Prize, Advanced Market Commitments, and Pharmaceuticals for Developing Countries

Executive Summary

This brief paper discusses the strengths of the patent system and its weaknesses in terms of creating incentives for innovation. It considers how Advanced Market Commitments (AMCs) may supplement the patent system, and introduces a Comprehensive Advance Market Commitment (CAMC) proposal. It shows how both AMCs and a CAMC could increase incentives for R&D into diseases of the poor, and examines administrative requirements and the political situation of these supplementary initiatives.

1. Introduction

Can prizes and other mechanisms usefully supplement the patent system for drugs for neglected diseases? Several proposals have been made in recent years, in response to the failure of the patent system, by itself, to provide adequate incentives for development of such drugs, or access on reasonable terms in case they are developed. This brief paper considers a variety of proposals, which range from simple prizes to comprehensive advance market commitments. I begin with a brief description of the different proposals, and then offer some comments on the comparisons, and finally discuss issues with implementation.

It is helpful to begin by describing the system of incentives we already have, which is composed of patents and research grants.[1]

1.1 Patents and Research Grants

A patent is a government grant allowing the exclusive use of a given innovation for limited period of time, as a reward for the development and disclosure of that innovation. The value of the patent is dependent on the profits to be had from this exclusive exploitation. Generally, a patentee is unable to completely appropriate all the value that is created by an innovation, for a number of reasons. First, patentees are generally unable to perfectly price discriminate, i.e. charge different prices for the same product to different buyers, depending on the value each buyer attaches to the product. This may be a particularly important problem in pharmaceutical markets in developing countries, as shown by Hollis, Flynn and Palmedo (2007). Second, patents are time limited to twenty years. The time limit is more stringent in pharmaceutical markets: because of testing and approval requirements, patentees of medicines rarely obtain much more than about twelve years of exclusivity following commercialization of the product. Third, a patent is in many cases insufficient to prevent inventing around by competitors. Fourth, patentees frequently face imperfect markets, and this is particularly true in developing countries because of the lack of health insurance. A sick person without health insurance may have insufficient cash to buy medicines and may be unable to borrow when sick. Thus, there is likely to be a wedge between the revenues the patentee can extract from a sick person, and the social value of saving the person's life. This demand-side imperfection is of great importance in pharmaceutical markets in developing countries.

Because of incomplete appropriation through the patent system – especially in the case of drugs and vaccines used in developing countries – there is likely to be an inadequate investment into innovation, compared to what would be efficient. However, even when the patent system does generate an innovation, the pricing must be relatively high, in order to ensure a return to the

patentee. High pricing, in poor countries where consumers lack health insurance, will ensure that many sick people are not served by the innovation during the period of patent protection.
The inadequacy of patents has led them to be supplemented by monetary grants to researchers. Such grants can be directed to projects for which the appropriability is particularly low, such as projects with distant pay-offs or projects related to neglected diseases. However, grants are problematic. All grant applicants emphasize the importance and potential value of their research program, so that it is difficult for the grantor to identify the best projects. Research grants resemble a "central planning" system, since the grant administrator chooses what research to fund, compared with patents, which resemble a market, since researchers choose what to investigate based on their private information.

2. Supplementary incentives

Given the deficiencies of patents and research grants, supplementary incentive systems should be of interest. I consider three types of supplementary incentive: simple prizes which consist of a one-time payment for some achievement; Advanced Market Commitments, which consist of a promise to pay some award for each unit of vaccine delivered; and Comprehensive Advanced Market Commitments, which consist of a promise to pay, over a period of years, a cash award per unit of measured health improvement from a patented treatment.

2.1 Prizes

The simplest and most familiar prize system is a fixed dollar award given to the first firm to meet some technical target, or the firm to get closest to that target within a given period. The X-Prize foundation, for example, awarded $10m for the first spaceship that could carry three people into space twice in two weeks. The application of this kind of prize to medical technologies is not straightforward, however, since it is extremely difficult to specify a suitable medical target. For example, a malaria vaccine might meet the technical qualifications but have serious side effects. How serious could the side effects be without disqualifying the vaccine? Since it is impossible to completely describe the required technical standard in advance, it would be necessary for the prize committee to make a subjective decision afterward. This in turn would effectively require the prize to be more flexible: for example, it might reward the "best new malaria medicine for 2007." In turn, this leads to problems for the prize authority, since it is very possible that they may have to give a prize to a relatively unimportant drug.

