Immunization Focus

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

GAVI

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Immunization Focus is issued quarterly on the GAVI website at www.VaccineAlliance.org
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NEWS

Triple attack on African meningitis outbreak

FOR the second year running, Burkina Faso is struggling with an outbreak of meningitis exacerbated by a virulent strain of meningococcus called W135. But as the epidemic season peaks this month, officials are hopeful that a three-pronged strategy combining mass campaigns with a newly licensed vaccine, better case management, and more efficient surveillance are already beginning to reduce the impact of the disease.

So far this year in Burkina, there have been almost 6000 cases of meningitis and more than 800 deaths. A number of survivors have also suffered permanent disabilities, such as hearing impairments.

The African "meningitis belt" is accustomed to outbreaks caused by the more familiar meningococcal strains, or serogroups, known as A and C. But last year the W135 serogroup, which had until then appeared only sporadically in Africa, emerged to kill more than 1700 in Burkina Faso. The vaccine that was available at the time protected only against the A and C serogroups. A vaccine against W135 already existed, but its high price had put it beyond the reach of most African governments. Last September, African governments issued an urgent call for an affordable vaccine that would also protect against W135.

WHO contacted several vaccine manufacturers and a trivalent "ACW" vaccine was developed by GlaxoSmithKline (see *Immunization Focus*, November 2002). In December 2002, the Belgian authorities granted the ACW vaccine a licence. In February, after surveillance reports indicated that meningococcal disease was increasing and that W135 was present in several districts, the vaccine was released at the request of the Burkina government by the International Coordinating Group on Vaccine Provision for Epidemic Meningitis Control. WHO and the health ministry are now assessing the vaccine's impact. The results will be available to help plan for the 2004 epidemic season.

Dr Chris Nelson of WHO's department of Vaccines and Biologicals said that the tight timetable could not have been met without the leadership of key individuals and collaboration between WHO, GSK and the Bill & Melinda Gates Foundation.

Mackay/WHO

Getting better: a recovering child in Burkina Faso

But vaccination is only part of the strategy for controlling the disease, said Nelson. Equally important is prompt treatment with an affordable antibiotic, oily chloramphenicol. The proportion of sick individuals who are dying from the disease (the case-fatality ratio) has fallen from as high as 15% to 10% in most districts as the epidemic has progressed, indicating improved case management, he said. He has also observed a marked improvement in the quality of surveillance data this year, due to improved training and collaboration between WHO and the ministry of health, which has received extra resources for the work. ■

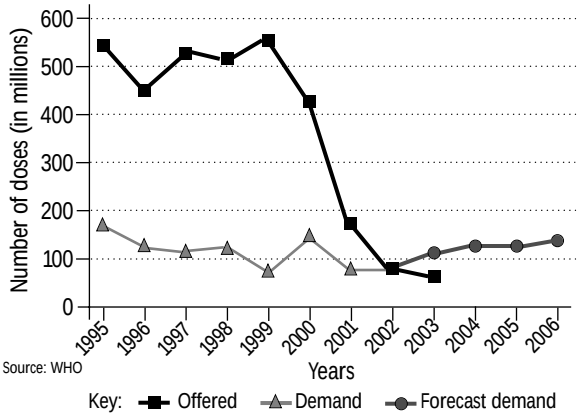
Inside this issue

Strengthening the vaccine regulators

While vaccines procured through UNICEF meet quality standards set by WHO, the same quality assurance is not always guaranteed when governments buy their vaccines direct. As vaccine supply patterns change, WHO is working with developing countries to build their own capacity to regulate vaccines, whether locally produced or imported

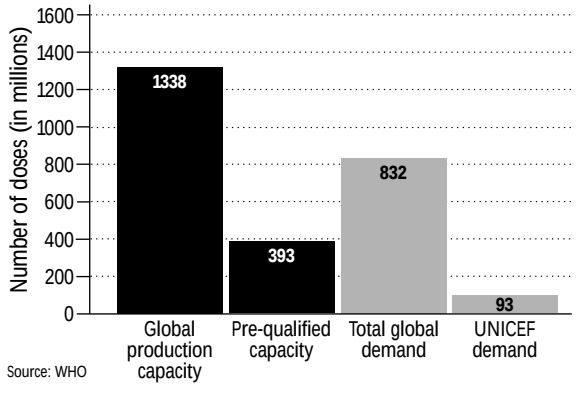
BASIC children's vaccines are in increasingly short supply worldwide. Take, for example, the case of DTwP, the diphtheria, tetanus and pertussis vaccine containing a whole-cell form of pertussis. Many industrialised countries now use acellular pertussis, so the interest of the big pharma in the whole-cell vaccine is diminishing rapidly. Last year, only three manufacturers offered DTwP to UNICEF, with the bulk of this supply coming from developing countries. And this year, for the first time in decades, UNICEF's demand for this vaccine outstrips supply (Fig.1).

