An Efficient Reward System for Pharmaceutical Innovation

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Abstract
Because pharmaceutical markets are dysfunctional, the patent system does not effectively stimulate drug research and development. Instead, it induces large amounts of research into drugs with little incremental therapeutic value, while providing inadequate incentives to innovate in really novel areas. At the same time, patents result in high prices which exclude many users from access to potentially life-saving therapies. In this paper, I propose a novel reward system for pharmaceutical innovation, in which innovators are rewarded based on the incremental therapeutic benefits of their innovation. This would align innovators' incentives with social objectives, and lead to the best possible allocation of research investment. With rewards paid directly to innovators, patents could be compulsory licensed to enable competitive pricing, thus solving problems of drug access. Government expenditures on rewards could be largely funded through reduced expenditures on patented drugs, and pharmaceutical innovators could continue to earn a healthy return on their investments.

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 prescription medicines at their cost of production. The key to unblocking the impasse of high drug prices is to reward drug innovators based on the therapeutic value their products create through national government-funded Pharmaceutical Innovation Funds. Depending on the size of the funds, incentives for pharmaceutical innovation could be made stronger or weaker than at present, but total annual rewards on the scale of $120bn a year globally would 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

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– since they would save so much on pharmaceutical purchases. And because therapeutic benefits of drugs can be reasonably identified using standard techniques, it is possible to make rewards proportional to therapeutic benefits in a predictable, meaningful way. This is exactly the outcome that the patent monopoly system is designed to obtain, but which it fails to achieve in the pharmaceutical market. In this paper, I describe how to implement such a system.

The proposed approach is intended to be complementary to the patent system. It maintains the institutions of patent system but replaces the existing 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). 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 would retrospectively determine the therapeutic benefit of an innovation in order to make a payment to the patentee. 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. Indeed, it is comparable in many respects with the commonly observed system in which the government provides drug insurance and controls prices.

An underlying limitation to this proposal is that it applies only to pharmaceuticals whose primary purpose is to improve human health outcomes, since this is the basis for valuing innovations. There are a number of widely used techniques for measuring health outcomes such as Quality Adjusted Life Years, or QALYs. These measures can be used to roughly aggregate health effects of medicines across individuals with different levels of health. While imperfect, the use of QALYs enables a comparison to be made between the therapeutic benefits of different drugs in a standardized way and thus to find a meaningful measure of the social value of an innovation. 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 to reward pharmaceutical innovations.[2] While there are problems with QALYs (as discussed in Section 5.4 below), they are also a reasonable measuring stick for health outcomes.

There are a number of reasons for thinking that innovation in pharmaceutical markets should be treated differently from innovation in other areas. First, patents are exceptionally important in pharmaceuticals, more so than in almost all other industries. Second, pharmaceutical markets are extraordinary because the person choosing the medicine (the physician) is not the consumer, and often the consumer does not pay, at least directly. Thus similar but not identical medicines do not typically create strong price competition, as I discuss below.[3] So the usual incentives to control costs appear to be ineffective in pharmaceutical markets and there is a mismatch between the rewards to the

[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] For a discussion of this point, and the effect of me-too medicines, see Lee (2004).

innovator and the therapeutic benefit of the product.[4] 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 in pharmaceuticals it is health outcomes that are valued.

There have been a number of other proposals for change to patent systems. The two principal directions for reform are funding research through direct grants from a government agency such as the NIH and replacing patents with government-funded prizes or rewards (Wright, 1983). Evidently, this proposal falls into the latter category. The main problem with prize and reward systems is in determining how large the prize should be: historically, prizes and rewards have typically been a small fraction of the social value of innovations (DiMasi and Grabowski, 2004). Scotchmer (2005, chapter 2) offers a discussion of the issues that arise in systems of prizes, and a review of their interesting history. Gallini and Scotchmer (2001) argue that a system of prizes will be the best possible mechanism for eliciting innovation "if the size of the prize could be linked to the social value" of the innovation, exactly what is proposed here.[5]

