



# State of the world's vaccines and immunization

Third edition

## Executive summary



# State of the world's vaccines and immunization

Third edition

Executive summary

© World Health Organization 2009

All rights reserved. Publications of the World Health Organization can be obtained from WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel.: +41 22 791 3264; fax: +41 22 791 4857; e-mail: [bookorders@who.int](mailto:bookorders@who.int)). Requests for permission to reproduce or translate WHO publications – whether for sale or for noncommercial distribution – should be addressed to WHO Press, at the above address (fax: +41 22 791 4806; e-mail: [permissions@who.int](mailto:permissions@who.int)).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention, or photographic illustration, of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.

Printed in Switzerland.

## Overview

Since the Millennium Summit in 2000, immunization has moved centre stage as one of the driving forces behind efforts to meet the Millennium Development Goals (MDGs) – in particular, the goal to reduce deaths among children under five years old (MDG 4).

More children than ever before are being reached with immunization: over 100 million children a year in 2005–2007. And the benefits of immunization are increasingly being extended to adolescents and adults – providing protection against life-threatening diseases such as influenza, meningitis, and cancers that occur in adulthood.

In developing countries, more vaccines are available and more lives are being saved. For the first time in documented history the number of children dying every year has fallen below 10 million – the result of improved access to clean water and sanitation, increased immunization coverage, and the integrated delivery of essential health interventions.

More vaccines have been developed and others are already in the late stages of clinical trials, making this decade the most productive in the history of vaccine development. More money is available for immunization through innovative financing mechanisms. And more creative energy, knowledge, and technical know-how is being put to use through the development of public-private partnerships – forged to help advance the immunization-related global goals.

Yet despite extraordinary progress in immunizing more children over the past decade, in 2007, 24 million children – almost 20% of the children born each year – did not get the complete routine immunizations scheduled for their first year of life. Reaching these vulnerable children – typically in poorly-served remote rural areas, deprived urban settings, fragile states, and strife-torn regions – is essential if the MDGs are to be equitably met.

In response, a major global push is under way to ensure that these difficult-to-reach children – most of them in Africa and Asia – are immunized. At the same time, new initiatives have been launched to accelerate both the development and deployment of new life-saving vaccines.

The stakes are high. WHO has estimated that if all the vaccines now available against childhood diseases were widely adopted, and if countries could raise vaccine coverage to a global average of 90%, by 2015 an additional two million deaths a year could be prevented among children under five years old. This would have a major impact on meeting the global goal to reduce child deaths by two-thirds between 1990 and 2015 (MDG 4). It would also greatly reduce the burden of illness and disability from vaccine-preventable diseases, and contribute to improving child health and welfare, as well as reducing hospitalization costs.

But even when the global goals have been met, success will be measured against an additional benchmark – whether the achievements are sustainable. Solid building blocks are

being put in place – strengthening of health systems and immunization programmes, new public-private partnerships for vaccine development and immunization, new long-term global financing mechanisms, innovative and sustainable delivery strategies, and improved advocacy and communication strategies – to ensure that long-term progress is not sacrificed for short-term gains.

In addition, continued investments will be needed to accelerate the research and development of urgently needed vaccines against diseases such as malaria, tuberculosis, and acquired immunodeficiency syndrome (AIDS), which together account for over four million deaths a year and a high burden of disease, mainly in developing countries.

This edition of the *State of the world's vaccines and immunization* focuses on the major developments in vaccines and immunization since 2000. [Part 1](#) (Chapters 1–5) examines the impact of immunization on efforts to meet the MDGs, especially the goal to reduce deaths among children under five. It looks at the development and use of vaccines and at the safeguards that have been put in place to ensure their safety, efficacy, and quality. It sets out the progress and challenges in meeting the immunization-related global goals, and looks at the cost of scaling up immunization coverage to meet these goals, and efforts to ensure that the achievements are sustainable in the long term. Finally, it looks beyond 2015 to likely changes in the immunization landscape.

