Immunization Focus

A quarterly publication of the Global Alliance for Vaccines and Immunization www.VaccineAlliance.org

GAVI

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Immunization Focus

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NEWS

The ball is rolling

THE FIRST countries to receive approval for support from the Global Fund for Children's Vaccines have received the good news. Letters from GAVI were sent to the countries just before *Immunization Focus* went to press. The first payments and supplies of vaccine are on track to be released by November.

An independent review committee met to assess the proposals in mid-July. Its six members, from Ghana, Tanzania, the Philippines, Mali, the US and Thailand, included immunization programme managers and a health minister (1). The committee's recommendations were endorsed by the GAVI Board. In total, 17 countries submitted proposals that contained enough information for review. Of these, 15 received approval, conditional in some cases on the countries' ability to demonstrate that they could meet specific requirements. Remaining countries have been asked to re-submit their proposals.

Some clear lessons emerged from this brand-new process, however. One is that the guidelines and proposal application form need to be improved. Some governments appeared not to have understood fully the need for detailed quantitative information about their immunization programmes. In fact, the review committee decided that all the approved countries need to provide further information before funds can be released – for example, in spelling out how they plan to mobilize the resources to pay for newly introduced vaccines in the medium to long term. "In GAVI we should foster quality," says Maritel Costales, a member of the committee, and previously the immunization programme manager for the Philippines. The countries have been asked to produce the information by 1 September.

"This was our first time; it was difficult," said Costales. "We have learnt from our experience, but I am confident that the process is a good one."

The countries that received approval for one or both forms of Fund support, subject to providing additional information, are: Bhutan, Cambodia, Côte d'Ivoire, Ghana, Guyana, Kenya, Kyrgyz Republic, the Laos People's Democratic Republic, Madagascar, Malawi, Mali, Mozambique, Pakistan, Rwanda (for immunization services); and Tanzania. ■

● For more about the proposal process and its effects in some African countries see page 2 ◗

(1) A list of the committee members is available from the GAVI Secretariat.

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Injection of hope: in June, Norway's PM Jens Stoltenberg pledged US$125 million over five years to children's immunization in low-income countries

Inside this issue

Bringing it all together

The first set of governments have been through the process of seeking support from the Global Fund for Children's Vaccines. Here's how it felt in some African countries

FOR anyone involved in applying to GAVI for support from the Global Fund for Children's Vaccines, the past few months have been a hectic and exciting time. Tight schedules have been made tighter by face-to-face meetings, often between people who have never sat down together before, even though they all work in immunization in a given country. Data from sometimes scattered sources have been gathered together and reviewed to meet the requirements (see How GAVI and the Fund will support countries, page 3). But, whether governments joined the first round of proposals for support, or decided to wait for the second, the experience has been a useful one, according to many of those involved. And all the players have learnt lessons that will stand them in good stead for the future.

Several key messages emerged. First, the process allowed countries a unique opportunity to assemble their key immunization "players" and review their current services. Second, the process sometimes served as a catalyst for change, for example by triggering a specific commitment by a health minister to improve the safety of immunization equipment or vaccine quality control. And third, in certain situations, it was better to wait and gather the information for a good proposal in the second round than to rush to submit an incomplete one for the first.

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Special delivery: vaccine supplies leave Maputo for flooded regions of Mozambique earlier this year

"The time to talk brings a lot of change. It has been a useful process," says Dr Tarande Manzila, medical officer for new vaccines in WHO's regional office for Sub-Saharan Africa, temporarily in Harare, Zimbabwe, who has worked with a number of countries in the region in preparing their proposals.

"It was a very good experience for all of us to get involved and get to know where we are," says Eva Kabwongera, UNICEF project officer for health in Kampala, Uganda.

In Mozambique, says Miguel Aragon Lopez of UNICEF's Maputo office, the process has been catalytic. For example, seeing that GAVI would supply autodestruct syringes with new and under-used vaccines, Mozambique – which has been using re-sterilisable syringes until now – has decided to match GAVI by using disposable ones for all the other vaccines it administers within its programme, such as BCG, measles and tetanus. Also, says Rose Macauley, technical adviser to the Mozambique immunization programme at the Ministry of Health, the process has triggered a rethink of the role of the national Immunization Coordination Committee (ICC). Before, this committee focused only on polio eradication. Now, the committee's scope of work is to be extended. In a year in which Mozambique's immunization services are still reeling from the effects of catastrophic flooding, the pace of recovery has been fast.