A number of recent papers have tried to develop proposals for alternative ways of setting up prizes which would enable adequate (but not excessive payments) to be made to innovators, in exchange for placing their patents in the public domain. Kremer (1998) suggests a "patent buyout mechanism", with a prize amount determined by the price at which firms would be willing to purchase the patent. Shavell and van Ypersele (2001) propose a system of optional patent rewards, in which government could offer a reward greater than the patentee's monopoly profits, but smaller than the social value of the innovation. Such a system would increase innovation and – if the rewards were not excessive – welfare. Guell and Fischbaum (1995) propose that governments pay a reward based on the profits obtained by a product in a test market. Abramovicz (2003) offers a comprehensive discussion of these and other proposals, and argues that, whatever mechanism is used, retrospectively assessed rewards could be helpful, and that the problem of under-rewarding of innovations could be avoided by requiring the rewarding agency to disburse all its funds while at the same time allowing firms the option of choosing between a reward and a patent monopoly. The key contribution made in my proposal is identifying an efficient method of determining the payment to be made to innovators, based on the therapeutic contribution of their innovation. Unlike the other proposals, mine offers both a way of alleviating inefficiencies caused by high drug prices and a method of directing pharmaceutical research towards the most socially valuable innovations. I agree that a fixed sum of rewards should be determined in advance (to avoid the problem of inadequate rewards), but defer the question of whether the reward program should be optional for firms.

In the following sections, I begin by describing the special problems inherent in the interaction between the pharmaceutical market and the patent monopoly system. I

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

[5] Will Masters (2004) proposes a more modest use of prizes as a supplement for patents in agricultural innovation. He suggests that prizes should be awarded with the amount to be equal to a fixed fraction of economic value of the innovation over a pre-determined time period.

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 marketing, to inefficiently high prices, to high volumes of counterfeit drugs, to parallel imports, and, indirectly, to price controls.

2.1 Misdirected Innovation

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. Underlying this trade-off between high prices and innovation is the understanding that if people are willing to pay high prices for a good, that indicates 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. This means, in turn, that the incentive for innovators is to undertake research that is valuable to society, since such innovations will earn high rewards. If rewards are not proportional to the social value, then the patent system cannot work well: it will lead firms to invest in innovations which have little social value, while ignoring avenues of investigation which could be of immense social value.

Unfortunately, pharmaceutical markets are among the least well functioning of all markets, undermining the connection between value and reward. 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.[6] In these circumstances, price is a relatively unimportant strategic variable for competition between drugs – detailing of doctors may be more important. In addition, prices in many countries are regulated by government. The result is that prices may be either too high or too low compared to the ideal market (one in which consumers are informed about the choices they make and then bear the full cost of those choices).

Since prices in pharmaceutical markets do not necessarily reflect value to consumers, profits are not likely to be proportional to the social value of an innovation. 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

[6] Agency problems in drug markets have been well-understood for a long time: Senator Kefauver noted in his 1959 hearings into drug pricing that "The drug industry is unusual in that he who buys does not order, and he who orders does not buy." (Cited in Maeder 2003)

the marketplace.[7] Drug companies may obtain substantial rewards by developing products with relatively little incremental therapeutic value over pre-existing products. If product X is slightly better than product Y, it may be able to charge a huge price premium, because doctors will prescribe it based on its therapeutic properties, without regard for the price disparity. Lu and Comanor (1998) using American data, and Ekelund and Persson (2003) using Swedish data, have shown that drugs categorized by the FDA as having "little or no therapeutic gain" are typically introduced at around the same price as existing therapies in the US and at about twice the price of existing therapies in Sweden.[8] Drugs with "modest therapeutic gain" were priced at around 2 times competing therapies in the US and 4 times as high in Sweden. 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 profitability, which is only weakly related to the incremental therapeutic value of a medicine. Exactly the same sorts of problems are created by poorly designed systems of price controls: the incentives to invest are distorted by the expectation of what price will be permitted by the regulator.

