Pre-Commitments to Purchase New Vaccines: Rationale *

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Executive Summary

Malaria, tuberculosis, and HIV kill approximately 5 million people each year. The overwhelming majority of deaths occur in poor countries. Despite recent scientific advances, research on vaccines for malaria, tuberculosis, and African strains of HIV remains minimal. This is in large part because potential vaccine developers fear that they would not be able to sell enough vaccine at a sufficient price to recoup their research expenditures. This paper discusses the rationale for a vaccine purchase fund that would pre-commit to purchase vaccines for these diseases and distribute them in developing countries. Such pre-commitments would both create incentives for vaccine research and ensure that if vaccines were developed, they would reach people in developing countries.

There is a strong case for public, global action to spur vaccine development and ensure that vaccines are available to those who need them. The public subsidies most countries provide for vaccination are justified, because people who take vaccines not only benefit themselves, but also benefit others by helping to break the chain of disease transmission. Moreover, if vaccines were sold under patent at a monopoly price, they would not reach many people who need them. Large public vaccine purchases offer the potential to bring down the price per dose and enlarge the market, potentially benefiting both vaccine producers and consumers. Global coordination is needed because research on vaccines is an international public good – each individual country has an incentive to free-ride on the research incentives provided by other countries. Incentives for vaccine research should be put in place before vaccines have been developed, because once vaccine developers have invested large amounts in developing a vaccine, governments face the temptation to force them to sell at prices that cover manufacturing, but not research, costs. Anticipation of this discourages vaccine research. Rough calculations suggest that private incentives for vaccine development may be an order of magnitude less than the social value of vaccines.

Historically, governments have stimulated vaccine research by paying for research inputs, for example through grants to researchers. The development of the biotech venture capital industry makes it easier for scientists with prospects of producing viable products to attract investors, as long as a substantial market for their product is anticipated. This increases the scope for encouraging the later, more applied stages of vaccine research by pre-committing to purchase vaccines. Pre-committing to purchase vaccines has several advantages relative to paying for research inputs. First, it gives researchers strong financial incentives to focus on developing a marketable vaccine rather than pursuing other goals, such as publishing academic articles. Second, paying for vaccines, rather than funding research expenditures, gives pharmaceutical firms and scientists strong incentives to self-select only those research projects that have a reasonable chance of leading to a vaccine. With purchase pre-commitments, the public pays only if a vaccine is actually developed. Finally, purchase pre-commitments help ensure that if vaccines are developed, they will reach those who need them.

Purchase pre-commitments are also attractive relative to other ways of rewarding developers of vaccines, such as extensions of patents on other pharmaceuticals, cash prizes for vaccines, and paying more than necessary for existing vaccines.

A companion paper, “Purchase Pre-Commitments for New Vaccines: Design Issues,” explores how pre-commitments to purchase vaccines could be designed.
Malaria, tuberculosis, and HIV kill an estimated 5 million people each year. In the past fifty years, these diseases have claimed six times as many lives as all wars [WHO, 1999b]. Virtually all malaria cases, and more than 95% of new HIV and tuberculosis cases, are in developing countries [UNAIDS, 1998; WHO, 1998], although the spread of drug resistance threatens increased infection and death in developed countries as well. Almost 90% of malaria cases and 70% of new HIV infections occur in sub-Saharan Africa [WHO, 1999a; UNAIDS, 1998].

Recent scientific advances have increased the potential for development of effective vaccines. Yet, despite the huge toll of these diseases, very little vaccine research is directed towards malaria, tuberculosis, and African strains of HIV. Potential vaccine developers fear that they would not be able to sell enough vaccine at a high enough price to recoup their research investments. This is both because these diseases primarily affect poor countries, and because vaccine markets are severely distorted. One way to create incentives for vaccine development would be to establish a vaccine purchase fund which would pre-commit to purchase vaccines and provide them to developing countries at an affordable price. This paper sets forth the economic rationale for pre-committing to purchase new vaccines.

Section 1 of this paper provides background information on malaria, HIV, and tuberculosis, and reviews the current state of scientific progress towards vaccine development.

Section 2 examines the economic rationale for public, global action to support the development and wide distribution of vaccines, and argues this action should take place now, before vaccines have been developed. The subsidies almost all countries provide for vaccination are justified for four reasons. First, individuals have inadequate incentives to take vaccines, since those who take vaccines benefit not only themselves, but also benefit others by breaking the cycle of infection. Second, the chief beneficiaries of vaccination are often children. Third, consumers
are often more willing to pay for treatment than prevention, perhaps because it takes time to learn about the effectiveness of vaccines. Finally, monopoly pricing of vaccines would prevent many people who need vaccines from obtaining them. Large public purchases could potentially make both vaccine producers and consumers better off than under monopoly pricing by reducing the cost per dose and expanding the market.

Global action is needed because research on a vaccine is a public good. In the absence of a global program, each country would have an incentive to free ride off the research programs and research incentives provided by other countries. Programs to compensate vaccine developers should be put in place now, because once a vaccine has been developed, governments and international organizations will be tempted to use regulation or compulsory licensing to obtain vaccines at prices which cover only manufacturing costs, not research costs. Anticipation of this deters vaccine research. Rough calculations suggest that the social benefits of vaccines may exceed the returns to a private developer by a factor of ten.

Section 3 examines the appropriate roles of “push” and “pull” programs in encouraging vaccine research. “Push” programs pay for research inputs, for example through grants to researchers, while “pull” programs pay for an actual vaccine. Push programs are well suited to financing basic research, because it is important that the results of basic research be quickly communicated to other scientists. Grant-funded researchers have incentives to publish quickly, while researchers with strong financial incentives to develop a vaccine might wish to withhold information from competitors. Historically, governments have relied heavily on push programs to encourage even the later, more applied stages of vaccine development, in part because it was necessary to finance research expenditures in advance of the development of a vaccine. However, with the development of the biotech venture capital industry, it is now much easier for scientists to attract investors to finance research, as long as a substantial market is expected for the product. Pull programs can provide such a market, and they have several attractive features
relative to traditional push programs for encouraging vaccine development. First, pull programs provide strong financial incentives for researchers to focus on developing a marketable vaccine, rather than pursuing other goals, such as publishing academic articles. Second, under pull programs, the public pays nothing unless a viable vaccine is developed. This gives researchers incentives to self-select projects with a reasonable chance of yielding a viable vaccine, rather than to oversell their research prospects to research administrators. Finally, pull programs help ensure that if vaccines are developed, they will reach those who need them.

Section 4 argues that a vaccine purchase fund is superior to other pull mechanisms designed to increase incentives for vaccine research. Rewarding vaccine developers with extensions of patents on other pharmaceuticals would inefficiently and inequitably place the entire burden of financing vaccine development on patients who need these other pharmaceuticals. Cash prizes for research are economically similar to a vaccine purchase fund, but provide a weaker link between vaccine quality and the compensation paid to vaccine developers. They are also likely to be politically less attractive and therefore less credible to potential vaccine developers. Encouraging vaccine development through research tournaments is likely to be difficult, since there is no guarantee that a vaccine could be developed within a fixed time period. Paying more than necessary for existing vaccines is an expensive and potentially ineffective way of encouraging research on future vaccines.