Figure 1: DTwP offered to UNICEF



Moreover, UNICEF's purchasing requirement is only part of the total global need. More than 60 countries do not buy their vaccines through UNICEF but direct, from manufacturers within their borders or by importing. WHO figures suggest that some 90% of the DTwP available globally is now made in developing countries. Of this, only about one-third has been shown to meet WHO's quality assurance "prequalified" standards (Fig.2).

Figure 2: Global DTwP supply and demand 2002



To safeguard children and to ensure an adequate future supply of high-quality vaccines, WHO says that its member states should use only vaccines of assured quality in their immunization programmes. The key question is how to do this. Vaccines may be "prequalified" by WHO, that is, shown to meet agreed quality standards for purchase by the UN agencies, or they may be licensed by a fully functional national regulatory authority (NRA).

> **'In some countries, the weakness of the regulatory system has proved a bottleneck to manufacturers that have already invested heavily in new plant'**

WHO has provided the "prequalification" service to UNICEF and the other UN agencies in assessing the acceptability of vaccines that they may wish to buy from a variety of different sources. The service gives purchasing agencies independent advice on the quality of vaccines and their suitability for use. WHO prequalified vaccines must meet quality, safety and efficacy standards: for example, they must show consistent potency and thermostability. They are monitored for their compliance with programme specifications on presentation and labelling, and are also monitored once in use to detect and document any possible suspected adverse effects.

However, WHO has recognized that its own staff cannot assess every new candidate vaccine and that for a sustainable system to exist, governments must take responsibility for regulating domestic and imported products themselves. Since 2000, the UN agency has therefore placed increasing emphasis on building the regulatory capacity of national governments. Before a vaccine can be considered for prequalification, the manufacturer's host country must have a competent NRA in place, and this authority must be clearly independent from the manufacturing industry.

In the past, some governments have been unable to separate manufacture from regulation, and several public manufacturers in developing countries have had close, or overlapping, links with the regulatory system. In some countries, the weakness of the regulatory system has proved a bottleneck to manufacturers that have already invested heavily in new plant and high-quality production processes. So WHO is investing, first, in training regulatory staff until each NRA can fulfil its necessary functions. Good manufacturing practice can then be enforced.

Fully functional NRAs should fulfil six specific functions, says WHO (see Box 1). Clearly, it is not realistic to expect every country, however low its income, to have the same type of authority. For a country that is host to a vaccine industry, the regulatory authority must fulfil all six functions. For a country that procures all vaccines through UN agencies, the WHO prequalification process takes care of some aspects of the process, and only the first two functions must be fulfilled. For a country that buys vaccines direct, but does not produce any, the first four functions must be fulfilled.

1: Six functions of an independent national regulatory authority

- **A** published set of requirements for licensing
- **S**urveillance of vaccine field performance to identify any suspected adverse events following immunization
- **S**ystem of lot release
- **U**se of laboratory when needed
- **R**egular inspections to allow enforcement of good manufacturing practice
- **E**valuation of clinical performance for safety and efficacy

There is now growing evidence that some major vaccine-producing countries, such as The People's Republic of China, are strengthening their capacity to regulate the industry. Last December, an international expert team appointed by WHO went to China to review the functions exercised by its national vaccine regulatory system. The team found major advances since 1998, when a new State Drug Administration had been established as an independent authority, separate from the ministry of health and from the state vaccine manufacturers. The law on registration and licensing of vaccines had been revised. A system for monitoring the lot release of vaccines had been put in place in 2001.

