

# Immunization Focus

A quarterly publication of the Global Alliance for Vaccines and Immunization

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GAVI

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## Immunization Focus

*Immunization Focus* is issued quarterly on the GAVI website at [www.VaccineAlliance.org](http://www.VaccineAlliance.org)

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## Early gains in Africa's 'biggest ever' attack on polio

NEWS

IN the largest synchronized peacetime operation the region has ever seen, 17 countries in West and Central Africa have begun a campaign to immunize 70 million children against polio. With the second round due to start in late November, the early results from the first round, conducted during October, indicate that the campaign has reached a higher proportion of children than any before it.

"Now countries are really getting up to the levels where they can interrupt the transmission of the virus," said Bruce Aylward, coordinator of the Global Polio Eradication Campaign at WHO in Geneva. "No countries have ever cooperated on this scale except in times of war, and that is extremely exciting."

For the first time, many of the countries involved did house-to-house visits, using hundreds of thousands of volunteers to immunize children and then mark the houses. Compared with previous years, the first round has reached 5% to 20% more children than had ever been immunized before.

Political commitment at the highest level was key to the operation's success, said Deo Nshimirimana, regional coordinator for WHO in Abidjan. "President Konare of Mali launched the first day and he stayed all morning, vaccinating the children himself," he said. The campaign went ahead even in countries disrupted by conflict.

The organizers also targeted national borders, where migrants

and victims of conflict tend to miss out on polio immunization. "These synchronized campaigns are an opportunity for peace-building," said Carl Tinstman, UNICEF's senior advisor for polio eradication.

Despite the success, there is still room for improvement, said Nshimirimana. "We still have villages that were not covered in hard-to-reach areas, and we need to do more to train some of the volunteers." A third round will follow early next year in some countries.

**Chalk it up:**  
a volunteer marks a house in Sokoto, Nigeria, in the first round last month



The success of a coordinated and synchronized cross-border campaign could be adapted for other public health purposes, said Aylward, including malaria control or even anti-smoking programmes.

The countries involved are: Benin, Burkina Faso, Cameroon, Chad, Côte d'Ivoire, Gambia, Ghana, Guinea, Guinea Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone and Togo. Key to the effort is Nigeria, the largest remaining reservoir of endemic polio in the region. ■

Phyllida Brown

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# Coming to grips with the big one

**A new plan to attack measles is gathering widespread support, as Phyllida Brown discovers**

MEASLES kills more children than any other other vaccine-preventable disease. This year it will claim the lives of about 880 000 children—a staggering 30% of all vaccine-preventable deaths and 40% of those in children. How can this be, when an effective vaccine costing just 26 cents, including safe injection equipment, has been widely available for more than 20 years?

It's an easy enough question to ask, but, predictably, the answer is tougher. Measles virus is difficult to control because of its contagious nature and the characteristics of the existing vaccine (see Box 1). Disagreements about how best to tackle it have continued for a decade.

The Americas have made dramatic progress towards eliminating the disease.<sup>a</sup> But some other regions have seen their situation worsen steadily. Amid an overall stagnation in immunization programmes, the percentage of children vaccinated against measles worldwide appears to have actually fallen, from 80% in the early and mid-1990s to 72% in 1999. In many countries in sub-Saharan Africa, coverage is much lower.

Determined to change the current situation, the World Health Organization and UNICEF, together with the US Centers for Disease Control and Prevention (CDC), developing country health experts and others, have hammered out a consensus on what should be done. A plan<sup>1</sup> to be published this month by WHO and UNICEF should be endorsed by the

partner organizations and finalised by the end of the year. The plan has two broad goals:

- To cut measles deaths by two-thirds, saving 3 million lives, by 2005; and
- To continue to prevent at least 600 000 deaths a year, sustainably, after 2005.

In addition, the plan sets a timetable to collect data to indicate whether, after 2005, measles can feasibly be eradicated worldwide.

The plan sets out details of how these goals may be reached (see Box 2). The core of the plan is to increase routine coverage with measles vaccine and then use supplemental campaigns to cut the death toll further. "We have an agenda now to substantially reduce measles mortality," says Ana Maria Henao-Restrepo, who coordinates measles activities at WHO.

The consensus underlying the plan marks a welcome resolution to a protracted debate between key players in global public health. The argument has not been about the need to reduce the number of deaths—after all, few would question this—but about whether the world should embark on a campaign to eradicate measles, and if so, when. By deferring the eradication decision until more data have been gathered, the plan allows the opposing camps to move forward.

"The programme was at a standstill," says Edward Hoekstra, medical coordinator for measles activities at UNICEF. "Now everyone is agreed." ■

## Box 1: Why measles is a tough challenge

Measles is the most contagious infection known to humans. It may cause fever, cough, rash, conjunctivitis, diarrhoea, ear infections and pneumonia. A less frequent but serious consequence of infection is encephalitis, or inflammation of the brain. Measles can also cause permanent disabilities such as blindness.