A companion paper, “Purchase Pre-Commitments for New Vaccines: Design Issues,” discusses how pre-commitments to purchase vaccines could be structured.

The idea of an HIV Vaccine Purchase Fund was proposed by a coalition of organizations coordinated by the International Aids Vaccine Initiative at the 1997 Denver G8 summit. Since then, the idea has been explored by the World Bank Vaccine Task Force [World Bank, 1999]. Kremer and Sachs [1999] and Sachs [1999] have advocated the establishment of a fund in the popular press. This paper draws on earlier work on vaccines, including Batson [1999], Dupuy
and Freidel [1990], Mercer Management Consulting [1998], and Milstien and Batson [1994], and on the broader academic literature on research incentives, including Guell and Fischbaum [1995], Johnston and Zeckhauser [1991], Lanjouw and Cockburn [1999], Lichtmann [1997], Russell [1998], Scotchmer [1997], Shavell and van Ypsel [1998], and Wright [1983]. This paper sets out the case for pre-commitments to purchase vaccines in terms of the underlying economic principles. In particular, this paper argues that information asymmetries between research funders and researchers make a vaccine purchase fund advantageous relative to push programs, such as grants to researchers. It also argues that pre-commitments to purchase vaccines are necessary because governments have time-inconsistent preferences: they would like to encourage research on vaccines, but once vaccines have been developed, they would like to obtain them at the lowest possible price. Finally, it compares pre-commitments to purchase vaccines to other pull programs.

Readers who are already familiar with the burden of malaria, tuberculosis, and HIV; the scientific prospects for vaccines; and existing vaccine research may wish to skip section 1, while those familiar with the rationale for public, global support for vaccine research may wish to skip section 2, and proceed directly to section 3, which examines the role of “pull” programs.

1. Background on Malaria, HIV, and Tuberculosis

This section reviews the burden of the major infectious diseases, discusses scientific prospects for vaccines, and argues that current research efforts are paltry relative to the burden these diseases impose.

1.1. The Burden of Malaria, HIV, and Tuberculosis
Estimates of the burden of infectious disease vary widely, but it is clear that the burden is huge. The World Health Organization estimates that each year there are 300 million clinical cases of malaria and 1.1 million deaths from malaria [WHO, 1999a]. Malaria is particularly likely to kill children and pregnant women. Resistance is spreading to the major drugs used for treating malaria and for providing short-term protection to travelers.

Each year, approximately 1.9 million people die from tuberculosis. More than 98% of these deaths occur in developing countries [WHO, 1999a]. However, with up to 17% of tuberculosis infections resistant to all five major anti-tubercular drugs, the spread of resistance poses a threat to developed as well as developing countries [WHO, 1997]. The existing BCG vaccine, which is distributed widely, provides only temporary and imperfect protection against tuberculosis.¹

More than 33 million people are infected with HIV worldwide, over 95% of whom live in developing countries. In 1998, about 2.3 million people died of AIDS, 80% of whom lived in sub-Saharan Africa. Approximately 5.8 million people were newly infected, 70% of whom were in sub-Saharan Africa [WHO, 1999a; UNAIDS, 1998]. New life-extending HIV treatments are far too expensive for most individuals and governments in low-income countries. Since people with compromised immune systems are especially vulnerable to tuberculosis, the spread of HIV is contributing to the spread of tuberculosis. Indeed, of the 1.9 million people who die annually from tuberculosis, 400,000 are infected with HIV.

1.2. The Prospects for Vaccines

Vaccines have proved effective against many other infectious diseases, and in the long

¹ The vaccine seems much more effective in some trials than others: trials in Britain suggest effectiveness up to 80%, while those in the southern United States and southern India suggest close to zero effectiveness.
run, they are likely to be the most effective and sustainable way to fight malaria, tuberculosis, and HIV. The potential of vaccines is demonstrated most vividly by the success of the smallpox vaccination program, which led to the eradication of the disease in the 1970’s. About eighty percent of the world’s children receive a standard package of cheap, off-patent vaccines through the Expanded Program on Immunization, and these vaccines are estimated to save 3 million lives per year [Kim-Farley, 1990]. However, only a small fraction of children in poor countries receive newer vaccines, such as the Haemophilus influenzae b (Hib) vaccine, which are still on patent and hence more expensive.

The question of whether vaccines can be developed against malaria, tuberculosis, and HIV remains open, but there is reason to be optimistic. A recent National Academy of Sciences report [1996] concludes that the development of a malaria vaccine is scientifically feasible. Candidate vaccines have been shown to protect against malaria in several rodent and primate models. Moreover, the human immune system can be primed against natural malaria infection. People who survive beyond childhood in malaria endemic areas obtain limited immunity which protects them against severe malaria, although not against parasitemia and milder illness. Since vaccines prime the immune system by mimicking natural infection, vaccines may similarly provide protection against severe disease. Recently, candidate vaccines have been shown to induce protection against tuberculosis infection in animal models. The example of the existing BCG vaccine suggests that the human immune system can be primed against tuberculosis infection. A number of candidate HIV vaccines protect monkeys against infection and induce immune responses in humans.

Nonetheless, formidable scientific and technological obstacles remain in the way of development of malaria, tuberculosis, and HIV vaccines. All three diseases have many variants and evolve rapidly, making it difficult to design vaccines which are effective against all variants of the disease and which remain effective for a long time.
Recent advances in immunology, biochemistry, and cloning have given scientists new tools to understand the immune response to these diseases, find correlates of protection useful in testing whether candidate vaccines are likely to succeed, and develop better animal models. Genetic sequencing of the organisms causing tuberculosis, HIV, and malaria is either complete or far advanced. This may help scientists create vaccines which target many different antigens, and thus are more effective in the face of genetic diversity.

1.3 Current Vaccine Research

Despite the likely scientific potential, current research on vaccines for malaria, tuberculosis, and HIV is paltry relative to the burden of these diseases. According to a Wellcome Trust study, public and non-profit malaria research amounted to about $84 million in 1993, with vaccine research making up only a small fraction of the total [Wellcome Trust, 1996]. This amounts to about $77 per malaria fatality, compared with research expenditures of up to $789 per fatality for asthma. The amount of private sector spending on malaria is unknown, but is generally considered to be far lower than public spending. Less is known about total expenditures on tuberculosis research, but the United States National Institutes of Health, one of the world’s leading funders of basic research, spends around $65 million per year on tuberculosis research, compared with $2.7 billion on cancer research [NIH, 1999].

Applied AIDS research is overwhelmingly oriented towards treatments which would be appropriate for people with AIDS in the United States, rather than towards vaccines appropriate for less developed countries. The multi-drug treatments for HIV are not feasible for poor countries, since they cost $10,000-16,000 a year [PhRMA, 1999], require ongoing immune monitoring, and need to be taken in perpetuity according to a precise protocol. To the extent that vaccine research is conducted, it is primarily oriented towards the HIV strains common in rich
countries. Most candidate HIV vaccines tested worldwide are based on clade B, the strain of the virus transmitted in the United States, Europe, Australia, and Southeast Asia, rather than the clades most common in Africa, where two-thirds of new infections occur. It is uncertain whether a vaccine developed for one clade would protect against other clades.