[Part 2](#) focuses on over 20 vaccine-preventable diseases and reviews progress since 2000 in efforts to protect populations against these diseases through the use of vaccines.

## Immunization and human development

[Chapter 1](#) outlines the progress in vaccines and immunization over the past decade against the backdrop of a changing health and development landscape.

In September 2000, leaders of more than 190 countries signed the United Nations Millennium Declaration, which committed the international community to eight development goals aimed at reducing poverty and improving human development. One of these goals calls for a massive reduction in deaths among children under five years old – a two-thirds drop in the under-five mortality rate between 1990 and 2015. Most of the effort in achieving these goals is focused on developing countries, which account for over 90% of deaths among children in this age group.

In 2005, the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) published the Global Immunization Vision and Strategy (GIVS) for the decade 2006–2015. With an overriding focus on the need to ensure equity in access to vaccines and immunization, the strategy sets out the steps that the immunization community needs

to take in order to contribute fully to the attainment of the MDG mortality reduction targets. Implementing the strategy calls for four main approaches: protecting more people; introducing new vaccines and technologies; integrating immunization with other components in the health system context; and immunizing in the context of global interdependence.

The global goals have added a sense of urgency to vaccine-related activities and spurred renewed efforts to complete, as far as possible, what the GIVS refers to as “the unfinished immunization agenda”. The chapters which follow chart the progress made so far in completing this agenda and in meeting the global goals.

## A new chapter in vaccine development

Chapter 2 highlights the surge in vaccine development over the past decade and outlines the reasons for this. It documents the unprecedented growth in the volume of traditional childhood vaccines now being produced by manufacturers in developing countries. And it reports on progress in efforts to assure the quality, safety, and effectiveness of vaccines.

The first decade of this century has been the most productive in the history of vaccine development. New life-saving vaccines have been developed for meningococcal meningitis, rotavirus diarrhoeal disease, avian influenza caused by the H5N1 virus, pneumococcal disease, and cervical cancer caused by human papillomavirus (HPV).

The vaccine industry is experiencing a new, more dynamic period. Since the year 2000, the global vaccine market has almost tripled – reaching over US\$ 17 billion in global revenue by mid-2008, and making the vaccine industry one of the fastest growing sectors of industry. Most of this expansion comes from sales in industrialized countries of newer, more costly vaccines, which account for more than half of the total value of vaccine sales worldwide.

The recent surge in new vaccine development is largely due to three key factors: the use of innovative manufacturing technology, growing support from public-private product development partnerships, and new funding resources and mechanisms (see Chapter 4).

At the same time, there has been unprecedented growth in the capacity of manufacturers in developing countries to contribute to the supply of the traditional childhood vaccines. Overall, the demand for these traditional vaccines has also grown since 2000, partly to meet the massive needs of the major initiatives put in place to eradicate polio, and reduce the burden of measles and of neonatal and maternal tetanus.

Since the early 1990s, the vaccine market has changed. Growing divergence between the vaccines used in developing and industrialized countries, a drop in the number of suppliers in industrialized countries, and a reduction in excess production capacity led to

a vaccine supply crisis beginning in the late-1990s. In response, UNICEF – which procures vaccines to reach more than half (55%) of the world’s children – established the Vaccine Security Strategy to ensure the uninterrupted and sustainable supply of vaccines that are both affordable and of assured quality. While the strategy succeeded in reversing the fall-off in the supply of vaccines to UNICEF, vaccine supply remains heavily reliant on a limited number of vaccine manufacturers and continued vigilance is needed.

Making sure that vaccines are safe, effective, and of good quality is a pivotal element of vaccine development and deployment. It begins with the “infancy” of the vaccine, usually in the laboratory, where its components are tested for criteria such as purity and potency. It continues with clinical testing for safety and efficacy in humans, followed, after licensure, by post-marketing testing of vaccine batches for consistency of the production process, as well as surveillance to identify any potential cases of vaccine-related adverse events.

