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• Together with the partners of the Global Alliance for Vaccines and Immunization (GAVI) and its financing arm the Vaccine Fund (VF), WHO provided support to countries to expand the use of new and underused vaccines, and helped 28 countries develop financial sustainability plans to ensure that the progress made is sustained.

• Progress was achieved in the area of immunization safety. By end-2003: 174 Member States (91%) were using vaccines of assured quality; 67 Member States (35%), which account for 62% of the world's children under five, had functioning systems to monitor and manage adverse events following immunization (AEFI); and 91 developing countries (55%), including 78% of African countries, were using autodisable (AD) syringes for routine immunization.

• The "Reach Every District" (RED) strategy was launched in order to improve access to immunization services and strengthen managerial capacity at the district level.

• One of the major achievements of the biennium was the certification of the European Region (EUR) as polio-free. This was the third region to be certified after the Americas Region (AMR) and the Western Pacific Region (WPR). The Global Polio Eradication Initiative published its Strategic Plan for 2004–2008. By end–2003, polio had been eliminated in all but six countries: India, Nigeria, Pakistan, Afghanistan, Egypt and Niger, of which the first three accounted for more than 90% of all cases.

• The number of measles deaths fell in almost all regions with the Eastern Mediterranean Region (EMR) showing a 32% drop, the Africa Region (AFR) 21%, the South-East Asia Region (SEAR) 14% and WPR 10%. The Americas have eliminated indigenous transmission of measles. The countries in EMR, EUR and WPR have established regional measles elimination goals.

• Progress continues to be made towards elimination of maternal and neonatal tetanus (MNT). Of the 57 countries that had not achieved MNT elimination by 2000, five had provisionally done so by the end of the biennium and 32 had developed plans of action.

• The African AIDS Vaccine Programme (AAVP) was established to promote HIV vaccine research and evaluation through capacity-building and regional and international collaboration, and to support the creation of national AIDS vaccine plans.

• Accelerated Development and Introduction Plans (ADIPs) were established by the GAVI/VF partners to help speed up the development and introduction of pneumococcal and rotavirus vaccines.

• The Measles Aerosol Project was launched, aimed at development and licensing of a vaccine and a device for respiratory delivery.
1. INTRODUCTION

The immense scientific achievement of vaccines and immunization – targeting children and women of childbearing age in all countries – represents one of the most successful and cost-effective public health interventions in history. Immunization has eradicated smallpox, substantially reduced morbidity and mortality from diphtheria, pertussis, tetanus and measles, and is on the verge of eradicating polio. Since its inception in 1974, the Expanded Programme on Immunization (EPI) has provided guidance and recommendations to national authorities on how to design, develop, and manage immunization services to efficiently deliver needed vaccinations. Meanwhile, during the 1980s, the global push to achieve Universal Childhood Immunization (UCI) resulted in the establishment of national systems of immunization and rapidly-rising immunization coverage. Global immunization coverage levels increased dramatically during the 1970s and 1980s. In the 1990s, global immunization coverage remained around 70%, but with wide variation both within and between countries and declining coverage in Africa and South-East Asia. (Figure 1)
As a partner in the Global Alliance for Vaccines and Immunization (GAVI) and its financing arm the Vaccine Fund (VF), WHO undertook to increase substantially its

This report, structured according to the three main IVB objectives, highlights the accomplishments of WHO in this field in 2002–2003, at the country, regional and global levels.

support to national immunization programmes. To this end, WHO has worked in close collaboration with the United Nations Children’s Fund (UNICEF) and other agencies such as the US Centers for Disease Control and Prevention (US CDC), non-governmental organizations (NGOs) and academia to expand technical and financial cooperation with countries. In 2003, as a result of efforts to strengthen immunization services, 78% of children under one year of age were immunized by their first birthday (measured by coverage with three doses of diphtheria–tetanus–pertussis [DTP] vaccine). As a result, more than 2 million deaths from vaccine-preventable diseases (VPDs) will be prevented, together with an additional 600,000 hepatitis B-related deaths from liver cirrhosis and hepatoma that would otherwise have occurred in adulthood among the children immunized in 2003. During this period, global efforts to eradicate polio and reduce measles mortality also made great strides.

Figure 2: Score card: global immunization

<table>
<thead>
<tr>
<th>Activity/Goal</th>
<th>Percentage of Countries (# of countries)</th>
<th>&quot;Job to be Done&quot; to achieve Goal (estimated population to reach)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine immunization: (% of developing countries with 80% routine coverage in all districts)</td>
<td>28% (46) / 72% (119 &lt;80%: No data)</td>
<td>At least an additional 9.2 million children &lt;1 year</td>
</tr>
<tr>
<td>Eradication of polio:</td>
<td>59% (113) / 41% (73 non-endemic; 6 endemic)</td>
<td>&gt; 500 million children 0–5 years</td>
</tr>
<tr>
<td>Measles mortality reduction by 50% (1999 levels): (% countries with ≥90% coverage) (% countries with 2nd dose opportunity)</td>
<td>49% (≥90% coverage) (94) / 51% (≥90% coverage/ND) (98)</td>
<td>13 million additional children &lt;1 year with routine</td>
</tr>
<tr>
<td></td>
<td>85% (2nd opportunity) (164) / 85% (no 2nd opportunity) (28)</td>
<td>400 million children with 2nd opportunity</td>
</tr>
<tr>
<td>Elimination of MNT:</td>
<td>70% (135) / 30% (57)</td>
<td>100 million CBA women (to be vaccinated 3x in high risk areas)</td>
</tr>
<tr>
<td>Vitamin A: (% of countries combining delivery of vitamin A with immunization)</td>
<td>56% (76) / 44% (60)</td>
<td>&gt; 500 million children under 5 years at risk of VAD</td>
</tr>
<tr>
<td>Introduction of new vaccines: HepB (% of countries using hep B) (% of countries with hep B)</td>
<td>73% (introduced) (147) / 27% (not introduced) (51)</td>
<td>125 million children &lt;1 year</td>
</tr>
<tr>
<td></td>
<td>56% (≥80% coverage) (83) / 44% (&lt;80% coverage/ND) (64)</td>
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</table>
By end-2003, significant progress had been achieved towards global immunization goals including: routine immunization coverage in districts; measles-mortality reduction; the distribution of vitamin A capsules; and the introduction of vaccines against hepatitis B and *Haemophilus influenzae* type b (Hib) (Figure 2). However, these advances have not occurred in all countries. In sub-Saharan Africa only about 60% of children are immunized during their first year of life. Wars, natural disasters, extreme poverty, discrimination and geographical isolation have meant that one quarter of the world's children are still not protected against common diseases.

In 2003, an estimated 27.5 million infants worldwide and 40 million pregnant women remained in need of immunization. In that same year, it is estimated that over 28 million children (21% of all births) were born in 32 countries where coverage is less than 70%, including 10 million in countries with coverage under 50% (Figure 3). Overall in 2003, only 28% of developing countries reported that all districts had achieved over 80% coverage among infants with the basic three doses of DTP. As a result, each year around 1.5 million children die needlessly from VPDs.

There is a need to not only expand immunization services but also to ensure their sustainability, since every year over 100 million children are born and need to be immunized. In an increasingly globalized world, the global community has a clear interest in the widespread use of current vaccines and the rapid development of new vaccines against emerging diseases.
The WHO strategy directly addressed the three over-arching objectives of the Immunization, Vaccines and Biologicals (IVB) Department: *innovation in vaccine and delivery systems, strengthening of immunization systems and accelerated disease control*. Within these three objectives, specific emphasis was placed on three selected priorities during 2002–2003:
- accelerated vaccine introduction;
- immunization safety;
- polio eradication.

Five IVB functional groups combine their work towards achieving these objectives and addressing priority targets (Figure 4). This report, structured according to the three main IVB objectives, highlights the accomplishments of WHO in this field in 2002–2003, at the country, regional and global levels.

