with the use of QALYs (as discussed below) but while imperfect they are also a reasonable measuring stick for health outcomes.

There are other reasons for thinking that innovation in pharmaceutical markets should be treated differently from innovation in other areas. Patents are exceptionally important in pharmaceuticals, more so than in almost all other industries, because similar but not identical medicines do not typically create strong price competition. Pharmaceutical markets are also special because the person choosing the medicine (the physician) is not the consumer, and often the consumer is also not paying, at least directly. So the usual incentives to control costs appear to be ineffective in pharmaceutical markets[3] and there is a mismatch between the rewards to the innovator and the therapeutic benefit of the product. The current system makes the incentives for innovation dependent on this seriously dysfunctional market. The proposed system rewards innovation based on health outcomes, not willingness to pay or unmeasurable "utility", and this makes sense for pharmaceuticals, since it is health outcomes that are valued.

The proposal described here is related to Hubbard and Love (2004), but differs significantly from their approach because it includes a specific method for rewarding innovation based on the therapeutic contribution of a medicine. It also draws on proposals by Kremer (1998) and Abramowicz (2003). Kremer proposes a patent buyout mechanism which relies on prices at which firms would be willing to purchase patents.[4] Abramowicz

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[2] Indeed, there is a sense that in countries such as Canada, Australia, NZ, the UK, and some others, where cost-utility evaluation of pharmaceuticals is common, that rewards already are in part determined on the basis of QALY analysis.

[3] The limited effectiveness of competition pharmaceutical markets is of course one of the reasons that so many countries impose price controls only on pharmaceuticals.

[4] Notably, this proposal may solve the problem of deadweight losses but does little to direct research spending to therapeutically valuable areas.

proposes a flexible retrospective reward system. I begin by describing the special problems inherent in the relationship between the pharmaceutical market and the patent monopoly system; then present the details of the proposal, and finally address both how it could create value and what obstacles there could be to its implementation.

2. The Patent Monopoly System and Pharmaceuticals

The patent monopoly system functions particularly poorly for pharmaceuticals. As I describe in this section, it leads to misdirected innovation and advertising, to inefficiently high prices, to high volumes of counterfeit drugs, to parallel imports, and, indirectly, to price controls.

2.1 Misdirected Innovation and Wasteful Advertising

It is well known that monopoly exploitation of innovations under the patent system can reduce the benefits or "surplus" available to society from an innovation. This inefficiency is tolerated because the monopoly profits create an incentive to innovate, and in the absence of innovation, even less social surplus is created. The key to this trade-off between high prices and innovation is that the fact that people are willing to pay high prices for a good is an indicator that it is a valuable innovation. The greater the value to consumers, the higher the price the innovator can charge, and the greater the profits. Thus the reward to the innovator is at least roughly proportional to the value to society of the innovation. This means, in turn, that the incentive for innovators is to develop innovations that are valuable to society, since those innovations earn high rewards.

Unfortunately, the connection between value and reward is weak in pharmaceuticals. The reason is that pharmaceutical markets are hindered by exceptionally awkward agency problems. Doctors prescribe medications based on their beliefs as to the best medicine, somewhat influenced, presumably, by the extensive detailing and advertising focused on them. Since doctors do not pay for the medicines they prescribe, price is not an important component of their decision-making process. Consumers are typically ignorant of possible choices, and of the differences between various therapies and medicines and how these would relate to their own physiology, and may be paying only a fraction of the price of any medicine, or may pay nothing at all. The other part will be paid for by an insurer – possibly government or a private company – which has limited influence over the medicine prescribed.[5] In these circumstances, price is a relatively unimportant strategic variable for competition between drugs – detailing of doctors may be more important. Therefore, prices do not reflect value to consumers. For example, a product such as Nexium® which is therapeutically extremely similar to generically available versions of omeprazole is able to command a significant premium in the marketplace.[6] Drug companies can thus obtain substantial rewards by developing products with relatively little incremental therapeutic value. If product X is slightly better than product Y, it may be able to charge a huge price premium, because doctors will

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[5] Insurers typically use different levels of co-payment to influence drug choice.

[6] On the therapeutic value of Nexium ®, see Therapeutics Letter, June-September 2002, at http://www.ti.ubc.ca/PDF/45.pdf, last accessed June 13, 2004. The preference for many consumers of high priced branded products over essentially identical (but much lower priced) generics also provides interesting evidence for the weak role of price competition in pharmaceuticals.

prescribe it based on its therapeutic properties, without regard for the price disparity. The incentives to innovate are thus seriously distorted, because the rewards to innovation are based not on creating therapeutic value – which is what is valued by society – but on prices, which may or may not be related to therapeutic value.