Good news, but, of course, not everything in the region went perfectly. As with many large and highly devolved partnerships, GAVI's partners' activities in Africa suffered from some muddles and overlaps in the initial stages. Early in the year, governments and officials in certain countries were confused by uncoordinated messages from individual partners.

No time to spare

Also, once the process was set up, time pressure was a problem. Several officials said they would have liked more time to get ready. The proposal packs were sent out in mid-May for return by 30 June for consideration in the first round. "It's a very short time, and there are many things to do, not only GAVI," said one. "But people have worked very hard."

And then there was the inevitable risk of a dash for cash. Some health ministers reportedly returned from the World Health Assembly in Geneva and demanded that their immunization officials complete and submit a proposal form in the first round, even when officials warned that some of the information required to complete the proposal was lacking. Although the system is not competitive, it does rely on countries providing all the necessary information. Countries whose proposals are incomplete will be encouraged to resubmit them at a later date: redoubled efforts are needed to ensure that all countries are adequately briefed on the process, says Dr Manzila.

To ensure the best use of the proposal process, the African regional offices of WHO and UNICEF held an informal meeting in Abidjan, Côte d'Ivoire, in mid-April. They clarified GAVI's mechanisms and examined some of the key issues, such as how governments will plan to sustain support for immunization services beyond the five years of support from GAVI and the Global Fund for Children's Vaccines. ◗

Then WHO officials worked with individual countries to provide guidance on their proposals, focusing initially on those best equipped to provide the information needed in the short time available. Where there was enough time for discussion at higher political levels, in-person visits were strikingly productive. For example, in Tanzania, discussions with high-ranking officials in the health ministry resulted in a renewed and specific commitment by the government to sustaining immunization services.

In some cases, consultants for the GAVI partners advised countries to wait for the second round to submit their proposals. Uganda was one of several such countries. "At first, we thought, why?" says Kabwongera. "But in the end we agreed that with more time it [our proposal] will be much better."

Assembling scattered data

Most of the required information for the proposal exists, says Kabwongera, but it was scattered and needed to be assembled. Uganda's immunization services have suffered in recent years, possibly due to the introduction of policies such as the decentralization of health delivery services, and reforms of the civil service that resulted in some immunization workers being laid off. Some have now been reinstated, however, and, says Kabwongera, strategies have been developed to revitalize the immunization programme.

Predictably, there is a range of views on how and whether GAVI and the Fund should refine or develop the conditions for support. Perhaps the newest feature of the mechanism for funding countries is the "share" concept, which represents the Fund's contribution to the cost of fully immunizing one child (see How GAVI and the Fund will support countries, this page). Nominally, this has been set at $20 per child. Some commentators (2) argue that the real cost varies from country to country, and that shares should therefore be scaled to take account of population size and other factors. Others welcome the share concept's flexibility, contrasting it with the red tape that traditionally surrounds donor support. "The only conditionality is a commitment to really vaccinate the children," says Miguel Aragon Lopez in Mozambique.

Which, after all, is what this entire effort is about. ■

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Phyllida Brown

How GAVI and the Fund will support countries

What? GAVI and the Global Fund for Children's Vaccines will support countries initially to:

- Strengthen their immunization services for existing vaccines such as diphtheria, tetanus and pertussis (DTP3), polio and measles; and
- Introduce under-used vaccines such as hepatitis B and Hib.

Who? All low-income countries with GNP per capita of US$1000 or less are eligible for support. In China, India and Indonesia, special arrangements are envisaged.

How? To receive support, a country must have:

- A functioning mechanism for coordinating the activities of all immunization players, usually an Interagency Coordination Committee;
- A recent assessment of immunization services; and
- A multi-year plan for immunization.

Which type of support is most suitable for which countries?

- Support for immunization services is to be given to countries where coverage for DTP3 is below 80% of the target population. The aim will be to strengthen health systems to improve the service in all districts.
- Support for the introduction of new and under-used vaccines will be provided to countries where DTP3 coverage is above 50%. Where it is lower, countries are encouraged to focus on improving their overall immunization system before introducing new antigens.

How will the money be disbursed?