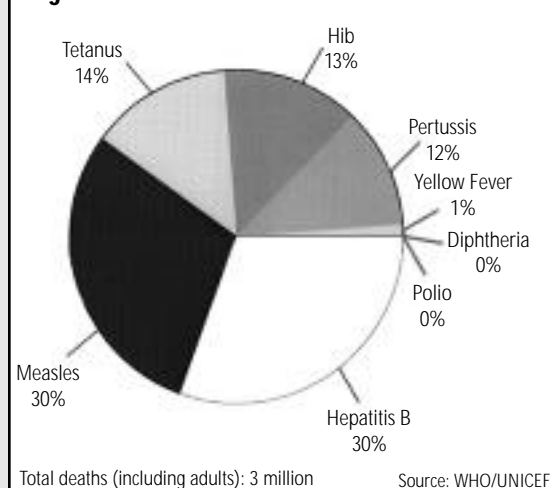
Measles accounts for fully 30% of all deaths from vaccine-preventable diseases including adult deaths caused by hepatitis B (See Figure 1). Twenty countries account for 85% of the deaths, and half of all deaths are concentrated in just four countries—India, Nigeria, Ethiopia and the Democratic Republic of Congo.

Complications of the disease are much more common in low-income countries, and in malnourished children, than in industrialized countries. However, in some high-income countries, particularly in Europe, complacency about measles has created situations where vaccination coverage levels are lower than required to prevent outbreaks.

With the introduction of measles vaccine to the majority of the world's children, the estimated yearly death toll has fallen by about 80% from the pre-vaccine era. However, because measles is so contagious, and because a small minority of those who are vaccinated do not develop immunity, vaccination coverage levels need to be very high—above 90%—to stop the transmission of the virus.

Measles vaccine is given no earlier than 9 months. Before this time, it fails to stimulate immunity in the infant because the mother's antibodies to the virus are still present. Thus, immunization against measles must be delivered much later than the rest of the immunization schedule of vaccines against tuberculosis (BCG), polio and diphtheria, tetanus and pertussis (DTP). This means that,

**Fig 1: Deaths from Vaccine-Preventable Diseases**



even where coverage rates for BCG and DTP vaccines are at 80% or above, coverage for measles vaccine is usually lower because a large number of parents do not maintain contact with health workers after the first few months. Measles vaccine is also more difficult to handle than some other vaccines: it has to be reconstituted and is highly sensitive to heat.

Research to identify new vaccines against measles, particularly those that could be delivered earlier in life and/or by inhalation, is continuing.

The grounds for the debate have shifted quickly. As recently as 1996 experts at a meeting held by WHO, the Pan American Health Organization (PAHO) and the CDC concluded that global measles eradication was feasible and that a target date should be set for between 2005 and 2010<sup>2</sup>. But others were less certain. The World Bank, for example, has long argued against embarking on an eradication campaign before the costs of doing so—including the diversion of resources from other immunization efforts—have been carefully weighed.

The Americas have almost eliminated indigenous measles, but only through a highly aggressive and active campaign. Elsewhere, in the poorest high-burden countries, such tactics are currently “unthinkable”, says Henao-Restrepo. Fifteen countries, all but five of them in Africa, immunized less than half of their one year-olds against measles in 1998. Measles is killing children in these countries mainly because their routine immunization programmes are struggling on all fronts.

“The consensus is building that the world is not ready for a measles eradication campaign,” says Mark Kane, of the Bill and Melinda Gates Children’s Vaccine Program. One reason, he believes, is that the Global Polio Eradication Initiative has proved more labour-intensive and costly in its final stages than most experts predicted. Even at a predicted cost of US\$2.5 billion spread over 20 years, the cost is likely to be dwarfed by the predicted \$1.5 billion annual savings that will flow from polio eradication<sup>3</sup>; but, experts fear, before that final goal is achieved, a second disease eradication initiative could sap resources and attention from the critical final stages of the polio campaign.

**Finish off polio first**

This view is also supported by Ciro de Quadros, head of vaccines and immunization at PAHO, who is credited with being the driving force behind both the polio and the measles elimination initiatives in the Americas. “It is essential that we act to reduce measles mortality, but of course we cannot think about global eradication of the disease at this stage,” he says. “The top priority must be to eradicate polio.”

Also, it has become clear that countries’ current needs are too diverse to be straitjacketed into a single measles eradication campaign. Each has different pressures and priorities.

In Pakistan, for example, Rehan Hafiz, the national manager for the Expanded Programme on Immunization (EPI), says the programme’s resources are fully devoted to the polio campaign at present, and any additional campaign on measles should only be considered later and after careful thought. “Campaigns are very labour-intensive,” says Rehan. “The basis for a strong programme should always be routine immunization.”