The result is that innovative effort is misdirected. 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 existing drugs.[9] 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.[10] Drugs such as Celebrex® and Vioxx® are examples of such products, as are the Viagra® imitators Cialis® and Levitra®, and numerous statins. It is not clear what proportion of research spending is devoted to me-too products, as the industry does not release data on spending by product. However, over 50% of R&D spending is used for clinical testing (DiMasi, Hansen, and Grabowski, 2003). Public data on the number of subjects in clinical tests suggests that only 20% of the R&D budget allocated to clinical testing is used for drugs which the FDA categorizes as offering a "significant improvement" compared to marketed products – the other 80% is used for products which do not offer a significant improvement (Love, 2003). It is not my contention that "me-too" drugs are without value. Evidently variety is important since not every patient reacts the same way to all drugs, and in some situations (such as antibiotics) having more drugs can help to protect against resistance, a point which Calfee (2000) makes eloquently. However, since me-too drugs do not typically result in large price reductions, it is likely that they attract more investment than is socially optimal.

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[7] 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. Another interesting case in which small (or even negative) therapeutic benefit has led to huge profits is the case of the two pain-relievers Celebrex ® and Vioxx ® (Juni, Rutjes and Dieppe 2002).

[8] Similarly, Lichtenberg (2004) finds that drugs which the FDA lists as "priority review" create a significant impact on population longevity, while "standard-review" drugs, which have therapeutic properties the FDA considers to be similar to those of already-marketed drugs, have no discernible effect on longevity. Prices of standard-review drugs are, however, typically similar to those of the previously introduced priority-review drugs.

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

[10] For more on me-too drugs, see Angell (2004) and Goozner (2004, chapter 9).

Not only is the R&D investment into "me-too" drugs likely excessive, me-too products harm the returns available to pioneer drugs by capturing market share from them even before patent expiry. This harms the incentive to undertake research into pioneer drugs, to the extent that the innovator expects a reduction in its period of exclusivity. So the result of the supranormal profitability of me-too drugs is both excessive investment in research with little therapeutic benefit and a reduction in the incentives for investment in truly pioneering research.

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 at the monopoly price. The welfare loss caused by this is called by economists the "deadweight loss" (DWL) of monopoly pricing, since there is a pure loss to society when consumers do not obtain a product which they value more than the cost of producing it. Guell and Fischbaum (1995), using highly aggregated data, claim that the scale of deadweight loss in the US drug market is on the order of $3bn- $30bn annually; in a more detailed paper (1997) the same authors estimate deadweight losses of $5bn on $8bn of sales, which indicates very large DWL for the market overall.[11] Baker and Chatani (2002) construct a very rough estimate for DWL of $5bn - $20bn annually for the US. Globally, the DWL is certain to be many times this figure, because in many markets, drug insurance is unavailable and so consumers are more price-sensitive.

Hollis and Flynn (2003) show 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 WTO Doha agreement to allow compulsorily 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. The problem of "access" to drugs worldwide is also creating a crisis of confidence in the pharmaceutical system worldwide, particularly as so many people in developing countries have been unable to afford drugs for HIV/AIDS, aggravating a humanitarian disaster.

2.3 Counterfeit Drugs

The high prices of patented drugs compared to production costs, and the difficulty of verifying the legitimacy of products, have led to a flood of counterfeit medicines. Counterfeits comprise a substantial share of the global market for pharmaceuticals.[12] 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.

[11] Douglas and Guell (2004) use US and Canadian data to argue that the DWL in the US market for a large number of drugs is at least 25% of sales.

[12] Lybecker (2003) claims that counterfeits may constitute up to 10% of the global market for pharmaceuticals.

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 cause a variety of market inefficiencies.

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 comparisons between US and foreign prices are 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.[13]

The prospect of price controls in the US 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."[14] 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

[13] For example, Pfizer's recent reduction of prices for low-income and uninsured consumers was widely seen as a strategic move to counter "legislative momentum behind price controls." ("Pfizer to discount drugs for the Poor," July 8 2004, *Financial Times*, p.1) At the same time, large private sector buyers have recently been active in establishing "buyer groups" in order to create leverage for price discounts ("Big Employers Join Forces in Effort to Negotiate Lower Drug Prices" by Milt Freudenheim, *New York Times*, June 12 2004).