In general, little research is oriented toward tropical diseases. Of the 1,233 drugs licensed worldwide between 1975 and 1997, only 13 were for tropical diseases. Two of these were modifications of existing medicines, two were produced for the U.S. military, and five came from veterinary research. Only four were developed by commercial pharmaceutical firms [Financial Times, 1999]. (Of course, many other drugs are relevant for both developing and developed countries.)

2. The Economic Rationale for Public, Global Support for Vaccine Development and Distribution

This section argues that support for the development and wide distribution of vaccines should be 1) public, 2) global, and 3) put in place before vaccines have been invented. A rough calculation suggests that the social benefits of vaccines are likely to be ten times as much as vaccine developers could realize from their work, implying that private incentives for vaccine development are currently far too small, and that a great deal of public support for vaccine development is warranted.

2.1 The Case for Public Subsidies for Vaccines

In the vast majority of countries, governments purchase vaccines and distribute them to the population either free of charge or at a highly subsidized price. These subsidies are justified
on several grounds. First, individuals who take vaccines not only benefit themselves, but also help break the chain of disease transmission, thus benefiting the rest of the population. Second, the chief beneficiaries of vaccines are often children, who are not able to make decisions on their own behalf. Third, consumers seem much more willing to pay for treatment than prevention. This may be because consumers may not immediately observe the effectiveness of vaccines. The benefits of vaccines, unlike those of drugs for treating diseases, are not evident until considerably after they are taken.

The fourth reason is more subtle. Because vaccine development is expensive, but manufacturing additional doses of vaccine is typically cheap, large government purchases can potentially make both vaccine producers and the general public better off than they would be under monopoly pricing, by increasing the market for vaccines and bringing down the cost per dose. If the price paid by the government is not too much below the monopoly price, the vaccine developer can be made better off, because the larger market created by government purchases can more than make up for the lower price per dose. Those consumers who would have been willing to pay the monopoly price are better off, as long as the taxes they would have to pay to finance government vaccine purchases are less than the monopoly price. The consumers who valued the vaccine at more than the production cost but less than the monopoly price can also be made better off, as long as the value they place on the vaccine is greater than the increase in taxes necessary to finance government purchases.

Figure 1 shows a situation in which government purchases can potentially make everyone better off than under monopoly pricing. The downward-sloping line shows the willingness to pay of different potential consumers for the vaccine, which depends on their income. The lower horizontal line represents the cost of producing an additional dose of the vaccine once the research costs have been incurred and the factory has been built. A monopolist will choose a price to maximize profits. Area A represents the surplus of revenue over marginal manufacturing
costs under monopoly pricing. These funds can be used to cover the costs of research and development on the vaccine, the costs of building the factory, and any profits. Note that many people who are not willing to buy the vaccine at the monopoly price would be willing to pay more than the amount it costs to produce an additional dose of vaccine.
**Figure 1: Vaccine Pricing and Usage Under**

Monopoly Pricing and Government Purchases

Monopoly Price

Manufacturing Cost

Willingness to Pay

Fraction of Population Vaccinated
To see why large government purchases that expand the market and bring down the average cost per dose may potentially be able to make everybody better off, suppose that the government agrees to pay the vaccine manufacturer an amount equal to the sum of areas A, B, C, and D in exchange for enough vaccines for the entire population. If these purchases are funded by taxing people based on their income, with all people who would have paid the monopoly price paying just under that price, and all other people paying just over the actual production cost, vaccine producers and the general public will both be better off than under monopoly pricing.²

Note that while large government purchases could potentially make everyone better off, if they are at too low a price, they would make vaccine developers worse off, thus discouraging research.

### 2.2 The Case for Global Support for Research

Not only is there a strong case for public purchases of vaccines, there is also a strong case for international action to encourage the global public good of vaccine research. Each country has an incentive to free ride off research financed by other countries’ governments or induced by

² Pharmaceutical manufacturers may try to sell the vaccine to different customers at different prices, through a system of tiered pricing. However, the ability of pharmaceutical manufacturers to discriminate between customers in this way is limited, because all customers will try to obtain the vaccine at the lower price. The government has the power to tax higher income earners at a higher rate. Pharmaceutical manufacturers may come up with crude income indicators, for example by selling at a discount to groups of hospitals, but they have less scope to vary prices with income than the government does to vary taxes with income.

³ Note that if the willingness to pay for vaccines depends on factors other than income, and if these factors are difficult to measure, then tax-financed government vaccine purchases will not make literally everyone better off, because some people would not want to take the vaccine at any price. It is useful to contrast the cases of malaria and HIV. If a safe, cheap, and effective malaria vaccine were developed, almost everyone living in areas with malaria would presumably want to purchase it. On the other hand, some people might not want to take an AIDS vaccine, even if it were free, because they believe that they have a very low chance of contracting the disease. Since taxes would presumably fall equally on people with a low and a high risk of contracting AIDS, large government purchases of an AIDS vaccine might not literally make everyone better off, because the willingness of people in low-risk groups to pay for the vaccine might be less than the increase in their taxes necessary to pay for vaccine
their intellectual property rights protection by financing little research or providing little or no intellectual property rights protection itself. Individual countries could simply rely on the intellectual property rights protection provided by other countries to stimulate vaccine research, but aggressively bargain using the threat of regulation or compulsory licensing with vaccine developers to obtain the lowest possible price for themselves. In particular, some countries, particularly small countries, might be tempted to demand vaccine at prices that cover manufacturing costs, but do not provide any surplus over manufacturing costs to help compensate research expenditures. A large country, such as the United States, would know that if it did this, it would risk cutting off the flow of future research. Small countries, such as Uganda, can assume that taken individually, their actions will have little effect on total research incentives. However, if all African countries act this way, there will be little incentive for development of a malaria vaccine.

This problem is particularly severe for countries that are only a small fraction of the world market and so reap only a small fraction of the worldwide benefits of research. Pharmaceutical prices are controlled at prices approximately \( \frac{1}{2} \) of United States levels in the European Union, while in Japan, they are controlled at \( \frac{1}{4} \) of U. S. levels [Robbins and Freeman, 1988]. The world’s three leading infectious diseases primarily affect small developing countries, which have even less reason to internalize the benefits of drug development than the European Union or Japan. Prices for vaccines in developing countries are often a tiny fraction of U. S. prices.

Historically, developing countries have not provided much protection for intellectual property rights for pharmaceuticals. Several large developing countries, including India and Brazil, have recently agreed to enhance intellectual property rights for pharmaceuticals, but only under intense trade pressure from the United States. It remains to be seen whether the promised purchases.
intellectual property rights protection will be enforced, and many pharmaceutical firms are skeptical. Weak intellectual property rights protection makes it harder for developers of vaccines against diseases affecting developing countries to recoup their investment.

Note that if intellectual property rights are enforced globally, the same arguments which suggest that national vaccine purchases are more efficient than individual purchases also suggest that global purchases are potentially more efficient than national purchases. If vaccine developers charge a monopoly price to governments, some countries will not be able to afford to purchase the vaccine. The vaccine developer, the poor countries, and the rich countries all could potentially be better off if vaccines were purchased for the entire world at an appropriate price. All countries could potentially be made better off than they would under monopoly pricing, as long as the rich countries paid no more than the monopoly price they would have paid otherwise, and the poor countries pay less than the amount at which they value the vaccine, but more than the actual production cost.  

