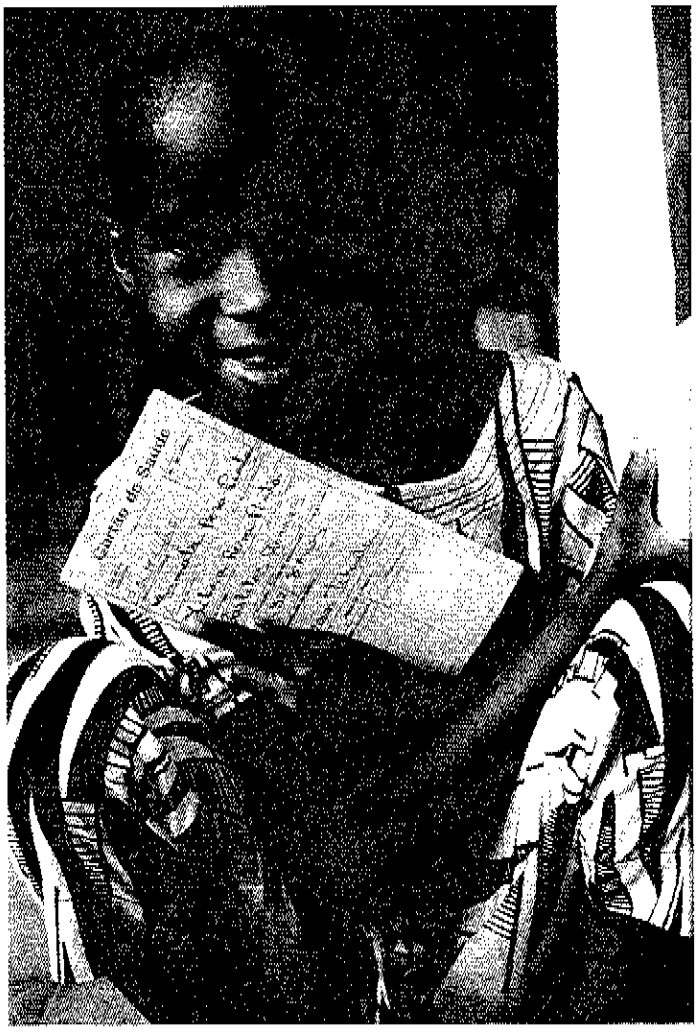
EXECUTIVE SUMMARY

WHO/GPV/PR/96.01
Distribution: General
Original: English



State of the world's vaccines and immunization

World Health Organization

United Nations Children's Fund

NOT TO BE DISTRIBUTED UNTIL 25 SEPTEMBER 1996

WHO/GPV/PR/96.02

Two decades of progress

UNICEF/Adrain Pennink (93-BOU1104)

The Victories	1974	1996
Children immunized against EPI diseases	5 %	80 %
Yearly child immunization contacts	31 million	500 million
Annual lives saved by immunization	less than 1 million	3 million
Children affected by crippling diseases	450 000	50 000

The Downside

Of the 12 million children under the age of 5 who die each year, 2 million die from EPI vaccine-preventable diseases.

Vaccine research and development costs are rising.

The Challenges

To save up to nine million more children each year through development of new vaccines.

To efficiently immunize children against diseases that strike in adulthood (e.g., hepatitis B, tuberculosis, AIDS).

To find new funding to meet rising cost of vaccines for the poorest countries.

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Executive Summary

The vaccine challenge

The *State of the World's Vaccines and Immunization*, jointly produced by the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) highlights the current vaccine situation in the world today, showing not only the successes that have been achieved, but the dramatic challenges we can expect in the future. Yet while immunization programmes have grown and advances in technology allow us to envisage a range of new and improved vaccines, immunization is today at a crucial juncture. The cost of developing and producing vaccines is increasing significantly—and will be accompanied by dramatic increases in the cost of new immunization programmes, thus focusing new attention on the critical gap between rich and poor nations and the ability to pay. Meanwhile, donor funding for immunization shows signs of declining. Will governments be willing—or able—to pay for the new vaccines? Can they afford not to? Millions of lives depend on these factors, as this summary of the report outlines below.

