Historically, societies have encouraged research in a variety of ways:

- Patents grant inventors monopolies over the goods that are produced from their ideas.
- Government directly funds research through such programs as the National Science Foundation and the National Aeronautics and Space Administration.
- Prizes also have been used to spur research and development. For example, in 1714, after a British fleet got lost and struck rocks off England’s coast, drowning 2,000 sailors, the British government established a £20,000 prize for a method of determining longitude at sea. That prize led to the development of the chronometer.

Today, the United States government spurs research mainly through direct funding and the granting of patents. Both methods are vitally important, but each causes serious problems—and each has proved inadequate in spurring the research needed to develop effective vaccines against HIV, tuberculosis, and malaria.

**PATENTS**

**The Consumer’s View** The monopoly pricing of patented goods prevents some people who need those goods from buying them. This problem is illustrated vividly by the recent dispute between the United States and South Africa over AIDS drugs. Up to 20 percent of pregnant women in South Africa are infected with HIV. AIDS drugs cost more than $10,000 annually, well beyond the reach of most South Africans. Alternative, generic versions of the drugs would be much cheaper, but buying these products would violate the patent rights of the original drug developers. To enable its citizens to obtain AIDS drugs more cheaply, South Africa is considering legislation to compel patent holders to license their discoveries to generic manufacturers and to allow the importing of cheap generic drugs from countries that do not respect the original patents. Opponents of the legislation argue that if intellectual property rights are not respected, private firms will lose their incentive to develop new drugs. The United States initially opposed the legislation. However, when AIDS activists began protesting against Al Gore, who had raised the issue as a chair of the U.S.-South Africa Bina
tional Commission, the United States rapidly backed down. The issues raised by the confrontation are deep. Patents, and the resulting legal monopolies, create incentives for research and development that drive medical progress. But under our current institutions, those same problems—and each has proved inadequate in spurring the research needed to develop effective vaccines against HIV, tuberculosis, and malaria.
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firm would be amply compensated and the world’s vaccinologists would turn most of their attention to other deadly diseases. However, the patent system creates an incentive for other firms to design around the first patent so as to produce a competing vaccine and obtain a share of the market. Sixty percent of patented innovations are imitated within four years; the average cost of an imitation is typically two-thirds the original cost of an invention. Not only is this use of scientific talent socially wasteful, but it reduces incentives for developers to undertake original research.

Although patents give potential inventors too little incentive to do original research, they create too strong an incentive to conduct "me too" research aimed at designing around existing patents. Suppose, for example, that a biotech or pharmaceutical firm developed a 100-
percent effective, safe, single-dose AIDS vaccine. In an ideal world, the
firm would be amply compensated and the world’s vaccinologists would turn most of their attention to other deadly diseases. However, the patent system creates an incentive for other firms to design around the first patent so as to produce a competing vaccine and obtain a share of the market. Sixty percent of patented innovations are imitated within four years; the average cost of an imitation is typically two-thirds the original cost of an invention. Not only is this use of scientific talent socially wasteful, but it reduces incentives for developers to undertake original research. Although patents can create too much incentive to develop substitute products designed around original patents, they can also block needed improvements that draw on the ideas covered by the original patents. For example, the development of the high-pressure steam engine was blocked by James Watt’s patent covering all steam engines. Watt’s steam engine was blocked by a previous patent until he found a way to invent around it; and Thomas Edison’s improved version of the telegraph was blocked by a prior patent for many years.

GOVERNMENT RESEARCH AND DEVELOPMENT

An alternative to patents as a way of encouraging research is for government to fund research directly, through such entities as the National Institutes of Health. Government can be more effective in financing basic research, but government programs to finance commercial R&D have a mixed record. To take a few examples, the supersonic transport plane, the Carter administration’s synthetic fuel program, and the Clinch River Breeder Reactor were spectacular failures.