As with public purchases at the national level, the danger is that these purchases will be at so low a price that declines in vaccine revenues from rich customers would not be offset by increased revenue from poor customers, so that overall research incentives decline. The danger of reducing research incentives by reducing the vaccine price in rich countries is probably great enough that international vaccine purchases should be limited to poor countries, which would not have paid much for vaccines in any case.

4 Alternatively, the market could reach efficient size if vaccine developers charged each nation a separate price based on what they were willing to pay, through a system of tiered pricing. In fact, pharmaceutical firms do charge different prices to different countries. However, tiered pricing is limited by the possibility of resale and by fear of a political backlash in rich countries. Politically, it may be difficult for pharmaceutical firms to justify charging high prices in one country when they charge lower prices in another country. At a congressional hearing, Senator Paula Hawkins asked a major vaccine manufacturer, “How can you justify charging nearly three times as much to the United States government as you did to foreign countries…” [Mitchell, Philipose, and Sanford, 1993]. Since then, U.S. manufacturers have not submitted bids to UNICEF to supply vaccines. When President Clinton announced his childhood immunization initiative in 1993, he said, “I cannot believe that anyone seriously believes that America should manufacture vaccines for the world, sell them cheaper in foreign countries, and immunize fewer kids as a percentage of the population than any nation in this hemisphere but Bolivia and Haiti.” [Mitchell, Philipose, and
2.3 The Case for Pre-Committing to Reward Vaccine Developers

Finally, action to encourage the development and wide distribution of vaccines should not just be public and global, but should take place now, before vaccines have been developed. This is because of what economists call the “time consistency” problem. Vaccine research is very expensive, but once vaccines have been invented, they can usually be manufactured at low cost. Before vaccines have been invented, governments would like to encourage vaccine research. After vaccines have already been invented, governments may be tempted to try to obtain them at a price that would cover manufacturing costs, but not research costs. Governments are in a strong bargaining position at this point, because they are monopsonistic vaccine purchasers, they can regulate vaccines, and they can threaten to violate intellectual property rights of the vaccine developer. For example, governments can impose compulsory licensing of the vaccine to alternative suppliers without paying royalties sufficient to cover the cost of research, adjusted for the risk of failure and the opportunity costs of research expenditures. Thus, while in theory government purchases of vaccines could make both vaccine producers and consumers better off, in practice, they are often used as a vehicle to transfer wealth from vaccine producers to consumers. Since potential researchers anticipate this redistribution, they invest less in research than they would otherwise. This probably plays an important role in the low levels of research on malaria, tuberculosis, and even HIV vaccines discussed earlier.

The time-consistency problem that leads governments to pay low prices for vaccines is exacerbated by political economy problems that make vaccines a lower political priority than

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Sanford, 1993].

5 As an example South Africa is threatening to impose compulsory licensing of treatment of AIDS in order to drive down the price.

6 Large liability awards can also be seen as a way that governments extract resources from vaccine developers.
Section 2: Economic Rationale for Supporting Vaccines

curative care or health worker salaries in many developing countries. In particular, since vaccines deliver a widely distributed benefit, they may receive less political support than expenditures which benefit more concentrated and politically organized groups, including curative care and salaries for health workers.

2.4 Social vs. Private Return: Some Quantitative Estimates

The arguments above suggest that the tendencies for governments to free ride on the research incentives offered by other governments and to insist on low prices once vaccines have already been developed would tend to reduce the private return to research considerably below the social return. A very crude estimate suggests that the social benefits of vaccines may be ten times the private benefits appropriated by vaccine developers. Since potential vaccine developers will consider only these private benefits in setting their research budgets, incentives for vaccine research are almost certainly far too small.

For example, consider the benefits from a vaccine which reduced malaria mortality and morbidity by 80%. A standard way to measure the burden of the disease is the number of Disability Adjusted Life Years (DALYs) lost to the disease. The WHO recently estimated that malaria creates 39.3 million DALYs per year [WHO, 1999a]. Assuming that the marginal manufacturing and delivery cost for this vaccine would be about $1.50 per child vaccinated, and that the 52.6 million children born annually in low-income and lower-middle-income countries

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7 The fall in mortality and morbidity depends on the epidemiology of the disease and the percentage of people immunized, as well as the efficacy of the vaccine in protecting individuals.

8 The addition of both the hepatitis B and the yellow fever vaccines (which are relatively expensive) to the Expanded Program of Immunization increased the $15 cost of the program by 15%, or $2.25. Almost all of this constitutes manufacturing and distribution costs, rather than profits for pharmaceutical firms, since those vaccines are no longer under patent. It therefore seems reasonable to assume that the manufacturing and distribution cost of adding one more vaccine would be about $1.50.
with high enough prevalence to make vaccination cost-effective were inoculated, mass
administration of this vaccine would cost about $3.51 per DALY saved. In its 1993 World
Development Report, the World Bank defined a highly cost-effective health intervention as one
which cost less than $100 per DALY saved. (A moderately cost-effective intervention was one
which cost less than $1,000 per DALY saved). If one interprets $100 per DALY as the social
benefit of reducing DALYs\(^9\), the annual net social benefit of this vaccine would be about $96.49
per DALY saved, equivalent to $2.17 billion, or about $41.29 per immunized child. Note that
these figures do not take into account the potential economic benefits of reducing malaria
prevalence.\(^10\)

Table 1 shows the annual social benefit and the benefit per immunized child for other
vaccines.

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<th>Malaria</th>
<th>HIV</th>
<th>Tuberculosis</th>
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<tr>
<td>Number of children born annually in high-prevalence, poor countries</td>
<td>52.6 million</td>
<td>81 million</td>
<td>102.9 million</td>
</tr>
<tr>
<td>Annual social benefit of vaccine at $100 per DALY</td>
<td>$2.17 billion</td>
<td>$3.7 billion</td>
<td>$927.5 million</td>
</tr>
<tr>
<td>Annual benefit per child vaccinated</td>
<td>$41.29</td>
<td>$45.30</td>
<td>$9.01</td>
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Notes: Marginal manufacturing and delivery costs assumed to be $1.50. DALY burdens from WHO [1999a]. Each country’s DALY burden per capita assumed to be that for its region. 75% of the population assumed to be vaccinated.

The revenues generated from vaccines would almost certainly be much less than this
social benefit, limiting the incentives to invest in vaccine research. To give some indication of

\(^9\) This requires making judgements about the dollar value of DALYs, which some are reluctant to do.
\(^10\) These are difficult to assess. Gallup and Sachs [1998] use a cross-country regression approach to estimate that
countries with severe malaria grew at 1.3% lower per year.
this, while 23% of vaccine doses produced globally are sold to UNICEF [Russell, 1997], these
doses generate only $240 million of revenue – 6% of the $4 billion annual global vaccine
revenue. The total developing country market for childhood vaccines is $200 million annually.
The combined cost of the six vaccines in the standard Expanded Program on Immunization (EPI)
package is about $0.50 per dose [Robbins and Freeman, 1988]. It seems likely that the developer
of a malaria or HIV vaccine would receive payments less than a tenth of the conservatively
estimated social value of $40 per immunized child. Of course, a vaccine under patent would
likely generate greater revenues than off-patent vaccines. However, when the hepatitis B vaccine
was first introduced and priced at $30 per dose, it was not used widely in developing countries
[Muraskin 1995; Galambos 1995].