- For the improvement of immunization services in countries with DTP3 coverage below 80%, GAVI and the Fund have developed a radical new approach. Rather than tie up funds for specific restricted uses, as with traditional donor support, the approach allows governments and ICCs to decide how best to use the funds, requiring in return a strict set of performance monitors.

Funding will be based on the concept of a "share" of US$20 for each fully immunized child. Total funds will be divided into two equal amounts. The first half of the money will be invested up-front on the basis of the number of children that the government intends to immunize in the next two years, over and above the percentage currently immunized. The second half will be awarded in the form of "rewards" for each additional child actually immunized.

- For the introduction of new and under-used vaccines the Fund will supply vaccines and safe injection equipment. Governments are advised to plan to transfer the costs of these items to their own budgets, or to seek external support for their purchase, before the end of the funding period. These plans will be reviewed in 2002.

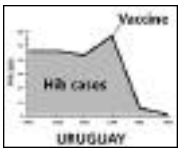
How long will the money last? The Fund's current resources have been budgeted to provide all eligible countries with five years of support. GAVI's partners recognize the need for sustained support, and are taking steps to extend the Fund beyond five years. However, they will also help governments to plan how to sustain their improved performance and seek other support.

When is the next deadline? Proposals for the next round should be received by the GAVI secretariat by 15 October.

Lisa Jacobs

The invisible culprit

An avoidable disease continues to kill more than a thousand children every day. Phyllida Brown finds out why, and asks what is being done to overcome the problem



IT has been virtually eliminated from the industrialized countries. Safe, effective vaccines that protect infants from it have been licensed for about a decade. Yet in many developing countries, the bacterium *Haemophilus influenzae* type b (Hib) goes almost unchecked. Worldwide it is estimated to kill 400 000 to 500 000 young children each year. Most die of pneumonia, and a smaller number from meningitis.

So far, very few developing countries use Hib vaccines in routine immunization programmes (see Map). Why? First, because the vaccines are relatively expensive. Even though prices have fallen sharply, the cost of a three-dose schedule is still at least US$6, compared with just cents for traditional vaccines such as diphtheria, tetanus and pertussis (DTP). Second, and equally important, many governments are simply not convinced that the disease is a problem in their country. Despite being one of two leading causes of pneumonia, Hib can be difficult to diagnose, so its role often goes unrecognized.

Only the highlighted countries routinely use Hib vaccine

Source: WHO

Now, however, years after international efforts began in earnest to increase children's access to Hib vaccines in developing countries (1), some key gains have been made. First, researchers now have dramatic and solid evidence of the impact of these vaccines on the incidence of pneumonia and meningitis in some low-income countries (2). This evidence has helped to clarify the size of the Hib burden. Second, cost-effectiveness estimates suggest that, provided Hib vaccines are delivered within existing immunization programmes, they can deliver excellent returns. And third, convinced that the introduction of Hib vaccine is a sound investment for countries' health systems, the GAVI Board has decided that low-income countries should receive at least initial funding from the Global Fund for Children's Vaccines to do so.

Hib vaccines are safe and effective. The World Health Organization has published a position paper on Hib which concludes that, "in view of the demonstrated safety and efficacy of the Hib conjugate vaccines, Hib vaccine should be included….in routine infant immunization programmes" (2). WHO recognizes that individual nations must take account of their own capacity and priorities in deciding whether to adopt the vaccine, but, overall, supports its use.

Yet despite WHO's position, and even with the prospect of new funding in the short term, many countries' health officials consider Hib to be a relatively low priority among under-used vaccines, preferring instead to introduce immunization against hepatitis B, a virus whose prevalence is relatively well known. In some cases, governments fear that the addition of Hib vaccine to their immunization programmes will strain already-overstretched systems.

Still a low priority

For example, in Mozambique, the national immunization programme is not considering introducing this vaccine at the moment. "The programme does not have the capacity for the introduction of a new antigen," says Rose Macauley, technical adviser to the programme at the Ministry of Health.