**Figure 4: Strategic and structural features of the WHO Immunization, Vaccines and Biologicals Department**

<table>
<thead>
<tr>
<th>Functional Groups</th>
<th>Innovation (4 targets)</th>
<th>Immunization Systems (3 targets)</th>
<th>Accelerated Disease Control (2 targets)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality Assurance and Safety</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research and Development IVR: The Initiative for Vaccine Research is composed of 3 teams that work on R&amp;D for bacterial, viral and parasitic vaccines</td>
<td>Priority target: accelerated vaccine introduction</td>
<td>Priority target: safety of immunization</td>
<td>Priority target: polio eradication</td>
</tr>
<tr>
<td>Assessment and Monitoring</td>
<td></td>
<td></td>
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<tr>
<td>Access to Technologies</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Expanded Programme on Immunization</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

All Groups contribute to the 9 Strategic Plan Targets.

In November 2002, UNICEF, WHO and the World Bank issued *State of the World's Vaccines and Immunization* – a joint report which focused on the increasing divide between the rich and poor in:
- the provision of immunization services,
- access to new vaccines, and
- research and development (R&D).

A multi-city launch of the report took place in Bangkok, Cairo, Dakar, Geneva, London and Paris and attracted extensive press coverage. Readers are encouraged to consult this document for further information and analysis on global aspects of immunization.
Key events 2002–2003

Governing and Advisory Bodies

• Executive Board and World Health Assembly (WHA) 2003 passed resolutions on reducing global measles mortality; a strategy for child and adolescent health development; and SARS.
• WHA Technical Briefing on ensuring the safety and efficacy of medicines, vaccines and products of human origin, with an emphasis on the strengthening of national regulatory authorities (NRAs).
• The Technical Consultative Group on the Global Eradication of Poliomyelitis met twice during the biennium.
• Two meetings of the Expert Committee on Biological Standardization.
• Two meetings of the WHO Strategic Group of Experts (SAGE) provided guidance to WHO in the field of immunization and vaccines, with a high level of implementation of recommendations.

Innovation and research

• Updated guidance on safety of vaccines from human or animal transmissible spongiform encephalopathies.
• New guidelines issued for the biosafety of inactivated polio vaccine (IPV) manufacture from wild poliovirus.
• Review of cell-substrate safety issues associated with primary cells for vaccine manufacture to ensure that vaccines are safe.
• Establishment of the pneumococcal and rotavirus ADIPs by GAVI (the WHO Initiative for Vaccine Research [IVR] acted as the secretariat for the GAVI R&D Task Force) and memorandum of understanding with IVR.
• Establishment of a new partnership (supported by the Bill & Melinda Gates Foundation) to develop an aerosol measles vaccine.
• Launch of the African AIDS Vaccine Programme (AAVP), supported and funded by several partners.

Immunization systems

• Reaching Every District (RED) strategy launched in July 2002.
• Hepatitis B vaccine included in most national immunization schedules, no longer a “new vaccine”.
• 102 developing countries (62%) using autodisable syringes for routine immunization.
• The Global Training Network expanded to encompass cold chain and logistics. Greatly increased awareness about issues on vaccine quality and freezing of vaccines whose formulation does not permit freezing; use of vaccine vial monitors (VVMs) to detect heat exposure; and adverse events following immunization (AEFIs).
• In 1998–2003, the number of vaccines produced in low-income and economic-transition countries increased from 21 to 33.
• 50 assessments were carried out with the national regulatory authorities on vaccine quality of vaccines either produced nationally or imported.
• 30 out of 48 vaccine-producing countries – but only 16 out of 144 non-vaccine-producing countries – have a functioning NRA.
• Worldwide, 91% of countries and 77% of infants benefit from vaccines of assured quality.

Accelerated disease control

• For reasons of both epidemiology and financial constraint, there was a tactical shift in polio eradication activities in 2003: supplementary immunization activities were focused exclusively on the remaining seven endemic and six highest-risk countries.
• By end-2003, indigenous polio was reported in only six countries – the lowest number ever.
• Polio resolutions emerged from the meetings of the G8 countries in Kananaskis, Canada (2002) and Evian, France (2003), and a Decision on Polio Eradication was issued by African Union (AU) Heads of State at a Summit Meeting in Maputo, Mozambique (2003).
• In its second major fund-raising drive among its membership, Rotary International raised over US$125 million for accelerated polio eradication efforts worldwide.
• Measles Partnership: comprehensive strategy developed (combining routine vaccination, periodic campaigns and surveillance).
• Meningitis and yellow fever: two deadly epidemics hit Africa.
• Yellow fever and meningitis surveillance carried out, building on polio surveillance.
• Hib and invasive pneumococcal disease surveillance carried out, building on the meningitis surveillance network.
• Burden of disease and cost-effectiveness analyses of vaccine introduction carried out (for Hib in Asia and yellow fever preventive campaigns in Africa).
2. **Innovation in Vaccine Introduction and Delivery Systems**

Figure 5. Accelerated vaccine introduction: hepatitis B, 2003

- **HepB3 ≥ 80%** (83 countries or 43%)
- **HepB3 < 80%** (19 countries or 20%)
- **HepB vaccine introduced but no coverage data reported** (25 countries or 13%)
- **HepB vaccine not introduced** (45 countries or 24%)
  (In 5 countries HepB administered for adolescence)

Source: WHO/PV database, 2004. 192 WHO Member States
Date: October 2004
Through the support of GAVI/VF, there have been large strides in making new vaccines available in low-income countries. These advances are revolutionizing the way vaccines are conceptualized, manufactured, presented and administered.

Introducing new vaccines
In recent years, there has been a marked increase in the number of countries including hepatitis B, Hib and yellow fever vaccines in their routine infant vaccination schedules (Figures 5 and 6). However, much more remains to be done in order to make them available for all children in all countries where they are indicated – both through expanding introduction to the remaining countries and strengthening immunization systems so that countries can improve access to services. By the end of 2003, 134 of 165 (81%) developing countries and economies in transition had successfully introduced hepatitis B vaccine into their national immunization schedules and 63 (38%) had introduced Hib vaccine. In low-income countries, these new vaccine introductions were greatly facilitated by support from GAVI/VF. Critical issues which emerged during this biennium included how the introduction of new vaccines could help immunization systems reach more people and command community, country

WHO and its partners, according to their respective mandates, continued to fulfil their roles in supporting countries to regulate and assure the quality and availability of new products through the strengthening of regulatory and delivery systems.

and partner commitment to ensure the long-term financial sustainability of these products. Partner coordinating bodies in countries, such as the Interagency Coordinating Committees (ICCs), supported governments in their efforts to harmonize and maximize the use of national and international contributions to immunization, while ensuring the long-term operational and financial sustainability of immunization services after the introduction of new products.

Figure 6. Accelerated vaccine introduction: Haemophilus influenzae type b, 2003

<table>
<thead>
<tr>
<th>Year</th>
<th>Vaccines Introduced</th>
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</thead>
<tbody>
<tr>
<td>1997</td>
<td>26 countries</td>
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<tr>
<td></td>
<td>Hib vaccine</td>
</tr>
<tr>
<td></td>
<td>introduced but no</td>
</tr>
<tr>
<td></td>
<td>coverage data</td>
</tr>
<tr>
<td></td>
<td>reported (26 countries)</td>
</tr>
<tr>
<td></td>
<td>Hib vaccine not</td>
</tr>
<tr>
<td></td>
<td>introduced</td>
</tr>
<tr>
<td></td>
<td>(166 countries)</td>
</tr>
<tr>
<td>2003</td>
<td>89 countries</td>
</tr>
<tr>
<td></td>
<td>Hib3 ≥ 80%</td>
</tr>
<tr>
<td></td>
<td>(57 countries 30%)</td>
</tr>
<tr>
<td></td>
<td>Hib3 &lt; 80%</td>
</tr>
<tr>
<td></td>
<td>(10 countries 5%)</td>
</tr>
<tr>
<td></td>
<td>Hib vaccine</td>
</tr>
<tr>
<td></td>
<td>introduced but no</td>
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<tr>
<td></td>
<td>coverage data</td>
</tr>
<tr>
<td></td>
<td>reported (22 countries 11%)</td>
</tr>
<tr>
<td></td>
<td>Hib vaccine</td>
</tr>
<tr>
<td></td>
<td>not introduced</td>
</tr>
<tr>
<td></td>
<td>(103 countries 54%)</td>
</tr>
</tbody>
</table>

* In 2 countries partial introduction

Research and development: Initiative for Vaccine Research (IVR)
The Initiative for Vaccine Research (IVR) was launched in 2001 with a mandate to provide a centralized source of leadership, vision, priority-setting and coordination of global vaccine R&D programmes. IVR is WHO's key body responsible for drawing together the necessary expertise and efforts to address both global priorities and identified gaps in vaccine research. It benefits from the wide expertise of IVB in the domain of vaccine introduction, as well as from knowledge acquired by WHO in the area of parasitic and HIV vaccine development, ethics, clinical trials and capacity-building. IVR activities are linked with those of the UNDP/WHO/World Bank Special Programme for Research and Training in Tropical Diseases (TDR). Meanwhile, the UNAIDS/WHO HIV Vaccine Initiative (HVI) is an important component of IVR.