The huge disparity between private incentives to invest in

research and the social benefits of a vaccine suggests that research will be far too low in the
absence of public support, and that substantial public encouragement is needed.

To summarize, there is a strong case for a global, public effort to spur vaccine
development and ensure that vaccines reach those who need them. Vaccine research is an
international public good, since efforts by one country to develop a malaria vaccine will benefit
others as well. Commitments to reward vaccine developers need to be made now, since once
vaccines are developed, governments may be tempted not to compensate vaccine developers for
their research expenditures. A rough quantitative estimate suggests that the social benefits of
malaria, tuberculosis, and HIV vaccines are far greater than the profits that vaccine developers
could hope to realize from their work. Given all these factors, encouraging vaccine research
should be high on the list of priorities for any development assistance rich countries wish to

\[11\] Even if the entire pharmaceutical budget in many African countries went to malaria vaccines, the benefit to a
vaccine developer would be far less than the social benefit. The social benefits of a malaria vaccine in 25 African
countries for which health expenditure data are available would be $648 million annually, even using conservative
assumptions on DALYs. [Note: This number needs to be updated.] These countries spent $1.7 billion on health in
1996 [World Bank, 1998]. Generally, pharmaceuticals account for between 10-30% of recurrent costs in health
[World Bank, 1993]. This would amount to $170-510 million. (Of course, pharmaceutical expenditures could
provide. The next two sections discuss various options for encouraging vaccine research.

3. The Roles of Push and Pull Programs in Encouraging Vaccine Research

The literature on vaccine research distinguishes between “push” and “pull” programs. Push programs provide direct funding for vaccine research, for example, through grants to academics, public equity investments in vaccine development, or work in government laboratories. Pull programs increase rewards for development of a vaccine, for example, by promising to purchase a vaccine if it is developed. Roughly, the distinction is between paying for research inputs and paying for research outputs. Sub-section 3.1 argues that the development of the biotech venture capital industry has broadened the scope for pull programs, and that while such programs are attractive for the later stages of the vaccine development process, push programs should be used to finance basic research. Sub-section 3.2 reviews the history of AID's malaria vaccine program, which illustrates the problems associated with push programs.

3.1 The Potential Role of Pull Programs

change in response to vaccine development.
Historically, there were relatively few sources of finance available for commercial pharmaceutical research outside a few major pharmaceutical companies. Programs designed to encourage such research therefore had to finance research inputs ahead of time rather than simply paying for a vaccine. However, with the rise of the biotech venture capital industry in recent years, it is now much easier for researchers with reasonable scientific prospects of developing a product with to attract outside investors, as long as a sufficient market is expected for their product. Pull programs could create such a market. It is worth reevaluating methods of supporting research in light of this changed financing environment.

Pull programs create strong financial incentives for actual vaccine development, and these incentives are likely to be desirable, especially in the later stages of vaccine development. Scientists are likely to be much better informed about their work and about the prospects for vaccines than research administrators, and in the absence of strong financial incentives, this creates temptations for scientists to 1) exaggerate the potential for success in order to obtain grants, and 2) divert effort away from developing a vaccine and towards other objectives, such as publishing academic articles. I discuss each of these issues below.

Perhaps the chief advantage of pull programs that provide strong financial incentives for production of a vaccine is that they help in selecting research projects. Under a system of grant-financed research, advocates for particular diseases and scientists working on the disease have an interest in exaggerating the scientific potential for advances on that disease. Similarly, researchers working on a particular line of research have an interest in exaggerating the promise of their own lines of research. Politicians and government scientific administrators may have trouble deciding which diseases are worth working on, and which vaccine approaches, if any, are

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12 Several vaccines were therefore developed primarily in the public sector, and only later licensed out to the private sector for production. For example, the meningococcal meningitis vaccine was developed almost entirely at the Walter Reed Army Institute of Research, and a hepatitis B vaccine was designed by the Hepatitis B task force [Muraskin, 1995]. However, it is not clear that the development of these vaccines in the public sector reflects so
worth pursuing. They may wind up financing ideas with only a minute probability of success, or worse, failing to fund promising vaccine research because they do not have confidence that its backers are presenting objective information on its prospects.  

Purchase pre-commitments or other strong financial incentives tied to research outputs have an advantage over research grants precisely because the scientific potential for vaccines is difficult for those outside the field to assess. With an assured vaccine purchase, taxpayers pay nothing unless and until an effective vaccine is produced. Politicians and the public do not have to worry that they are investing millions in a malaria vaccine that may be technically infeasible. Pharmaceutical firms contemplating pursuing a line of research and scientists contemplating joining biotech ventures in exchange for stock options will only take the risk of investing their money and time if they believe the scientific prospects are worth pursuing. If scientists and pharmaceutical firms believe a malaria vaccine is feasible, they will risk their time and money. If not, they won’t.

Opinion polls suggest that the U.S. public believes that most foreign aid is wasted, but that they would be willing to support foreign aid if they felt the money was reaching the intended beneficiaries [Kull and Ramsay, 1997]. Under a system of grants to research laboratories, the public would not know whether funds are being wasted, thus making support for vaccines less politically appealing. If public funds are spent only for an actual vaccine, the public can be much more confident that its tax dollars are going to good use.

The second problem with push programs is that because politicians and the public cannot completely monitor researchers’ activities, grant-funded researchers have an incentive to divert some of their effort away from producing a marketable vaccine, and towards other objectives,
such as publishing academic articles. Many academic and government researchers have career incentives and intellectual interests that orient them to fundamental science. The later, more applied portions of the vaccine development process include some activities that are not particularly interesting intellectually, but are expensive. Techniques for manufacturing sufficient quantities of candidate vaccines in sufficient purity for clinical trials must be developed. Animal models for the disease must be created. Vaccine trials in the field must be conducted. Nobody wins a Nobel Prize for these important steps in vaccine development. Under a system of grant-financed research, some researchers may therefore be tempted to use funds earmarked for applied vaccine research and development to finance their time while they devote much of their effort to pursuing more theoretical scientific objectives. In contrast, if governments purchase vaccines, they pay for research output rather than research inputs, and thus provide strong financial incentives to actually develop a marketable vaccine.\(^\text{14}\)

Although pull programs have an advantage in the later stages of development, basic research should continue to be financed with grants, rather than pull programs which link rewards to research outcomes. The difficulty of evaluating the quality of basic research output makes paying for research output problematic. It is not simply a matter of testing if a vaccine works, or a product sells. Moreover, basic research, by definition, is as valuable for the information it provides to other researchers as for the products it produces. With strong financial incentives tied to product development, researchers would be more inclined to keep their research results private longer in order to have an advantage in the next stage of research. In contrast, grant-funded academics and scientists in government laboratories have career incentives inclined to seek equity investment.

\(^{14}\) Subsidizing private research through targeted tax credits is subject to problems similar to those affecting grants to researchers. Currently, U.S. companies are eligible for a 20% research and development tax credit. A bill recently introduced in the United States Congress, the Lifesaving Vaccine Technology Act, proposes increasing this credit to 30% for research on vaccines for diseases that kill more than one million people a year. Like direct funding of research, tax credits may be difficult to target. Firms doing research with only indirect implications for these
to publish their results quickly.