Two hundred years after the discovery of the first vaccine—against smallpox—the world is on the threshold of a series of major scientific developments that will change the face of preventive health care for children. Over the next 5-15 years a new generation of vaccines will come on line that could save the lives of up to 8 million children a year.

Dramatic advances in molecular biology and the use of genetic engineering techniques have produced a raft of candidate vaccines that will:

- simplify immunization;
- improve the performance of existing vaccines;
- protect against diseases for which no vaccines currently exist;
- protect against diseases that are becoming untreatable due to rapidly increasing microbial resistance to antibiotics.

Scientists are studying a range of potential new vaccines against over 60 different diseases. They include vaccines against:

- the major childhood killers—diarrhoeal diseases, acute respiratory infections, and malaria;
- diseases that can remain dormant and strike in adulthood such as hepatitis B—a vaccine is already on the market but not universally accessible—and major killers such as tuberculosis (where an improved vaccine is needed) and HIV/AIDS. Immunization in childhood against these diseases could save millions of adult lives a year.

But there is a catch. The new generation vaccines are expected to be many times more expensive than those in use today. Vaccines are likely to cost not cents but dollars a dose from now on, even perhaps in the poorest countries. Research and development costs today for a single vaccine can range from US$ 50 million to US$ 200 million—depending on the length and complexity of the research. On top of that, new vaccines will be constrained by a web of intellectual property rights—each adding a fixed percentage to the price of a single dose as well as restricting its manufacture elsewhere.

As donor funding for immunization declines, will governments be willing—or able—to pay for the new vaccines? Can they afford not to?

Over 12 million children die every year—3 million of them before they are even a week old. As many as 2 million of those deaths are from diseases that could be prevented by the vaccines already on offer through the Expanded Programme on Immunization. They occur for two main reasons: because vaccines are not 100% effective and because each year about 20% of the world's children are not fully immunized during their first year of life with the original six EPI vaccines against diphtheria, tetanus, whooping cough, polio, tuberculosis, and measles. Work is now under way to boost immunization coverage rates and cut delivery costs through simplifying immunization—cutting down on the number of contacts needed and developing new vaccines that can be given at an earlier age. This would help protect children against diseases such as measles which can strike before they are old enough to be immunized, as well as reaching more children with vaccines before they lose contact with the health

care system. New vaccine delivery concepts under development or in field tests include vaccines that can be inhaled, single-dose vaccines with built-in slow-release booster shots, and conjugate vaccines in which antigens are combined with a "vaccine carrier" such as tetanus toxoid.

The two-pronged approach to transform immunization—boosting coverage through improving existing vaccines and immunization and adding a range of new vaccines against diseases that are not yet vaccine-preventable—will be a severe test on immunization finance and delivery systems. But, perhaps more importantly, the new approach will require a fundamental re-think of the value of disease prevention through immunization. What is a vaccine really worth?

The availability of new, more expensive vaccines will focus attention increasingly on the relative value of alternative disease prevention measures. The cost-effectiveness of each possible intervention—whether immunization, efforts to improve sanitation and hygiene, environmental protection, or the adoption of a healthier lifestyle—will need to be carefully weighed to ensure that the choice is based on the most effective and efficient use of resources available. But even at a higher price, vaccines will remain one of the most cost-effective means of preventing disease and avoiding treatment costs.

The Expanded Programme on Immunization (EPI)

In 1974 when the Expanded Programme on Immunization was launched by the World Health Organization (WHO), less than 5% of the world's children were immunized against the initial six target diseases—diphtheria, tetanus, whooping cough, polio, measles, and tuberculosis—during their first year of life.