An alternative mechanism is the patent buy-out, in which the government purchases the patent rights of the innovator. While there are difficulties inherent in such a system, especially related to the problem of knowing how much to pay (see, e.g. Kremer 1998), the chief shortfall in patent buy-outs is that they do nothing to change the incentives of researchers. Thus, patent buy-outs are ineffective as a solution for creating new incentives for firms to develop new drugs for neglected diseases.

2.2 Advance Market Commitments (AMCs)

An Advanced Market Commitment consists of a promise by some international body to make a supplementary payment to a firm which sells a qualifying vaccine at a fixed price. The Advanced Market Commitment espoused by several countries for a pneumococcal vaccine and funded to the tune of $1.5bn is the best developed of these schemes.

The standard AMC is relatively well understood and is thoroughly explored in Kremer and Glennerster (2004), the Tremonti report (2005), and the Pilot AMC for Pneumococcal Vaccines

Framework Document (2006). The essence of the AMC is that funds are committed in advance to make payments to any firm which can produce and sell a qualifying vaccine. The total amount of funds is set in advance, and once the money is used up, the AMC is finished. To qualify, a vaccine has to meet a certain "Technical Product Profile" determined in advance, relating to the efficacy and safety of the vaccine. The payments made to the firm under the AMC are set at a payment per unit, less the price the firm charges to governments. For example, if the AMC guarantees a payment of $9 per vaccine delivered, and the firm charges governments $2 per unit, the AMC would pay the firm $7 per unit. The vaccine seller can choose its price, but whatever price it chooses must remain the same following the AMC. Thus, the firm must balance the gain from a low price – increased sales during the period of the AMC – with the loss from a low price following the AMC.[2]

The AMC is a simple contractual arrangement. The funders are agreeing in advance to pay $x per unit sold for any vaccine which meets the technical requirements, in exchange for the seller agreeing to hold its price fixed over some period of years. The seller need not enter into this agreement, but could simply exploit its patent exclusivity as profitably as possible, selling its vaccines at whatever price it could obtain. The chief benefit of the AMC is that it creates an additional incentive to accelerate the development of vaccines thought to be of great importance.
The AMC scheme can be thought of as a prize per unit of vaccine delivered, rather than per new medicine. AMCs have the attractive characteristic that the payment depends on the commercial success of the product, which in turn depends on its effectiveness. A vaccine with serious side effects, for example, would likely have relatively small sales, so that the amount paid under the AMC would also be relatively small. AMCs therefore represent a significant improvement over any kind of simple prize.

There remain, however, difficulties of identifying the technical requirements which must be met for a product to be eligible for payments under the AMC. This is an exceptionally important problem since the technical requirements must be fully stated before the research and development process, and it is therefore impossible to capture all the relevant contingencies. As a result, while AMCs are likely to be very productive for specific vaccines, they do not cast a very wide net, and do nothing to stimulate innovation outside the specific technical parameters of the specified vaccine.

2.3 Comprehensive Advance Market Commitments

The limitations of AMCs suggest that a modified version which had broader reach might be valuable. A more general system of Advance Market Commitments, which I will label Comprehensive Advance Market Commitments (CAMC) has been proposed by Hollis (2005, 2007a, 2007b) and Pogge (2005). In this system, a payment is made to the patentee over a period of years for innovative drugs or vaccines based only on the measured health effects of the products. The CAMC eliminates the requirement for the administrator to state a technical standard in advance, and replaces it with the requirement to form an estimate of the effectiveness of the product, where the estimate is obtained after the product is developed or even after it has been commercialized for some years. Health effects are often measured in terms of a standardized measure, the "Quality-adjusted life-year" or QALY.