Even in countries that are keen in principle to introduce Hib, there is a need for data to justify the decision. "We would like to introduce Hib vaccine, but we have no concrete data or statistics on the burden," says Eva Kabwongera, project officer for UNICEF in Kampala, Uganda. She contrasts this with the situation for hepatitis B. "For hepatitis B we have the statistics, we have identified it as a burden, so it is appropriate to introduce the vaccine." In Sub-Saharan Africa only Kenya, Malawi and Rwanda have so far requested support for Hib in their proposals to GAVI and the Fund, although a group of countries in West Africa including Côte d'Ivoire, Benin, Burkina Faso, Ghana and Togo is also planning to work with partners to introduce Hib. ◗

Box 1: Hib: the basics

- Among all strains of *Haemophilus influenzae*, type b accounts for about 90 per cent of the invasive disease. Hib disease kills an estimated 400 000-500 000 children each year
- An estimated 3 million cases of severe disease are attributed to Hib each year. One in five children who develop meningitis suffer permanent brain damage
- In industrialized countries before immunization was widespread, meningitis was the most frequent manifestation of Hib disease, but worldwide there are probably about five cases of severe Hib pneumonia for every case of Hib meningitis
- Hib resistance to antibiotics is growing
- Since the introduction of conjugate Hib vaccines from 1990 onwards in industrialized countries, the incidence of invasive Hib disease in these countries has fallen by more than 90 per cent
- Outside the industrialized countries, Hib vaccines have been shown to protect against meningitis and pneumonia in Chile, Uruguay and The Gambia

For Jay Wenger, coordinator of the Accelerated Vaccine Introduction Priority Project at WHO, the invisibility of Hib is a key reason for the lack of demand in many countries. "People are not going to introduce a vaccine for a disease they cannot diagnose," he says. Among the diseases that doctors see regularly, pneumonia is among the most common – but its causes are multiple and the Hib cases look no different from the others. The bacterium is difficult to isolate without invasive procedures and special laboratory materials that may not be available in some developing countries. "If you never isolate the bacterium, then the clinicians are unlikely to think about the disease," says Wenger.

Box 2: Is there an evenly distributed burden of Hib disease worldwide?

Based on the available estimates, the incidence of invasive Hib disease varies between regions.

- In the US before widespread immunization, there were an estimated 40 to 60 cases of Hib meningitis and an estimated 67-130 cases of all Hib disease per 100 000 children under 5 years of age annually.
- Sub-Saharan Africa appears to have similar or greater rates for Hib meningitis.
- Asia, by contrast, may have a lower incidence of the disease with estimates of less than 5 cases of Hib meningitis per 100 000; yet Hib has been found to be the leading cause of bacterial meningitis in most hospital-based studies, including in Asia.
- Further studies in China, Korea and Vietnam are under way to quantify the burden in Asia further.
- Latin American studies at the end of the 1980s, before the introduction of vaccines, suggest that, for the region overall, there were 15 to 25 cases of Hib meningitis per 100 000 children, and 21 to 43 cases of all Hib disease. However, more population-based studies are needed to confirm these estimates.

And even when samples are obtained, infection may be masked in children who have been treated indiscriminately with inappropriate antibiotics. Although a few large city hospitals in Sub-Saharan Africa do perform laboratory diagnoses of Hib disease, data on the burden of disease due to the microbe have not been widely disseminated.

Measuring the burden

Joel Ward, director of the UCLA Center for Vaccine Research in Torrance, California, believes that there is also a problem of perception. In some countries Hib is wrongly perceived to be a problem only of the industrialised world. "I have been told that Hib is a Western disease," he told delegates at the Third Annual Conference on Vaccine Research in Washington, DC, earlier this year. Yet antibodies to Hib are found in all populations, as are the diseases it causes.

Since the mid 1990s, however, the evidence that Hib is a major cause of pneumonia worldwide has strengthened dramatically. In The Gambia, West Africa, between 1993 and 1995, researchers assessed the impact of a Hib conjugate vaccine on the incidence of pneumonia overall in a double-blind trial involving more than 40 000 infants. They found that in the Hib-vaccinated group, the incidence of severe pneumonia, diagnosed on chest X-ray, was reduced by 21 per cent (3). By implication, the researchers concluded, one in five episodes of severe childhood pneumonia in the Gambia is Hib-related. This is at least twice as high as earlier estimates, which had attributed at most 10 per cent of pneumonia episodes to Hib. Adding weight to these findings, researchers in Chile have performed similar studies and found very similar results (4). With the aim of increasing the spread of data in Asia, a similar Hib vaccine trial, with a measurement of the impact on pneumonia overall, is under way in Lombok, Indonesia, coordinated by the Program for Appropriate Technology in Health and the France-based nongovernmental organization, Association pour l'Aide à la Médecine Préventive (AMP). For English or French briefings, see www.aamp.org/lombok.html