During this biennium, IVR continued to consolidate WHO's various vaccine R&D programmes into an integrated effort. While vaccines such as Hib, yellow fever, Japanese B encephalitis and rubella were readily available but underused, new vaccines such as rotavirus, pneumococcal, meningococcal, and human papilloma virus (HPV) vaccines were in advanced stages of testing. In addition, new vaccines were being developed against major infectious pathogens such as malaria, HIV/AIDS and tuberculosis, as well as against some of the "orphan" infectious diseases including leishmaniasis and hookworm infestation.

In addition, various new immunization-linked methods and products were being investigated to enhance the ease, safety and efficacy of immunization delivery. It is anticipated that several of these – for example, new formulation methods to increase vaccine stability, devices for the non-parenteral administration of vaccines, and rapid biomedical tests to monitor and evaluate the impact of immunization – will be helpful in accomplishing immunization goals. Once tested, these new methods and devices will need to be marketed at an affordable price if they are to be used widely in low-income countries.

Highlights of IVR progress
By end-2003, highlights of progress achieved by IVR include:

- **Pneumococcal and rotavirus vaccines**: WHO participated in the development of the GAVI Accelerated Development and Introduction Plans (ADIPs) for rotavirus and pneumococcal vaccines that were approved in June 2002. The rotavirus ADIP was established at the Program for Appropriate Technology for Health (PATH) in Seattle, and the pneumococcal ADIP at John Hopkins University, Baltimore. Each of the ADIPs will receive US$30 million from GAVI/VF over three years. WHO has established memoranda of understanding with both ADIPs and is a strategic partner in these efforts.

- **Meningitis Vaccine Project (MVP)**: The project was formed in 2001 as a partnership between WHO and PATH. The ambitious 10-year programme aims to prevent the meningitis epidemics which currently plague sub-Saharan Africa. The Bill & Melinda Gates Foundation awarded the partnership US$ 70 million over a 10-year period to develop and produce a conjugate meningitis vaccine tailored for children and adults in Africa. To produce the vaccine, MVP secured agreements with two commercial partners to provide the vaccine components and manufacture the complete vaccine.

- **Vaccines against HPV infection and cervical cancer**: Two study results of a candidate vaccine showed very high levels of efficacy in protecting vaccinated women against HPV infections. Large Phase III efficacy trials are now starting in several Latin American and Asian countries in areas with high disease burden. In parallel, WHO international collaborative studies were launched to establish HPV reference reagents for harmonization of global HPV diagnostic procedures.
• **HIV/AIDS:** More than 30 candidate HIV vaccines were developed and tested in multiple Phase I/II clinical trials in both developed and developing countries. Two Phase III efficacy trials with one HIV vaccine concept (VaxGen rgp120 candidate vaccine) were completed by the end of 2003 in Thailand and the USA with no significant efficacy results. A third Phase III trial to evaluate a "prime-boost" vaccine concept using a combination of ALVAC (canarypox vector) and rgp120 (VaxGen) was initiated in 2003.

WHO provided continuous technical and scientific advice to developing countries with regard to review and approval of clinical-trial protocols to be implemented in developing countries. Two protocols for Phase III trials in Thailand were reviewed and technical recommendations provided to the Ministry of Health of Thailand by the UNAIDS/WHO HIV Vaccine Advisory Committee. WHO also provided continuous support to strengthen vaccine-trial capacity in developing countries, with a special focus on Africa through the development and implementation of the National AIDS Vaccine Plans/Strategies and the African AIDS Vaccine Programme.

A major obstacle in HIV vaccine research is the lack of multiple vaccine-trial sites in developing countries for the conduct of Phase III efficacy trials. The HIV vaccine trials need to be conducted with the best known vaccine candidates at the most appropriate vaccine-trial sites, in line with the highest scientific and ethical standards.

For the first time, the superiority of some of the new TB vaccine candidates over the traditional BCG vaccine has been demonstrated.

• **Tuberculosis (TB):** A network was established for the evaluation of TB candidate vaccines in non-human primates that more closely reflect human immunity against TB than the currently-used mouse and guinea pig standard challenge models. Long-term experiments in non-human primates have, for the first time, demonstrated the superiority of some of the new TB vaccine candidates over the traditional BCG vaccine.

• **Measles:** The measles vaccine aerosol project is being supported jointly by a partnership involving the American Red Cross, the Bill & Melinda Gates Foundation, the US CDC and WHO. The Bill & Melinda Gates Foundation provided funding to WHO to ensure the implementation of all activities needed for the development and licensure of this new formulation of measles vaccine. Since the inception of the project, preliminary bench studies have been completed that assess different delivery devices, as well as immunogenicity and safety studies in monkeys.

• **Malaria:** WHO has sponsored a Phase I clinical trial of a new candidate vaccine in Shanghai, China. This trial started in June 2003 and will test the immunogenicity of a candidate vaccine developed under WHO/TDR funding by a Chinese investigator. WHO is also engaged in research that will lead to establishment of norms and standards for evaluation of candidate vaccines.

**Setting norms and standards for new products**

WHO biological standardization activities have contributed to global public health through written guidance on production and quality control issues. This guidance defines international technical specifications for the quality and safety of biological medicines.

**Recommendations for the production and quality control of influenza vaccines were revised ... and new guidelines drawn up to meet the challenge of developing and administering suitable influenza vaccines against new strains of the virus with pandemic potential.**

New guidelines were established on the safe manufacture and quality control of inactivated poliovirus vaccines manufactured from wild-type poliovirus starting materials. These specify steps to minimize the risk of reintroducing wild poliovirus into the community from a vaccine manufacturing facility.
Recommendations for the production and quality control of influenza vaccines were revised in response to significant developments since the last revision of WHO requirements. Since subunit and split vaccines were being widely used, the effective dose of haemagglutinin was established. In addition, recommendations for vaccines containing adjuvants were developed and approved. Meanwhile, new guidelines were drawn up to meet the challenge of developing and administering suitable influenza vaccines against new strains of the virus with pandemic potential. The new recommendations are designed to facilitate the production of vaccines against pandemic strains by establishing specifications for the use of cell cultures for influenza vaccines, and also for the use of reverse genetics to derive suitable prototype strains for vaccine production.

New guidelines were also issued for the production and quality control of pneumococcal conjugate vaccines. The guidelines include a summary of experience gained in identification of reference levels of antibodies that supported the successful licensure of a single product in a number of countries and will guide the review of clinical-trial data from other countries and with other products.

Work was also carried out in a number of high-profile areas, including the alleged toxicity of preservatives used in vaccines, the restarting of smallpox vaccine production in response to fears of bioterrorism, and safety issues relating to the production of certain vaccines and other biological products:

- **Thiomersal**: A new guidance document was issued which sets out the general principles of evaluating a vaccine following the elimination, reduction, removal or replacement of thiomersal from an already-licensed vaccine. Making changes to licensed thiomersal-containing vaccines is a complex issue that requires careful consideration. The elimination or reduction of the preservative from an existing product may have some unexpected effects on vaccine quality, safety or efficacy, including effects on vaccine stability. A product with altered thiomersal content may, in some cases, be considered as a new vaccine requiring further clinical trials.