**Box 2: Gaining the upper hand: a strategy to reduce measles deaths worldwide**

The WHO-UNICEF mortality reduction strategy will be focused on the 20 countries that account for 85% of all measles deaths. Initially, it is being adopted by a subgroup of those countries that are already free of endemic polio (Mozambique, Tanzania, Uganda, Indonesia and Myanmar), allowing the remainder to concentrate first on polio eradication. Countries will draw up 3 to 5-year plans to achieve and sustain the targets.

Countries are advised to:

- Increase their routine coverage of at least one dose of measles vaccine to at least 80% of infants aged 9 months.
- Ensure a “second opportunity” for measles vaccination, either through a supplemental campaign or a routine second dose. The second opportunity is needed both to increase the probability that everyone gets at least one dose, and to increase the proportion of the population that is successfully immunized. (At 9 months, up to 15% of infants will not respond to a single dose of measles vaccine, but will be protected after a second dose later.) This advice is new and based on evidence that high measles mortality is more frequently found in settings where children have only one opportunity for measles vaccination.
- Establish an effective system for monitoring coverage and maintaining measles surveillance.
- Provide vitamin A supplements where needed alongside vaccination.
- Improve the management of complicated measles cases.

For more details, and for separate guidelines for countries aiming to eliminate measles, see reference 1.

In contrast, Uganda is under popular pressure from parents to conduct measles campaigns. Issa Makumbi, the national manager for the EPI in Uganda, says that there is strong demand from ordinary people to act swiftly with mass vaccination campaigns to protect infants from resurging outbreaks of measles. Routine measles vaccination coverage is around 53%. “We cannot wait to revitalise the routine programme while our people are dying,” says Makumbi. “We have to do campaigns first to reduce morbidity and mortality a bit and then put all our efforts into improving routine coverage.” Uganda, with support from UNICEF and WHO, is currently doing mass campaigns in 20 districts. “We have to respond to this demand,” he says. “It is a reality.”

As polio’s devastating effects have begun to recede, the burden of measles has looked increasingly unacceptable, and some in Uganda—and in other countries in Africa where polio is no longer endemic—have questioned the resources that polio attracts compared with the resources available for measles control within routine programmes. “From the community’s point of view, polio is not the priority,” says Makumbi. “It is measles that kills them every minute.” Like some other countries, Uganda has made a virtue of this situation by combining polio campaigns with measles

campaigns. In this way, staff resources are used efficiently and the uptake for polio vaccine remains high, even though the threat of the disease is less visible, because families have strong motivation to get their children immunized against measles.