Because of the growing data on the importance of Hib, the GAVI Board has concluded that there is justification for introducing the vaccine in Sub-Saharan Africa, the Americas and the Middle East. Countries in Asia may also be justified in introducing Hib if epidemiological data confirm the need. Indeed, one of GAVI's targets is to introduce Hib vaccine to 50% of high-burden, low-income countries by 2005 (5).

Rapid assessment tool

But many countries prefer to have their own data on the size of the Hib burden before they go ahead and introduce the vaccine. "The problem is that, at the moment, countries still have to take the WHO's word for it," says Wenger. "So it is still not a definite buy-in." Thus there is also a need for a tool to enable governments to rapidly assess the burden of Hib in their own population. To this end, WHO, the US Centers for Disease Control and Prevention and other partners have been developing such an assessment tool. Chris Nelson at WHO describes how it works.

First, officials scour the records of the main hospital in a district to identify all logged clinical cases of meningitis over a set period, usually 12 months. They also check laboratory records for microbiological records of Hib meningitis and cross-check lab data with clinical records. The number of Hib meningitis cases, set against the whole population in the district under age 5, gives an estimate of the incidence of this condition. Measuring Hib pneumonia is more difficult, but the trials in The Gambia, Chile and elsewhere suggested that there are about five pneumonia cases to each meningitis case in a year.

The rapid assessment tool assumes a similar ratio and uses the meningitis incidence figure to estimate the pneumonia figure. Field tests of the tool have begun: six countries have already either tested it or have planned to test it over the coming weeks, says Nelson. "We are moving very quickly," he says. There will be a meeting in October and a draft by the end of November, says Nelson. ◗

With better data on disease burden, says Tore Godal, Executive Secretary of GAVI, many countries will see the benefit of introducing the vaccine.

But affordability continues to be a concern to many governments, given that commitments to immunize children must be sustained well beyond the five years of support from the Global Fund for Children's Vaccines. Nonetheless, different strands of evidence suggest that the cost should not be seen as an insurmountable barrier. First, an increasing number of studies indicate that Hib vaccines are cost-effective. In January 2000, researchers commissioned by the former Children's Vaccine Initiative published estimates of the cost-effectiveness of Hib in Sub-Saharan Africa which indicated that vaccine could be delivered for US$21-22 for each year of healthy life gained (6). That would make the vaccine an excellent "buy", given that, according to analyses performed for the World Bank, any health intervention that costs less than $25 per year of healthy life gained would be regarded as a highly cost-effective investment (7). Earlier studies by the same researchers had also indicated that the vaccine could be cost-effective in low-income Asian countries.

Cost savings

There are also some individual national studies, including some that actually predict *cost savings* – rather than just cost-effectiveness – from Hib immunization. For example, in an analysis published in 1995, researchers in South Africa measured the costs of the disease against the benefits of the vaccine there. They calculated that the estimated economic costs of Hib disease in the 1992 Cape Town cohort ranged from Rand 10.7 million to R11.8 million. The costs of introducing the vaccine would have been less, amounting to R8.3 million. They concluded that the vaccine's benefits would have exceeded its costs in Cape Town alone by up to R3.5 million (US$500 000) – a substantial return (8). Since 1999, South Africa has introduced Hib vaccine into its national immunization programme.

Impressive as the data on investment returns may be, some governments nonetheless are still likely to find $6 or more per immunized child unaffordable for the longer term. This situation may change, however, as the cost of the vaccine continues to fall or as resources are freed up for immunization from other sources.

As for the strain on overstretched immunization programmes, Wenger argues that the difficulties may have been overstated. WHO and the other partners in GAVI strongly advocate the use of combination vaccines where possible, and some combinations of Hib and DTP are available (see reference 5).