- **Smallpox vaccines**: The *WHO Recommendations for Production and Control of Smallpox Vaccines* were completely revised. Since there are few remaining global stocks of this vaccine, production would need to be restarted to meet the kind of major demand on vaccine supply that might follow an intentional release of smallpox virus, for example. The revised recommendations provide state-of-the-art guidance for new vaccine manufacture and for the testing for each type of substrate.

- **Human and animal transmissible spongiform encephalopathies**: A WHO consultation on biological and pharmaceutical production issues related to transmissible spongiform encephalopathies was held in Geneva in February 2003. The resulting guidelines included a new categorization of tissues from humans, cattle, sheep and goats used in biological medicines into high risk, lower risk and no detectable risk. It also covered risk analysis procedures for vaccines and other biological products.
In many countries, continued efforts are needed to strengthen immunization systems. Many countries have not yet established national and district level immunization workplans; district level management is often weak or overburdened, and in some cases disoriented by an ongoing national decentralization process. Poor management in some countries is evidenced by high dropout rates and missed opportunities for immunization. However, some valuable lessons have been learned that can be applied to strengthen immunization services. Experience from disease control activities for polio, measles, neonatal tetanus, yellow fever and epidemic meningitis demonstrates that when appropriate policies, programmes and resources are in place, children and women can be reached with immunization even in the most difficult and remote areas.

In many countries, immunization forms an integral component and often acts as the backbone of maternal and child health services. It figures prominently among the health interventions that are the most frequently and regularly accessed by communities. In order to capitalize on this and maximize the use of available human, logistic and financial resources, interest has grown in linking immunization to other specific health interventions. Immunization contacts, whether at fixed health centres or less commonly in places distant from these facilities, represent an opportunity for communities to access additional preventive and curative information, as well as goods and services in support of child health, primary care and reproductive health. Vitamin A, for example, has been successfully distributed through supplementary and routine polio or measles immunization activities.

**Reaching Every District (RED)**

In 2002, the economic plight of many developing countries was severe. Poor infrastructure and lack of capacity at the district level hampered implementation of accelerated disease control activities, as well as the expansion of routine immunization coverage in low-performing countries and districts. The infrastructure, so vital for maintaining the day-to-day running of health services, was in many instances crumbling or run by dedicated individuals with a minimum of equipment, often without being paid for months at a time. In addition, the political climate in areas of conflict has made it hard for even the most committed government to maintain the pressure they would have liked in the area of child immunization.

In response to the 2002 United Nations (UN) General Assembly Special Session on Children goal of achieving 80% DTP3 coverage in every district by 2010, the Children's Vaccine Program (CVP) at PATH, UNICEF, the United States Agency for International Development (USAID), US CDC, WHO, and other partners identified five operational components that contribute to strengthening immunization services at the district level: re-establishment of outreach services, supportive supervision, community links with service delivery, monitoring and use of data for action, and planning and management of resources. In January 2003, IVB and partners began implementing a global policy to reach every district (RED) with routine immunization services. National RED workshops, in collaboration with partners, were launched in Afghanistan, Cambodia, Ethiopia, Pakistan, and Sudan, and an intercountry workshop was held for Afghanistan, Djibouti, Pakistan, Somalia, Sudan and Yemen. Each workshop focused on obtaining national commitment to...
reaching 80% coverage in every district, training national and international staff on methods for strengthening routine services, developing better quality district microplans, using experience gained in polio eradication, and maximizing the use of national funds for district activities aimed at increasing coverage.

In AFR, special efforts were made in 2002 and 2003 to implement the RED strategy in the “Big Four” African countries – Angola, DR Congo, Ethiopia and Nigeria – which account for 40% of the African population and 70% of the unimmunized in Africa. By end-2003, in 30 of the 43 countries in this Region an increased proportion of districts had achieved 80% routine immunization coverage.

Immunization safety
WHO continued to provide global leadership on immunization safety in 2002–2003 through the Priority Project on Immunization Safety, which aims to establish a comprehensive system to ensure the safety of all immunizations administered through national immunization programmes. Injection safety assessments were carried out in 19 countries in 2002 and 18 countries in 2003. The use of safe injection equipment such as autodisable (AD) syringes and safety boxes continued to increase. By end-2003, 102 (62%) developing countries, including 76% of countries in the African Region, were using AD syringes on a routine basis. This significant achievement is partly due to the financing of safe injection equipment/funds for injection safety by GAVI/VF and the transfer of AD syringe technology to a number of countries. Increasingly, countries included injection safety in their national workplans (Figure 7).

Efforts to improve facilities for the management of immunization-related waste also made considerable progress. Guidelines were disseminated widely in order to inform countries of the different waste disposal options available. A number of countries strengthened their understanding and capacity in this area as a result of mass immunization campaigns. Cooperation was extended to India and Viet Nam in preparing plans for safely collecting and destroying or recycling used syringes. In early 2002, the “Focus” Project was established in order test the range of WHO immunization safety tools and expertise in two countries, Burkina Faso and the Syrian Arab Republic. A number of activities were held during 2002, including capacity-building for the development of information, education and communication (IEC) materials and the training of trainers.

The Global Advisory Committee on Vaccine Safety (GACVS) provided valuable technical support throughout the biennium on issues relating to vaccine safety. The committee, which meets twice a year, has a mandate to respond promptly, efficiently and with scientific rigour to vaccine safety issues of potential global importance. Issues discussed at meetings held in 2002–2003 included: the safety of thiomersal-containing vaccines; hepatitis B vaccine and leukaemia; hepatitis B vaccine and multiple sclerosis; Bell’s palsy following intranasal vaccination; mumps-measles-rubella (MMR) vaccine and autism; and the safety of smallpox vaccines. The outcome of these meetings was published in the WHO Weekly Epidemiological Record.

Improvement of country systems for monitoring and managing AEFIs followed recommendations that emerged from the assessments of NRAs. By end-2003, 67 (35%) Member States had functioning AEFI monitoring and management systems, which covered 62% of the global population under five years of age.

A network of partner websites, the Vaccine Safety Net Project, has been created to improve global dissemination of information on vaccine safety ...

A WHO website on immunization safety (www.who.int/immunization_safety/en/) and another on the GACVS (www.who.int/vaccine_safety/en/) were launched. The Vaccine Safety Net Project, a network of partner websites, was also created to improve global dissemination via the Internet of information on vaccine safety that adheres to good information practices. At the end of the biennium there was continuing concern about the need to sustain and improve political commitment to injection safety, as well as uncertainty about the capacity of countries to sustain injection safety supplies once the GAVI/VF support ends.
Figure 7. Countries including injection safety as a component of national workplans, 2003

- Yes (123 countries 64%)
- No (23 countries 12%)
- No data or not applicable (46 countries 24%)

192 WHO Member States
Date: October 2004
3. STRENGTHENING IMMUNIZATION SYSTEMS

Training
IVB training experts and partners developed and revised simple, practical training materials for health workers (Immunization in Practice) and mid-level managers (Global MLM modules). These training materials, based on appropriate adult-learning techniques, were tailored to the skills required at each level. Immunization in Practice (issued in September 2003) contains eight modules targeting district and health facility staff. It includes materials adapted from the polio eradication programme on planning, monitoring and use of data to improve immunization services. It is currently available in English, and translations are planned in French, Russian and Spanish.

Training materials have been developed, revised and adapted and a training partnership website has been established.

Also under development was a set of eight modules for national and sub-national level staff aimed at improving their technical skills in management, planning, monitoring, and evaluation. The emphasis here is on problem solving and creating efficiencies by combining the activities included in individual accelerated disease control plans.

A set of 13 modules was also developed by WHO’s Africa Regional Office, addressing key issues in the Region. The modules were field tested and used in several intercountry and national training courses. The set of modules is available in English, French and Portuguese. Financial support for this project was provided by the United Nations Foundation (UNF).