2.2 "Deadweight losses"
The patent system as now implemented also causes substantial welfare losses because consumers who would buy the product if it were priced at somewhere nearer production cost do not buy it when priced at the monopoly price. The welfare loss caused by this is called by economists the "deadweight loss" of monopoly pricing, since there is a value lost to society when consumers do not obtain a product which they value more than the cost of producing it. In pharmaceutical markets, this effect is more severe the lower the level of insurance coverage, which means that it is especially important in developing countries. Hollis and Flynn (2003) show also that the incentives to innovate generated by monopoly pricing in developing countries may be very small in comparison to the deadweight losses created by high prices. The 2003 Doha agreement to allow compulsory licensed drugs to be supplied to developing countries is testament to the importance of finding a solution to the welfare losses (including death and suffering) caused by high pharmaceutical prices.

2.3 Counterfeit Drugs
The high prices of patented drugs, and the difficulty of verifying the legitimacy of products, has led to a flood of counterfeit medicines. Counterfeits comprise an estimated 10% of the global market for pharmaceuticals (Lybecker, 2003). Many counterfeit products are ineffective, do not contain the claimed amount of the active ingredient (if any), or are produced under unsanitary conditions, and may therefore have adverse health effects on consumers. Counterfeits also harm the innovating drug company by stealing their sales and, if the counterfeit product is ineffective, damaging their reputation. Counterfeits can thus also reduce the incentives to innovate.

2.4 Price Controls
Because of agency problems in drug markets, as well as the substantial deadweight losses caused by high prices discussed above, most developed countries with extensive government health insurance programs have implemented price controls. These price controls require extensive government interference in drug markets and are likely to be very inefficient.

Even in the United States, where the government has emphatically rejected the use of price controls, special price mechanisms regulate the prices at which pharmaceuticals are bought for some government departments (such as Veterans Affairs). The frequent legislative attempts in recent years to allow imports of drugs from other countries with some form of price controls is of course another mechanism for introducing price controls; and the constant comparison between US and foreign prices is a constant reminder to Americans that other countries seem to benefit from price controls. This suggests that even in the US, there is a possibility that price controls may eventually be introduced in various guises.

The prospect of price controls is also becoming more likely as pharmaceuticals become an increasingly important – and costly – component of health care, and as the willingness to pay of insurers is being tested by manufacturers' high pricing policies. Recently, a number of very high introductory prices, and substantial price increases of older drugs, have indicated that manufacturers are experimenting with the limits of what the system will accept in terms of high prices. A recent Forbes article pointed out that in 1994, cancer drugs could be used to extend a patient's lifespan by an average 11.5 months, at a cost of $500. In 2004, better drugs could be used to extend a patient's lifespan by an average 22.5 months, but at a cost of approximately $250,000, or 500 times as much. The article suggests that this model is unsustainable and that "it's likely that drug costs will have to come down and that some patients will be denied medicine because their chances are too slim."[7] Very high prices, particularly when government is the buyer, are extremely problematic. The government faces three choices. Either it uses its bargaining position as government to impose a price, or it declines to cover the drugs, or it simply includes drugs no matter what the price. Since not including the drug in the formulary leads to inferior patient outcomes and no profits for the drug innovator, this is not a good solution. That leaves the choice between price controls and simply paying whatever price is asked. Private insurance companies, in these circumstances, can negotiate a price, and are willing to back up their negotiating position with the threat of exclusion from coverage. But what is the back-up position of government? The threat of exclusion is essentially a way of enforcing price controls (Hollis, 2002). When drugs cost $500 for a treatment, they were simply included in the coverage. When drugs cost $250,000 for a treatment, governments can no longer ignore the option to bargain.[8]

As shown above, the patent monopoly system does not serve the pharmaceuticals market very well – it leads to misdirected innovation, to substantial deadweight losses, to counterfeit drugs, and to price controls. These features are not observed to the same extent in other markets. (For example, in automobile markets, consumers are relatively competent to assess product quality and to make informed decisions about purchasing based on prices, quality, and their own budgets. Automobile makers therefore have incentives to develop differentiated products which respond to consumers' demands. Deadweight losses are relatively small in automobile markets because prices are close to the cost of production, counterfeits are relatively rare, and price controls are not used.) This suggests that there are two requirements for an effective system of funding innovation in pharmaceuticals. First, the rewards for innovation in pharmaceuticals should be proportional to the value of the innovation to society. And second, prices should be near average production cost, in order to minimize deadweight losses and counterfeit drugs, and to eliminate the need for price controls. The following section details a proposal for a system which meets these requirements.

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[7] Cancer's Cost Crisis, Matthew Herper, Forbes Magazine, June 8, 2004. Garattini and Bertelé (2002) present similar information on the relationship between the incremental effects of new cancer drugs and their prices.