As countries grapple with competing demands on their highly restricted resources, Hib vaccine may not appear to be a top priority today. Yet, when in future the vaccine is introduced, and the crushing burdens of childhood pneumonia and meningitis begin to lift, health workers and parents may look back with astonishment at the reasons given for delaying now. ■

Box 3: Hib vaccines

The new generation of "conjugate" Hib vaccines contain two components - the Hib polysaccharide capsule and, attached to it, a "carrier" protein antigen such as tetanus toxoid that stimulates a strong, T-cell related, immune response. These vaccines are effective in infants and reduce the number of Hib bacteria carried by healthy people in their nasopharynx, reducing the spread of Hib infection not only in vaccinated but also unvaccinated people. There are several licensed Hib conjugate vaccines, including combinations with DTP and DTP and hepatitis B.

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Vaccine impact graphs are adapted from *The Jordan Report* 1998. NIAID, Bethesda, Maryland, USA.

No more business as usual

Although AIDS vaccines may still be years away, policy makers must act radically and swiftly to ensure global access to them, say two new analyses

EVEN if the scientific hurdles to developing AIDS vaccines can be overcome, low-income countries may still wait decades for access to those vaccines, warns a hard-hitting report (1) released last month. The report, from the International AIDS Vaccine Initiative (IAVI), concludes that unless there is a "monumental shift" in the world's approach to the use of vaccines, millions of people will be needlessly infected with HIVwhile they wait for those vaccines to "trickle down" to them. The report calls for immediate and radical changes in the global approach to vaccine production, licensure, pricing, purchasing and distribution, and sets out a five-point action plan.

Reality check

The report comes soon after a separate analysis of the prospects for developing and using AIDS vaccines, from José Esparza of the WHO-UNAIDS HIVVaccine Initiative and Natth Bhamarapravati of Mahidol University, Thailand (2). The authors urge that trials of vaccine candidates be stepped up and that plans for universal access be made now. "The ultimate irony would be that a vaccine developed in collaboration with less-developed countries could actually contribute to increasing the gap and inequalities that the AIDS pandemic has created," they say.

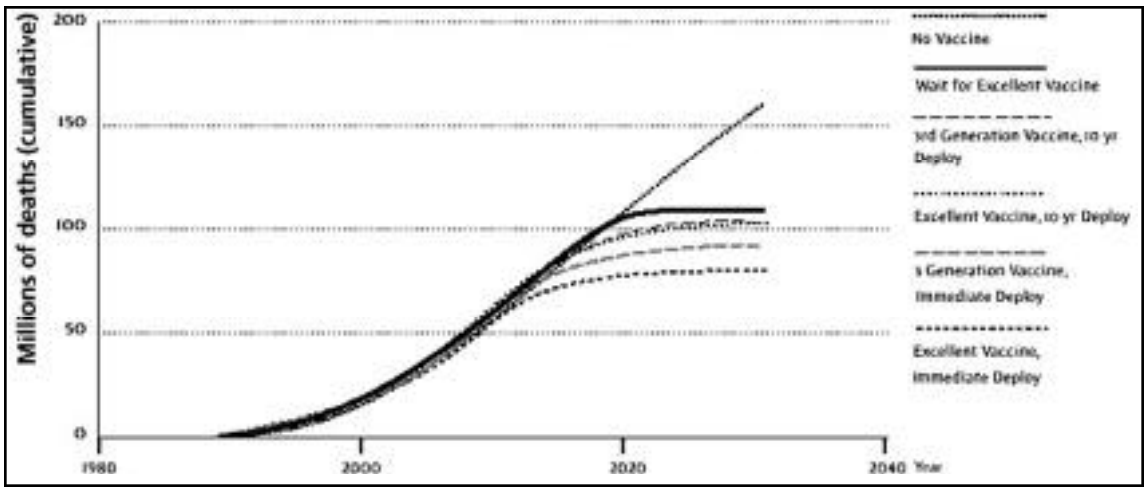
Esparza and Bhamarapravati focus mainly on getting vaccines tested. "The first step to increasing access to an HIV vaccine is to develop one," says Esparza. Only two efficacy trials are currently under way, with results from the first available as soon as 2001. WHO and UNAIDS will hold a consultation in October to estimate demand for vaccines, should current candidates show any protection.