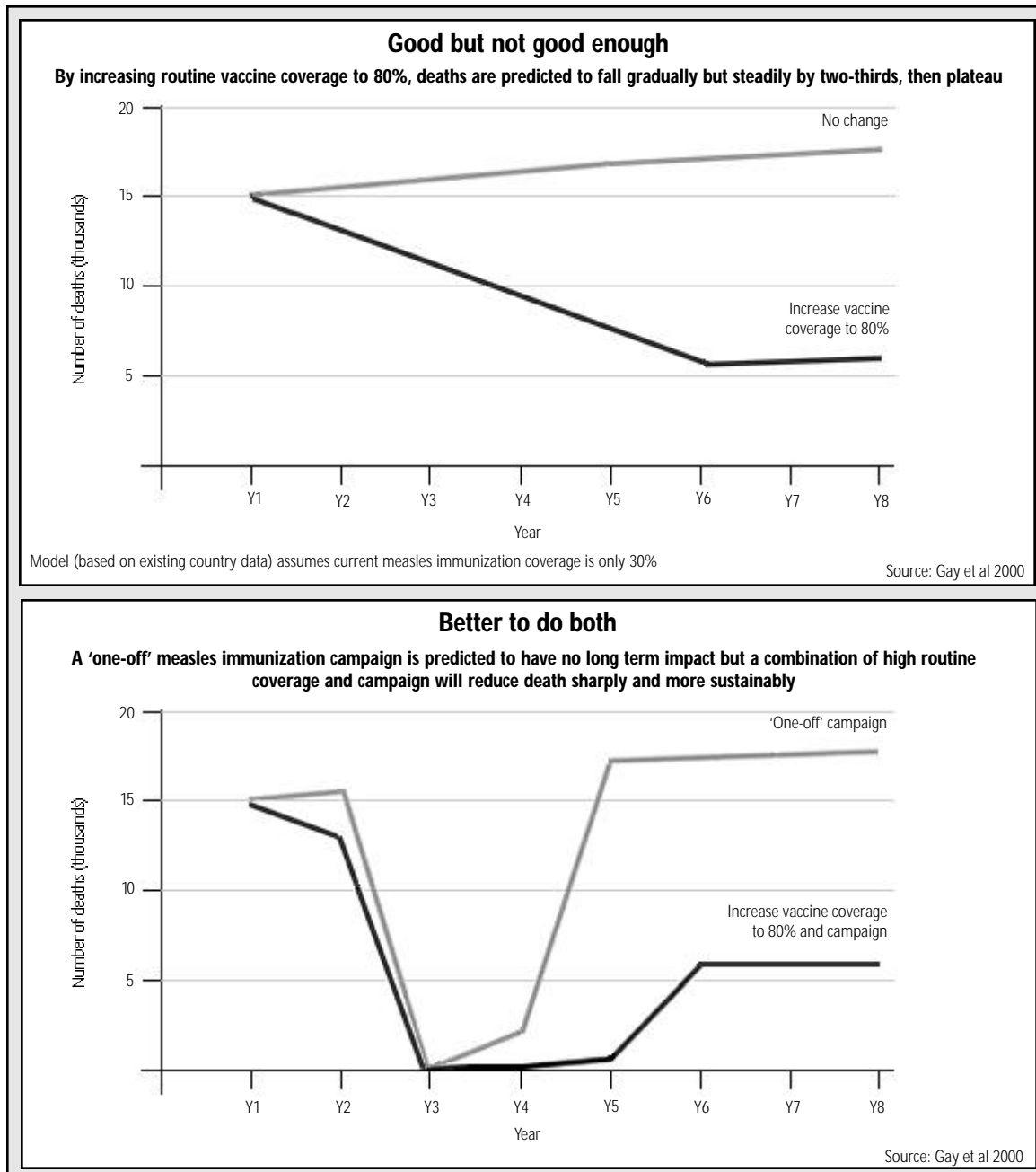
The new WHO-UNICEF plan recognizes countries' different needs and sets out a framework for good practice. It is based on analyses of the evidence of what works, says Henao-Restrepo. All countries, whatever their current measles status, can use the plan to reduce their measles deaths, while countries or regions that wish to be more ambitious, such as the Americas, Europe and the Eastern Mediterranean, which have elimination plans, can also work within the framework to achieve their aims.

The targets for saving lives can be pursued by all countries immediately—and the economic arguments for doing so are convincing. Preliminary estimates of

the cost of achieving the mortality reduction goals in the twenty highest-burden countries are \$150 million a year, says Hoekstra, a relatively modest sum. What is more, WHO and UNICEF say that governments can achieve the goals extremely cost-effectively. In high-burden countries, improving coverage from 50% to 80% is estimated to cost around US\$2.50 for each life-year gained. In general, health interventions that can be delivered in low-income countries for less than US\$25 per year of life gained are considered to be excellent "buys" for governments, so this represents exceptionally good value for money.

The core of the plan is to increase routine immunization coverage with measles vaccine to 80% by 2005. But WHO and UNICEF recognize that this will be only a first step. Even when fully implemented, routine coverage of 80% would still result in more than 250 000 children dying of measles each year. ▀

**Figure 2:** Models used by WHO and UNICEF show the expected impact of different approaches to vaccination



To reduce the worldwide death toll beyond this level, supplementary campaigns will be needed, implemented as part of a long-term and comprehensive strategy.

The recommendations are based on the results of models devised by Nigel Gay and colleagues at the Public Health Laboratory Service in London, England. Using real data from a typical high-burden country where measles vaccination coverage is only 30%, Gay and his colleagues modelled the impact on mortality of increasing coverage to 80%, enacting one-off campaigns, and doing both. Their results are shown in Figure 2. If coverage is increased to 80%, the number of deaths will fall by two-thirds over five years, then plateau. If, on the other hand, the country attempts to reduce measles deaths with a one-off campaign, deaths will fall sharply but transiently, returning to the previous high level within a couple of years. If, however, routine coverage is increased to 80% and a supplemental campaign is added, deaths will be sharply and sustainably reduced.

“You have to do both things,” says Hoekstra. “With high coverage and a campaign, it’s a few years before the number [of deaths] goes up again, so you have a longer period to work on improving routine immunization.” Repeated campaigns will, of course, reduce the death toll further. “Measles campaigns could not replace routine immunization programmes,” says Hoekstra. “They can only be in addition.”

One critical issue is the supply of vaccine: officials estimate that it will take up to two years for the manufacturers of measles vaccine—some 12 companies in all—to scale up production to a level needed for countries to carry out the recommended steps in the mortality reduction strategy. The targets in the WHO-UNICEF plan take these delays into account. “We are watching the situation closely and will review it every 3–6 months,” says Henao-Restrepo.