[8] Robert Wittes ("Cancer Weapons: Out of Reach", Washington Post, June 15, 2004, p. A23) characterizes the drug industry's rapidly escalating prices as "effectively daring the government to impose price controls."

3. The Proposal

This section describes a method for rewarding patented pharmaceuticals with payments or rewards paid out of a government-financed Pharmaceutical Innovation Fund (PIF). When a drug is approved for use in a country, it would be registered by a firm, normally by the owner of related patents required in the production of the drug.[9] The PIF would make payments to registrants, and in exchange for such payments, registrants would be compelled to grant zero-priced licenses for all listed patents when used to make and sell the drug. The payments would be annual during the period in which the registrant's patents would, in the absence of the licenses, be sufficient to prevent other firms from producing bio-equivalent products. Rewards would also be paid for patented cost-reducing process innovations, for exceptional discoveries not protected by patents, and for court verdicts of invalidity or non-infringement which allowed for generic production without a compulsory license. The purpose of this section is to outline how the fund should determine the reward for a given innovation.

Payments from the PIF would be made based on the proportion of points attributable, according to the following scheme:

1. Drugs which advance health should 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 sold by the registrant and by other manufacturers in a given year. Therapeutic value is determined by multiplying the QALYs of the treatment by the dollar value of a QALY. (In determining the next best treatment, the PIF 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 PIF 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, based on the available information about a drug.[10] See the appendix for more details on how this amount should be quantified.

2. Cost-reducing innovations should be granted points equal to the price reductions enabled by implementation of the patented innovation. Specifically, points allocated for cost-reducing innovations should be equal to the difference between the average price of the medicine set by all sellers using the patented innovation and the average price of those not using the innovation, times the number of pills in which the innovation was implemented. See appendix for more details on how this amount should be quantified.

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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] Annual analysis would be useful mainly in cases where the therapeutic benefit of a product is not fully understood when it is introduced.

3. Drugs representing significant breakthroughs in treatment, but which advance the field in a way not well captured by traditional patents, may be *exceptionally* rewarded with points. These exceptional rewards may not exceed 2%[?] of the PIF.

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

Payment of monetary rules would be according to the following ordering. First, the PIF would pay out any awards under (4). Each registrant (for type (1)) or patentee of a cost-saving process (for type (2)) would obtain a payment equal to the total available monetary reward multiplied by its share of the total points allocated under (1), (2) and (3). PIF payments of type (1) or (2) above 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.

2.1 Rationale for awards

Category (1) awards give to the drug registrant an award commensurate with the net benefit created by the drug. The net benefit is the benefit over existing therapies. Note that this is very different from the current system in which a me-too drug (one which is similar to another product already available) may be able to capture a large share of the market and make immense profits without adding much therapeutic value. The approach of using net benefit of a drug may be controversial; however, the rewards given under such a scheme must be more proportional to the real gain introduced by a therapeutic innovation than other approaches, including the current system. 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, perhaps through random sampling of doctors.

Note, for clarity's sake, that the registrant obtain points for every sale of its drug, no matter who produces or sells the product, so that the reward is really for the innovation and clinical testing 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 number of units on which it could earn points. Note that rewards would not be large for imitator drugs under this proposal, which would probably lessen the incentives to develop such products. Thus firms which developed first-in-class drugs would benefit from large sales volumes, less advertising expense, and high rewards based on therapeutic value.

Category (2) awards give to the innovator rewards which are due to the development of cost-lowering techniques. Note that the innovator is not required to share the cost-reducing process – if not patented, it can be used to lower only that firm's costs.

If patented, then it becomes protected and other firms will want to use it if it in fact lowers their costs. Since the innovating firm benefits from cost reductions at all firms adopting the low-cost process, it would in general be profitable to patent the cost-reducing technique. Rewards for cost-reducing innovations are also important to prevent the registrant from disclosing an inefficient, high-cost process when it registers the drug and then making money through selling the medicine at a price far above its true cost of production. (Without category (2) awards, no independent firm would have an incentive to invest in discovering a lower cost production method.)

Category (3) awards are potentially important in exceptional cases, particularly for products which have opened up new therapeutic avenues which cannot be fully patent protected. Similarly, certain types of therapies – such as taking Vitamin E – may be very effective therapeutically, but the patent system does not provide any incentive to undertake studies to demonstrate therapeutic effectiveness because of competition in the Vitamin E market (Hay and Lu, 1999). Awards might be made for studies of this type. Note that the discretionary payments should be limited to a small proportion of the PIF in order to minimize the risks of lobbying and collusion.

Category (4) awards are necessary since they would provide an incentive for firms to eliminate invalid or "incomplete" 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 non-infringing processes and invalid patents would free up resources in the PIF to pay for genuine advances in drugs.[11] 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.[12]

Before trying to evaluate the possible gains from this proposed system, I discuss in the next section some of the substantial, obvious problems that would arise in its implementation.