The government often has difficulty in selecting appropriate research projects and in motivating researchers to focus on developing viable projects. Researchers applying for grants have an incentive to present the prospects of success in the best possible light to increase their chances of receiving funding. Research administrators in turn have incentives to tell their superiors that prospects for success are bright in order to increase the budgets of their divisions. Once research grants have been made, researchers may not focus intensely on developing viable products. Many academic and government researchers have career incentives and intellectual interests that orient them to fundamental science, whereas the later stages of product development often include activities that are not intellectually interesting. It can be difficult to determine whether a researcher is focusing on development of a product, trying to publish an academic paper, or preparing the next grant application. In contrast, a private firm pursuing a patent is paid only if it develops a successful product; thus its incentive is to choose projects with an realistic chance of success and then to focus intensely on developing viable products.

Another problem with direct government financing of R&D is that organized interests (e.g., defense contractors and AIDS activists) may lobby to influence these decisions, diverting research expenditures from objectives that are scientifically meritorious or economically viable. Members of Congress may support research projects because they are located in member’s districts, not because those projects are likely to succeed. Once projects have been started, they acquire their own bureaucratic and political momentum, making them difficult to shut down, even if the scientific prospects for success appear dim.

In view of the politics of government-funded research, it is not surprising that empirical studies suggest that the rate of return on publicly financed R&D is much lower than that of privately financed R&D.

PRIZES AND PATENT BUYOUTS

Through the early nineteenth century, prizes were used widely as an alternative to patents and government sub-

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R E G U L A T I O N 2 3 , N O . 2
Malaria, tuberculosis, and HIV have in the past 50 years killed several times as many people as all wars. Together, they kill five million people a year, mostly in developing countries.

Through the buyout of Daguerre’s patent a valuable technology was placed in the public domain and more fully used. Further research was spurred because developers of improved lenses or photographic chemicals did not have to worry that their work would be blocked by Daguerre’s patent. And because Daguerre’s sale of the patent was voluntary, not coerced, incentives for invention were not weakened by setting a precedent for the expropriation of intellectual property rights.

Of course, prizes can be used only when it is possible to describe the desired invention ahead of time. Who would have thought of establishing a prize for the Post-it note?

**FINDING VACCINES FOR MALARIA, TUBERCULOSIS, AND HIV**

**The Threat** Malaria, tuberculosis, and HIV are the world’s most deadly communicable diseases. In the past 50 years, those diseases have killed several times as many people as all wars. Together, they kill five million people a year, mostly in developing countries.

Malaria kills 1.1 million people annually and is particularly likely to kill children and pregnant women. Resistance is spreading to the major drugs used to treat malaria and to provide short-term protection for travelers.

Tuberculosis kills 1.9 million people a year. Although most cases of tuberculosis now occur in developing countries, drug-resistant strains are spreading rapidly, posing a threat to developed countries.

In 1998, about 2.3 million people died of AIDS, and 5.8 million people were newly infected, 70 percent of them in sub-Saharan Africa.

**The Promise of Vaccines** Vaccines have proved effective against many other infectious diseases, and in the long run, they are likely to be the most effective and sustainable way to fight malaria, tuberculosis, and HIV. The potential of vaccines is illustrated most vividly by the eradication of smallpox in the 1970s. A standard package of cheap, off-patent vaccines reaches three-quarters of the world’s children and is estimated to save 3 million lives a year.

It is an open question whether vaccines can be developed...
against malaria, HIV/AIDS, and adult tuberculosis, but there is reason to be optimistic. Recent research on animals looks promising and advances in immunology, biochemistry, and cloning have given scientists new tools with which to develop and test vaccines. Genetic sequencing of the organisms causing malaria, tuberculosis, and HIV is complete or far advanced.

Obstacles to Private-Sector Research There is little private-sector research on vaccines for malaria, tuberculosis, and African strains of HIV. Most of the people who suffer from those diseases are poor and cannot afford to spend much on vaccines. Most applied AIDS research is on treatments, which tend to be more lucrative than vaccines. AIDS activists also tend to focus more on lobbying for treatments than for vaccines. The little AIDS vaccine research that is conducted is overwhelmingly oriented towards the strains of the disease prevalent in rich countries, not the strains prevalent in Africa, where most people are dying.