**Action by the year’s end**

WHO and UNICEF are keen to move ahead quickly with seeking endorsement for the plan from their technical experts, then implementing it. This month, the GAVI Board will also be asked to decide on the role that the Alliance and its partners should play. As well as declaring measles a high priority, GAVI will be asked to help in practical ways.

One of GAVI’s key milestones is to increase routine immunization coverage to 80% by 2005<sup>3</sup>, putting it firmly in line with a central goal of the measles plan. Also in line with the plan, GAVI’s partners are already working with countries to improve the systems used to monitor vaccine coverage and safety. At present, measles vaccine coverage is not included in GAVI’s monitoring system, with the main indicator being the percentage of children who receive diphtheria, tetanus and pertussis (DTP) vaccine. In future, measles coverage may be added to the indicators.

Decisions about whether or how the Global Fund for Children’s Vaccines might provide support for the measles strategy will be made in the near future. One of the Fund’s three sub-accounts provides support for countries to improve their routine immunization services so, in principle, this could be used in part to help improve routine measles vaccination coverage. A more controversial question is whether the Fund might also support supplemental measles campaigns or even buy vaccine supplies. Different experts hold different views. For example, Kane, a member of the GAVI Working Group, says that he personally does not believe that the limited resources of the Fund should be used for buying measles vaccine or paying for campaigns today. But in 2-3 years’ time, if routine coverage and monitoring has improved in the high-burden countries, he personally believes that the GAVI Board may want to consider using Global Fund resources for well-planned supplemental campaigns, if other support is not available. Hoekstra, meanwhile, argues that the Fund should be used, for example to make strategic grants valued at, say, one-third the size of individual partner grants.

“Measles is the number one public health problem



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**Swift action: measles vaccination campaigns, like this one in East Timor, can only supplement a good routine programme**

among vaccine-preventable diseases of children,” says Hoekstra, “and GAVI now has the opportunity to bring it under the umbrella of its programme.” In today’s atmosphere of consensus, next year’s one year-olds could be the first to see progress. ■

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**Footnote**

a. Measles elimination is defined as a situation where endemic transmission has stopped over a wide geographic area and secondary spread from imported cases will end naturally, but continued intervention is needed. Measles eradication is defined as the interruption of transmission worldwide.

# Research that delivers results

## As GAVI decides on its R&D priorities, Karen Birmingham investigates neglected areas

ASK anyone in public health to name some priorities for vaccine research in developing countries, and it's a fairly safe bet that they will mention new vaccines against HIV, tuberculosis and malaria. But some will mention other equally pressing problems. One in four children worldwide is still not immunized routinely with existing, inexpensive vaccines. Up to half of all vaccinations given worldwide may be unsafe, putting children at risk of fatal bloodborne infections. And some important vaccines are stagnating in the development process because current, market-based systems offer manufacturers little incentive to produce them for developing countries.

A growing number of specialists believe that these problems must be addressed, perhaps even before another dollar is spent on making new vaccines.

"There are things we already know how to do, and for those we don't need research, we need implementation,"

says Mark Kane, director of the Bill and Melinda Gates Children's Vaccine Program. "But we also need to do some operational research to learn more and document the effectiveness of newer approaches and technologies."

This month, the GAVI Board will begin to answer the question of how the partners in the Alliance, and the Global Fund for Children's Vaccines, should support R&D to accelerate the introduction of immunization products, systems and technologies that will benefit the world's poorest. The Fund will be one channel of support. The size of the budget for R&D has yet to be determined (see Box).

GAVI was formed to close the gaps in the world's current immunization efforts, not to duplicate the efforts of others. It is therefore expected to support a few carefully targeted areas of R&D that are currently

relatively neglected, rather than duplicate other funding sources.

Some of these targeted areas may include operational research—for example, analyses of what incentives companies need to develop products that benefit mainly the poorest populations; measuring the outcomes of training health workers in safe practices; or measuring the burden of diseases in developing countries where data are scarce.

*Immunization Focus* asked a number of major funding bodies in infectious disease research for information about the relative amounts they spend on basic, clinical and operational research. Not surprisingly, comparable data are not available, because research is categorized differently in different institutions. However, the institutions contacted largely agreed that operational research is underfunded.

To define its priorities, GAVI will look at proposals from several sources,

including its newly formed R&D Task Force. The Task Force, co-chaired by Myron Levine of the Center for Vaccine Development at the University of Maryland and a member of the GAVI Working Group, Yasuhiro Suzuki of WHO and Rino Rappuoli, of Chiron, has consulted widely to help clarify GAVI's role. The group asked Peter Wilson, a consultant with more than 20 years' experience of working with the pharmaceutical and vaccine industry, to canvas the opinion of a broad range of individuals with a stake in immunization.