The IAVI report, whose principal author is Roy Widdus of the former Children's Vaccine Initiative, says that the traditional paradigm for fostering the use of new vaccines in developing countries has been "a colossal public health failure". Because vaccine development is risky and usually privately financed, manufacturers tend to market their vaccines at first in high-income countries whose consumers can afford to pay the full price. Over time, typically around 15 years, the price falls as production capacity and efficiency increase; external aid donors and a few developing countries' governments then start to buy the vaccines and they are introduced piecemeal over many years. The use of vaccines against hepatitis B and *Haemophilus influenzae* type b (Hib) has followed this pattern, for example, with millions of preventable deaths as a result.

"This approach – deplorable for any serious disease – is utterly unacceptable in the case of HIV," says the IAVI report. At the current rate of infection, even a delay of five years between the licensing of an AIDS vaccine and its widespread introduction in low-income countries would mean up to 30 million needless HIV infections.

"The ultimate irony would be that a vaccine developed in collaboration with low-income countries could actually contribute to increasing the gap and inequalities that the AIDS pandemic has created"

IAVI identifies key reasons for the slow introduction of existing vaccines into low-income countries. These include lack of money, the low priority placed on disease prevention by most governments, and, in some high-income countries, the political unpopularity of differential pricing policies for health products. In addition, manufacturers must navigate the "fragmented and uncoordinated" regulatory systems of different nations for approving vaccines, and must scale up production for global needs.



Source: IAVI

Figure 1: Projected global AIDS deaths with different vaccine strategies

The top curve shows projected deaths in the absence of a vaccine. Lower curves show the likely effects of using vaccines of different efficacy, either immediately on licensure, or after delays.

In the case of AIDS vaccines, these problems are compounded, the IAVI report says, by additional challenges: crucially, in the poorer countries there is little or no infrastructure for distributing vaccines to the population groups that most urgently need immunizing against HIV – adolescents and sexually active adults. Most vaccines are given to infants and, although some have argued that HIV vaccines could also be given to this age group, the IAVI report says that such an approach could introduce further delays. The efficacy of a vaccine administered in infancy might not be known until many years of trials have passed, and the duration of protection would also be difficult to determine, says Widdus. "You could end up postponing [implementation] for 10 years and then still find that you need a booster in adolescence." On top of these problems, planning now for large-scale production is difficult because experimental AIDS vaccines are evolving fast.

Moving target

Whereas "first-generation" vaccines, as defined by IAVI, may provide only 40% protection and may require multiple doses, a "third-generation" vaccine might offer 90% protection, be administered orally, and require only occasional boosters. Clearly, each vaccine type would have its own specific requirements for volume, delivery and counselling. Overall, choices about the types of vaccines used and the speed at which they are introduced could decide the fate of millions of people over the course of the epidemic (Figure 1).

A third critical problem with HIV vaccines is that no one yet knows whether a vaccine based on one strain of the virus will protect against other strains. In many communities, particularly in Sub-Saharan Africa, multiple strains are now circulating. The report says that studies to establish whether vaccines can protect against several strains must be run in parallel and must be strategically coordinated. Otherwise the assessment process could take several additional years.

IAVI lists five key requirements to ensure rapid access to vaccines:

- **Effective pricing and global financing mechanisms**
- **Reliable estimates of demand and required production capacity**
- **Appropriate delivery systems for adolescents, sexually active adults and other at-risk populations**
- **Harmonization of national regulations and international guidance for vaccine approval and distribution**
- **Immediate steps to widen access to existing, under-used vaccines against other major diseases, using mechanisms such as GAVI and the Global Fund for Children's Vaccines**

Political leaders and the private sector are challenged to endorse the use of tiered pricing for AIDS vaccines, so that low-income countries will be able to pay what they can afford while manufacturers will still get a satisfactory return on their investment. The report calls for "credible" financial commitments from the industrialized nations to buy and deliver vaccines to developing countries.

Much more effort is also needed, it says, to convince finance ministers and donors of the value of preventing disease, particularly AIDS which is almost always fatal and which affects young, productive adults. The report suggests that, on the basis of existing knowledge, an HIV vaccine could be cost-effective at prices up to 50 times higher than the traditional children's vaccines. Detailed studies on the cost-effectiveness of hypothetical HIV vaccines have not been done yet. But the President of IAVI, Seth Berkley, says they are a priority.

As for the design of delivery systems that would reach adolescents and young adults, Widdus argues for radical rethinking of the traditional approach. "We have basically got to think about lots of different points of access and forget about a single system that reaches 95% [of the target population]", he says. Instead of traditional delivery systems, vaccines might need to be given in a variety of settings including some outside the usual framework - for example, through schools and outreach services that promote condom use with sex workers and street children.