3. Obstacles to Implementation

There are a number of obvious difficulties in implementing the proposed mechanism. First, substantial government resources would be required to finance the rewards. Second, there is a legitimate concern over how large the PIF would need to be to induce the efficient amount of innovation. Third, a large federal agency would be required to perform comparative analysis of the therapeutic effectiveness of medicines and their costs. This would be costly and fraught with the risks of bureaucratic inefficiency and collusion. And fourth, there is a concern that it is not possible to identify therapeutic benefits of medicines with enough precision to make judgements over how to allocate rewards from the PIF. I address these in turn.

3.1 The cost of financing the reward fund
The PIF would require substantial investment to finance the rewards. If the fund were set to pay out $50bn annually, that would represent approximately 2% of the US federal

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[11] It is important to preserve incentives to demonstrate invalidity since the PIF agency would then not have to have the expertise to determine patent validity.

[12] The current system already suffers from a great deal of patent litigation.

government budget for 2005. To the extent that the proposed system required increased expenditures by government, it would require additional taxes to pay for the PIF. However, the government would also reap considerable savings from paying lower prices on the drugs it buys, and consumers could in principle pay more taxes given lower personal drug spending and insurance costs.

The savings to governments from lower pharmaceutical prices would be substantial and could allow even a very large PIF to be approximately revenue neutral. Currently, US federal, state, and city government spending on pharmaceuticals is approximately $100bn[13], of which around $10bn is spent on drugs available generically. Under the proposed plan, assuming little expansion of the quantities of drugs financed, and a 65% decrease in average price for branded products, government spending on pharmaceuticals would fall to approximately $42bn annually, for a savings of $58bn. Suppose that the US financed its own national PIF of $50bn (with other national governments funding their own PIFs for another $50bn, approximately in line with current global pharmaceutical revenues). Then US governments would require less, not more, revenues under the proposed system. In other countries, where the government share of pharmaceutical spending is higher, savings could likely be realized even with very substantial contributions to the PIF.

3.2 The problem of setting the fund at the right amount
$100bn annually would likely be large enough to provide incentives for more spending on innovation than we currently observe. Evidently the size of the PIF would be related to the rate of innovation. As the current scale of private-sector research spending *globally* is on the order of $50bn annually (Fleck, 2004), it should be possible to provide enough incentives under the proposed model to generate that much spending in the future. Given the importance and expense of drug marketing, however, it seems reasonable to propose that the size of the fund should be perhaps twice the size of total current R&D spending. It is difficult to estimate how large the fund should be; but even if it does not generate the "optimal" amount of investment in R&D, it is also true that the current system does not generate the optimal amount of R&D.[14] In order to make the proposed system credible, it is necessary that the incentives be large enough to stimulate at least as much R&D as occurs currently; and so this is why I propose that such a substantial annual payout from the PIF.

3.3 Bureaucratic/Political Control of the PIF
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 in general suffer from poorly-defined

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[13] This is a very raw guess – but Medicaid spending on retail pharmaceuticals is around $40bn, so including hospital spending plus city and state governments $100bn seems in the ball park.

[14] Economists (such as Kremer 1998) often assume that in order to induce the efficient amount of R&D spending, it is necessary for the reward to innovation to be equal to the entire social surplus created by the innovation. This is of course not true: all that is necessary to achieve efficiency is that the marginal reward should be equal to the marginal social surplus. Neither the proposal in this paper, nor the current implementation of the patent system, nor any other known mechanism, can make any pretension to being able to achieve efficiency in this sense.

objective functions 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 PIF 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 PIF 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 PIF employees could always be a risk. Sharing a fixed sum between innovators would also help to alleviate concerns of under-rewarding (Abramowicz 2003, p. 226), since the PIF agency would not have discretion to reduce total rewards if they felt that the innovations were inadequately productive.

Political interference with rewards might also be a concern. Government preferences for giving points to domestic firms would certainly be a problem. This suggests that the rationale for how points were to be awarded would have to be made public and fully documented.