An immunization training partnership was launched in 2002, which brings together partners from the public and private sectors and provides a forum for information sharing and collaboration on training activities. The second meeting of the training partnership was held in April 2003. The training partnership also has a website (www.who.int/vaccines-diseases/epitraining) where partners can post training events and materials for review. These activities have resulted in greater information exchange about training opportunities available to national staff and have stimulated the exchange of training curricula and materials among partners.

Production and supply of quality-assured vaccines
Efforts to sustain and expand immunization services depend on the sustainable and reliable supply of affordable vaccines of assured quality. Grouped procurement operated by UNICEF and the Pan American Health Organization (PAHO) enables national immunization programmes in developing countries to obtain vaccines of assured quality at reduced prices. To support this, WHO operates a vaccine prequalification scheme which assesses the quality, safety, immunogenicity and efficacy of all vaccines procured by UN agencies, including newer vaccines.

During the biennium, 22 new requests for evaluations were received by WHO from manufacturers and 11 were completed. These assessments included newer vaccines such as Hib, two combined vaccines (DTP–Hib) and one recombinant hepatitis B vaccine. In addition, 47 vaccines already listed by WHO were reassessed for continued acceptability for purchase by UN agencies. To monitor compliance with UN tender specifications, a total of 168 lots of vaccines that had been shipped to countries through UN agencies were subject to independent testing by two reference laboratories. The rapidly increasing demand for the prequalification of vaccines has been difficult to meet due to the shortage of WHO staff specialized in this field and the scarcity and limited availability of outside experts.

Essentials to the success of maintaining global supplies include accurate forecasts, financial planning and adequate stock management and distribution systems.

Although temporary shortages in global supply do occur, resulting in national stockouts, overall the outlook for the vaccine supply market was more positive
than it had been over the previous five years. The components that proved to be essential to success include accurate forecasts, financial planning and adequate stock management and distribution systems. A continuing concern was the divergence of the vaccine markets, which has occurred mainly due to factors such as cost, differences in disease burden and concerns about potential side-effects. As a result, developing countries today increasingly provide different vaccine antigens or different vaccine formulations to their populations than those used in industrialized countries. To help bridge this growing gap, there was a promising trend towards increased vaccine production in low-income and economic-transition countries where the number of manufactured vaccines prequalified by WHO grew from 21 to 33 in 1998–2003.

WHO's role in vaccine production and supply focused on efforts to improve vaccine demand forecasting, national regulatory mechanisms and the prequalification of vaccines. WHO also established a database on vaccine production capacities worldwide in order to predict, prevent or correct vaccine shortages. The database – containing updated information on 36 types of vaccines from 98 manufacturers worldwide – has enabled WHO to target and prioritize its efforts when shortages occurred of DTP, meningococcal, polio and yellow fever vaccines. In addition, WHO conducted a study on vaccines containing different types and amounts of preservatives (thiomersal or alternative preservatives) to determine whether they were suitable for use in accordance with the WHO multidose vial policy.

Strengthening national capacity to oversee the quality of vaccines produced locally or procured

In every country, the NRA should exercise regulatory oversight over the production and control of vaccines, according to six critical functions defined by WHO: licensing; surveillance of AEFIs; lot release; laboratory access; Good Manufacturing Practices (GMP) inspections; and clinical evaluation of vaccine safety and efficacy. A survey conducted in the early 2000s found that 30 out of 48 vaccine-producing countries but only 16 out of 144 non-vaccine-producing countries had a functioning NRA. WHO performs periodic assessments of NRAs to determine their capacity to fulfil the required functions and, where necessary, suggest ways to improve their performance. Such NRA assessments were conducted in China, Cuba, Egypt, France, India, Islamic Republic of Iran, Japan, Pakistan, the Philippines, Thailand and Viet Nam. WHO embarked on several activities to upgrade NRAs through training and other forms of capacity building.

An initial meeting for the establishment of a Network of National Regulatory Authorities brought together eight of the strongest NRAs in low-income and middle-income countries (Brazil, China, Cuba, India, Indonesia, Republic of Korea, Russia and South Africa) with the aim of fostering mutual recognition and cooperation. A collaboration with the European Medicines Agency (EMEA) led to the development of a procedure which enables EMEA to issue, at the request of WHO, a Scientific Opinion on vaccines which are produced anywhere in the world but are for use only in developing countries. This procedure will facilitate considerably the WHO prequalification scheme.

NRAs are responsible for the inspection and enforcement of GMP in vaccine production facilities in their country. Several workshops were conducted in China and India to train GMP inspectors and strengthen local manufacturers. National capacity-building activities also included the establishment of three training centres in Russia, Sri Lanka and Tunisia where courses were conducted on the monitoring of AEFIs. Other courses were conducted on a range of activities including: GMP, regulation of vaccines, laboratory quality systems, and quality control methodologies. A new training curriculum on clinical evaluation was developed, tested and implemented. The Global Training Network (GTN) held 18 training courses and organized the placement in host institutions of 208 trainees from NRAs, national control laboratories and surveillance systems in 50 countries.
In 2002–2003, WHO conducted 10 new NRA assessments and 25 NRA reassessments, as well as follow-up visits in relation to specific regulatory functions. While all NRA assessments aimed to assess strengths and weaknesses and support institutional development, 15 of these were also critical to enable access to the vaccine prequalification scheme (since the functioning of the NRA is a prerequisite for initiation of the prequalification process). By the end of 2003, much progress had been achieved towards the strengthening of NRAs worldwide, but there were continuing gaps in the capacity of developing countries to fulfil all six critical regulatory functions. In some countries, lack of political commitment for the establishment of functional and independent regulatory authorities remained an obstacle to progress.

Immunization financing

Immunization is currently a relatively inexpensive and highly cost-effective health intervention. Although immunization financing should be primarily a national public responsibility, many low-income countries have relied heavily on international assistance for this. As a result, financing can be volatile and vulnerable to shifts in donor priorities. The most prominent feature of international cooperation on immunization over the past few years has been the coordinated effort to enable low-income countries to introduce more expensive vaccines such as hepatitis B and Hib. The expansion of vaccination schedules to include such vaccines has greatly increased the level of resources that need to be mobilized. While some relief may be obtained over time from the fact that the procurement of increasing volumes of vaccine and greater competition among manufacturers may help bring prices down, past experience has shown that it takes several years before increased demand for new vaccines is matched by lower prices.

WHO made efforts to ensure that external financial support to countries is provided in ways that strengthen national ability to gradually assume financial responsibility for immunization.
While co-financing strategies were developed to reduce the financial barriers to the introduction of new and existing vaccines and technologies, efforts were made to ensure that external financial support to countries is provided in ways that strengthen national ability to gradually assume financial responsibility for immunization. WHO coordinated the technical assistance to mainly GAVI/VF-supported countries for the development and implementation of Financial Sustainability Plans (FSPs), which are intended to help countries determine the overall cost of their immunization programmes, the sources of funds, the gaps that remain to be filled and the impact that a new vaccine introduction will have. To support these efforts, WHO developed a number of tools, including a Financial Sustainability Diagnostic Tool, Financial Sustainability Plan Guidelines and a Costing and Financing Tool; the latter two were translated into French, Portuguese, and Russian. Regional workshops were held in Cameroon, Russia and Uganda in 2003 to support 22 countries in developing their FSPs. In addition, an Immunization Financing Database website was created (www.who.int/immunization_financing/en/) containing data and analysis from all FSPs. While the development of an FSP was an important first step, countries also need guidance on how to integrate these plans into their multi-year plans for immunization, how to update them on a regular basis, and how they can mobilize the resources needed to fill the gaps.

**Vaccine management**

WHO and UNICEF have continued to collaborate closely on the development of strategies and tools to ensure that vaccines are adequately managed at all levels of the immunization programme. Efforts have been focused on the development of a new WHO–UNICEF initiative to encourage countries to procure and maintain equipment and to adopt management and training practices that fully protect vaccines in primary and intermediate vaccine stores. The WHO–UNICEF Effective Vaccine Store Management (EVSM) initiative provides countries with self-assessment tools, guidelines and model standards, focused specifically on vaccine storage and distribution. Countries use these tools and documents to assess weaknesses in equipment and operating procedures and to make the improvements necessary to meet the 10 global criteria set out in this initiative. To date, 29 assessments have been conducted in all regions except the Americas. The Sultanate of Oman (October 2002–September 2003) was the first country to be awarded a certificate in recognition of its achievement in meeting the global WHO–UNICEF EVSM standards (Figure 8).