Any firm accepting payments under the CAMC must also freely license its patent rights for the relevant product, while ensuring access at a competitive price. The innovating firm would then be rewarded based on the total sales of the product by itself *and* generic firms. The innovator might

receive payments over some fixed period (say, 10 years) following approval of an innovative drug. (A single-time prize or patent buy-out would not work well: it would be difficult to estimate in advance the sales volumes and the effectiveness of the product; and the firm, having received its prize, would have no incentive to engage in promoting its product for optimal use, as noted by Kieff, 2001. Therefore, like AMCs, the CAMC system is designed so that payments are made based on sales of the product over a period of years.)

A CAMC could be specifically targeted at products which addressed neglected diseases; or it could be limited to payments for health effects in developing countries. However, it could also be global and unrestricted in terms of diseases. Since the vast majority of the world's population – and therefore the vast majority of the global burden of disease – resides in relatively poor countries, the incentives to develop drugs treating the poor would be very strong. Unlike profits from exclusive exploitation of patent rights, incentives under the CAMC are not related to the wealth of the consumer. Thus, it would create incentives which would be efficient in the sense of maximizing the health gains per dollar invested.

3.0 Comparisons

In this section, I contrast the AMC and CAMC proposals from a number of different perspectives. It is clear that there are advantages and disadvantages to either of these systems, which are in any case likely to be complements, rather than substitutes.

3.1 Budgetary requirements and source of funds

The AMC proposal requires a *relatively* modest budget, since payments depend on the achievement of specific technical targets and on the sales volume of the product. In addition, it is only granted for a specific kind of vaccine. However, this modest budget comes at the cost of modest inducement of incremental innovation: if the system is extended to a wide set of vaccines, the required budget balloons into the tens of billions of dollars; and this still only applies to vaccines. The GAVI initiative for a pneumococcal vaccine, which is in fact very close to commercialization, has a $1.5bn budget, and the amounts proposed for other disease vaccines further from commercial development are in the range of $5bn to $10bn (Tremonti Report, 2005, p.9).

The CAMC system would require even larger funding, since it addresses not only vaccines for particular diseases but other pharmaceutical products as well. For example, a reasonable starting point would be a promise of annual payments of at least $2bn per year. The CAMC relies on a flow of innovations in order to achieve attractive properties, which means that it would be necessary for it to apply to a large set of diseases and conditions. While the budget would be fixed, its impact on incentives for R&D in any given field would be dependent on the size of the fund awarded annually. If the annual budget were too small, the fund would be unlikely to work well.[3]

The most likely source of such funds is national governments, probably of OECD countries, which have already demonstrated a willingness to invest in the pneumococcal vaccine AMC. Charitable foundations with an interest in health might also contribute seed funding. In addition, developing countries might also make some contribution to a rewards fund in proportion to their GNP per capita. The proposal made by Hubbard and Love (2004) sets up a standard for what might be reasonable here.

3.1.1 Supplementary funding

If an organization wished to focus on one disease – for example, HIV/AIDS – it could do so in a very simple way by offering to pay a supplementary amount for any treatment dealing with that disease. Both AMCs and CAMCs could easily administer supplementary incentives for drugs or vaccines treating diseases believed to be of particular importance.

3.2 Risks for Innovators

Innovators bear technical risks under any system in which payments are conditional on technical success. Research grants are thus an exception since they impose all risks on the funder. However, patent exclusivity, AMCs, and CAMCs all have their own specific risks.

Under patent exclusivity, innovators of drugs face risks of (a) competition from firms which invent around their patent, (b) compulsory licensing, and (c) inability to obtain the anticipated revenues. AMCs mitigate the revenue risks in some ways, since a successful innovator is assured of being compensated a fixed amount for all the units sold, until the AMC's funding is used up or some time limit expires. AMCs also increase revenue risks since they require the innovator to maintain the same price following the AMC period as during. Even if the firm is unsuccessful in obtaining substantial sales under the AMC, it cannot increase its price afterwards. AMCs eliminate the risk of compulsory licensing, since the patentee can offer a low price during the period of the AMC payments. However, AMCs carry a higher technical risk than patent exclusivity since in order to obtain payments under the AMC, the firm must achieve a pre-specified technical profile. Failure to match this profile may result in zero payments under the AMC.