Private research on vaccines for malaria, tuberculosis, and African strains of HIV is limited not only by the poverty of potential customers, but also by the limited ability of private developers to reap the benefits that those vaccines would produce. Individuals who take vaccines not only benefit themselves, but also help break the chain of disease transmission, thus benefiting the rest of the population. Customers would not pay for this side benefit of vaccines. In addition, the beneficiaries of vaccines are often children. Keeping children disease free would allow them eventually to earn enough to compensate vaccine developers, but of course, there is no way children can sign a contract to compensate vaccine developers when they become adults. Furthermore, some potential customers may be unwilling to pay much for vaccination because they are unaware of its benefits, a problem that is particularly acute in poor countries, where many potential customers are illiterate and may not trust health officials.

Moreover, governments often use their power as buyers, their regulatory power, and their power over intellectual property rights to keep vaccine prices low. Many governments drive down the price of vaccines and other pharmaceutical products by limiting intellectual property rights and by producing or importing cheap generic versions of drugs and vaccines. This practice is widespread in poor countries, but even such countries as Japan, Switzerland, and Sweden were not awarding patents on pharmaceuticals as recently as the 1970s. That strategy avoids the high prices associated with patents but also discourages R&D.

As a result of such policies, vaccines used in developing countries typically sell for pennies a dose. Those vaccines that cost as much as a dollar per dose do not reach most people in the poorest countries. Rough calculations suggest that, even at a cost of $40 per immunized person, vaccines against malaria and HIV would be cost-effective in poor countries. But because private firms would be lucky to receive even a tenth of that amount in those countries, they are—unsurprisingly—not rushing to develop vaccines.

Government-Funded Research Not the Answer Given the obstacles to private research into vaccines for malaria, tuberculosis, and HIV, one option would be for the government to finance research directly. This makes sense for basic research. However, direct government financing is ill-suited to the subsequent development of useful products—a task that is much better left to the private sector. In The Malaria Capers, Robert S. Desowitz chronicles the sad story of the efforts of the U.S. Agency for International Development (USAID) to promote the development of a malaria vaccine. USAID decided in the 1980s to finance three teams seeking a malaria vaccine. One team developed a candidate vaccine, but only two of nine volunteers tested were protected from malaria, and the tests indicated that the vaccine created side effects. Those results, mixed at best, did not prevent USAID from issuing wildly optimistic statements. 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” (p. 255). Fifteen years later, the world is still waiting for a malaria vaccine.

Early work by a second team yielded disappointing results, but, not surprisingly, the principal investigator argued that his approach was still worth pursuing and requested an additional $2.38 million from USAID. The expert consultants assigned to review the project recommended against funding the research, but James Erickson, USAID’s malaria vaccine project director, told the USAID Office of Procurement that the expert panel “had endorsed the scientific methodology and the exceptional qualifications and experience of the researchers” (p. 258). Once the grant was awarded, the principal investigator transferred grant funds to his personal account. He was later indicted for theft.

Although outside evaluations of the third team’s proposal called it mediocre and unrealistic, Erickson arranged
An advance commitment to purchase a certain quantity of a vaccine at a certain price, if it were invented, could take the form of a contractual agreement to buy any new vaccine that meets specified criteria.

A patent buyout would allow firms to compete freely to manufacture a vaccine, but given the technical complexity of manufacturing vaccines and the arduous process of securing regulatory approval, competition might not be intense even if patents were put in the public domain.

The Promise of Purchase Commitments: Alternatively, the government (or a private foundation) could make an advance commitment to purchase a certain quantity of a vaccine at a certain price, if it were invented. The commitment could take the form of a contractual and binding agreement to buy from a prospective vaccine developer any new vaccine that meets specified criteria (e.g., it must be FDA-approved and effective at least 80 percent of the time). The sponsor could then make the vaccine available to developing countries in exchange for modest co-payments.

Incentives: Unlike direct government financing of research, a purchase commitment allows the private sector to decide which projects to pursue; that is, research priorities are not centrally planned by government, but independently decided by private firms reacting to the market incentive offered by the purchase commitment. Pharmaceutical firms and scientists will take the risk of investing their money and time only if they believe the scientific prospects are worth pursuing. A firm that thinks a vaccine is impossible to produce, given current scientific knowledge, will not invest its money in research and, thus, no government funds will be wasted on a futile effort. Moreover, a purchase commitment gives researchers a strong financial incentive to focus on developing a marketable vaccine. Researchers are unlikely to be distracted by such other pursuits as publishing academic articles; they will be paid only for producing a viable vaccine.