![Sultanate of Oman’s winning EVSM score](image-url)
In the face of pressures such as the need for multi-skilled health staff, high staff turnover rates, and the introduction of new vaccines and technologies, the need for training in better vaccine management practices has become a priority. In response, a Vaccine Management (VM) cluster was created in 2002 under the GTN. Its aim is to improve vaccine management practices at country level through a series of training courses (offered by selected vaccine management training centres) and defined follow-up procedures. In 2003, GTN/VM established two WHO-accredited training centres (Department of Communicable Diseases Surveillance Control in Sultanate of Oman and the Collaborative Centre for Cold Chain Management in South Africa). In 2003, GTN/VM conducted three different types of courses: a vaccine store-management training course targeting vaccine store and cold chain managers; a vaccine management training course targeting national immunization programme managers; and a training skills course targeting GTN/VM training centres. These training courses, based on adult learning techniques and focusing on competency-based skills introduced new approaches to training.

A global meeting to review progress in the implementation of vaccine vial monitors (VVMs) brought together national immunization programme managers, technical agencies and representatives of public and private vaccine manufacturers, determined that VVMs should be applied to all vaccines.

The listing of tested equipment in the Product Information Sheets has been replaced by a newly developed prequalification scheme for immunization technologies.

A newly developed Performance, Quality and Safety (PQS) system, a prequalification scheme for immunization technologies which replaces the 15-year old Product Information Sheet system, aims to make available specifications and independent performance assessment results for equipment and devices used in immunization programmes. The new approach will be based on three key criteria: performance, quality and safety. All examples of a selected product must have performance characteristics that meet the relevant specification standards; quality and reliability characteristics that are appropriate for field conditions; and safety characteristics that ensure that no harm is caused to users, patients, or to the environment over the course of the product's life cycle. It is planned that the system will be functional by the end of 2005. Among the key issues that will need to be addressed are uncertainties about continued financing for the provision and renewal of equipment, and the need to develop new strategies to prevent damage to vaccines through freezing.

Measuring and monitoring progress
Over the past decade, considerable progress has been made in establishing monitoring and surveillance systems capable of determining immunization coverage and trends and the impact of vaccination on VPDs, as well as guiding public policy, strategies and programme action. Building on an extensive and growing laboratory network, polio and measles surveillance has not only generated critical information to guide the respective eradication and mortality reduction initiatives, but has also supported the early detection of and response to other diseases...

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In addition, improvements in surveillance for all VPDs, coupled with laboratory diagnosis where appropriate, provided crucial information to guide programmes and determine the burden of disease in order to monitor national and global mortality and morbidity attributable to each VPD.
• **Strengthening routine monitoring systems:** An analysis was undertaken of countries’ reporting and monitoring systems. The main problems identified included weaknesses in areas such as: charting coverage, data use, vaccine and supply stock log, recording practices, AEFI surveillance implementation, and poor computer back-up procedures. Major efforts are under way to support the use of local data for time management and planning. A set of 12 national core indicators was selected to provide a comparable and representative profile of immunization systems.

• **Burden of disease:** The global burden of VPDs (by country, region, age and gender) has been modelled for hepatitis B, measles, pertussis, and for neonatal, non-neonatal and maternal tetanus. Current efforts are focused on modelling the burden of yellow fever and rotavirus diarrhoea as well as Hib and streptococcal pneumonia. By 2003, the Hib disease-burden rapid assessment tool had been used in a number of countries including Egypt, Ghana, Iran, Jordan, Malaysia, Sultanate of Oman, the Pacific Islands, Tunisia, Uganda and Yemen.

Two new guideline publications were released: one for estimating costs of introducing new vaccines and the other for estimating the potential cost effectiveness of Hib vaccine.

• **Cost-effectiveness analysis:** In 2002, work was continued on the costs and financing database. Two types of guidelines were published: guidelines for estimating the costs of introducing new vaccines into the national immunization system, and guidelines for estimating the potential cost-effectiveness of Hib vaccine. Work began in early 2003 on the preparation of guidelines for estimating the potential treatment costs averted through the introduction of rotavirus vaccine. Cost-effectiveness and cost-utility studies carried out in 2002 and the first half of 2003 are nearing completion for Hib (Albania, Russia), streptococcal pneumonia (South Africa), rotavirus (South Africa), neonatal tetanus (Pakistan), measles (Burkina Faso), hepatitis B (Mozambique) and yellow fever (Nigeria), in addition to a cost analysis of post-certification polio vaccination in low-income countries.

Laboratory network (polio, measles, rubella)

In 2003, the polio laboratory network detected wild polioviruses in 15 countries. However, the genetic characteristics of these viruses revealed that endemic viruses circulated in only six countries (Afghanistan, Egypt, India, Niger, Nigeria and Pakistan). The viruses in the remaining nine countries were imported from Nigeria and Pakistan. No outbreaks associated with vaccine-derived polioviruses (VDPVs) were detected by the laboratory network in 2003, although VDPVs were isolated in a few cases.

As of end-2003, 671 labs in 148 countries were receiving samples from suspected measles cases and most were testing and reporting using standardized methods (Figure 9).

A quality assurance and proficiency testing programme has been established by WHO and more than 97% of 106 national laboratories tested passed a measles proficiency test. WHO coordinates a network of 145 laboratories that support the Polio Eradication Initiative, of which 96% were accredited by WHO in 2003.

IVB coordinates a programme of work to minimize the risks of re-introduction of polioviruses into communities through potential release from laboratories.

IVB coordinates a programme of work to minimize the risks of re-introduction of polioviruses into communities through potential release from laboratories. During the pre-eradication era all countries are requested to conduct a national survey of biomedical laboratories and prepare an inventory of those holding stocks of wild polioviruses or materials potentially infected with such viruses. During the biennium, such surveys were initiated in 153 countries. As of end-2003, surveys had been completed in 103 countries, with 196 482 laboratories surveyed and 757 (0.4%) of these identified as having wild poliovirus or potentially infected materials.
3. STRENGTHENING IMMUNIZATION SYSTEMS

Figure 9. Global Measles and Rubella Laboratory Network, 2003

The designation employed and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the secretariat 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.

Date as of Dec 2003
**Trends in immunization coverage:** WHO and UNICEF conducted a retrospective review of data available on national immunization coverage for the years 1980–2001 to determine the best estimates of immunization coverage. The outcome of this review was published by WHO and UNICEF.

Accurate monitoring of immunization coverage is necessary to measure success in delivering vaccines and to determine the causes of the continuing incidence of a VPD. However, there is ample evidence of poor recording and reporting practices at various levels of the system that lead to inaccurate coverage figures. In many countries, administrative coverage data do not coincide with coverage survey data. Few countries have implemented recall systems for defaulters or use data to direct immunization programmes.
Global immunization partnerships, such as GAVI/VF, the Measles Partnership, the Partnership for Maternal and Neonatal Tetanus Elimination and the Partnership for Polio Eradication, have been created to jointly pursue shared goals. They bring together major stakeholders in immunization from both the public and private sector, including the vaccine industry.

Through the Global Polio Eradication Initiative, for example, countries have clearly demonstrated the capacity to achieve high coverage and implement high performance disease surveillance, even in areas affected by political turmoil or other difficult circumstances. However, specially designed strategies are needed to reach hard-to-reach populations on a regular basis as well as those affected by outbreaks and emergency situations.

The Global Polio Eradication Initiative has not only achieved great progress towards meeting its goals but has had a wider impact on health service delivery. It has explored new ways to engage communities in health actions benefiting them; succeeded in involving private partners and the commercial sector in immunization efforts; created high quality information systems; systematized logistics and the financial management of field programmes; and stimulated the establishment of surveillance mechanisms supported by laboratory networks which have contributed to the detection and control of a variety of epidemics. A global laboratory network monitors the circulating virus strains of influenza and all countries must have up-to-date preparedness plans in the event of a global influenza pandemic.