Licensure, or approval for human use, is the most crucial step in the process. The official body that grants the licence – the *national regulatory authority* – is the arbiter of whether established standards have been met to ensure that a vaccine is of assured quality.

All industrialized countries have a reliable, properly functioning vaccine regulatory system, but only about one quarter of developing countries do. The international health community has launched a series of initiatives, spearheaded by WHO, to ensure that vaccines used in national immunization programmes are “vaccines of assured quality”. The initiatives include a prequalification system established by WHO to advise UN vaccine procurement agencies on the acceptability, in principle, of vaccines available for purchase, and efforts to ensure that every country has a reliable, properly functioning national regulatory authority.

## Immunization: putting vaccines to good use

Chapter 3 highlights the achievements of immunization over the past decade and reports on progress and challenges in efforts to reach more people with more vaccines, to boost immunization coverage at the district level, and to target difficult-to-reach children who have not been immunized. It also sets out some of the key elements of an effective immunization programme.

Over the past decade, immunization programmes have added new and underused vaccines to the original six – diphtheria, tetanus, pertussis, measles, polio, and tuberculosis – given to young children. They include vaccines against hepatitis B, *Haemophilus influenzae* type b (Hib) disease, mumps, pneumococcal disease, rotavirus, rubella, and – in countries where needed – yellow fever and Japanese encephalitis.

Immunization averts an estimated 2.5 million child deaths a year, but despite the successes, millions of children in developing countries – almost 20% of all children born every year – do not get the complete immunizations scheduled for their first year of life.

Reaching these children will require overcoming a number of critical barriers that have slowed progress. A major barrier is the underlying weakness of the health system in many developing countries. Another is the difficulty in delivering vaccines through an infrastructure and logistical support system that is often overloaded. Yet another is a lack of understanding about the importance of vaccines – especially among the poorest populations – and a failure to actively demand access to immunization services. The threat posed by false or unsubstantiated rumours about vaccine safety is also a barrier to progress, as is the projected shortfall in funding needed to reach the global immunization-related goals (see Chapter 4).

Efforts under way to overcome the barriers to expanded immunization include the use of immunization campaigns and “outreach” operations that seek out population groups not adequately covered by routine immunization programmes. In addition, special initiatives, such as the Optimize project, have been launched to help countries manage the growing complexity of immunization logistics (delivery and storage of vaccines, for example) underpinning immunization activities.

The Reaching Every District (RED) strategy, launched in 2002, is designed to strengthen immunization delivery at the district level, by encouraging district-level immunization officials to adopt the principles of “good immunization practice”, such as the identification and resolution of local problems, the organization of regular outreach vaccine delivery services, and the involvement of communities in ensuring adequate functioning of immunization services.

Another strategy aims to integrate immunization activities with other services provided by the health system. Any contact that a health worker has with a child or mother at a health facility is also an opportunity to check immunization status and, if need be, to administer vaccines. Conversely, a mobile team offering immunization to a community can also distribute medicines, antimalarial bednets, and other health commodities or interventions.

Community participation is a key factor in raising vaccine coverage. Creating awareness of, and public demand for, the benefits of immunization is an essential component of an active immunization programme. However, it is also important to ensure that demand can be reliably met.

The availability of new vaccines against pneumococcal disease and rotavirus is expected to have a rapid and major impact in global efforts to reduce child deaths (MDG 4), prevent sickness, and, for pneumococcal disease, prevent disability. At the same time, vaccination against these diseases provides a key opportunity to actively promote the prevention and treatment of pneumonia and diarrhoea, which together account for over one third of all deaths among children under five years old.

Surveillance and monitoring are the cornerstones of immunization programmes, playing a key role in programme planning, priority setting, and mobilization of resources, as well as in monitoring trends in disease burden, and assessing the impact of disease control programmes and progress towards global goals. Since 2000, the increase in data-driven immunization initiatives (such as the RED strategy) and the need for disease data to monitor the impact of new vaccines have highlighted the need to strengthen surveillance and monitoring at all levels.