Wilson devised an 8-point questionnaire which asked respondents to prioritize aspects of R&D according to whether they are "central to, peripheral to or outside" the scope of the Task Force. The exercise identified three vaccines that are relatively near to market, but currently neglected, as strong candidates for support to overcome the final obstacles of development: pneumococcal conjugate vaccines that would protect against the strains of *Streptococcus pneumoniae* that are prevalent in developing countries; rotavirus vaccines; and meningococcal A vaccine. These three were selected because, as the Task Force puts it, they are "low-hanging fruit" that is almost ready to be plucked, and their potential benefit to public health is clear.

The Task Force recognizes that malaria, HIV and TB vaccines are high priorities, but says that there is already a "massive global effort" devoted to them, and points out that the infrastructures for delivering them in developing countries are not yet in place. By devoting resources instead to the three near-ready vaccines, the Alliance could also help to prepare the infrastructures for delivering vaccines against malaria, HIV

**"Countries are not going to consider paying for a vaccine for a disease they don't think they have"**

### GAVI and the role of the Global Fund in R&D

The Global Fund for Children's Vaccines has three separate sub-accounts: One for purchasing new and under-used vaccines such as hepatitis B; another for improving immunization services in the poorest countries; and the third for accelerating the development and introduction of immunization products, systems and technologies. While funds from the first two sub-accounts have already been allocated to countries, the ground rules for the third are still being established.

As GAVI sets priorities for R&D, it is clear that the Fund will support only some of them, while others will be supported by individual partners in the Alliance. Decisions on which projects to back will be taken by the GAVI Board.

It is agreed that the Fund should not support research that other bodies are already funding, nor replace traditional sources of money.

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and TB when these become available, says the Task Force.

In addition to the three products, the Task Force agreed to select up to three further projects. The direction that these will take is likely to emerge at the November meeting.

Respondents to Wilson's questionnaire also put a high priority on research to measure the burden of specific vaccine-preventable diseases in developing countries. Such data are valuable, not only to policy-makers but also for vaccine manufacturers, who increasingly rely on this information to calculate the potential market value of new vaccines.

Disease burden data have been shown to be one of three key factors influencing take-up of hepatitis B and *Haemophilus influenzae* type b vaccines into national immunization programmes<sup>1</sup>.

Orin Levine of the US National Institutes of Health (NIH), who organized a two-day meeting on disease burden at the WHO's headquarters in Geneva in October, sums up the need for this data: "Simply put, countries are not going to consider paying for a vaccine to prevent a disease that they don't think they have." However, Levine points out that for many diseases prevented by new vaccines, such as pneumonia caused by Hib and diarrhoea caused by rotavirus, establishing the local burden of disease is tricky. "Unlike measles or polio, there is no clinical disease entity that is unique to these agents. Carole Heilman, Director of the Division of Microbiology and Infectious Diseases at NIAID, whose organization is funding a trial in the Gambia of a 9-valent pneumococcus vaccine, also acknowledges the importance of this data. "The question high-burden countries have is, is this vaccine of use to them?" she says.

**Improving injection safety**

Spending on research to establish disease burden is probably very small at present, but figures are, once again, difficult to obtain. Heilman, for example, says she has hired a staff member specifically to work on the burden of Hib in the Gambia. However, she admits that she cannot give an estimate of how much money NIH invests in disease-burden research.

Sometimes, when disease burden data are lacking, it falls to investigators to collect this as part of a clinical trial. Take, for example, the Phase III trial of an 11-valent pneumococcus vaccine in the Philippines. Principal investigator, Hanna Nohynek of the Finnish National Public Health Institute, says: "Because the figures on prevalence of pneumococcal disease aren't available, we've built a disease burden component into the trial. On the basis of this, we should be able to calculate the savings of introducing the vaccine into such a community."

Developing countries also need better methods to monitor vaccine coverage. Chile is frequently held up as a model of success for its immunization programme. "But our system for monitoring coverage is

very primitive," says Rosanna Lagos of the Roberto del Rio Hospital in Santiago, and a member of the R&D Task Force. "Vaccination clinics have to resort to counting the number of doses at different ages—after a year or 6 months—to estimate the number of children vaccinated." Lagos says the programme desperately needs a computerized subject monitoring system.

Another concern is unsafe injection techniques. Millions of injections are delivered each year in developing countries. As many as 50% of injections have been estimated to be unsafe in one study<sup>2</sup>. One model estimates that unsafe injection techniques may account for approximately 2.3-4.7 million hepatitis C infections, 80,000-160,000 HIV infections, and a staggering 20% of all new hepatitis B infections in developing countries<sup>3</sup>. Research to document the impact of using auto-disable syringes on reducing these infections is

Say "aaah":  
Orin Levine investigates the burden of Hib in Alaska



Levine

on the R&D Task Force agenda.