[14] 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.

coverage. When drugs cost $250,000 for a treatment, governments can no longer ignore the option to bargain.[15]

2.5 Excessive Marketing

The problems in pharmaceutical markets that lead firms to undertake huge investments in order to develop products with relatively little therapeutic benefit can also lead to excessive marketing of the same drugs.[16] A product which offers little therapeutic benefit compared to other available products, but is sold at a high price, may nevertheless be marketed aggressively. Evidently, such marketing may be profitable for the firm, but it does little to generate real benefits for society to the extent that it reflects only competition for market share. Such competition for market share may even hurt real innovation, since the pioneer drug in a market must also engage in competitive marketing.[17] Looking forward, the pioneer firm knows that it will make less profits than if it were less likely to face such competition, and so the competition (which, recall, offers little additional therapeutic benefit) harms the incentives to innovate in the first place.

2.6 Summary

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, to price controls, and arguably to excessive marketing. 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 average cost of production, counterfeits are relatively rare, and price controls are not used.) This suggests that there are two crucial requirements for an effective system of funding innovation in pharmaceuticals. First, the rewards for innovation in pharmaceuticals should be proportional to the social value of the innovation. 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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[15] 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."

[16] Marcia Angell (2000) argued (plausibly, but without additional support) that "The fact is that marketing is meant to sell drugs, and the less important the drug, the more marketing it takes to sell it. Important new drugs do not need much promotion. Me-too drugs do."

[17] Note that competitive marketing is different from marketing when the firm is in a monopoly situation: monopoly marketing provides information to encourage prescribing of the drug and is presumably therefore useful. To the extent that competitive advertising is greater than monopoly advertising, it is likely that it is socially excessive. Note also that competition through marketing does not confer the same benefits on consumers as competition through price reductions.

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.[18] 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 drugs were patented. 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 categories:

(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 incremental QALYs of the treatment by the dollar value of a QALY.[19] (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.[20] See the appendix (S. 8) for more details on quantifying this amount.

(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 the appendix for more details on quantifying this amount.

[18] 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.

[19] The "dollar value of a QALY" is only material for determining the share of rewards between categories (1) and (2).

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

(3) 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 awards would be according to the following ordering. First, the PIF would pay out any awards under (3). Each registrant (for type (1)) or patentee of a cost-saving process (for type (2)) would obtain a payment equal to the total remaining monetary reward multiplied by its share of the total points allocated under (1) and (2). [21]

3.1 Some comments

Note that the registrant obtains points for every sale of its drug, no matter who produces or sells 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, perhaps through random sampling of doctors.

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 it remains secret and is 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 be profitable to patent the cost-reducing technique if the reward fund is large enough. 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.[22] (Without category (2) awards, no independent firm would have an incentive to invest in discovering a lower cost production method.)

Category (3) 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 invalid patents and non-infringing

[21] 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.

[22] Some countries require the patentee to disclose the "best" mode of implementing the innovation in the patent, which is similarly intended to avoid the problem of disclosing an inefficient process.

processes would free up resources in the PIF to pay for genuine advances in drugs.[23] 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.[24]

In the next two sections, I describe the possible gains from this proposed system, and some of the substantial, obvious problems that would arise in its implementation.

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, since category (1) awards give to the drug registrant an award commensurate with the net benefit created by the drug. Firms that developed products with high incremental therapeutic value would be highly rewarded, and firms that developed products which largely duplicated existing products would obtain relatively small rewards. This would increase the incentives to find new products with large incremental therapeutic value. And with fewer me-too products, and less incentive to advertise them (as discussed in section 2.5), profits of pioneer innovators would be even higher. While it is difficult to estimate the possible gain in terms of innovation, it would likely be substantial, since the incentives for socially valuable innovation would be increased. Thus it is no defence of the existing implementation of the patent system that the proposal would "undermine incentives for innovation."