Some VPDs occur periodically in the form of regional, widespread epidemics only to fade away for several years before reoccurring. Examples of these epidemic diseases include meningococcal meningitis, yellow fever and Japanese B encephalitis. Countries at risk of periodic epidemics need preparedness plans that are firmly rooted in their overall immunization plan and services. In the case of influenza, a global laboratory network monitors the circulating virus strains and all countries must have up-to-date preparedness plans in the event of a global influenza pandemic. However, many national preparedness plans are non-existent, out-of-date, or lack practicality. Efforts are under way by WHO and other international partners to stimulate and support the development of national preparedness plans and help scale up global capacity for influenza vaccine production.

Global Polio Eradication Initiative

The Global Polio Eradication Initiative, the largest international public health initiative in history, has become a showcase for public health. Nearly five million children are walking today who would otherwise have been paralysed by polio. Moreover, 1.25 million childhood deaths have been averted by the distribution of vitamin A during polio immunization campaigns. In addition to the humanitarian benefits, the eradication of polio will bring substantial financial savings due to foregone polio treatment and rehabilitation costs. Depending on national decisions on the future use of polio vaccines, these savings could exceed US$1 billion per year.

Nearly five million children are walking today who would otherwise have been paralysed by polio.

In 2002, the number of polio-endemic countries dropped to seven: India, Nigeria, Egypt, Pakistan, Afghanistan, Niger and Somalia (in descending order of cases). Within these countries, the extent of transmission was geographically limited, with 80% of cases confined to six states/provinces of India, Nigeria and Pakistan. However, the global case count quadrupled in 2002 (up from 483 virologically-confirmed cases in 2001 to 1919 in 2002) due to an epidemic in northern India and a rise in reported cases in northern Nigeria (Figure 10). With the exception of India, Nigeria and Egypt, all countries endemic in 2001 either stopped transmission or saw a decline in the number of indigenous polio cases. No polio cases were detected in Angola, Ethiopia or the Sudan in 2002 and there was a drop in the number of new cases in Afghanistan, Niger and Somalia. While some areas of Pakistan still had intense transmission in 2002, the number of new cases fell by 22%.
Figure 10. Polio eradication: progress by year

Source: IVB/WHO
The Technical Consultative Group on the Global Eradication of Poliomyelitis (TCG) held an interim meeting in November 2002 to review progress and identify strategies for stopping wild poliovirus transmission globally as quickly as possible. The TCG noted that, provided the quality of activities remained high and access to all children improved in Afghanistan, Niger and Somalia, those countries could be expected to stop transmission by mid-2003, with Pakistan following soon afterwards. However, the TCG warned that stopping transmission in Egypt, India and Nigeria would require multiple rounds of high-quality supplementary immunization activities (SIAs), backed by strong political engagement at every level.

India posed the largest country-level challenge to the Initiative. In India, the number of cases increased six-fold in 2002 as 1600 reported cases were confirmed, accounting for 83% of all cases worldwide. Worst affected was the northern state of Uttar Pradesh, which accounted for 65% of cases worldwide. The major epidemic that began in Uttar Pradesh in 2002 was largely the result of a reduction in the number of large-scale SIAs. For the first time in the Initiative’s history, extensive transmission was re-established in polio-free areas, as the epidemic in Uttar Pradesh spread into the Indian states of Gujarat, Rajasthan and West Bengal.

By end-2003, polio had been eliminated from all but six countries.

Despite tremendous international support for the Initiative in 2002, the programme continued to have a US$ 275 million funding gap for activities planned up to the end of 2005 – the greatest overall threat to achieving a polio-free world. The risks were highlighted at the end of 2002 as an acute funding shortfall for 2003 forced the scaling-back of a number of planned eradication activities, despite action by key immunization partners to bring forward future pledges of funding to fill the gap. In response to this financial crisis and current epidemiology, the programme was restructured to focus all SIAs on the remaining endemic and highest-risk areas – reducing the number of SIAs from over 100 in 2002 to about 20 in 2003. By end-2003, polio had been eliminated from all but six countries. However, the suspension of SIAs in northern Nigeria in mid-2003, due to unsubstantiated concerns about the vaccine used, led to an outbreak of polio that affected countries throughout West and Central Africa. By end-2003, 51 cases of polio due to imported poliovirus had been reported in Benin, Burkina Faso, Cameroon, Central African Republic, Chad, Côte d’Ivoire, Ghana and Togo. In all cases, the virus was linked to the outbreak that originated in northern Nigeria.

In 2003, WHO issued the Global Polio Eradication Initiative Strategic Plan 2004–2008 which outlined the activities required to: interrupt poliovirus transmission (2004–2005); achieve global certification and mainstream the Global Polio Eradication Initiative (2006–2008); and prepare for the Global OPV Cessation Phase (2009 and beyond). This Plan reflects the major tactical revisions that were introduced in 2003 to interrupt the final chains of polio transmission, the revised timeframe for certification of eradication, and the decision to stop immunization with oral polio vaccine (OPV) globally as soon as possible after global certification.

It is of critical importance to maintain active surveillance and rapid response capacity in the event of a suspected outbreak in the period between the interruption of polio transmission and certification of global eradication.

In the period between the interruption of polio transmission and certification of global eradication, it will be of critical importance to maintain active surveillance and rapid response capacity in the event of a suspected outbreak. The most effective way to sustain the gains derived from polio eradication will be to gradually incorporate polio activities into disease prevention, control and surveillance activities, while using the valuable experience accumulated through this Initiative to inform the development of future health policies and programmes.
Measles Initiative

In 2001, measles was still a leading cause of childhood death, with an estimated 30 million cases and over 700,000 deaths globally, of which 57% occurred in Africa, and over 98% in countries with a per capita gross national income (GNI) of less than US$1000. Global measles vaccination coverage in 2001 was 71.4%, with the lowest coverage (51.7%) in Africa and the highest (92.1%) in Europe (Figure 11).

Major progress was achieved in some parts of the world, particularly in the Region of the Americas which recorded its last indigenous measles case in 2002.

In February 2002, the Measles Initiative was launched, with the goal of vaccinating a projected 200 million children over 5 years of age and preventing an estimated...
1.2 million deaths. The Initiative is being spearheaded by the American Red Cross, UNF, UNICEF, US CDC and WHO. In 2003, the World Health Assembly passed a resolution on sustainable measles-mortality reduction, urging Member States to fully implement the WHO–UNICEF 2001–2005 strategic plan; to provide the financial support necessary for full implementation of national immunization programmes in which the measles-mortality reduction strategy is embedded; and to use measles-mortality reduction as a tool for strengthening national immunization programmes. Major progress was achieved in some parts of the world, particularly in the Region of the Americas where the last indigenous measles case was recorded in Carabobo, Venezuela, in November 2002.

Vitamin A supplementation
While much success has been achieved in linking vitamin A delivery with polio national immunization days (NIDs) and measles campaigns, uptake through routine immunization contacts has been slow. Efforts are now being focused on two specific opportunities: a post-partum maternal dose of vitamin A given with the first infant immunization contact; and a dose given to infants with measles immunization at nine months. In 2003, 60 (44%) countries at risk reported the distribution of vitamin A with routine immunization contacts. While the remaining 76 (56%) countries did not link vitamin A with routine immunization, 16 of these countries included vitamin A with immunization campaigns, and some pursued other ways such as "Vitamin A Days" or periodic distribution via community health workers.