By agreeing to purchase a large quantity of a vaccine, the sponsor can purchase it at a reasonable price, while providing a sufficient incentive for its development. Because the cost of R&D represents a large fraction of the cost of producing a vaccine, while the cost of manufacturing additional doses is usually modest, the total size of the market (not the price of a dose) will be most important in attracting potential developers. Thus, any commitment should specify the total value of the vaccine that will be purchased (i.e., price and quantity). To encourage development of a vaccine requiring as few doses as possible, the promised price should be set per immunized person, not per dose. A purchase commitment should cover as many countries as possible, in order to reduce the price per immunized person given the total promised market size. Participating countries would provide co-payments, scaled to their respective per capita incomes. The co-payments would...
help to ensure the participating countries' commitment to the effort and their satisfaction with a vaccine's effectiveness, given local needs and conditions.

Costs and Benefits A rule of thumb in the pharmaceutical industry is that an annual market of $250 million dollars is needed to attract strong interest from potential developers. If a commitment of that size were to result in the development of an effective vaccine, it would yield a high payoff. For example, in 10 years, more than 400 million people could be vaccinated against malaria at a per capita cost of $7.50. At least 216 million years of life could be saved at a cost of roughly $34 per year per life saved.

The benefits of a successful program would probably continue even after the expiration of the purchase commitment. It is likely that competing vaccines would become available, driving prices down and making purchases more affordable for developing countries and donors.

Potential Sponsors Recently, two institutions that traditionally have taken a centralized, statist, approach to vaccines have begun exploring market-oriented approaches. World Bank president James Wolfensohn said recently that his institution plans to create a $1 billion loan fund to help countries purchase specified vaccines if and when they are developed (Financial Times, February 2, 2000). It is not clear whether the Wolfensohn proposal will pass through the organization’s internal bureaucracy and win board approval.

The U.S. government, which sponsored the ill-fated U.S.A.P.O. effort to find a malaria vaccine, is now considering a more market-oriented approach. Private firms, rather than government bureaucracies, would make research decisions, knowing that they would be rewarded only if they develop effective vaccines. Specifically, the Clinton administration's budget proposal would match every dollar of qualifying vaccine sales with a dollar of tax credit, effectively doubling the incentives to develop vaccines for neglected diseases. A qualifying vaccine would have to attack an infectious disease that kills at least one million people a year and would have to be approved by the F.D.A. To qualify for the tax credit, sales would have to be made to approved nonprofit organizations or international institutions. The program’s matching feature could encourage the funding of vaccine purchases by nonprofit organizations, international institutions, and the governments of developing countries. The cost of the program would be capped at $1 billion and it would run from 2002 through 2010, but it could be extended for 10 years if no vaccine has been developed in that time.

Private foundations could also play a major role in creating markets for new vaccines. Because foundations have more continuity of leadership, they can more easily make commitments to purchase new vaccines. (The Gates Foundation, for example, has $22 billion in assets; one of its main priorities is to provide vaccines for developing countries.) U.S. law requires private foundations to spend at least 5 percent of their assets annually. A U.S. foundation could spend 5 percent of its assets annually on grants to expand the use of existing vaccines and to fund vaccine research, while using some of its principal to back a pledge to purchase and distribute effective new vaccines, if and when they are developed.

CONCLUSION The United States currently supports R&D through the granting of patents and government-funded research. It is time to consider supplementing these mechanisms. In particular, programs to help create markets for malaria, tuberculosis, and AIDS vaccines could harness the resources and expertise of the private sector in the fight against the world’s worst infectious diseases while avoiding the inefficiencies associated with many government programs.

Commitments to buy large quantities of vaccines could lead to the development and delivery of effective vaccines at low cost, saving millions of lives. Taxpayers would pay nothing unless and until those vaccines have been developed.

readings