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 50% to 80%. This would obviously be beneficial for consumers and insurers, with total savings in the US of on the order of $100bn annually. Globally, savings might be on the order of $200bn.[25]

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 immense in pharmaceutical markets. The gains from pricing drugs at approximately the average cost of production could easily be valued at $100bn, and gains in terms of saved lives would likely be very large.

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[23] 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.

[24] 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.

[25] This raises the question of whether global rewards totalling $120bn 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 reduce competitive marketing.

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 effectiveness (or ineffectiveness) during the period of commercial sales. Price controlled drugs are not usually priced near production cost, but may nevertheless fail to provide a sufficient reward to innovation. There is a more extensive discussion of how this proposal relates to price controls in Section 6.7.

4.5 More efficient marketing

The proposed system of rewards would not prevent marketing by the drug registrant. Indeed, promotions 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 marketing would be wholly beneficial: marketing which increased sales such that the net benefit was negative would decrease the reward obtained. So firms would have an incentive to promote the drug to obtain the largest number of users with a positive net benefit. However, the amount of promotion would be reduced under this proposal because there would be fewer copycat drugs competing to attract a limited number of prescriptions.

4.6 Reduction in total costs

The current system is wasteful, as described in Section 2, 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 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.

5.1 The cost of financing the reward fund

The PIF would require substantial investment to finance the rewards. If the fund for the US were set to pay out $60bn annually, that would represent approximately 3% of the US federal government budget for 2005.[26] 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 $80bn[27], of which around $10bn is spent on drugs available generically. Under the proposed plan, assuming modest 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 $35bn annually, for a savings of $45bn. Suppose that the US financed its own national PIF of $60bn (with other national governments funding their own PIFs for another $60bn, approximately in line with current global pharmaceutical revenues). Then US governments would require only a small increase in revenues under the proposed system. Consumers would benefit from substantial savings. 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.[28]

5.2 The problem of setting the fund at the right amount

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 I suggest here some rough figures to determine what amount would be necessary globally.[29] Evidently the size of the PIF would be related to the rate of innovation: I guess that global funds of about $120bn annually would likely be large enough to provide incentives for more spending on innovation than we currently observe. The fund would need to finance three major items: R&D, marketing, and profits.

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[26] An alternative calculation used below would base each national PIF on the share of world GDP: under this formulation, the US PIF would be approximately $40bn annually.

[27] This is a very raw guess – but Medicaid spending on retail pharmaceuticals is around $40bn, so including hospital spending plus city and state governments, $80bn seems in the ball park. There is likely to be a substantial increase in spending starting in 2006.

[28] For example, in Canada, the government share of drug expenditures is approximately 47% of US$14bn, so a reduction of 50% in brand prices would save the government around US$2.5bn, enough to pay for a PIF equal in size to 0.3% of GDP.

[29] I am using very crude guesses on current drug expenditures and costs at present and these are not intended to be more than illustrative.

The current scale of private-sector research spending *globally* is on the order of $50bn annually (Fleck, 2004), so we need to include at least that much for financing R&D. However, as noted above, the $50bn of R&D under the proposal described here would be better directed to generate real gains to health than under the current patent monopoly system. It is difficult to estimate how much total investment in R&D should be; but even if it does not generate the "optimal" amount, it is also true that the current system does not generate the optimal amount of R&D.[30] The uncertainty over the optimal size of the PIF is comparable to uncertainty over the optimal period of patent protection in the current system.

Second, under the proposed system, marketing would continue to be important, as described in Section 4.5, since the innovator would earn more profits if the drug was used more. The incentive to market the drug is desirable because the informational content of marketing, whether through physician detailing, free samples, journal advertising, study sponsorship, or directly to consumers, can be valuable. Globally, pharmaceutical marketing expenditures are on the order of $30bn.[31] Under my proposal, marketing expenditures would likely fall substantially as "copycat" drugs would have little incentive to advertise, and, in response, market leaders would also advertise less. In order to leave some room for marketing expenditures by innovators, the fund should be increased by approximately another $20bn.