By 1990 and again in the most recent statistics (after a slight interim drop in coverage), almost 80% of the 130 million children born each year were immunized before their first birthday. An achievement involving over 500 million immunization contacts with children throughout each year.

Within two decades the EPI was preventing the deaths of at least 3 million children a year. In addition, at least 750,000 fewer children were blinded, crippled, mentally retarded, or otherwise disabled. The immunization contacts have also opened up opportunities for other primary health care interventions—health education for mothers, vitamin and mineral supplements for children who need them, and routine health checks.

During 1995, in addition to the 500 million routine immunization contacts with children under one, a record 300 million children throughout the world—almost half the world's children under five—were immunized during mass campaigns against polio.

By the year 2000, polio is expected to be eradicated—eventually saving governments over US$ 1,500 million a year once immunization is no longer needed.

But will that money find its way back into immunization services—to help increase immunization coverage with existing vaccines or fund the introduction of new ones? While the war against polio may almost be over, the battle against other vaccine-preventable diseases is yet to be won. Almost 2 million children die every year from diseases that can already be prevented through immunization.

In 1994 over a million children died from measles, almost 500,000 from neonatal tetanus, and almost 400,000 from whooping cough. These were the children who slipped through the EPI net—among them some of the poorest and most disadvantaged children in the world. They included children who are caught up in wars, children on the move and who are never in the right place at the right time to be immunized, children who have had some but not all the doses of vaccine needed for full protection, or children who are living in sub-Saharan Africa where less than 60% of children are immunized.

The effort to sustain current levels of immunization coverage and reach out to more children as well—meeting the global target of 90% immunization coverage by the year 2000—is a major challenge, especially at a time of shrinking donor resources.

The EPI Plus

In its 1993 Development Report, *Investing in Health*, the World Bank maintained that in developing countries an EPI "package" that also incorporated vaccines against hepatitis B and yellow fever together with supplements of vitamin A and iodine (the "EPI Plus") would have "the highest cost-effectiveness of any health measure available today"—an assertion few would dispute. Yet neither hepatitis B nor yellow fever vaccine is available today in many of the countries that need them. The poorest countries are still having difficulty attracting donor funding. In addition, vitamin A and iodine supplements are not widely available where they are needed.

Of the 33 countries in Africa at risk for yellow fever, two thirds are classified by UNICEF as needing

continuing external support to obtain vaccines. But as donors have shown little interest in supporting the cost of yellow fever vaccine, few of these countries can afford to buy the vaccine today—even at the UNICEF discounted price of US$ 0.17 for the single dose needed. Instead, expensive mass immunization campaigns are mounted to control the increasing number of yellow fever epidemics as they occur—an illustration of how funds can be mustered for emergency efforts to contain the spread of disease but not for its prevention. Yet a 1993 cost-effectiveness study showed that routine delivery of the vaccine through the EPI would be seven times as effective as mass immunization campaigns in reducing the number of cases and deaths.

Hepatitis B vaccine has not fared much better. The licensing of the first plasma-derived hepatitis B vaccine in 1982 and a second generation recombinant vaccine in 1986 marked the beginning of a new era for vaccine development. But it also opened a Pandora's box—the implications of which are not yet fully understood. The dilemma lies in finding ways of ensuring that new vaccines are made available—right from the outset—to children in developing countries who also need them. The experience with hepatitis B vaccines has not been a very encouraging start.

Fourteen years after the first hepatitis B vaccine came on the market, millions of children throughout the world still do not have access to it—despite a dramatic drop in price. Allowing vaccines to slowly filter down to children in the poorer countries over 10-20 years is neither just nor equitable.

Vaccine prices

At today's prices, immunizing a child with the six original EPI vaccines (at UNICEF-discounted prices), costs no more than about US$ 1, with an additional US$ 14 in programme costs in delivery. Little wonder that the World Bank Development Report describes immunization as one of the most cost-effective public health interventions.