Disease surveillance systems are also expected to provide an early warning of impending or ongoing outbreaks of disease. The revised International Health Regulations, which entered into force in 2007, require WHO Member States to establish and maintain core capacities for surveillance at the local, intermediate, and national levels.

Over the past decade, progress has been made in setting up or improving surveillance systems for vaccine-preventable diseases. An example of a high-performance surveillance system is the polio surveillance network, which enables rapid detection of polio cases worldwide, and has been expanded in some countries to include measles, neonatal tetanus, yellow fever, and other vaccine-preventable diseases.

Meanwhile, as vaccine coverage has increased and the incidence of vaccine-preventable diseases has fallen – particularly in industrialized countries – there has been an increase in concern about the potential side-effects of vaccines.

Making sure vaccines are made, used, and tested in accordance with internationally accepted standards is one part of the effort to reduce the likelihood of a vaccine producing an adverse event (see Chapter 2). The other part is having an efficient post-marketing surveillance and investigation system in place that will rapidly pick up and verify any rumours or reports of adverse events allegedly related to the use of a vaccine.

Most industrialized countries have such a system, but many developing countries lack the resources or experience required. To address this, WHO has established a Global Advisory Committee on Vaccine Safety, made up of independent experts, to assess and respond to reports and rumours about vaccine safety. In addition, in 2009, WHO established a Global Network for Post-marketing Surveillance of Newly Prequalified Vaccines which have recently been introduced into national immunization programmes.

## Investing in immunization

Chapter 4 looks at the costs involved in scaling up immunization since 2000, and examines the response of both new and established sources of immunization funding.

Immunization is among the most cost-effective health interventions, but what does it cost, and is the investment worth making? In the 1980s, total annual expenditure on immunization in developing countries averaged out at an estimated US\$ 3.50–5.00 per live birth. By 2000, the figure had risen only slightly to about US\$ 6.00 per live birth. Since 2000, GAVI Alliance (formerly known as the "Global Alliance for Vaccines and Immunisation") support for immunization enabled many low-income countries to strengthen their routine vaccine delivery systems and introduce underused vaccines, such as hepatitis B, Hib, and yellow fever. Not unexpectedly, immunization expenditure began to rise again.

By 2010, the average cost of immunizing a child is projected to rise to about US\$ 18.00 per live birth. Beyond 2010, scaling up vaccine coverage with new vaccines – such as pneumococcal and rotavirus vaccines – to meet the MDGs and the GIVS goals is likely to raise the cost above US\$ 30.00 per live birth.

There are several reasons for these rising costs. For a start, new and underused vaccines cost more than the traditional vaccines, although as the market and demand expands, their costs should fall. A second reason is that the increased quantities of vaccines place considerable pressure on the existing vaccine supply chain, requiring expanded storage facilities and more frequent delivery of supplies. A third is the "hidden" costs of introducing a new vaccine into a national immunization programme, such as the costs of staff training, public information, and expanded surveillance and monitoring. Fourth, is the increased cost of providing immunization services for difficult-to-reach children.

Meeting the goals of the GIVS will mean protecting children against 14 diseases – diphtheria, pertussis, tetanus, measles, polio, tuberculosis, hepatitis B, Hib, rubella, meningococcal disease, pneumococcal disease, rotavirus, and (where needed) Japanese encephalitis and yellow fever. If all countries immunize 90% of children under five years of age with these vaccines, it is estimated that immunization could prevent an additional two million deaths a year in this age group – making a major contribution to the achievement of MDG 4.

A WHO-UNICEF analysis published in 2008 estimated how much it would cost to attain the GIVS goals in 117 WHO low- and lower-middle-income Member States between 2006 and 2015. The total bill came to US\$ 76 billion, including US\$ 35 billion for the 72 countries that have a gross national income (GNI) per capita below US\$ 1000 (as of 2006). These countries are eligible for GAVI Alliance funding and have received support for introducing underused and new vaccines as well as support to strengthen their immunization systems.