Finally, there are substantial assets employed in the pharmaceutical industry on which a return is required. Currently, global innovator profits are on the order of $50bn annually. This implies that, in order to sustain the current level of expenditures on R&D, allowing for marketing and a healthy return on capital employed in the industry, the global sum of national annual rewards should be on the order of $120bn. Note that there is not any inherent notion here of paying firms for marketing or profits; but successful drug firms do promote their products and need profits. Those with highly valuable drugs would obtain payments large enough to pay for innovation, to market their products, and to reward investors, just as under the patent monopoly system.

One problem that arises is that the value of pharmaceutical innovation may vary over time (see, e.g. Calfee, 2000, chapter 4). However, if the average number of QALYs generated by pharmaceutical innovation appeared to be changing, that would provide a useful signal that the size of the PIF should also change.

5.3 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

[30] Economists sometimes 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, implying that consumers obtain no surplus from the marginal dollar of R&D investment. 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. See Outterson (2004) for more on the question of the optimal amount of pharmaceutical R&D.

[31] This is only a crude guess. I guess current global revenues at $400bn with expenses of $30bn on marketing, $50bn on R&D, and around $50bn in profits. There is a large component in the income statements of drug firms entitled "marketing and administration" which is much larger than the sum of marketing I have assumed.

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 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. Brill-Edwards (1999) discusses some problems with regulatory capture in the context of pharmaco-economic evaluation.

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. The ALLHAT study of a few anti-hypertensive medications reportedly cost some $125m (Nash and Clarke, 2003). 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.[32] At present, there is a case to be made that there is significant under-investment in "post-marketing" studies of drugs.[33] 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 some extent simply replace existing pharmaco-economic evaluation and price-control agencies in countries where they already exist, and indeed, one option would be to conduct head-to-head trials along with placebo trials during phase III testing of drugs.[34]

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[32] Companies rarely undertake comparative studies voluntarily, since it is "playing with fire." Bristol Myers Squibb recently financed a study which discovered that a rival's drug was more effective in certain conditions ("Head-To-Head Studies Have Their Risks," Theresa Agovino, *Washington Post*, July 9 2004)

[33] 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). Angell (2004), Goozner (2004), and Reinhardt (2001) all propose a substantial increase in investment to undertake comparative post-marketing studies of drugs.

[34] The burden on a PIF would be heavier than on most price-control type agencies, since it would require on-going (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.

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, and even possibly outright corruption. 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 discussed in Section 2.4 above, there is a serious possibility of some price controls being implemented in the US in the near future.

To the extent that there is a concern that this proposal would impede the workings of the free market, one should be aware that drug markets are already distorted by agency problems and government interference. This interference operates at all stages in the product lifecycle, including: early government investment into undertaking basic research (Goozner 2004); drug approval; government enforcement of exclusive rights to patent exploitation; special regulations concerning sale and pricing of drugs; special regulations concerning patent infringement; regulations concerning mandatory substitution; etc. The market for drugs is currently far from free.

5.4 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.[35] 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.[36]

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 extensively used to value disabilities and compromised health status in terms of QALYs. 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). (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

[35] 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.

[36] 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.

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). Dickson, Hurst, and Jacobzone (2003) offer 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. 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. For an analysis of the theoretical validity of QALYs, see Doctor *et al.* (2004).

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 6.5 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 pharmaco-economic study estimating 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 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, etc.) in all regulatory decision-making by US government departments.[37] 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. In addition, with funding from eight states and two nonprofit organizations, the Center for Evidence-Based Policy at the Oregon Health and Science University is presently organizing reviews of twenty-five top-selling therapeutic drug classes (Morgan, Bassett and Mintzes, 2004, p. 275).

5.5 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 below in Section 6.6 would not violate TRIPS. Second, countries could simply offer a choice

[37] 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.