But the availability of low-cost vaccines through the EPI system is double-edged. The world has become inured to the topsy-turvy notion that, while antibiotics may be expensive, vaccines should come cheap.

The development of the second generation hepatitis B vaccine—the world's first genetically engineered vaccine—signalled that the days of cheap vaccines are over. Initially marketed at US$ 150 for three doses—150 times the cost of all six original EPI vaccines combined (at UNICEF-discounted prices)—by 1994 this one vaccine alone accounted for almost a third of the turnover from the global vaccine market, placing it firmly in the multi-million dollar drugs league. There is little to suggest that other new vaccines will be marketed—initially at least—with a less expensive price tag.

The spectre of vaccines that are unaffordable outside the industrialized countries is one of the reasons cited by several vaccine manufacturers for dropping out of the race to develop a vaccine against HIV. Adverse publicity surrounding the cost of treatment for HIV/AIDS with the drug AZT has made some manufacturers fear the political fallout from receiving sole rights to a vaccine that is affordable for the industrialized countries but out of reach for the developing countries where most HIV infections are occurring.

In its 1995 report *The State of the World's Children*, UNICEF noted that—as a result of an unprecedented social mobilization effort over two decades—immunization is the only medical breakthrough that has been made available not to 10% or 20% but to the vast majority of the world's children. But will it remain so?

The missing links

A range of additional measures is now needed to ensure that new and improved vaccines will be rapidly accessible to developing countries.

A lot more groundwork needs to be done in developing countries to assess the burden of disease and estimate the cost-effectiveness of introducing a new vaccine. Studies of disease burden and estimates of cost-effectiveness are of key importance in bringing a new vaccine to the market. This crucial information would help governments and donors prioritize in choosing, for example, between a new vaccine, alternative preventive measures, or treatment. It would also help manufacturers keep down the cost of the vaccine through advance knowledge of the size of the potential market in developing countries.

At present most vaccine development takes place within the private sector in the industrialized countries—where the most profitable vaccine market exists. As a result, most vaccines are tailored to diseases that occur in the industrialized countries among otherwise healthy children. But these diseases also occur in developing countries and may take a more severe form when they affect children who may also be suffering from malnutrition and other diseases.

Hib conjugate vaccine, which has been on the market now for six years, has been highly successful in reduc-

ing the incidence of Hib meningitis among children in the industrialized countries. But until recently, no one was sure whether it would be equally successful in lowering the annual death toll from Hib pneumonia and meningitis among children in developing countries, estimated to be at least 550,000.

Likewise, new vaccines against rotavirus have reached an advanced stage of development in the United States without being extensively tested in developing countries—where most rotavirus deaths occur. When children in Thailand were given a candidate vaccine against cholera in a limited trial it was discovered that they needed a dose at least 10 times greater than the level needed to protect a child in the United States.

Another handicap is the genetic diversity and geographical distribution of some of the organisms that cause disease. Individual organisms may have a wide range of serotypes and the ones that predominate in the industrialized countries may not be the same as those implicated in diseases in the developing countries. Since vaccine manufacturers in the industrialized countries tend to focus—understandably—on the development of vaccines against diseases that occur largely on their own doorstep, different vaccines may be needed to protect children in developing countries against diseases caused by the same or a genetically similar pathogen.

One example is the development of a vaccine against pneumococcal disease. In developing countries more than a million children a year die from pneumonia caused by the bacterium *Streptococcus pneumoniae*. More than 83 serotypes of this bacterium can cause disease, of which about 10 are implicated in up to 70% of cases involving children. But the predominant serotypes vary between industrialized and developing countries and between different forms of the disease, such as pneumonia or inner ear infection (otitis media). Until recently, pneumococcal vaccine research was driven not by the death toll from pneumonia in developing countries but by the bacteria's role in the increasing incidence of inner ear infections in the industrialized countries. However, new vaccines are now under development that are also designed to protect against pneumonia in developing countries.