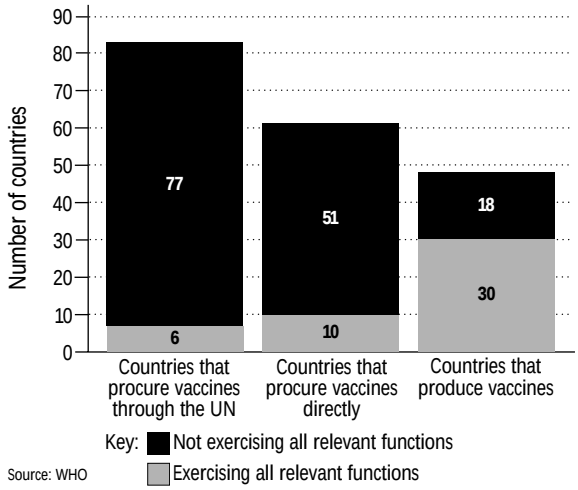
‘ Even in countries assumed to have robust and competent regulatory authorities, assessment can be a useful trigger for discussing ways to improve ’

Inspections to check that all producers were complying with good manufacturing practice had begun, and during 2002 most vaccine manufacturers were certified. Only the system for monitoring suspected adverse events following immunization needed to improve, and plans for that were set out clearly for the first half of this year. China had shown a "very strong" commitment to build up its regulatory capacity, the WHO inspectors found (1).

The existence of an independent and competent National Regulatory Authority (NRA) is one of the requirements for vaccines to become prequalified. Once the requirements are met, China's large industry will be able to help fill the gaps in the global supply of certain key vaccines by selling to the UN agencies, and to procuring countries abroad.

By late 2002, WHO had conducted assessments of 49 national regulatory authorities worldwide, including some in industrialised countries such as Australia, Japan and Sweden, and found that even in countries assumed to have robust and competent regulatory authorities, assessment can be a useful trigger for discussing ways to improve the way these six functions are carried out. Perhaps not surprisingly, the majority of governments worldwide have still some way to go before they can be said to exercise all their regulatory functions (Fig. 3).

Figure 3: Few countries' National Regulatory Authorities are yet performing all the appropriate functions



Obviously, countries with a vaccine industry are more likely than those without an industry to have a competent NRA, and in turn, those countries that procure their vaccines directly are more likely to have a fully functioning NRA than those that procure through UNICEF.

At this point, WHO is focusing its training initiatives on major producing countries. "Training is central to what we do," says Lahouari Belgharbi of WHO's department of Vaccines and Biologicals. WHO says it has trained more than 500 regulatory staff worldwide in the past seven years (2). The pace is accelerating as more and more new manufacturers come on line. In the coming year, WHO expects to have more potential pre-qualified manufacturers in India and China. Clearly, it is in the interest of governments and their WHO partners to increase the capacity for regulating this industry as soon as possible – as China has shown to be feasible. ■

Further reading

1. Vaccine Quality: Assessment of Vaccine Regulation in the People's Republic of China. Follow-Up visit 16–21 December 2002. WHO. From belgaharbil@who.int or WHO's regional office for the Western Pacific region.
2. Strengthening National Regulatory Authorities: A Global Overview. L. Belgharbi, WHO, address as above.

Not just better healthcare, but a better life as well

An ingenious development project in northern Mozambique aims to improve health service delivery, generate income from clean fuel sales, and even free up children to do their school work. Phyllida Brown reports

BACK in 2000, after Mozambique suffered some of the worst floods in its history, a Cameroon-born businessman called Blaise Judja-Sato went to help the relief effort. What he saw profoundly affected him. "I was struck by the weakness of the infrastructure and the impressive resilience of the local people, despite the daunting challenges they faced," he recalls. He met Graça Machel, the former minister of education and Nelson Mandela's wife, and asked how he could contribute.

Judja-Sato left his job as director of international business development for Teledesic LLC, a broadband satellite company co-founded by Bill Gates, and set up VillageReach, a nongovernmental organization based in the US. In 2001, VillageReach began working in partnership with Mozambique's Foundation for Community Development and its national government in the northernmost province of Cabo Delgado to increase people's access to healthcare, while also benefiting households, the local economy and the environment.

Cabo Delgado is a remote province, some 900 miles from the capital Maputo. Incomes are minimal, roads are poor, and healthcare is basic. Almost half the population lives more than two hours' walk from a health facility, and mothers taking their children to clinic have grown accustomed to finding no vaccines in stock, no appropriate medicines either, or that the fridge storing the vaccines has broken down. A survey (1) last year in the province found that only 29% of babies had been fully immunized, well under half the average rate for Mozambique.