There would also need to be a substantial investment in analysis of health outcomes and health economics by a "Pharmaceutical Innovation Fund Agency" to enable a reasonable allocation of points. With hundreds of significant drugs under patent at any given time, substantial resources would be required for determining QALYs and costs for all these medicines. Possibly such an agency would suffer from efficiency problems. However, there are several reasons for believing that such costs and inefficiencies are not an insuperably large problem. First, undertaking evaluations of drugs and treatments is socially valuable, since it enables better treatment. (At present, there is a case to be made that there is significant under-investment in "post-marketing" studies of drugs.[15]) Second, the costs of drug evaluation after the drug is already approved and on the market would be relatively small compared to the huge potential gains from the proposed system. Third, the bureaucracy would be less likely to suffer from inefficiency given a well-defined mandate of measuring therapeutic benefits and costs. Fourth, such an agency would to a large extent simply replace existing pharmaco-economic evaluation and price-control agencies in countries where they already exist.[16]

Aside from the expense of creating a PIF agency, such a process would inevitably engender significant lobbying efforts from innovators seeking to obtain the largest possible share of the pie. While this is undoubtedly true, it is also true that in most countries, there is already an active regime of price controls of pharmaceuticals, which must be subject to similar lobbying already. And even in the US, where price controls are not formally used, there is very substantial lobbying by the pharmaceutical industry. In addition, as I discussed in section 2.4 above, there is a serious possibility of some price controls being implemented in the US in the near future.

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[15] Indeed, the FDA sometimes mandates post-marketing studies of drugs; but a 2002 report found that only 882 post-marketing studies had been completed and filed with the FDA, out of the 2400 required during the period 1991 to 2000 (FDA, 2002)

[16] The burden on a PIF would be heavier than on most price-control type agencies, since it would require annual (not one time) assessments of therapeutic value in head-to-head tests. At the moment, most price control agencies only evaluate data submitted by companies, rather than commissioning their own studies. In principle, a PIF could continue to rely on such data, while requiring head-to-head studies of comparable drugs.

3.4 QALYs and economic valuation of drugs

An important requirement for the proposed system to be effective is that it has to be possible to make reasonably good assessments of the value 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.[17] 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.[18]

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), 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 during years 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 extensively used to value disabilities and compromised health status in terms of QALYs. (See Krupnick (2004) for an up-to-date summary of issues related to QALYs and similar measurements.) 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.[19] Nevertheless, there is a strong argument to be made that the inaccuracies inevitable in valuing health outcomes would lead to much smaller distortions in determining appropriate rewards for, and providing appropriate incentives for, pharmaceutical innovation, than the current system.

The most troubling set of conditions in terms of translation into QALYs are those treated by so-called "lifestyle drugs" such as Viagra®. The question of whether to reward products like Viagra® through the PIF would have to reside with the PIF agency; firms seeking to develop drugs for conditions such as male pattern hair loss might seek an exemption from the PIF if they expected that consumer valuations would be high in dollars but low in QALYs. (Section 5.5 below discusses another difficult set of drugs, those with both therapeutic and lifestyle uses.) However, in any case even Viagra® has been the subject of at least one rather controversial pharmaco-economic study trying to estimate its value in terms of QALYs (Smith and Roberts 2000).

A variety of other types of pharmaceuticals, such as psychotherapeutic drugs, present another difficult class to value in terms of QALYs. However, it is important to

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[17] 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.

[18] 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.

[19] For example, the NZ pharmaceutical management agency estimated that approval of a set of 5 drugs in the previous year had produced 199 QALYs (Pharmac, 2003, pp. 25-26)

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.

It is also worth observing that the OMB has recently been encouraging a greater use of cost-effectiveness analysis (using QALYs, DALYs, willingness-to-pay indices, etcetera) in all regulatory decision-making by government departments.[20] 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.

3.5 Other Risks

There are also some other risks to be considered in the proposal. Special care would be needed to minimize the risk of collusion between doctors or other buyers and drug registrants. If consumers were bribed to buy extra, unneeded units, the drug company could obtain extra points. This is the same sort of problem already faced by insurance companies, which have been successful in controlling it.

Whatever the rate of rewarding is, a point should never be worth more than one dollar, since if a point was worth more than a dollar, drug registrants would have an incentive to set their price below the marginal cost of manufacturing, thus eliminating competitive manufacturers and leading to inefficiently low prices.[21]

Finally, an important consideration in the proposal is the risk of other unforeseen problems. New and unknown, unexpected problems would arise. We already have a good knowledge of the problems inherent in the current implementation of the patent system in pharmaceuticals.

4. Benefits of Implementation of the Proposal

The potential benefits of the proposal are immense, including making drugs more widely accessible, eliminating inefficient pricing, improving the direction of research spending, and making marketing incentives more efficient.

4.1 Better direction of research expenditures.

The single most important effect of the proposal is that would make the incentives to innovate proportional in a meaningful way to social value. Firms that developed products with high therapeutic value would be highly rewarded, and firms that developed products which largely duplicated existing products would obtain relatively small rewards. Estimates of R&D spending in pharmaceuticals consistently show that a large fraction of expenditures are targeted at products offering little no therapeutic improvement over

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[20] See, for example, the speech by John Graham, Administrator of the Office of Information and Regulatory Affairs at the OMB on May 21 2002, available at http://www.whitehouse.gov/omb/inforeg/graham_speech052102..pdf, last accessed June 1, 2004.
[21] Points could be worth more than one dollar if costs were defined to include the price of the medicine as offered by other firms only. Alternatively, drug registrants could be discouraged from manufacturing and selling.

existing drugs.[22] In part, this is a function of the fact that it is difficult to develop new and highly effective drugs, of course; but it is also the case that firms find it profitable to imitate successful drugs.