Planning the delivery of vaccines must also take account of political and religious sensitivities that may affect people's demand for immunization, says Widdus. AIDS vaccines for adolescents would probably be most acceptable if they were offered together with other interventions, such as tetanus, rubella and hepatitis B vaccines and health education. "To think about intelligent healthcare packages takes time," says Widdus. "We need to start thinking about this now, not because there will be a vaccine next week, but because these things are intrinsically difficult and we are more likely to make mistakes if we rush at the last minute."

The IAVI report's fifth recommendation – that existing under-used vaccines against major diseases such as hepatitis B or Hib be rapidly and effectively introduced in developing countries through partnerships such as GAVI – will be the key test, it argues. If industry boardrooms are convinced that partnerships for the introduction of these vaccines can work, then partnerships for AIDS vaccines are also more likely to move ahead, says the report.

Tore Godal, Executive Secretary of GAVI says: "We must not be paralysed by problems that are still hypothetical. Instead we should work hard to develop the vaccines themselves and then use every mechanism at our disposal – including GAVI – to get them quickly to those who need them most." ■

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Phyllida Brown

Health promises at the G8 summit: the challenge is to deliver

A PROMISE to give priority to expanding children's immunization was among the less-widely reported outcomes of the summit of the Group of Eight (G8) major industrialized nations in Okinawa, Japan, which ended on 23 July. But after a summit widely criticized in the world's media for its lack of real progress, all eyes are now on those responsible for turning promises into action.

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A better chance: children like these in Haiti cannot afford to wait too long for results

"We have the political backing and promises of some new money: now the real test is to make something happen on the ground," Andrew Cassels, senior policy analyst at the World Health Organization, told *Immunization Focus.* Cassels said that the WHO had been strongly "encouraged" by the G8 leaders'recognition that better health is key to reducing poverty, but warned that there is "a huge agenda of work to be done over the next few months".

The seven rich nations plus Russia committed themselves to fight infectious diseases, especially AIDS, malaria, tuberculosis and childhood diseases. In their final communiqué (1) they set targets to halve TB deaths and the burden of malaria disease, and to cut by a quarter the number of HIV-infected young people, by 2010. The communiqué does not specify any mechanisms for achieving these targets, although a further meeting in the autumn will review priorities, discuss new ways of working and set a timetable for action.

New money has been promised from two of the rich nations: Japan will allocate US$3 billion in assistance to low-income countries for infectious and parasitic disease control over the next five years (2); and the United Kingdom is to double to US $160 million over the next three years, its development assistance for improving access to drugs and technologies for major communicable diseases. The European Commission, whose president also attended the G8 summit, is also understood to have promised significant new funding although no statement or specified sum had been announced as *Immunization Focus* went to press.

The leaders in Okinawa also heard confirmation that the International Development Association, the World Bank's concessionary lending arm, would treble its provision of credit to combat AIDS, malaria, TB and childhood diseases, including immunization, to at least US$1 billion. IDAprovides about US $7 billion per year overall for long-term credits to low-income countries. Eligible governments will be able to apply for IDAfinancing for a range of purposes, such as strengthening their infrastructures for delivering health interventions, or supporting disease prevention and control activities, says Amie Batson of the World Bank. The Bank's aim is to strengthen the capacity of governments to provide sustainable services, by complementing the actions of other GAVI partners and the Global Fund for Children's Vaccines. "The Fund can help to catalyze and complement more sustainable sources of funding," she says.

Besides setting targets on the three major killer diseases, the G8 communiqué also sets out a broader agenda which will need to be addressed if these targets are to be achieved. This includes "the development of equitable and effective health systems, expanded immunization, nutrition and micronutrients and the prevention and treatment of infectious diseases". And it commits the G8 nations and their partners to work "to make existing cost-effective interventions, including key drugs, vaccines and preventive measures more universally available and affordable in developing countries". ■

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Phyllida Brown

Immunization Focus

Editor: Phyllida Brown
Publisher: Dr Tore Godal, GAVI Secretariat, C/O UNICEF, Palais des Nations, 1211 Geneva 10, Switzerland. Email: Gavi@unicef.ch

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