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.

5.6 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.[38]

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.

6 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. This section is therefore intended for those readers who are interested in exploring the potential for practical application of the proposal.

6.1 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 offer a large therapeutic benefit over pre-existing products and yet not generate any sales, since the newer improved version would be

[38] 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.

preferred. This would lead firms to have weak or even negative incentives to improve products currently under patent.[39] Fortunately, there is a simple solution to this problem: when calculating the points attributable to a medicine, the PIF must not include any patented 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 should also not include medicines relying on the same patents in the comparison group for a given medicine.

6.2 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 patentability of the 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.)

Since the proposed system uses patents as the basis for establishing property rights to a medicine (where the property right includes the right to be compensated by the PIF, and to exclude others from the use of the patented innovation in any use other than the production of the registered medicine), whatever legal and administrative problems usually attend the patent system would continue. In addition, the patent term would continue to be 20 years.

[39] To see why, suppose that the old version offers a large improvement over pre-existing therapies, while the new version offers a small incremental improvement over the old version. Doctors will prescribe the new version, leading to small sales for the old version. If the new version is awarded points based on the incremental improvement over the old version, the firm will obtain only small rewards even though it is responsible for both new and old versions.

6.3 International Issues

On the one hand, this model is ideal for enabling wide international access to drugs, while eliminating inefficient parallel imports between countries having different prices. 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 dollar value for each 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 unavoidable. 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 here. 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 proposal outlined in this paper 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. (Such a mechanism is suggested in S. 6.9)

6.4 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, existing patented medicines could also be rewarded by the PIF; although some medicines would become less profitable 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.

6.5 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 to 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 medically indicated sales.

6.6 An Option for Restricting the Proposal

One possibility in 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. (Private insurance plans might match the government coverage, or offer insurance for additional drugs as well, recognizing that for the most part, high therapeutic value drugs would be rewarded by the PIF and be low priced, while low therapeutic-value patented drugs would be expensive.)

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 choosing to opt out of the PIF 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.

6.7 Comparison with Price Control Systems

A striking perspective on the proposal is how similar it is in many respects to a system in which there is government insurance for pharmaceuticals, and price controls. Such a

system is in place in most industrialized countries. In such systems, a government board typically determines prices largely on the basis of the therapeutic effectiveness of the medicine. The net result is that the revenues of the drug firm come from the government, and are equal to the price times the number of units sold, where the price is based on therapeutic effectiveness. Evidently, such a system is very similar to the proposal outlined in this paper; but it is also different in important ways.

First, price control systems still have high prices for drugs, compared to average production cost. This means that any buyers not covered by government insurance will face high prices, leading to some deadweight losses. Evidently, this problem may be small if most consumers are covered by government insurance.

Second, price controls tend to be arbitrary. In Canada, for example, prices are based on international reference pricing, with the Canadian price to be no higher than the price in a basket of seven reference countries. Prices may not increase (except for inflation) regardless of subsequent price changes elsewhere or new evidence of effectiveness. Although there is, in most price control schemes, some attention to therapeutic value, the way that it is introduced into pricing is not necessarily well conceived.

Third, in almost all such schemes, drugs with similar therapeutic effects are priced at very similar levels. This leads to inefficient research investments into copycat drugs, which are guaranteed to obtain the high price of the pioneer product, and to competitive marketing. At the same time, the inefficiently high investment into copycat drugs weakens the incentive to invest into pioneer drugs. A scheme in which rewards are based on the therapeutic contribution compared to pre-existing products will generate the greatest therapeutic progress.

Fourth, price control schemes, combined with government insurance and a fixed cap on the budget, tend to lead to exclusion of certain drugs with low benefit/price ratios. Since the price of the drug is typically not even close to the production cost of the drug, this exclusion of certain products is generally inefficient and creates deadweight loss.

