

## Vaccination: rattling the supply chain

The introduction of new vaccines, combined with a push to expand immunization globally to reach every child, is straining vaccine supply chains to the limit. New thinking on the way vaccines are delivered is needed. Gary Humphreys reports.

The first decade of this century was perhaps the most productive in the history of vaccine development, seeing the release of a plethora of new life-saving vaccines for rotavirus diarrhoea, types of meningitis and pneumonia, and for human papillomavirus (HPV) infections that cause cervical cancer. “We are in a very different situation now compared to 10 years ago,” says Dr Osman Mansoor at the United Nations Children’s Fund (UNICEF) in New York. Mansoor, who is UNICEF’s senior health adviser for the Expanded Programme on Immunization and New Vaccines, notes that more vaccines are in the pipeline. In fact more than 80 vaccines are in the late stages of clinical testing, and 30 of them are designed to protect against major diseases including dengue and malaria.

At the same time, the global vaccine market is booming: since 2000, global revenue from the sale of vaccines has almost tripled reaching more than US\$ 17 billion by mid-2008. While most of this expansion is accounted for by sales of new and more costly vaccines in industrialized countries, more vaccines are also reaching developing countries due to the efforts of the GAVI Alliance (formerly the Global



Health worker in Niger shows bottles with vaccine vial monitors.

WHO/Umit Kartoglu

Alliance for Vaccines and Immunization), a public–private partnership established in 2000 to increase immunization in poor countries.

The World Health Organization (WHO) and UNICEF estimate that just over 80% of the world’s children now have access to immunization, as measured by coverage of the third dose of DTP (diphtheria, tetanus and pertussis) vaccine, while an increasing number also have access to powerful new vaccines. “In the past, countries relied on a package of vaccines against six diseases,” says Project Optimize Coordinator Modibo Dicko, referring to WHO’s Expanded Programme on Immunization, which was launched in 1974. “Now some countries are doubling the number of vaccines they offer.”

As encouraging as all this seems, the scaling up of immunization programmes and the introduction of new vaccines is putting an unprecedented strain on delivery systems that have not changed in decades. James Cheyne, a supply-chain consultant, who started his career in vaccine logistics in Burma (now Myanmar) in 1977, is in a good position to judge those systems since he has had a hand in designing several himself.

Cheyne cites the unnecessary layering of distribution networks as one of his main concerns. “Typically there is a central store that supplies the regional stores,

which then feed the provincial stores and district stores that in turn supply the local health centres,” he says, pointing out that while this layering made sense 30 years ago, because the lines of communication were weak, these days low-cost telecommunications technology has changed things. “You don’t need a store for each administrative level anymore because we have cell phones and the person from the health centre can call the central store directly,” Cheyne says.

Making better use of that kind of technology is a core aspect of the work being done by Project Optimize, a collaboration between WHO and PATH (formerly the Program for Appropriate Technology in Health), a nongovernmental organization.

For Michel Zaffran, the director of Project Optimize, information technology is key in combating one of the biggest problems faced by vaccine distribution systems – overstock in supply. On the face of it the idea that immunization programmes are hampered by too much vaccine seems paradoxical. But, in fact, the overstocking of vaccines increases cold storage costs and generates waste (when vaccines are lost, damaged or not used before their expiry date, and when not all vials in a multi-dose vial get used).

“We want to have as little buffer stock as possible, but still we want to



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It is important to have adequate supplies of vaccine for each vaccine session, especially when women and children, such as these in Niger, must travel long distances on foot.

have enough vaccine to vaccinate the children,” Zaffran says, arguing that this means putting in place information systems and technologies that give managers a real-time picture of how much stock they have throughout a country and whether the quantities meet the requirements of their immunization strategy.

According to UNICEF’s Mansoor, an even more pressing problem is when there are shortages of vaccine supplies to meet demand for children who turn up for vaccination sessions.

These problems can be further exacerbated when the volume of vaccine flowing through the system increases, as has been the case since 2000, and vaccines have become bulkier, partly due to manufacturers’ packaging policies. As Zaffran explains, increased price is one of the main drivers of this trend: “In the early days when the vaccine cost around US\$ 0.10, WHO encouraged health workers to open a vial for one child even if it meant wasting nine doses. There were wastage rates of 60% or 70%. Now that we are introducing vaccines, which cost several dollars a dose, things have changed.”

“Countries are postponing the introduction of these vaccines because they do not have the capacity.”

Michel Zaffran

According to Dicko, the cost of newer vaccines is between US\$ 3.50 and US\$ 7.50 per dose (when procured through UNICEF) and sometimes more. Newer vaccines are often in single or two-dose packages. While this helps to reduce wastage, it also means that they require more cold chain space per dose compared with the traditional EPI (Expanded Programme on Immunization) vaccines that come in 10- and 20-dose vials.

Another significant driver of increased bulk is more sophisticated packaging. Until 2009, the only pneumococcal conjugate vaccine (against a range of child infections including pneumonia and meningitis) was only available in a pre-filled syringe that required nearly 20 times as much storage space as in a 10-dose vial. “New vaccines require upwards



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Vaccine supplies packed in cold boxes and strapped to a motorbike for delivery in a rural area in Niger.

of five times the amount of physical space in cold storage,” says Dicko, who cites the problems faced by Turkey as an example of the sort of challenges that result. “In 2005 Turkey needed only 2600 m<sup>2</sup> of cold storage in order to accommodate its stocks of vaccine. When they introduced the first generation of pneumococcal vaccine in 2008, Turkey’s storage space requirement jumped (four times) to 11 400 m<sup>2</sup>. They had to rent cold storage space.” Turkey found a solution, but not every country does. For Zaffran it is not too strong to describe the situation faced by many countries as a “crisis”. “Countries are postponing the introduction of these vaccines because they do not have the capacity,” he says. “Some countries are actually delaying the time when the vaccines arrive, even when they have been paid for by others because they do not have the capacity either at the central level or in the country.”

The kind of problem faced by Turkey is also causing people to rethink the use of the cold chain, the temperature controlled supply chain, which has traditionally been used for virtually all vaccine delivery. “Most vaccines are stored at a temperature of between 2 and 8 degrees Celsius,” explains Cheyne, referring to guidance that is described on the vaccine packaging.

“One vaccine has the potential of being kept for six months at 45 degrees, but the requirement is still to keep it at temperatures between 2 and 8. It makes absolutely no sense at all,” he says. Moving some vaccines from the cold chain to a

temperature-controlled chain at, say, 25 degrees, would make room for other vaccines or enable countries to cut back on storage costs Cheyne argues. UNICEF’s Mansoor sees another advantage. “For me, the issue is not so much getting vaccines out of the cold chain but getting them beyond the cold chain to reach into areas where there is no refrigeration so that more children can benefit,” he says.

For Mansoor the move makes even more sense given the availability of vaccine vial monitors (VVM), which are now on the label of virtually all vaccines shipped by UNICEF. The labels carry the image of a circle containing a white square. “The white square gets darker with cumulative heat exposure. If the vaccine has been subjected to heat that risks making it subpotent, the VVM shows this when the colour of the inner square is the same or darker than the outer circle,” Mansoor explains. Currently there is no equivalent detection method for freezing, which is much more damaging to some of the newer vaccines than heat in current cold chain arrangements. Like Cheyne, Dicko thinks there are many candidates for removal from the cold chain, citing as examples the vaccines against hepatitis B, Japanese encephalitis, cholera, diphtheria, tetanus and HPV infections. However, he says, this list cannot be drawn up without the consent of the manufacturers and the regulatory authorities. “It cannot be done outside that process,” he says, “but we are building evidence that it can and should be done”.