

# Childhood Vaccines: The R&D Factor

Pharmaceutical companies contend that a proposal for the federal government to buy childhood vaccines and distribute them free of charge would undercut the development of new products

The measles epidemic that slammed the United States in 1989, infecting more than 18,000 people and killing 41 children, shocked a lot of parents. But it didn't surprise some public health officials, who had been warning for years that the United States has a disturbingly low vaccination rate among young children and that a killer epidemic was a disaster just waiting to happen. And those officials argued that measles was merely a harbinger of things to come. Polio-myelitis, pertussis, rubella, and mumps might all follow in killer outbreaks.

As tragic as the measles epidemic was, it finally focused public attention on the nation's immunization problems. The National Vaccine Advisory Committee, an influential body that advises the Public Health Service, urged the government to spend more than \$40 million annually to improve access to and delivery of childhood vaccines. The United States helped launch the Children's Vaccine Initiative, an international drive to research and develop vaccines. And state and local governments stepped up efforts to vaccinate more children.

That kind of action is all to the good. Four years later, however, a disaster is still waiting to happen. The Centers for Disease Control and Prevention (CDC) estimates that although nearly all children are fully immunized by the time they enter public schools at age 5, vaccine coverage of 2-year-olds is still staggeringly low: As few as 37% in that age group nationwide have been vaccinated. In light of that kind of inertia, a growing band of public health experts are arguing that it's time for a drastic step: The federal government, they say, should purchase vaccine for every child in the country and distribute the material free of charge.

The scheme, known as "universal purchase," is under serious consideration by the Clinton Administration, and it may be included in legislation being drafted by Senator Edward M. Kennedy (D-MA), chairman of the Senate health committee. The three main vaccine manufacturers in the United States—Lederle-Praxis Biologicals, Con-

naught Laboratories, and Merck & Co.—have reacted with horror to the idea, however, warning that if the federal government becomes the sole purchaser of childhood vaccines, competition will be squashed, returns on investment will plummet, and research and development on new vaccines will be



**Too expensive?** President Clinton says new vaccines are fine, but many parents can't afford existing ones.

devastated. "It's bad for the immunization enterprise across the board," says Connaught president David Williams.

Though proponents of universal purchase concede that providing vaccines for free will do little if the distribution system for childhood vaccines isn't improved, they maintain that the potential benefits outweigh the risks (see sidebar). And they also argue that industry exaggerates the threat to R&D. "There's no question that R&D is important, but there is a question of how much R&D the manufacturers are now doing," says Joseph Tiang-Yau Liu, a health analyst for the Children's Defense Fund (CDF), a chief advocate of universal purchase. There's also no question that the universal purchase idea is shaping up as a major test of the new Administration's health policies.

## The R&D equation

The vaccine manufacturers say now is an ironic time to launch a program that could undercut their R&D efforts, since, after a long dry spell, an explosion of vaccine research is under way—an explosion that could be short-circuited by the universal purchase plan. For more than a decade, vaccine R&D

has been in a precarious position in the United States. Much of the trouble stemmed from the growing number of multimillion-dollar lawsuits being filed by people who believed that they or their children had been injured by vaccines. As a result, more than a dozen manufacturers closed up shop, leading to threats of vaccine shortages.

To bolster the vaccine industry, Congress in 1986 created the National Vaccine Injury Compensation Program, a no-fault system that pays children injured by vaccines and relieves manufacturers of most of their liability burden. "Liability was the largest barrier to innovation in this field," says Connaught's Williams. Universal purchase, he believes, jeopardizes the many new products in the pipeline. "It would be a crime to set that [progress] aside."

New childhood vaccines currently on the horizon include preparations for varicella, the chickenpox that afflicts 3 million children each year; otitis media, or inflammation of the ear; respiratory syncytial virus, which can cause severe respiratory distress in young children; and rotavirus, the chief cause of the often lethal infant diarrheal disease. Equally important is the push to simplify delivery with new combination vaccines—Merck and Connaught are now jointly attempting to make a cocktail of diphtheria, tetanus, pertussis, *Haemophilus influenzae* type B (Hib), hepatitis B, and polio. And then there is a renaissance of vaccine research in smaller biotechnology companies—which the large pharmaceuticals often invest in or buy outright—for AIDS, herpes, malaria, rheumatoid arthritis, cancer, and lupus.

But those advances won't do much good if parents can't afford to get their children inoculated. "We cannot possibly justify financing research and development in future vaccines based on prices that will assure that children will not receive the vaccines that are available today," Clinton railed while visiting a health clinic on 12 February.

Indeed, much of the interest in universal purchase is driven by the sharply increasing price of childhood vaccines: A full series has jumped from \$23 to \$244 over the past decade. But the manufacturers contend that 80% of the increase is due to new vaccines added to the schedule (Hib and hepatitis B) and a new federal excise tax that funds the National Vaccine Injury Compensation Program. And they note that they already sell at



## A Question of Distribution

Offering free vaccine in a "universal purchase" scheme won't, by itself, solve the country's immunization woes—even the most polar opponents in the vaccine debate agree on that. The key problems, they say, are access and delivery. Improvements currently being called for include keeping clinics open longer, tracking newborns with a national registry and notifying parents when children are due for immunizations, and providing better public education about the benefits of vaccines.