Is the investment worth making? Data on the cost-effectiveness of immunization confirm that it is. For example, the global eradication of smallpox, which cost US\$ 100 million over a 10-year period up to 1977, has resulted in savings of US\$ 1.3 billion a year in treatment and prevention costs ever since.

In addition to being a significant contributor to childhood deaths, vaccine-preventable diseases also constitute a major cause of illness and long-term disabilities among children both in industrialized and developing countries. The classic example of prevention of serious disability has been the prevention of paralytic polio in hundreds of thousands of children since the advent of the Global Polio Eradication Initiative (GPEI).

Of the new vaccines, the pneumococcal vaccine has been shown to be associated with a 39% reduction in hospital admissions due to pneumonia from any cause. Among children who survive an episode of pneumococcal meningitis, a large proportion are left with long-term disabilities. Similarly, the rotavirus vaccine has been shown to reduce clinic visits and hospitalizations due to rotavirus diarrhoea by 95%.

Thus, while the impact on child deaths alone would be sufficient justification for the use of vaccines in children in developing countries, the reduction of long-term disability among children and the savings from reductions in clinic visits and hospitalization more than justify their use in children everywhere.

Immunization has other far-reaching benefits beyond the positive impact on individual and community health. A recent study by a Harvard School of Public Health team found that by keeping children healthy and in school, immunization helps extend life expectancy and the time spent on productive activity – thereby contributing to poverty reduction (MDG 1).

Who pays the bill and how? In 2007, WHO's 193 Member States were funding an average 71% of their vaccine costs (33% in low-income countries). Of these, 86% of countries reported having a separate line item for vaccines within their national budget – a measure associated with increased budget allocations to vaccines and immunization and with long-term political commitment to immunization. From the WHO-UNICEF costing analysis, it is estimated that 40% of the costs of immunization for the period 2006–2015 will be met by national governments.

Since 2000, immunization funding from multilateral, bilateral, and other funding sources has increased by 13% (not adjusted for inflation). At the same time, there has been a shift both in the way funds are channeled and in the way they are used. At the global level, some bilateral donors have increasingly used the GAVI Alliance as a channel for funding. At a country level, there has been a move away from a project-based approach to the use of broad-based funding mechanisms to support the health sector as a whole.

Health and immunization systems benefit substantially from targeted immunization efforts such as the GPEI. A substantial proportion of the investment in polio eradication has been spent on strengthening routine immunization and health systems, and on achieving the goals of the GIVS.

In recent years, several innovative public-private partnerships and new financing mechanisms have been introduced to provide predictable and sustainable external financial support to help countries meet the immunization-related global goals. The GAVI Alliance is a public-private global health partnership that provides support to countries with a GNI per capita below US\$ 1000, to strengthen their health systems and immunization programmes, increase routine immunization coverage, and introduce new and underused vaccines. As of the end of 2008, the Alliance had received a total of US\$ 3.8 billion in cash and pledges from public and private sector donors, and disbursed US\$ 2.7 billion to eligible countries. Over the period up to 2015, the Alliance has an estimated US\$ 3 billion funding gap out of the estimated US\$ 8.1 billion total funding needed.

During its first phase (2000–2005), the GAVI Alliance focused on the introduction of new and underused vaccines (hepatitis B, Hib, and yellow fever). During the second phase (2006–2015) support is being expanded to new vaccines (rotavirus and pneumococcal vaccines). In addition, the GAVI Alliance Board has approved for possible future support a further package of vaccines to be offered to countries, including HPV, Japanese encephalitis, rubella, and typhoid.

To meet concerns about financial sustainability, all GAVI-supported countries were required to prepare a comprehensive multi-year plan for immunization, or cMYP. In 2007, the Alliance introduced a new co-financing system, which requires countries to pay a gradually increasing share of the cost of their new vaccines, based on a country's GNI per capita. By the end of 2008, 30 countries had begun using this system to pay for the introduction of the pentavalent vaccine (DTP-Hepatitis B-Hib), rotavirus vaccine, and pneumococcal vaccine.