4.2 Lower Prices and Elimination of "Deadweight Loss" (DWL)
Prices of medicines under this proposal would fall to approximately the average cost of production. Based on experience with drugs facing generic competition today, this implies that patented drug prices would decrease by on average 60% to 80%. This would obviously be beneficial for consumers and insurance companies, with total savings in the US of on the order of $150bn annually. Globally, savings might be on the order of $250bn. (This raises the question of whether a global $100bn PIF would provide adequate incentives for new innovation. The key is that the payment for innovation would reflect the value created to society, rather than the value created for the innovator given the dysfunctional pharmaceutical market. A more efficient reward system would enable large savings; and equally a reduction in copy-cat drugs would make advertising less valuable to firms.)

Aside from the reduction in total expense to consumers, there would be a welfare gain from increased consumption of lower-priced medicines. The deadweight loss (DWL) from the current patent system is certainly huge for pharmaceuticals. (Baker and Chatani construct a very rough estimate of $5bn - $20bn annually for the US. Globally, the DWL is certain to be many times this figure.) The DWL is, of course, really a health outcome measured in dollars. So another way of thinking about the impact of monopoly prices on welfare is that some consumers die or suffer needlessly because they do not buy essential medicines.

4.3 Reduction in counterfeit products
The proposal would substantially lessen the incentive to produce counterfeit drugs, since prices would fall to close to average production costs. Of course, some counterfeiting might still take place for products with relatively high production costs, but with lower prices, the profits from counterfeiting would be lower.

4.4 Elimination of price control regimes
The proposed system would allow for the elimination of price control regimes in countries where they exist, since prices would be near average production cost, and no significant gains could be realized by trying to push prices lower. There are several reasons why the patent plus price controls approach is inferior. Price controls, first of all, imply at least as much government interference and lobbying as the mechanism I have proposed, without all the corresponding benefits. Price controls are typically not sufficiently sensitive to the net therapeutic contribution of a new product, thus distorting incentives to innovate. Price controls are usually determined only on the basis of clinical trials before the drug is approved, and do not benefit from demonstrations of efficacy (or inefficacy) during the period of commercial sales. Price controlled drugs are not usually priced near production cost, but may not be priced in such a way as to provide a sufficient reward to innovation.

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[22] Love (2003), Lexchin (2003), and National Institute for Health Care Management Research and Educational Foundation (2002).

4.5 More efficient advertising
The proposed system of rewards would not prevent advertising by the drug registrant. Indeed, advertising which expanded demand could be profitable, since the registrant obtains points for additional sales, based on the average net benefit. However, the effect of this advertising would be wholly beneficial: advertising which increased sales such that the net benefit was negative (i.e. to consumers who had relatively low valuation of the treatment) would decrease the average valuation. So firms would have an incentive to advertise to obtain the largest number of users with a positive net benefit. Note that this is quite different from the current standard, in which advertising will typically increase both price *and* quantity sold. This means that advertising may be excessive, from a social perspective, since it enables the firm to charge higher prices, which do not increase social value. In addition, currently advertising to increase sales even to people for whom the net private benefit is negative may be profitable since the drug firm obtains a large mark-up on each sale.

The amount of advertising would also be reduced under this proposal because there would be fewer copycat drugs competing to attract a limited number of prescriptions. One way that firms compete is through advertising, implying that when there are fewer firms with competitive products, advertising may be reduced. The proposal in this paper would likely reduce the incentives to develop copycat drugs, leading to less head-on competition between close substitutes, and implying less advertising.

4.6 Reduction in total costs
The current system is wasteful, as described in the previous points, since it leads to large expenditures in marketing and in research into copy-cat drugs and line extensions. The proposed system could therefore actually cost less in total, with substantial savings to consumers. Criticisms of the proposal based on the assumed inefficiency of the management of the PIF should counterpoise this inefficiency against the immense inefficiency of the current system.

5. Other Issues

In this section, I consider a number of other issues not discussed above: the treatment of sequential innovation; the use of the patent system; international issues; transition issues; and drugs with dual uses.

5.1 Treatment of sequential innovation
An important feature of much current pharmaceutical innovation is small improvements in use and formulation of existing products. Therefore it is extremely important that any proposal on pharmaceutical innovation provide appropriate incentives for such incremental improvements. At present, as discussed above, there are some very inappropriate incentives for development of small modifications to existing products since they may enable firms to effectively extend monopoly prices.