To address the logistical problems of the health service, VillageReach has a contract with the health ministry to deliver vaccines and medicines to clinics in Cabo Delgado. The contract, which began last year, also covers the supply and maintenance of cold-chain equipment – mainly fridges – and other clinic essentials such as lamps and sterilisers. And, because the central aim is to reach underserved households, VillageReach is also working with the health ministry to increase staff outreach, for example by providing them with bicycles.

VILLAGEREACH

Fresh thinking: Blaise Judja-Sato

But the Northern Mozambique Project, as the partnership is called, is not just about health service delivery. "We're developing an innovative model to improve lives in a number of ways for the hardest-to-reach populations," says Judja-Sato. Rather than define the need in terms of the health system alone, VillageReach and the Foundation for Community Development have identified a broader development need and set about meeting it.

VILLAGEREACH

They explored several options for generating income alongside the healthcare logistics work, such as using the trucks that deliver vaccines to return with a load of local farmers' vegetables for sale. Most were rejected as unworkable. Judja-Sato discussed the issue with colleagues in Mozambique and abroad, including Dr Michael Free, vice president for technology at the Program for Appropriate Technology in Health (PATH) in Seattle.

Then they hit on an idea: to supply a clean and reliable fuel, not only to the cold chain, but also to the community as a whole. "We were spinning ideas ◗

Hard labour: time freed up from gathering firewood can be put to better use

VILLAGEREACH

and this one came out of the spin," says Free. A reliable power supply is critical for the effective function of a cold chain. Rural clinics in low-income countries such as Mozambique have traditionally run their fridges and lamps on kerosene. But kerosene deliveries can be erratic, and kerosene-powered fridges are inefficient, unreliable and difficult to repair.

Outside the clinics, fuel shortages are equally pervasive and disruptive. Most families rely on gathering firewood or buying charcoal to cook their meals, but the trees are dwindling and the bare soil is eroding. The task is becoming more and more time-consuming, occupying hours of each day for women and children. Along the coast, people are starting to burn mangrove, but this is beginning to deplete the habitat of several species of fish and prawn that have been important to the local fishing industry. The only alternative is kerosene, but it causes many domestic fires and poisons too many young children in accidents.

"We realised that the cold chain was the central problem, but knew that we could not focus solely on that," says Judja-Sato. "You have to have a comprehensive and rigorous approach, and try to bring business experience to the problem."

VillageReach and the Foundation for Community Development decided to replace the old kerosene-powered fridges with new and more efficient models that run on liquefied petroleum gas (LPG), sometimes called propane. To ensure a steady supply of the gas, they have set up a company called VidaGas, a Mozambican for-profit entity, with its own distribution plant in Pemba, the main town in Cabo Delgado. The gas comes up from the port by tanker and is stored at the distribution plant, opened last November, from which it is sold to the Ministry of Health in 11-kilogram cylinders. VidaGas is also working with the government's energy and environment ministries and is now starting to sell gas commercially to households and small local businesses, such as restaurants and hotels. The profits of these commercial sales are intended to help fund the activities of VillageReach in Mozambique. And the gas will make a big difference to daily life and the environment.

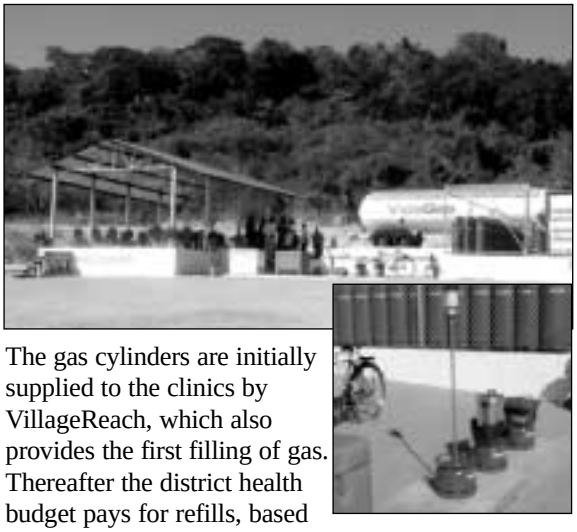
Instead of spending hours gathering firewood, children can go to school and women can devote more time to education, childcare and small businesses. After dinner is cooked, the stove burner can be removed from the gas cylinder and replaced by a lamp attachment. For the first time, children can do their homework after the daylight has faded. Adults who cook dinner over a gas stove suffer fewer respiratory problems than when they cook over firewood or charcoal, and their babies suffer fewer infections. VidaGas is selling a starter pack consisting of the burner, lamp and 5 kg of gas to households for around $45. VillageReach and its local partners are setting up microloan schemes to enable families to pay for the equipment over a period.