CAMCs offer a more complicated risk profile. The risk of inventing around an innovation is considerably reduced because with zero-cost licenses there is little benefit to inventing around. Similarly, there are no risks of compulsory licensing since prices are already competitive. However, there are risks that the firm won't meet its revenue targets, which relate to the rate at which health improvements are compensated. Since each firm obtains payments based on its *share* of measured health improvements achieved by products in the CAMC system, its payments are dependent not only on its own product, but also on other products. For example, if a firm develops a perfectly effective vaccine for cancer, that vaccine might soak up much of the available payments under the CAMC for many years, leading to relatively low payments for other firms' products. However, this risk is mitigated by substitutability between patent exclusivity and the CAMC system. If payments are too low under the CAMC, firms will choose to exploit their patent exclusivity instead, increasing the payments for those firms that remain in the CAMC system. (Similarly, if payments are relatively high under the CAMC, more firms will forgo their patent exclusivity, thus lowering the payments.) Thus the market mechanism built into the CAMC system automatically adjusts the payment so that for a given health improvement, the rate of payment under the CAMC is comparable to that available for firms exploiting their patent exclusivity.[4]

3.3 Breadth of the Incentives

An objection to the AMC approach is that it only incentivizes research in a particular direction, one chosen by the administrator. This limited scope, of course, allows it to focus resources on some particular outcome. The CAMC system, however, allows for any innovation which has measurable health effects. Thus, for example, if a drug treatment could treat malaria more effectively in the absence of an effective vaccine, it would be incentivized under the CAMC

approach but not under the AMC system. This is an important issue since it allows innovators, who have the best information, to make decisions on what to invest in; under the AMC system, investment in innovation is effectively directed by the administering body. In a sense, the AMC system suffers from the same problem as research grants, in that the administrator must identify the most promising directions for research, instead of leaving it to innovators to determine what sort of product is most likely to be developed with the greatest cost-effectiveness. Only if the administrator believes that it has greater knowledge of potential innovations, their value and their expected costs, than do innovators themselves, should it try to direct research.

3.4 Pricing and Access

Under the CAMC system, the innovation must be openly licensed – and therefore become generically available – to be eligible for payments. This ensures that the price is at a competitive level, and is probably the best that can be done for access. Generic competition, of course, may not work well in some circumstances – for example, for complex biologics, since they may not have approved generic versions. Any CAMC system would have to deal with that problem.

Under the AMC system, the proposed mechanism to control price is that the patentee must choose a permanent price. This creates unclear incentives for the patentee and the effects are difficult to anticipate. If the patentee wishes to maximize sales of its vaccine because it anticipates competition for the limited funds of the AMCs, it may price its vaccine at below variable cost. It does so, however, knowing that in the future, following the AMC, it will be obligated to offer its vaccine at the same low price. It is, however, not clear that this will really be a binding constraint: how is this obligation to be enforced?

3.5 Choosing the Level of Payments

The level of payments is another important point of comparison. The AMC system sets a price which must be somewhat arbitrarily chosen. When justifying the price, AMC proponents have referred to the cost-effectiveness of the proposed mechanism, in terms of its cost per DALY.[5] They show that if the AMC is effective in stimulating the development of a vaccine, it will be very cost effective, with an estimated cost per DALY saved of approximately $15. This is indeed very low. The attractiveness of the CAMC system is that if the expected payment per DALY under the CAMC were $15, it would encourage not only such vaccines but also any interventions which had even greater cost-effectiveness. The CAMC system does not require the administrator to choose a level of payments: firms do that by competing for the available money. In time, firms will be able to form expectations of the payment for a given product.

3.6 Administrative Expense

Any kind of supplementary system offering payments to innovators would require the creation of an Independent Assessment Committee to decide on rules and regulations of how payments would be made and who would qualify, and then to actually disburse payments.

The cost and difficulty of assessing how large payments should be is an important difference between the CAMC and AMC systems. With the AMC system, the size of the payment per unit of the product is determined in advance. Following development of the vaccine, it is only necessary to determine (a) whether it meets the technical requirements, (b) the number of units sold, and (c) whether it was sold at the stated price.