Suppose that a firm develops an improved version of its own product (e.g. once-a-day instead of twice-a-day doses, leading to improved patient compliance). If the old

version of the product is no longer protected by patents, then this raises no particular problems. The firm could obtain some payment from the PIF based on the therapeutic improvement of once-a-day versus twice-a-day formulation.

If the old version is still protected by patents, however, then one needs to be more careful. The net benefit of the new product is the small therapeutic benefit over the older product. The older product might, in comparison with the newer product, have no net benefit. This would lead firms to have weak or even negative incentives to improve products currently under patent. Fortunately, there is a simple solution to this problem: when calculating the points attributable to a medicine, the PIF must not include any medicine registered to the same firm in the set of alternative therapies.

If the sequential innovation is patented by a firm other than the registrant, then in general it will raise patent issues: that is to say, that the new improved version of the drug will infringe on patents held by the firm which registered the older drug. In these circumstances, the new company may not sell the new and improved version without obtaining a license from the patentee of the old drug. It is desirable to have improved versions of products, but if the two products are therapeutically similar, then the newer product will not obtain substantial points, unless the older one is excluded from the set of comparison therapies when calculating the net therapeutic benefit. Therefore, to encourage sequential innovations, the PIF would not include medicines relying on the same patents in the comparison group for a given medicine.

Note that the treatment of drugs incorporating small improvements over prior versions would be much more sensible than in the current system. For example, in the current system, firms have been successful in introducing updated products with minor patented modifications which slightly improve outcomes. These products with monopoly prices replace older drugs which doctors do not prescribe. However, it is not evident that patients would choose the newer drug at the higher price if given a choice. The proposed system fixes this problem by providing an appropriate level of incentives for development of new and improved drugs.

5.2 Comments on the use of the Patent System

The proposed system employs patents as the method for determining whom the PIF rewards, and when. There are a number of reasons for using patents. First, using the patent system would allow for consistency between pharmaceuticals and other products in the treatment of intellectual property. Second, there is extensive experience with patents and their litigation. Maintaining patents as the basis for rewards would allow courts to continue to use their knowledge about patent procedures and litigation. Third, this method allows for the smoothest possible transition, since it enables extension of current patent control into the new system: that is, firms that currently own or are developing technologies, based in part on their understanding of the patent system, would expect profits based on the same patented technologies. Fourth, the patent system would allow for effective licensing of patented innovations. For example, if the production of a given drug required the use of patents owned by two firms, the drug registering firm could license the other's technology using a standard license, with terms such as royalties, fixed payments, or even a share of the reward from the PIF. (Note that a firm which produces a registered drug, but is not the drug registrant, would not have to pay

any license fees. License fees would only be paid by the registrant to the other firm holding a relevant patent.)

5.3 International issues

On the one hand, this model is ideal for levelling the playing field between countries, if all adopt it. Innovators could be resident anywhere; and with prices equal to the average costs of production, even developing countries would be well served. However, if not all countries adopted this model, then one could expect substantial parallel imports into the non-adopting countries. The asymmetries could lead to some problems of coordination between adopting and non-adopting countries with respect to pharmaceutical trade. But the model if adopted by many countries could be designed to allow for small contributions in developing countries, basically by assigning them a small multiple on QALY.

Two possibilities arise for the PIF: either it could be a full-fledged international organization, under the control of an agency such as WHO, or there could be national PIFs. A global PIF, however, seems unlikely to be attractive to many countries, which suggests that national implementation might be more effective. However, it would be necessary to ensure that countries did not try to shirk from carrying an appropriate burden of supporting research through their contributions to their own PIF. Hubbard and Love (2004) propose a mechanism for countries to participate in a scheme such as that envisaged above. Their proposal suggests that each country should either continue with the existing monopoly patent system or, as an alternative, agree to commit some fixed proportion of measured GDP to a pharmaceutical reward fund. The mechanism outlined above provides a mechanism for countries to determine how to allocate the reward fund. The mechanism is evidently beyond the administrative capabilities of many small, less developed countries, so some alternative approach would be required for such cases.

5.4 Transition Issues

In general, the transition to the new system is anticipated to take the following form. The PIFA would be organized some years before the start date to begin the task of assembling therapeutic effectiveness information. This might take some years, since there is a large backlog of existing medications. Drug registrants would begin to make submissions on existing and new medications concerning effectiveness. Then as of the start date, the patents on all patent-protected medicines in the US would become compulsory licensed at zero cost. (Of course, only approved manufacturers could supply the market, given FDA safety regulations.) It would be as if all drugs suddenly lost patent protection. All producers from that date would be required to submit monthly information on sales to the FDA, and payments could be made from the PIF to drug registrants on a monthly basis. Thus, the value of existing patented medicines would be maintained; although some medicines would become less valuable and others more, depending on their relative net therapeutic effectiveness.