To set up the project Judja-Sato worked with a team, including Lionel Pierre, a Haitian who has worked for years in healthcare and transport logistics in developing countries with WHO and others and Didier Lavril, a French energy expert with particular experience of working with LPG in African settings.

Government commitment

Critical to the success of the project was the support of Graça Machel, who is the Foundation's president. "Graça gave us the credibility and enabled us to take the idea from concept to programme," says Judja-Sato. He attributes much of the success of the project to the Mozambique government, whose role has been key. "This project would not have been possible without the government's dedication and commitment. Their willingness to try new solutions to longstanding problems is commendable and has allowed us to work quickly and effectively."

Pierre describes the "before" and "after" scenarios in the clinics. Before, fridges were ancient, maintenance was appalling, and training of users nil. Health district staff were powerless to act; technicians had no means of transport and no money to intervene where necessary. Wastage for some vaccines had been as high as 80%. Now, gas fridges are up and running in 36 initial clinics, serving some 800 000 people or half the population; this will rise to 90 when all 17 districts in the province are equipped.



LLOYD/PATH

The VidaGas plant on its launch day and (inset) a burner and lamp for domestic use

The gas cylinders are initially supplied to the clinics by VillageReach, which also provides the first filling of gas. Thereafter the district health budget pays for refills, based on estimates of known consumption rates, says Pierre.

VillageReach's local staff, and government health staff, are all trained in maintaining the fridges, and spare parts are available. Training continues, and vaccine storage conditions have improved markedly and are now monitored monthly. VillageReach is also introducing equipment and procedures to improve injection safety. And the initiative includes a system to regulate the vaccine supply to avoid stock-outs and wastage, through proper management.

There are wider benefits for the local economy too; VillageReach has not only trained and employed its team of delivery and cold chain maintenance workers, but additional local work has been created, for example to maintain the trucks and look after the VidaGas distribution plant. "There are jobs, more self respect, and a virtuous spiral," says Free. And, as Lavril points out, the project should combat deforestation and reduce greenhouse emissions, by reducing the inappropriate use of biomass fuels. If fewer trees are felled, he adds, there should be less soil erosion and the impact of flooding should also be reduced.

Carlos Fumo, executive director of the Foundation in Maputo, is pleased by progress so far. "The ultimate aim is to ensure that children have greater access to vaccines, and to ensure that the quality of life of Mozambican communities improves." Even the most perfectly-stored and transported vaccines would be useless, says Fumo, if children did not actually get them. So he is delighted to report that the number of fully immunized children has risen by 40% in the project area in the short time since it began.

The key role of the Foundation now, says Fumo, is to educate and inform communities. "We need to make sure that there is local ownership of the programme." He is proud of the collaboration between private and public sectors.

No one pretends that the project is without risk. Can the commercial sale of the gas make enough money to sustain the project in the longer term? Can enough people afford the burner, the lamp and even the cost of the gas to make the commercial side self-sustaining? Even though it costs less to cook with gas than with charcoal, several weeks' worth of gas has to be paid for upfront, whereas charcoal supplies can be bought daily. Some families simply don't have that kind of cash in hand. "But I think this is an extraordinarily interesting, and very viable, model," says Free, a member of VillageReach's board. Free pays tribute to Judja-Sato's huge personal commitment to the project, to his networking skills in involving others and his ability to make the idea work.

Fumo does not believe that the cost of the equipment will be a significant barrier to most households. Many still use traditional fuels simply from habit, he says, and it is up to the Foundation to inform them about the alternative. "The very few people who have been exposed to this idea so far see a clear advantage in using gas instead of firewood."

Alfred Durão, former head of the Mozambican government's immunization programme and now working with VillageReach, is in no doubt about the difference the project has made so far. "There is no shortage of vaccines in the districts, and the fridges work. We have seen a good result and more vaccination of children."