A new, innovative source of funding is the International Finance Facility for Immunisation (IFFIm), which uses long-term legally binding commitments by donors to issue bonds on the international capital markets. The sale of these bonds provides cash that can be used by the GAVI Alliance to fund programmes. As of early 2008, the bonds had raised US\$ 1.2 billion from investors worldwide.

Another innovative financing mechanism is the Advance Market Commitment (AMC) – a new approach to public health funding designed to accelerate the development and manufacture of vaccines for developing countries. Conceived in 2005 by the Center for Global Development, a pilot AMC for pneumococcal vaccine was launched in 2007 by the Governments of Canada, Italy, Norway, the Russian Federation, and the United Kingdom of Great Britain and Northern Ireland; the Bill & Melinda Gates Foundation; the GAVI Alliance; and the World Bank; with an investment of US\$ 1.5 billion.

The good news is that more investment is being made in immunization and projected trends indicate growing financing in the future. Yet, without further growth, expected future funding from governments and donors will not be enough to sustain the gains already achieved towards GIVS goals and the MDGs. “The real challenge,” the WHO-UNICEF 2008 analysis report concluded, “will hinge on how national governments, and the international community at large manage their roles and responsibilities in reaching and financing the goals of the GIVS until 2015.”

## The view from the future

Chapter 5 looks forward over the next decade and considers how the immunization landscape may have changed by 2020.

By the 2020s, the strategies put in place to reach the MDGs should have brought deaths among children under five years old to an all-time low. Polio should be eradicated, and measles eliminated in all countries. Neonatal and maternal tetanus should no longer be exerting such a heavy toll on babies and mothers, and today's underused vaccines (against Hib disease, hepatitis B, and yellow fever) may have rid the world of the lethal burden of these diseases. The use of new vaccines against pneumococcal, rotavirus, meningococcal, and HPV disease may have inspired a new, more ambitious set of international health and development goals. Vaccines may have been developed that can turn the tide against malaria, tuberculosis, and AIDS.

Over the next decade or so, an increasing number of developing countries will be using the new vaccines coming onto the market. Some of these (such as the HPV vaccine) will be given to adolescents; others (such as the influenza vaccine) will be given to adults. However, there is as yet little knowledge or experience of reaching older age groups in developing countries, except through special immunization campaigns. School-based immunization is one possible solution, especially since school attendance is increasing in many developing countries.

New vaccine delivery systems are also anticipated. Devices that use needles may have been largely replaced with new approaches such as aerosol formulations sprayed in the nose (already available for an influenza vaccine) or lungs (currently being tested for several vaccines); adhesive skin patches; drops under the tongue; and oral pills.

Another potential breakthrough is the development of an increasing number of vaccines that are heat-stable. When supplied with a vaccine vial monitor to check exposure to heat, these vaccines should be available for use outside the cold chain – greatly relieving the pressure on the cold chain and logistics.

By 2020, manufacturers in developing countries may have acquired the capacity to make their own state-of-the-art vaccines tailored to meet their own specific needs. Moreover, their contribution to global vaccine supply may be on a more equal footing with the industrialized countries – a development likely to increase competition.

But the world will face fresh challenges. As of early 2009, countries throughout the world are facing economic recession and financial turmoil, which threaten to unravel hard-won gains. Climate change looms large and is likely to alter the epidemiological landscape in which vaccines and immunization operate – bringing new health challenges.

Despite this, the overall picture is one of cautious optimism, enthusiasm, energy, and dedication. Vaccines can make a major contribution to achieving the MDGs. Vaccine development is in a dynamic phase and more people are being reached with vaccines. New public-private partnerships and product development groups are becoming important drivers of vaccine development and deployment. And over the next two decades, public demand for vaccines and immunization is expected to rise. As it does so – and far into the future – there is every reason to believe that immunization will continue to be a mainstay of public health.