Some transition problems would arise. For example, existing licenses from patentees might become in effect worthless. Licensees and/or patentees might find that previously negotiated contracts were undermined. In such circumstances, if negotiation failed, arbitration might be required to ensure reasonable outcomes.

5.5 Drugs with Therapeutic and Lifestyle Purposes

Some medicines have dual purposes which span both medical and lifestyle purposes. For example, Seasonale®, which suppresses menstruation, may be indicated for women with endometriosis, but it may also be used as a "lifestyle" drug for women who value its effects. While both types of uses are valuable, only the former can be reliably translated into QALYs. It is not obvious how one would deal with such situations. One option, where lifestyle uses were significant, would simply be to exempt the product from the proposed system. A second option would be use monopoly pricing, where (1) patients who purchased the product based on a medical indication would qualify for a rebate on the product from the manufacturer, and (2) the manufacturer would receive rewards from the PIF agency for medical indicated sales.

5.6 An Option for Restricting the Proposal

One option for implementing this proposal would be to make inclusion in the PIF program optional for the patentee; but to tie inclusion into the PIF program to coverage under government insurance plans. Thus innovators would have a choice between exclusive exploitation of the innovation under the usual patent system, but with reduced sales since the product would not receive any coverage under government insurance plans; or submitting their product to the PIF system, losing their ability to exclude others from the use of the patented innovations, but earning a reward from the PIF and having their product covered under government insurance programs.

This approach has some obvious benefits. First, it eliminates the problems of how to deal with products such as Viagra® since the manufacturer would have to decide whether to seek awards for therapeutic value contributions or to seek high prices. Second, the rewards system would be clearly tied into the government's existing contribution to medical expenses. Thus, in areas where the government has no involvement, no government involvement would be needed. Third, it would not in any way affect national and international commitments regarding patent rights, since the decision of firms to drop their patent rights would be voluntary. Fourth, this approach would force governments to establish a large enough PIF to encourage firms to include their products in the PIF system, since if the PIF rewards got to be too small, firms with therapeutically valuable drugs would choose to forgo the rewards plus insurance coverage, providing a useful indication that the PIF rewards were inadequate.

The optional approach also suffers from some problems. First, firms could continue to invest in products with small therapeutic benefit as long as they could persuade doctors to prescribe them, leading to the same problems as discussed above in Section 2. Second, some drugs would likely not be included in government coverage, reducing the value (but also the costs) of the insurance. In general, drugs with the lowest therapeutic value would be the ones most likely not to be included in the PIF system.

5.7 International Commitments

The TRIPS agreement negotiated under the WTO in the Uruguay Round requires countries to provide patent rights, including the right to exclude others from using the patented innovation. Fortunately, the proposal can be implemented without necessarily violating TRIPS. There are a number of possibilities. First, the option suggested above in S. 5.6 would not violate TRIPS. Second, countries could simply offer a choice between

severe price controls or the PIF system to patentees. Since price controls do not in themselves violate international patent agreements, offering a choice between price controls and the proposed system of licensing plus rewards would not be a violation of TRIPS either.

Mathematical Appendix

This appendix shows the exact formulation for determining the number of points to be awarded for each patented medicine.

1. The points allocated to medicine A in any year in which it had patent exclusivity for the medicine should be $\sum_i \left[\left(vQALY_i^A - c_i^A\right) - \left(vQALY_i^B - c_i^B\right)\right]q_i^A$, 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.

2. Points should be allocated to cost-reducing innovations based on consumer benefits from implemented cost reductions. Suppose drug A already exists, and it is registered to firm X. Firm Y develops a new process for making the drug which enables the firm to lower the price of the medicine, so that the treatment cost using drug A falls from c_i^A to $\hat{c}_i^A$. If the new process is patented, it becomes freely available for use in pharmaceutical products, without license fees. Now firm X, firm Y and others may use the new process. Firm X continues to receive points equal to $\sum_i \left[\left(vQALY_i^A - c_i^A\right) - \left(vQALY_i^B - c_i^B\right)\right]q_i^A$, using the original cost of treatment, without the innovation. Firm Y obtains points equal to $\sum_i \left(c_i^A - \hat{c}_i^A\right)\hat{q}_i^A$, where $\sum_i \hat{q}_i^A$ is the number of units sold in which the lower cost process is used. Note that the reward is the same even if a firm improves the production process for its own medicine, i.e. if firm Y is firm X. In case all firms switch from the old process to the new process, an estimate would have to be made of the price at which the drug would have been sold in the absence of the process innovation.

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