The project is also attracting outside interest. "There is nothing like this in the world," says John Lloyd at PATH. "It is an extremely important piece of work." VillageReach itself is keeping a modest and cautious tone for the time being. Several governments have approached Judja-Sato and asked about pursuing a similar approach in their own country. VillageReach is definitely planning a series of other demonstration projects to ensure that the idea can work in a range of different settings. But it is not going to be rushed. The first step is to prove that the idea can work in just one province of just one country. So far, the signs are distinctly good. ■

LLOYD/PATH

Mozambique's immunization programme manager explains the project to President Joaquim Chissano (right) at the launch

References and further reading

(1) Survey conducted in 2002 by Foundation for Community Development, The Ministry of Health and VillageReach.

VillageReach, Seattle: www.villagereach.org

The Foundation for Community Development of Mozambique: www.synergos.org/partners/fdcenglish.htm

PATH: www.path.org. VillageReach works with PATH to field test new vaccination technologies. The Children's Vaccine Program at PATH provided seed funding for this project.

Is eighty percent coverage achievable?

Analysts review countries' performance and assess what steps are needed if the Alliance is to meet internationally agreed targets for immunizing more children

DESPITE early signs that a number of countries are improving their vaccination coverage, it looks unlikely that the GAVI goal of 80% of the poorest countries reaching 80% coverage in all districts by 2005 – the '80/80 goal' – will be reached. This is according to an analysis (1) carried out for the GAVI Board by management consultants McKinsey & Company.

The McKinsey team pored over the multiyear plans submitted to GAVI, examined data from UNICEF and WHO, and interviewed national, regional and international experts to assess the current coverage situation and forecast the likely evolution over the coming years. There are encouraging preliminary signs that GAVI may be contributing to a "modest" increase in overall coverage rates in countries supported by the Vaccine Fund in the past two years. However, the overall conclusion is that on current levels of activity, most GAVI-supported countries will not achieve 80% district-level coverage until after 2010.

'There can be no "one-size-fits-all" approach to improving the delivery of immunization – each country's solution is likely to differ'

Worldwide every year, about 34 million children miss out on immunization, resulting in nearly 3 million preventable deaths. At least 31 million of the unimmunized children live in countries supported by GAVI and the Vaccine Fund. Two out of every three unimmunized children can be found in five countries – India, Nigeria, China, Pakistan and Indonesia.

It is clear that unless countries increase vaccination coverage, the United Nations Millennium Development Goals (MDGs) will not be reached. The MDGs pledge to reduce deaths in children under age five by two-thirds before 2015. To support this goal, at the 2002 Children's Summit the UN General Assembly pledged to "ensure full immunization of children under one year of age, at 90% coverage nationally, with at least 80% coverage in every district or equivalent administrative unit", by 2010.

Faced with the findings of the McKinsey report, the GAVI Board is considering the most appropriate actions to meet the global goals. At its most recent meeting in New York on 6 March, Board members expressed a reluctance to launch brand new initiatives, wishing to work within established policies and programs. And, as the report warns, localized and tailored solutions are required to ensure sustainable improvements in coverage that eventually benefit the entire health system.

The McKinsey team was able to identify some broad groupings of countries by looking at the barriers they face. The team identified five key health system "drivers" that determine the performance of a national immunization programme: the degree of political and financial commitment; the physical infrastructure; the monitoring and information system; the management of service delivery and staff; and the degree of demand for immunization, or social mobilization.

While there are some countries that have all areas well in hand, most countries are lacking in at least in one or two areas, creating 'barriers' to improved performance. Weak management of service delivery and staff was found to be the most common barrier to improved performance, affecting some 40 countries. In a handful of countries, all barriers exist. A system-wide approach would be needed to overcome the barriers, according to the report.

On the positive side, McKinsey concluded that, when the value of immunization is well communicated, and social mobilization is strong, a "virtuous circle" can follow, with strong political commitment, ensured resource flow to districts, and appropriate service delivery with good monitoring.

One finding is clear: there can be no "one-size-fits-all" approach to improving the delivery of immunization – each country's solution would differ. Therefore the McKinsey report is being shared this month with countries; the GAVI Board will consider their reactions before taking decisions about how to accelerate the growth in coverage. ■

Lisa Jacobs and Phyllida Brown

(1) McKinsey & Company. *Achieving our immunization goal*. www.vaccinealliance.org

Immunization Focus

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Designed and produced by: Topics the Creative Partnership, 397 Topsham Road, Exeter, EX2 6HD UK Tel: +44 1392 876800 email: topics@eclipse.co.uk