6.8 Medical Devices

In principle, there is no reason that innovative medical devices could not also be included in this proposal, although in practice it is questionable whether there would be sufficient competition in manufacturing to lead to large price reductions; and whether the PIF agency would have sufficient knowledge to make judgements about therapeutic value outside of the area of pharmaceutical products.

6.9 A Special Fund for Least Developed Countries

Least developed countries would typically not be expected to create their own PIFs, as the administrative burden would be large and there is a reasonable justification not to expect such countries to make large payments to innovators. However, since many diseases primarily affect people in very poor countries, this would lead to inadequate incentives to innovate in drugs for such diseases, just as exists today. One way of resolving this problem would be to create a special internationally administered PIF for least developed countries which would give rewards on their behalf, using the system outlined above. Rewards would be allocated based on incremental therapeutic benefits of patented technologies, where the relevant patents were licensed at zero price. (Possibly the patents could be those filed in Europe or the US.) The only restriction on the size of

potential rewards to an innovator would of course be the size of the total reward pool available. This approach has the benefit of not favoring any particular innovation (e.g., vaccines for HIV/AIDS): wherever large therapeutic gains were available from a drug, it would be rewarded based on the relative value of the gains, compared to other medicines.

Notably, this special fund could be created independently from the adoption of the proposal in developed countries. Arguably, the need for such an approach is greatest in countries where drug insurance is rare, and so perhaps least developed countries should be the first ones to establish the type of system proposed in this paper.

It may be worthwhile to compare the proposal here to those proposals which have been made for prizes for pre-specified solutions, such as malaria vaccines. Those sorts of prizes, while perhaps desirable in themselves, are not very flexible, and hence cannot provide adequate incentives for innovation in a range of areas. The proposed special fund, however, if sufficiently large, would create large incentives to attack the entire range of health problems suffered in the least developed countries, with the greatest incentives for those drugs which would create the largest health benefits.

7 Discussion

The proposal outlined in this paper offers an efficient method of rewarding pharmaceutical innovation which delivers two major benefits. First, it aligns private research incentives with social objectives by rewarding innovations based on their evaluated therapeutic value. This is an improvement over the ordinary implementation of the patent system, which cannot be effective in eliciting pharmaceutical innovation given that pharmaceutical markets are extraordinarily dysfunctional. The proposal can therefore be used to increase the rate of drug development. Second, it allows for drugs to priced at approximately the average cost of production, allowing widespread access to drugs. Third, it continues to provide healthy profits to pharmaceutical firms which successfully bring innovative drugs to market. These advantages suggest that this proposal deserves serious investigation.

8 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. All conditions for which the drug is prescribed should be included in this calculation, including off-label uses.
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.

9 An Option to Replace the Fixed Fund with a Dollars per QALY reward

An alternative approach, to replace the fixed PIF, would be to reward innovators with a pre-announced amount per QALY.[40] Drugs would be assessed in the same way as described above to determine the incremental QALYs created over pre-existing therapies,

[40] This alternative approach was suggested to me by Joel Hay.

and then rewarded with a fixed dollar amount per incremental QALY. Such an award might be, say, $10,000 per QALY. (In calculating this award, the incremental costs of providing this therapy should be deducted.) This alternative would have exactly the same efficiency properties as the one outlined above. It offers some advantages: first, it removes some risks from innovators, since they could more reliably predict the size of the award they would earn; second, it is plausibly more equitable, as rewards would not depend on what other innovations were in the pool. Counterpoised against these advantages is the disadvantage that governments would be less able to predict their own budgetary requirements. In addition, innovators would not be playing against each other to earn rewards from a fixed pool: this would give the PIF Agency much more slack and would not allow it to benefit from the zero-sum game in which firms play against each other.[41] Possibly this option could be used to establish a ceiling on the reward per QALY.

[41] The problem of administrative inefficiency seems to me to be determinative here. If the PIF Agency does not have to make hard decisions with respect to which innovators get how many points, then it will simply allocate more dollars to everyone, resulting in huge bloat in the budget. At the same time, if the budget is unlimited, who will have any incentive to discredit exaggerated claims of effectiveness?

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