AIDS vaccine research is similarly hamstrung. Efforts to produce a vaccine against HIV-1 have so far concentrated almost exclusively on just one of the 10 subtypes of the virus. This sub-type occurs mainly in the industrialized countries but not in most developing countries where the incidence of HIV is highest.

Greater advocacy is needed to ensure that vaccine research and development is driven not only by commercial interests but by public health goals as well. However, vaccine manufacturers must have financial incentives—such as the guarantee of a large market in developing countries—to develop vaccines for the less profitable markets.

WHO has worked closely with vaccine manufacturers to help steer the development of meningococcal vaccines, for example—providing incentives through organizing and funding clinical trials of the vaccine in The Gambia and Niger. And in response to the re-emergence of tuberculosis—linked to the spread of HIV infection—and the increase in drug-resistant forms of the disease, the UN specialized agency has played a key role in the development of new vaccines.

The major stumbling block to the introduction of new vaccines will undoubtedly be the availability of sustainable funding. Efforts by UNICEF and WHO to ensure that the majority of governments assume responsibility for funding their own vaccine needs will release donor funds that can be redirected to the neediest countries. The problem is that, after shifting responsibility for the vaccine needs of 90% of the world's children, donor funding is still insufficient—at today's level—to provide the remaining 10% of the world's poorest children with new vaccines in addition to existing ones. According to recent estimates, by 1998, donor funding for the six original EPI vaccines for the neediest countries will be about US$ 21 million—without allowing for the extra cost of supplementary immunization with oral polio vaccine. The addition of hepatitis B vaccine for the highest risk countries would add another US$ 25-35 million.

The funding crisis is twofold. If donors are to fund both new and existing vaccines, they will need to guarantee a hefty increase in future in the overall amount currently provided for vaccines—even though only the neediest countries will qualify for assistance from now on. Most governments, on the other hand, are being asked to assume responsibility for their own vaccine funding—at the very time when the newer, more expensive vaccines become available. If UNICEF and WHO are to hold the line on targeting vaccine support to only the poorest countries, they will need firm political support from both donors and development agencies. If this strategy fails, there are fears that the existing tiered price structure could collapse—and with it all hope for the foreseeable future of access to new vaccines for these countries.

In the meantime, a concerted effort is needed to elevate the status of vaccines within the public health

sector. This will entail efforts to change public perception of what is an acceptable price to pay for a vaccine. The laudable efforts of the public sector to obtain very low vaccine prices for the benefit of the world's poorest nations have had an unfortunate knock-on effect. While governments and individuals are prepared to allocate large sums of money for hospitalization and high-cost treatment with drugs such as antibiotics, they now balk at the idea of having to pay out comparable amounts for a vaccine that can provide lifetime protection against disease—avoiding the costs of treatment and days lost at work.

One of the most serious obstacles to the provision of new vaccines to children in developing countries is that the higher cost of vaccines may not be weighed against the potential economic benefits. Governments and donors need to undertake rigorous cost-benefit analyses in order to make difficult choices within limited health care budgets. The danger is that, unless there is a fundamental shift in understanding of the value of vaccines, countries which have recently become self-sufficient in providing the EPI vaccines will not be prepared to fund the newer, more expensive vaccines. Each of which is likely to cost several times as much as the cost of the original six EPI vaccines combined.

The outcome of efforts to finance new vaccines will hinge on the success of four key strategies:

- targeting donor support to the neediest countries;
- tiered pricing by manufacturers;
- a commitment by governments and donors to increase the amount they now spend on vaccines;
- advocacy to encourage governments, donors, and the general public to recognize the value of vaccines on the basis of their health impact in individual countries.

Although undoubtedly a herculean task, changing attitudes to the value of vaccines would not cost large amounts of money. In the long run, treatment to save the lives of children not immunized against vaccine-preventable diseases and the legacy of disabled children will cost a lot more—both in money and needless suffering for children and their families.

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