Push programs centralize research decisions, while pull programs decentralize research decisions. While decentralization may lead to some duplication of effort, it also means that mistakes by a single decision-maker will not block progress towards a vaccine. In general, society seems to prefer to use direct government support for basic research, while relying on a patent system, rather than centralized government programs, to stimulate the applied work of actual product development. It probably makes sense to opt for a similar approach for vaccines.

Currently, some push programs are in place to spur vaccine research, although funding is modest. For example, IAVI supports ADIS vaccine efforts. Note that even if some push programs are used to encourage particular applied projects, it makes sense to complement those push programs with pull programs. That way, if any promising research leads slip though the cracks of the push system, researchers will still have an incentive to pursue the lead, albeit at their own risk.

If vaccine research were supported through a mix of push and pull programs, a lower price should probably be paid for vaccines that had already received support from push programs. For example, perhaps one condition of public push financing should be agreement to supply the vaccine to poor countries at a modest markup over manufacturing costs.

The administrators of push programs and the researchers financed by such programs often argue that they are somehow cheaper than pull programs. I believe that this view is mistaken. As a first approximation, a biotech or pharmaceutical firm will find it profitable to take on a project if the probability of success times the net present value of profits if the project succeeds is greater than the cost of undertaking the project. This implies that even in the best case, when the government funds only worthwhile research projects and government researchers focus all their energies on developing a vaccine, the expected cost of developing a vaccine, in net present value...
terms, is likely to be similar whether research is financed ahead of time directly by the government or induced by payments for a successful vaccine.\textsuperscript{15}

Why then do many government scientists argue that push programs are cheaper than pull programs? They overestimate their chances of success and underestimate the costs involved. Of course, scientists in pharmaceutical firms do the same. But pharmaceutical executives and biotech investors anticipate this overoptimism, and correct for it by requiring high hurdle rates before approving projects or investing funds.\textsuperscript{16} The net effect is that pharmaceutical executives and biotech investors wind up approving projects that are likely to have positive net present value. If policy makers make a similar correction, they would find that the costs of financing research expenditures and of inducing the private sector to undertake these expenditures are likely to be similar, but that paying only for a successful vaccine creates stronger incentives.

### 3.2 The AID Malaria Vaccine Program

The risks that grant-funded scientists and research administrators competing for budgets will overestimate the chances of success and divert resources away from vaccine research are far from hypothetical.

Desowitz [1991] chronicles the sad story of the U.S. Agency for International Development’s (AID) malaria vaccine efforts. Given the paucity of private malaria vaccine research, AID started a push program to support vaccine research. AID’s efforts in the 1980s

\textsuperscript{15} Governments have access to capital at interest rates only slightly better than pharmaceutical firms.

\textsuperscript{16} Pharmaceutical firms sometimes argue that they need very high rates of return to justify investment, because they have many alternative investment projects that would yield extremely high rates of return. It seems unlikely that pharmaceutical firms in fact have many projects that the financial market expects would yield rates of return higher than those routinely available in the stock and bond markets, because if everyone agreed that such returns were available, pharmaceutical firms could increase their return to shareholders either by borrowing to finance these investments, or by issuing new equity stakes. A more plausible explanation for the belief that extremely high rates of return are required to justify investment is that managers within the firm are overoptimistic about their chances of success, and that senior management corrects for this over-optimism by only approving projects that are estimated to
focused on three teams. A candidate vaccine was developed by the first team. Tests with 9 volunteers found that only 2 were protected from malaria, and suggested that the vaccine created side effects. These results, mixed at best, did not prevent AID from issuing wildly overoptimistic statements, such as “AID could put the first new major effective antimalaria weapon [the vaccine] since DDT to use in developing countries by 1990.” In 1984, the agency claimed that there had been a “major breakthrough in the development of a vaccine against the most deadly form of malaria in human beings. The vaccine should be ready for use around the world, especially in developing countries, within five years.”17 Fifteen years later, the world is still waiting for a malaria vaccine.

Early work by the second team yielded disappointing results, but not surprisingly, the principal investigator argued that his approach was still worth pursing and requested an additional $2.38 million from USAID. The expert consultants assigned to review the project recommended that the research not be funded. However, AID’s malaria vaccine project director told the AID Office of Procurement that the expert panel “had endorsed the scientific methodology and the exceptional qualifications and experience of the researchers.”18 Once the grant came through, the principal investigator transferred grant funds to his personal account. He was later indicted for theft.

The external evaluations of the third proposal called it mediocre and unrealistic. The AID project director ignored the report and arranged for the project to be fully funded. The principal investigator and his administrative assistant were later indicted for theft and criminal conspiracy in diverting money from the grant to their personal accounts. Two months before his arrest, the Rockefeller Foundation had provided him with a $750,000 research grant, and on the very day that he was arrested, AID announced it was giving him an additional $1.65 million for research.

have extremely high net present value.

17 All quotations are taken from Desowitz [1991], p. 255.
By 1986, AID had spent over $60 million dollars on its malaria vaccine efforts, with little progress. Not only the scientists, but also the research administrators, were guilty of exaggerating the prospects for vaccines to obtain more funding, and then diverting this funding away from vaccine research. Since AID believed that there would soon be many candidate malaria vaccines suitable for testing, it tried to obtain monkeys as test subjects for these vaccines. AID’s malaria vaccine project director, James Erickson, arranged for a contract to acquire monkeys to go to an associate who paid him a kickback. Erickson eventually pleaded guilty to accepting an illegal gratuity, filing false tax returns, and making false statements.

What about outside oversight? AID had arranged for independent oversight to be provided by the American Institute of Biological Science (AIBS). Erickson and the AIBS-assigned project manager were lovers.

The case of AID’s malaria vaccine program is extreme. The U.S. National Science Foundation and National Institutes of Health are not known as scandal prone institutions. Pharmaceutical firms internally run what amount to push programs. However, push programs in general are vulnerable to efforts by scientists and research administrators to overestimate the chances of success and to divert resources from vaccine development to other objectives. With pull programs, in contrast, biotech and pharmaceutical firms spend their own money on research, and the public pays only if a vaccine is produced.

Overall, it seems reasonable to have a two-pronged approach in which public sector and grant-funded university laboratories, with their weak financial incentives, focus on basic research, while strong financial incentives are created for private institutions to focus on the later stages of vaccine development. Institutions designed to help push vaccine development, such as the U.S. National Institutes of Health, already exist, and while they can always use more funding, their structure has already been worked out. A companion paper, “Purchase Pre-Commitments

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18 From Desowitz, [1991], p.258.
for New Vaccines: Design Issues,” examines how a vaccine purchase fund could be designed to create pull incentives for the private sector to develop vaccines. Section 4 argues that pre-commitments to purchase vaccines are likely to be superior to alternative ways of creating pull incentives for vaccine development, including cash prizes, research tournaments, buying existing vaccines at higher prices than would otherwise be necessary, and allowing vaccine developers to extend patents on other, more commercially profitable pharmaceuticals.