Another area that the GAVI partners will be exploring is the need to document the impact of communication efforts such as public education and advocacy campaigns. Barry Bloom, dean of Harvard School of Public Health and a member of the R&D Task Force, points out that the diseases prevented by newer vaccines, such as hepatitis B and Hib, may not be well understood by people in developing countries. "The concept of a vaccine that can prevent liver cancer many years later is hard for people to grasp," he says.

With only limited funds, the Alliance must be selective. But as key tasks are chosen, there is hope that each will bring the objective of safe universal immunization a little closer. ■

Karen Birmingham is news editor of the journal *Nature Medicine*

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# A smarter way to buy

**As demand for vaccines outstrips supply, Lisa Jacobs finds out how the system for buying them is modernizing**

IF only it were as easy as telling a company, “We need three times more vaccine this year than we did last year. If you can make it, we will buy it.” Crank up the manufacturing capacity and start producing, right? Not quite. A company must invest huge amounts of capital and time to build a new vaccine production unit, or create a significant expansion. So when vaccine needs change over time, supply can be hard to find.

The emergence of GAVI and the Global Fund has generated a great deal of new demand for hepatitis B (hep B) vaccine. And already, GAVI has run into a problem with supply. While global capacity for supply of monovalent hep B vaccine is sufficient to meet demand, a significant proportion of the demand is for combined diphtheria, tetanus and pertussis (DTP) and hep B. And while a number of companies are developing this combination vaccine, only one company, SmithKline Biologicals, currently has this combination pre-

qualified by WHO and available for sale. Significant increases in supply will not be seen very quickly.

In the meantime, GAVI Board has made a policy decision to reserve the available stock of combination vaccines for countries with relatively weaker systems. The burdens of introducing new vaccines—additional training, cold chain and logistics requirements—are minimized through the use of combination vaccines.

Furthermore, vaccines given in combination necessitate fewer injections per child, thereby enhancing safety. The countries with the stronger systems will be encouraged to introduce the monovalent vaccine into routine immunization.

“The situation is not ideal, but until combinations become available in greater quantity, we have tried to develop a transparent and equitable allocation policy that ensures the highest degree of safety and allows as many countries as

possible to access combination vaccines through the Global Fund,” says Steve Landry, of USAID and a member of the GAVI Working Group.

At press time, officials from UNICEF and WHO were to meet with a number of developing country health officials to discuss the available vaccines, and try to match need with supply.