The CAMC requires no determination in advance as to the amount of the payment for a given innovation or technical characteristics, but does require the administrator to make an estimate as to how effective the product has been in saving QALYs. This could be a very substantial exercise. Like the AMC system, it would be necessary to know how many units were sold – but it in addition, it would be necessary to make an estimate of the average effect of those units.
Determining the average effect on health of a unit of a drug would not be easy, but it would also not be without value, since such an exercise is in any case important in guiding effective prescribing. However, a less complex version could simply rely on estimates of the effectiveness of the drug obtained during clinical trials. These kinds of estimates are imperfect, to be sure, but not likely to be worse than a pre-determined payment established before the product has even been tested, as with the AMC system.

4.0 Relationship to Patent System

AMCs and CAMCs are intended as *optional* and *complementary* to the patent system. Both mechanisms leave patents exactly as they are, and entitle the patentee to additional payments. The essence of the CAMC system is that innovators must choose between accepting payments or exploiting the exclusivity rights created by the patent, while with AMCs, the innovator must choose between accepting the supplementary payments with a low price to the developing country, or exploiting the exclusivity rights with no limitation on price. In either case, firms will only accept the payments if doing so leaves them better off than unfettered use of the patent.

5.0 Political Obstacles

There are many political obstacles to any such system. As has been shown, the political obstacles can be solved for AMCs. It seems likely that this implies that they can also be overcome for other systems of supplementary incentives, provided the system does not derogate in any way from the rights normally accorded under the patent system. Of course, the decision to accept payment under the terms of the AMC requires the firm to give up the freedom to change the price of the vaccine in the future; but the firm is still completely free to reject payment under the AMC and sell its product without forgoing pricing flexibility. Similar rules would apply to the CAMC system: the firm could choose to exploit its patents in the usual way, or it could accept the payments, but not both. Thus, these systems are strictly additive, and do not detract from the rights or options of the innovator.

The CAMC model requires a sustained funding commitment, with persistent large annual payments to be made. This is clearly politically difficult, compared to the one time commitments which are required under AMCs. Most likely, in order to make such a sustained commitment feasible, some international agreement for funding, such as the one proposed by Hubbard and Love (2004), would be necessary. A CAMC would lack credibility in the absence of a significant multilateral funding agreement.

An important political obstacle to any kind of incentive system relates to avoiding the perception that the freedom of pharmaceutical innovators is being compromised in any way. For example, a system which bases payments on the QALYs saved by a given drug may appear to push national insurers further along the path towards cost-effectiveness analysis as a basis for pricing.

There are also legitimate concerns that if a product is sold at generic cost in a developing country, and at a monopoly price in developed countries, that is likely to lead to parallel trade between countries, and harm to the value of the patents in the developed countries. However, these fears

can be somewhat mitigated if the innovator does not sell product in developing countries, since then the low-priced product would all be made by generic manufacturers and would be readily distinguished at customs from the innovator's product.

6.0 Discussion

This paper has briefly considered how alternative incentive schemes such as Advance Market Commitments and Comprehensive Advance Market Commitments might help to create additional incentives for developing drugs and vaccines for neglected diseases. Both schemes ensure access; both create a substantial commercial reward for meaningful innovation. The AMC initiative is much more tightly focused on rewarding the development of specific vaccines, which makes it less expensive. The CAMC proposal would require greater resources but would enable a wider range of innovation.

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Endnotes

[1] For a more thorough discussion of innovation incentive mechanisms, see Hollis (2007b).
[2] It is not really clear what sort of results these incentives will create. According to the Tremonti report, the intention was to get prices close to variable cost of production; but the system proposed in the later Framework Document is not really consistent with this aspiration. A firm might simply choose a very low price – perhaps zero – to maximize its sales during the AMC, and then sell its patents to a third party following the AMC to avoid losses from low prices.
[3] The question of the minimum size of such a prize fund has not, however, been dealt with.
[4] It is important to note that this does not mean that this system would not increase incentives to develop drugs for neglected diseases. For most such diseases, the patent system offers little incentive since the potential consumers are indigent. The CAMC system would only account for changes in health, independent of the wealth of the consumers. Therefore, diseases which have high health costs among poor populations would become very attractive targets from a financial perspective.
[5] A DALY is a "disability-adjusted life-year." And is similar in conception to the notion of a QALY.