4. Alternative Pull Programs

Pull programs that reward successful vaccine research could take several different forms other than pre-commitments to purchase vaccines, including extensions of patent rights on other pharmaceuticals, cash prizes, research tournaments, and paying more than necessary for existing vaccines.\(^{19}\) This section argues that extensions of patent rights on other pharmaceuticals are not an efficient way to reward vaccine developers; that while cash prizes and commitments to purchase vaccines are economically quite similar, purchase pre-commitments are likely to be politically superior; that research tournaments are inappropriate for situations like vaccine development, in which it is possible that no satisfactory product will be created by a given date; and that paying more than necessary for existing vaccines is an expensive and potentially ineffective way of encouraging research on future vaccines. Studying the potential market for new vaccines may also be worthwhile, but it is likely to have only a minor effect on the amount

\(^{19}\) In a previous paper [Kremer, 1998], I discuss the possibility of buying out patents, using an auction to establish the patent’s value. This can be seen as a method of determining the appropriate cash prize in lieu of a patent. One advantage of this approach is that it can be used even for inventions such as the Post-It® note, which cannot be defined ahead of time and which would be very hard to create even a semi-objective procedure for valuing. On the other hand, the auction procedure for valuing patents described in that paper may be subject to collusion. For inventions such as vaccines, which are comparatively easier to define ahead of time and for which it is comparatively easy to evaluate effectiveness, advance purchase commitments may be just as effective as patent buyouts, and less subject to collusion.
of new vaccine research conducted.

4.1 Patent Extensions

Jonathan Mann, the late founding director of the WHO Global Program on AIDS, suggested compensating the developer of an HIV vaccine with a ten-year extension of patent rights on another pharmaceutical. With successful pharmaceuticals bringing in as much as $3.6 billion in annual sales [CNNfn, 1998] such a patent extension would be very valuable. Patent extensions may be politically appealing to advocates, in that they need not go through the budget process. However, they inefficiently and inequitably place the entire burden of financing vaccine development on patients in need of the drug for which the patent has been extended. To see this, note that extending the patent on Prozac as compensation for developing an HIV vaccine is economically equivalent to imposing a high tax on Prozac and using the proceeds to finance cash compensation for the HIV vaccine developer. High taxes on narrow bases are typically an inefficient way of raising revenue, since they distort consumption away from the taxed good. An extension of the Prozac patent would prevent some people from getting needed treatment for depression.

The potential countervailing advantage of patents is that when they are applied to the invented good, they closely link the inventor’s compensation to the value of the invention, since inventors will be able to charge more for valuable inventions. If a vaccine is more effective, causes fewer side effects, and is easier to administer, it will bring in more revenue. Patents therefore create appropriate incentives for potential inventors. However, rewarding the inventor of an HIV vaccine with the extension of a Prozac patent eliminates this link between the

20 As Michael Rothchild has pointed out to me, if governments and Health Maintenance Organizations (HMOs) purchase pharmaceuticals, patents may be equivalent to a broad-based tax. Nonetheless, patents may still be
usefulness of the invention and the magnitude of the compensation.

Another disadvantage of compensating vaccine inventors with extensions of patents on unrelated pharmaceuticals is that the right to extend a patent would be worth the most to firms holding patents on commercially valuable pharmaceuticals, and these firms may not be those with the best opportunities for vaccine research. This problem would not be fully resolved by making patent extensions tradable, since firms holding patents on commercially valuable pharmaceuticals would presumably receive some profits in any such trades. If vaccine developers were compensated in cash, rather than patent extensions, they could receive the full value of the compensation without sharing it with the holders of patents on unrelated pharmaceuticals. Cash payments are therefore likely superior to patent extensions as a way of rewarding vaccine developers.

4.2 Cash Prizes

Cash prizes in lieu of patents are economically similar to purchase pre-commitments. However, purchase pre-commitments more closely link payments to vaccine quality and are more politically attractive, and hence more credible. The disadvantages of government purchases are likely to be minor for vaccines.

Compared to cash prizes in lieu of patents, vaccine purchases provide a closer link between payments and vaccine quality. For example, suppose that a vaccine received regulatory approval, but was later found to have side effects. If a cash prize had been awarded at the date of regulatory approval, it might be difficult to get the money back. Vaccine purchases, on the other hand, could be suspended if countries wished to cease purchasing vaccines. Similarly, if a superior vaccine came on the market, countries could switch their purchases to that vaccine. A distortionary if HMOs and governments respond to pharmaceutical prices in their treatment decisions.
cash prize, on the other hand, would already have been awarded.

Moreover, purchase pre-commitments are likely to be politically more attractive than cash prizes, and thus more credible to potential vaccine developers. Vaccine developers are vulnerable to expropriation, even if the terms of the compensation program legally obligate the government to provide compensation for any qualifying vaccine: the funds could be extracted from them in a supposedly separate, unrelated action. For example, a pharmaceutical firm that had just earned a windfall on a malaria vaccine might be subject to stiff price regulation on another product. This suggests that it is important to design a compensation program in ways that are as politically acceptable as possible, and that generate the minimum amount of resentment. Purchasing malaria vaccine for the 50 million children born in Africa each year at $10 a dose for five years is likely to be more politically appealing than awarding a $2.5 billion prize to a pharmaceutical manufacturer. Conversations with pharmaceutical executives suggest that they do not like anything labeled as a prize.

Cash prizes in lieu of patents lead to free competition in manufacturing newly invented goods, whereas public purchases require the government to specify details of the goods purchased and to choose allocation rules. This would represent a significant advantage of prizes over purchases for most goods, but it is less important for vaccines. For example, if the government pre-committed to purchase high-definition television sets as a way of encouraging research, it would have to get involved in decisions about screen size, color, style, reliability, and other issues best left to consumers, and it would likely misallocate the television sets purchased, since it would have little way to determine how many high-definition television sets each household would be willing to pay for at the production cost. In contrast, governments regulate vaccine quality in any case. Moreover, an effective malaria vaccine would be easier to allocate,
since a single course should presumably be taken by all children in areas of high endemicity.²¹

### 4.3 Tournaments

In research tournaments, the sponsor promises a reward to whoever has progressed the farthest in research by a certain date. (See [Taylor, 1995] for a discussion of tournaments.) The design competitions often used to select architectural firms are examples of tournaments. In a vaccine tournament, a committee might be established with instructions to award a cash prize to whichever research team had made the most progress toward a vaccine as of a specific date. If no vaccine had been completed by that date, additional funds could be set aside for further rounds of the tournament.

Tournaments have several limitations, however, and may not be appropriate for encouraging vaccine research.

First, a payment must be made no matter what is developed. While tournaments provide incentives for researchers to devote effort to developing a product, they do not address the problem of determining whether research on a particular vaccine is worth pursuing at all. Advocates for a particular disease and scientists working on the disease will always want to encourage the establishment of tournaments for research on their disease, even if the prospects for ultimate success are low. With a vaccine purchase fund, nothing is spent unless a vaccine is developed.

Another problem with tournaments is that once research has been completed, the award committee might be tempted to allocate the reward on grounds other than progress in research. The committee might award the reward to a more politically correct firm, to a university team, or

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²¹ Not that many people are likely to live in areas where taking the vaccine is a borderline decision, and even in these areas, the appropriateness of vaccination depends primarily on technical issues rather than personal preferences.
to whoever had done the most scientifically interesting work, rather than to the team which had made the most progress toward a vaccine. Anticipating this, firms might invest in political correctness or scientific faddishness rather than in producing an effective vaccine. Of course, a committee making purchase decisions for a vaccine purchase fund could also be subject to bias, but judgments about who has made the most progress developing a vaccine are more subjective than judgements about whether a vaccine with a particular set of results from phase III trials should receive regulatory approval, or even how many lives have been saved by a vaccine.