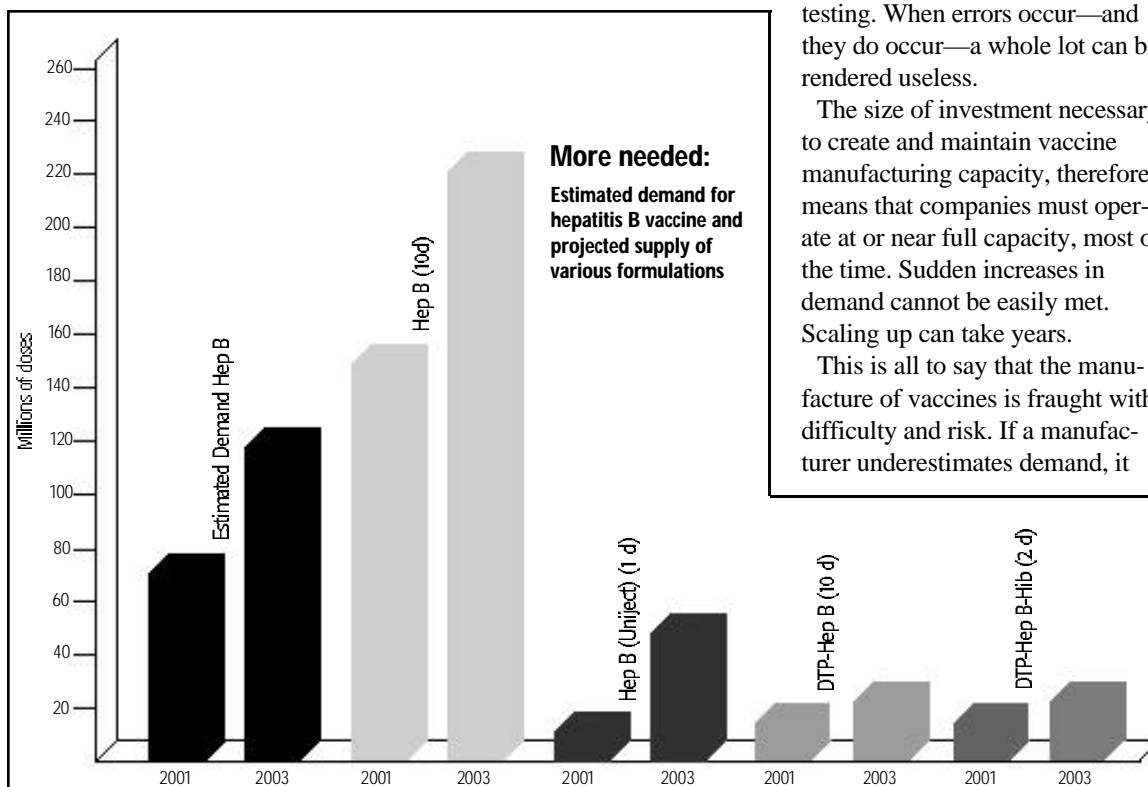
## A predictable supply

Vaccines are unlike most products—pharmaceutical and otherwise—in that they are biological compounds. They are alive, needing cultivation and care through their entire development process, sensitive to tiny discrepancies in manufacturing procedures.

All components for their manufacture must be constructed to very specific standards of temperature, moisture, air pressure and of course, safety and hygiene. Not only is scaling up capacity time-consuming, vaccine production is also highly regulated with each batch, or lot, requiring stringent testing. When errors occur—and they do occur—a whole lot can be rendered useless.

The size of investment necessary to create and maintain vaccine manufacturing capacity, therefore, means that companies must operate at or near full capacity, most of the time. Sudden increases in demand cannot be easily met. Scaling up can take years.

This is all to say that the manufacture of vaccines is fraught with difficulty and risk. If a manufacturer underestimates demand, it





risks losing market share; if demand is over-estimated, expensive facilities are underused, and investments turn into losses.

**Buying vaccines for the world's children**

The six vaccines introduced on a large scale in the developing world through the global Expanded Programme on Immunization, or EPI, were already mature products when the programme started. Product maturity in the vaccine field means that vaccine production is smoother, more manufacturers in the field means that demand can be more easily met, and more manufacturing capacity means that costs are reduced, and prices can

**“The companies have exceeded our expectations and there are many interesting offers on the table”**

follow costs down.

In this environment, it made sense for UNICEF to pursue a procurement policy that achieved the lowest prices possible. To do this, it has used what is known as a tender approach—issuing requests to all qualified manufacturers every or every other year for quotes on a specific amount of a particular vaccine.

This policy has its benefits; the low vaccine prices achieved through this method were critical in helping even the poorest countries introduce basic routine immunization into their health systems. But the singular focus on price—with the necessary attention to quality, of course—has downsides as well. For one thing, since EPI began in the 1970s with six vaccines, new vaccines have been

developed. Many children in the richer countries are now protected against 11 or 12 vaccine-preventable diseases. But the newer vaccines are not available for most children in developing countries, for two reasons that are inextricably linked: greater costs and limited supply.

Developing country health programmes have come to regard vaccines as low price commodities. In fact, vaccine costs are only a small fraction of the total estimated cost of providing routine immunization to a child. Of the estimated \$20 it costs to protect one child, the cost of the required doses of the six vaccines comes to less than \$1—the great majority of costs involved are staff, vehicles and maintenance, cold chain equipment, training and other overhead. The thought of paying more than a few pennies for the vaccine is anathema to many health officials.

But the focus on low prices has not helped to convince manufacturers that making the necessary investments on development and manufacturing capacity for vaccines for the developing world can make business sense.

**A new approach to procurement**

With the emergence of GAVI, and its focus on reducing the gap between the time that a vaccine becomes available in rich and poor countries, UNICEF Supply Division has taken the opportunity to restructure its relationships with companies. For the purchase of new and under-used vaccines, UNICEF has decided to use a ‘request for proposals’ method.

**Bulk orders**

With the global increase in immunization coverage—from about 5% in 1974 to nearly 75% today, UNICEF’s purchasing role has grown; in 1999, UNICEF supply division shipped 104 million doses of measles vaccines, 102 million doses of BCG, 100.4 million doses of tetanus toxoid, and 90 million doses of combined diphtheria/tetanus/pertussis (DTP) vaccine. Of course, with the increasing demands of the global polio eradication efforts, the bulk of UNICEF’s vaccine purchases in 1999 were for oral polio vaccine (OPV)—UNICEF shipped 881 million doses of OPV in 1999.

Through this route, UNICEF is asking companies to make offers that cover a longer term, affording companies more stable commitments over three to five years to ensure sustained supply of vaccines over longer periods. In addition, the vaccine industry has offered UNICEF additional components to contribute to the GAVI objectives including: training and materials, donations, bundling of vaccines to improve delivery, and injection equipment.

How have the companies responded? “The companies have exceeded our expectations,” says Steve Jarrett, Deputy Director of the UNICEF Supply Division. “There are many interesting offers on the table.”

“In the vaccine business, there are enough uncertainties during the development and manufacturing process; UNICEF is committed to working with industry to establish a reliable and predictable vaccine supply environment,” says Jarrett.

**Immunization Focus**

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