But supporters of universal purchase insist that it is the surest way to link all these fixes. One of the strongest—and best connected—advocates of universal purchase is the Children's Defense Fund (CDF), which used to include among its board members First Lady Hillary Rodham Clinton and Secretary of Health and Human Services Donna Shalala. CDF maintains that many children slip through the cracks when their private physicians, aiming to help families save money, refer them to public clinics for free vaccines. (Many insurers don't cover vaccinations.) "You never know if [the children] make it to the clinic," says Joseph Tiang-Yau Liu, a health analyst for CDF. "Universal purchase takes the vaccine and moves it to where the children are." The vaccine manufacturers counter, however, that providing free vaccine would not solve this particular problem. They point to a recent survey conducted by the Centers for Disease Control and Prevention (CDC) that shows that a dozen states that already

provide free vaccine to all residents don't have significantly higher vaccination rates of preschoolers (62% vs. 56%).

Yet universal purchase could also be the cornerstone of a national tracking and notification system. CDF envisions that the government, as the sole distributor of vaccine, could require pediatricians to report who was receiving what. If physicians did not cooperate, the government could refuse to replenish their vaccine stocks. The March of Dimes also makes this argument. "I personally don't believe you can do tracking without providing physicians free vaccine," says Kay Johnson, who handles government affairs at the March of Dimes. "We're not going to reach private physicians until there's an incentive."

The manufacturers like the idea of a tracking system but don't think it has to be linked to universal purchase. "Kids should be registered when they're born through Social Security," suggests R. Gordon Douglas Jr., head of Merck's vaccine division. In theory, notifications could routinely be mailed out and pediatricians could also access every child's immunization status.

Whatever the fate of universal purchase, Walter Orenstein, director of the CDC's division of immunization, welcomes all this attention on improving the vaccination rates of preschoolers. "I'm excited there's this much interest," he says. "If we can't do it now, it can't be done."

—J.C.

a discount half of the country's childhood vaccines to states and the federal government, which then distribute them for free through a variety of programs.

The impact universal purchase would have on the development of new vaccines would depend in part on the price the government would be willing to pay. CDF's Liu contends that the government should pay manufacturers the weighted average between the current public and private-sector prices. "If their revenue doesn't change, how can it affect research?" asks Liu. But R. Gordon Douglas Jr., head of Merck's vaccine division, says the essential problem is that R&D requires a long-term investment, and "we don't believe the federal government is a reliable partner."

How much profit would be needed to ensure that sufficient R&D is maintained? It's difficult to gauge. For one thing, the companies will not reveal how much they spend on vaccine-related R&D. Companies claim to reinvest up to 15% of their vaccine profits into R&D, but even the size of the childhood vaccine market is a mystery, with guesstimates ranging from \$500 million to \$800 million. Moreover, a substantial amount of vaccine research is conducted by the federal government, and that would not be affected by universal purchase. "I think more research is done in the public sector than the private," says John LaMontagne, head of the lead vaccine division of the National Institute of Allergy and Infectious Diseases, "but I have no way of



**Summit meeting.** (From left) Connaught's David Williams, Lederle's Ronald Saldarini, and Merck's R. Gordon Douglas Jr. talk R&D with Donna Shalala.

confirming that." The National Institutes of Health itself devotes nearly \$200 million to adult and pediatric vaccine research each year, and more than \$70 million is spent by the Department of Defense, the Agency for International Development, the CDC, and the Food and Drug Administration.

Though Boston University's Anthony Robbins, a leading proponent of universal purchase, doubts that the large pharmaceuticals conduct a substantial amount of vaccine research, he also believes that the federal government should couple universal purchase with a plan to pay industry to develop new vaccines—just as the military funds the development of new weapons. "We'd double or

triple the actual number of vaccines in this country," he predicts. "I think the evidence is that the current rate of profit is insufficient to drive them at an appropriate rate. We could be a lot further along than we are now."

### If it's Monday, I'm for it

Many vaccine experts are on the fence about universal purchase. As Walter Orenstein, head of the CDC's division of immunization, says, "On Monday I'm for it, on Tuesday I'm against it." Orenstein believes the threat to R&D is real, but concurrently thinks that universal purchase offers a long-term benefit: As new vaccines are developed, they could automatically be added to the armamentarium.

A clearer definition of the vaccine R&D equation is expected to emerge in June when the Institute of Medicine completes a study to evaluate the United States' role in the Children's Vaccine Initiative. And it may take the Clinton Administration that long to decide where it stands on the universal purchase issue. Currently, Administration officials are in a research mode themselves, holding several closed door meetings with Merck, Connaught, and Lederle. Following one such meeting on 1 March, Health and Human Services Secretary Donna Shalala told *Science* that R&D was discussed, adding, "We don't have a formal position on universal purchase." But clearly, the Administration does have a bottom line on immunization reform: the sooner, the better.

—Jon Cohen