Collusion among potential researchers may be particularly harmful in tournaments. If only a few pharmaceutical firms had done a significant amount of work, they could collude to exert low effort on doing further research, since the reward would be paid whether or not a vaccine was developed. In contrast, collusion under the vaccine pricing mechanism discussed in the companion paper could lead to higher vaccine prices, but would not prevent development of a vaccine.

Tournaments may lead researchers to put their efforts into looking good on the tournament completion date, rather than a completing a vaccine. Firms which discovered promising research leads that were unlikely to yield solid results before the deadline might ignore their leads, while firms that received information that the research line they were pursuing would not yield a vaccine might not reveal this information.

Tournaments are also politically unattractive. Governments may not find it politically attractive to pay large amounts for research that may have not progressed very far. Since there would be no clear-cut way to decide who was ahead in research, awards might be subject to litigation and charges of favoritism.

Finally, rewards in tournaments would have to be in cash, rather than in guaranteed sales, since no vaccine may have been developed by the end of the tournament. As noted earlier, however, cash rewards are less politically attractive than guaranteed markets.
Section 4: Alternative Pull Programs

4.4 Expanded Purchases of Existing Vaccines

Although the standard EPI package of vaccines is widely distributed, a number of effective vaccines that are already available, such as the hepatitis B vaccine, are not fully used.\(^{22}\) While there is a strong case for purchasing and distributing existing vaccines which are not widely used in developing countries, these purchases should be justified on their own terms, rather than as a way of encouraging more research. Paying more than necessary for existing vaccines is likely to be an expensive and potentially ineffective way of encouraging research on future vaccines.

Note that in order to encourage firms to invest in vaccine research, it would be necessary to buy vaccines from the original developer at a markup over the manufacturing cost. This typically means purchasing the vaccine while it is still under patent, because once a vaccine is off patent, competition among manufacturers, or even the threat of competition, typically drives prices down much closer to the manufacturing costs.

A few new vaccines are under patent. There are four new conjugate vaccines against Haemophilus influenzae b (Hib), which causes pneumonia and meningitis. Vaccination has virtually eliminated Hib disease from many industrialized countries. In developing countries, the WHO estimates that 400,000 to 700,000 children die each year as a result of Hib disease, although further epidemiological surveys are needed to get a precise figure. A full course of treatment with a Hib conjugate vaccine currently sells for $45-$60 to private purchasers, and for $15-$22 to governments of industrialized countries. The Pan-American Health Organization

\(^{22}\) An effective vaccine for malaria or one of the other major killers would likely be consumed much more widely than the hepatitis B vaccine, since the disease burden of hepatitis B is small relative to that of AIDS, tuberculosis, or malaria. Moreover, malaria kills young children very quickly after infection and the onset of symptoms, whereas hepatitis B infection can remain asymptomatic for decades, and many people may not understand its relation to the
(PAHO) has negotiated a special price of $10, but this is still too expensive for most developing countries.

The newly developed rotavirus vaccine is also under patent. Rotavirus vaccine has been used in industrialized countries, but recently there were reports of side effects, and the vaccine has been withdrawn from the U. S. market. In the United States, diarrhea induced by rotavirus is only rarely life-threatening, so even rare side effects might justify not using the vaccine. In developing countries, where an estimated 600,000 children die each year from rotavirus-induced diarrhea [PATH, 1999], a case could be made that vaccination might be worthwhile, despite side effects from the vaccine.

A new vaccine may soon be available against pneumococcus (Streptococcus pneumoniae), which is one of the most common causes of bacterial pneumonia worldwide, killing an estimated 1.2 million children annually [WHO, 1999c].

Purchasing existing vaccines for developing countries is certainly justified in its own right. However, buying currently available vaccines at a higher price than necessary is an expensive and potentially ineffective way of encouraging future research.

Given that the Hib and rotavirus vaccines were developed without any expectation of realizing significant profits in developing countries, paying a developed country price for these vaccines now would provide extra profits to pharmaceutical firms. Providing these extra profits might be worthwhile if it were the only way to establish a reputation for paying remunerative prices for future vaccines. Not surprisingly, pharmaceutical manufacturers argue that the best way to persuade them that work on future vaccines would be rewarded would be to buy currently available vaccines at a high price. However, if it were possible to commit now to purchase future vaccines at a remunerative price, there would be no reason to spend more than necessary for

Note that estimates of rotavirus and pneumococcus deaths were not necessarily prepared using the standard WHO
vaccines which have already been developed. Paying high prices for both current and future vaccines as a way of encouraging future research amounts to paying twice, and is thus a waste of funds.

Purchasing vaccines that are currently under patent may not make pharmaceutical firms confident that they will be rewarded for developing new vaccines for developing countries. Since international interest in health in developing countries is fickle, pharmaceutical firms might well feel that the availability of funds to purchase Hib vaccine now does not guarantee that the international community would be prepared to pay for future vaccines. If pre-commitments to purchase vaccines through a vaccine purchase fund could be made binding enough, they offer a potentially more credible way of spurring research.

In summary, purchases of existing vaccines should be justified on their own terms, and purchasers should bargain for the best possible price. If new programs, such as those sponsored by the Gates Foundation, purchase these vaccines in large quantities, they should seek to negotiate prices significantly below those currently available.

4.5 Commissioning Market Studies

Some argue that pharmaceutical firms conduct little research on vaccines for tropical diseases because they underestimate the potential developing country market for vaccines. This has led to calls for studies of potential demand for vaccines in developing countries, and dissemination of the findings to pharmaceutical firms.

Public funding of these studies may have some merit insofar as the information provided is a public good for many pharmaceutical firms, which no single pharmaceutical firm would collect as thoroughly on its own. However, it is not clear that consultants hired by public burden of disease methodology, and that estimates prepared with that method might be lower.
institutions are as skilled as the pharmaceutical firms themselves in estimating the potential profits from a malaria vaccine. Moreover, pharmaceutical firms may suspect that any such assessment of the potential market might be inflated, given that the institutions sponsoring these studies have an interest in arguing that the demand for such vaccines would be high. Finally, one must consider the logical possibility that further investigation would suggest that the market for vaccines is smaller, not greater, than currently believed by private industry. Market studies of potential vaccine demand may be useful, but by themselves they are unlikely to substantially increase vaccine research.

4. Conclusion

This paper has argued that public, global action is needed to encourage vaccine research and ensure that vaccines are widely distributed once they are developed. Grant-funded research has an important role, especially for basic research, but the development of the biotech venture capital industry has made strong financial incentives tied directly to development of a marketable vaccine appropriate in encouraging the later stages of vaccine development. Pre-commitments to purchase vaccines can both provide incentives for development of vaccines, and ensure that vaccines reach those who need them most. Taxpayers would pay only if a vaccine were developed.

A companion paper, “Pre-Commitments to Purchase New Vaccines: Design Issues,” discusses the design of purchase pre-commitments for vaccines.
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