Elimination of maternal and neonatal tetanus
Efforts to eliminate maternal and neonatal tetanus (MNT) are well under way: by 2003, MNT had been eliminated from 140 countries (including 5 awaiting confirmation), while 52 were still confronting this problem in one or more districts (Figure 12). To increase coverage in populations at high risk of neonatal and maternal tetanus, supplementary national immunization activities were implemented in 30 countries. In the 540 districts targeted, 22.5 million women were immunized with at least two doses of tetanus toxoid (TT). WHO collaborated with UNICEF to accelerate activities in the 57 priority countries that had not yet achieved MNT elimination. Using a protocol developed by WHO, 4 of the 57 priority countries/states (Malawi, South Africa and Eritrea in Africa, and the state of Andhra Pradesh in India) were validated as having eliminated MNT. An ad hoc committee of experts approved the method as suitable to validate elimination, and advised on a series of other monitoring issues. WHO also maintained a global database containing district-level data on MNT and shared it with partners. MNT disease-burden surveys were conducted in Lao People Democratic Republic and Nigeria. WHO participated in evaluating MNT activities in Ethiopia and Pakistan and assisted extensively in developing plans of action in Gabon, Myanmar, Nepal and Uganda. WHO developed a methodology to estimate the burden of neonatal and maternal tetanus, and is in the process of modelling the impact of various control strategies. MNT surveillance standards were set with SEAR and WPR and joint WHO/UNICEF coordination meetings were held with AFR, EMR, SEAR and WPR. A special effort was made to publish experiences and findings, underlining the need to sustain ongoing efforts to curb neonatal and maternal mortality resulting from tetanus. Of particular concern is the lack of attention to the problem in countries or areas where MNT remains “hidden” because its incidence may be below detection level, especially among populations with poor access to services.

Pertussis
Pertussis remained a major cause of childhood morbidity and mortality with case-fatality rates in developing countries as high as 4% in infants. In 2002, there were an estimated 18 million pertussis cases and 294 000 pertussis-related deaths globally, with 45% of these deaths occurring in Africa. In 2003, global coverage for DTP3 was estimated at around 78%, ranging from a low of 60% in sub-Saharan Africa to a high of 95% in industrialized countries. While pertussis control has not received sufficient emphasis in recent years, despite the high disease burden, it is anticipated that it will benefit from ongoing efforts to strengthen routine immunization systems and improve access to immunization services, particularly in the 75 GAVI/VF-eligible countries.
Figure 12. Maternal and neonatal tetanus (MNT) elimination status, 2003
Meningitis

During 2003, the WHO/AFR Paediatric Bacterial Meningitis (PBM) Surveillance Network was in its third year of activities in 26 countries. This network of sentinel surveillance sites focuses on issues related to the development, introduction and sustained use of vaccines where they are needed. Although epidemics in the meningitis belt are traditionally associated with *Neisseria meningitidis* serogroup A and sporadic cases of Nm W135 are not uncommon, in 2002 serogroup W135 (et37 clone) emerged for the first time as the cause of a large-scale epidemic in Burkina Faso. During 2002, a total of 14,453 cases and 1,743 deaths (case–fatality rate 12%) were reported in Burkina Faso.

In September 2002, a consensus meeting was held in Ouagadougou with countries of the meningitis belt and major stakeholders to review short-term, medium-term and long-term strategies for epidemic meningitis control. In view of the fact that a long-term strategy of developing a conjugate meningococcal vaccine and a short-term strategy of surveillance and case management were both in place, the meeting adopted a medium-term strategy of making a W135-containing polysaccharide vaccine available. Although such a vaccine was already on the market (containing four serotypes, including W135), there was only a limited supply and the price ruled out its large-scale use in developing countries. It was decided that the best response would be to develop a different formulation of the vaccine, containing only the three serotypes most prevalent in Africa, including W135. WHO contacted several vaccine manufacturers to explore the possibility of developing this new formulation and GlaxoSmithKline (GSK) responded positively with an offer to produce three million doses of a trivalent Nm ACW135 polysaccharide vaccine within record time. WHO worked promptly to establish a public–private partnership with the Bill & Melinda Gates Foundation and GSK Biologicals to develop and procure this vaccine at an affordable price. By January 2003, the new vaccine formulation had been fully licensed by the Belgian National Regulatory Authority and registered in Burkina Faso, and two million doses were sent to this country for epidemic response. By the end of that year, a six million-dose stockpile had been established to ensure rapid availability in the event of future Nm W135 meningitis epidemics in the African meningitis belt.

While the epidemic response in Burkina Faso was under way, WHO agreed to conduct an impact evaluation including an assessment of the efficacy and immunogenicity of the vaccine as well as AEFIs. Several components of this activity received technical support from US CDC. Most of the funding for the supply of vaccine in 2003 and partial funding for the trivalent vaccine impact assessment activities was provided by the Bill & Melinda Gates Foundation. This response to an emerging disease helped curb the meningitis epidemic in Burkina Faso in 2003. In addition, it also highlighted how an effective public–private partnership could succeed in making a new, quality-assured product rapidly available. Never before had a vaccine been developed so promptly to respond to the specific needs of a developing country.

Meanwhile, WHO continued to work closely with PATH towards the development of an affordable conjugate vaccine against meningitis type A for future use in routine childhood immunization in Africa. It is anticipated that the vaccine will become available for public health use in 2007–2008.

Yellow fever

A sharp rise in yellow fever cases was reported in 2000–2002, mainly due to low immunization coverage in countries where the disease is endemic, widespread infestation of *Aedes aegypti* mosquitoes in cities near endemic areas, and frequent travel to and from endemic areas. Considerable progress has been made to include yellow fever vaccine as part of routine infant immunization schedules.

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preventive campaigns has been both the availability and the affordability of vaccine. In response, in November 2002, the GAVI Board funded a six million dose stockpile of yellow fever vaccine for a period of three years. The number of African countries that have embarked on case-based surveillance of yellow fever has increased from 6 countries in 2001 to 13 countries by 2003. In addition, the number of national laboratories which were established, equipped and trained to perform diagnostic testing for yellow fever has increased from 5 in 2001 to 17 in 2003. This has led to the early detection of – and rapid response to – outbreaks in a number of countries, thereby preventing many cases and deaths.

Rubella

There has been substantial progress over recent years in the introduction of rubella vaccine. In 2003, 111 countries (58%) were using rubella vaccine in their national immunization schedule compared with only 67 countries (35%) in 1996 (Figure 14). Rubella vaccine coverage varied by stage of economic development: 100% for industrialized countries, 71% for countries with economies in transition, and 48% for developing countries.

Two WHO regions - AMR and EUR - have embarked on intensified rubella immunization towards the elimination of congenital rubella syndrome (CRS) by 2010.

Two WHO regions have embarked on intensified rubella immunization towards the elimination of congenital rubella syndrome (CRS). The PAHO/AMRO Governing Bodies passed a resolution in 2003 to eliminate CRS and rubella from the Region by 2010. The European Region included rubella immunization together with measles in its Regional Strategic Plan with the goal of achieving less than one case of CRS per 100 000 births by 2010.
Figure 14. Countries using rubella vaccine in their national immunization system, 2003

Yes
(111 countries or 58%)

No
(81 countries or 42%)

WHO Member States
Date: October 2004
WHO and its global partners have made great strides in some areas of immunization but less progress in others. While in many developing countries the focus remains on increasing routine coverage, in higher-income countries immunization is taking on new challenges and additional age groups are now benefiting from vaccines. For some years, during polio and measles campaigns, vaccines have been given not only to infants but to older age groups as well. Meanwhile, additional and booster doses of infant vaccines such as a fourth dose of DTP are now being administered in an increasing number of countries. In addition, countries are continuing efforts to immunize all women of childbearing age with tetanus toxoid before they first conceive. This trend to involve wider age groups is likely to continue as more financial resources are attracted to immunization. It is hoped that this expanding age range will fit well with the need for delivery of the “under-five health package”. Even in the lowest-performing countries, it may be possible to introduce crucial new vaccines in the coming years.

A number of new vaccines are in the process of development; some are likely to be ready in the short term, while others, such as a malaria vaccine, are still frustratingly far off. Over the next decade, vaccines against HIV/AIDS, herpes simplex virus and human papilloma virus are likely to become available. Such vaccines may well need to be given to 10–15 year olds before their first sexual experience. However, efforts to ensure high coverage with these vaccines among the target age groups will be a challenge for conventional delivery strategies – especially in developing countries that have often been unable to deliver even routine infant vaccines. While the prospect for some countries is daunting, it also offers an opportunity for the international community to respond supportively and creatively to these impending needs.

Another challenge is the need to ensure the safe disposal of the waste material from vaccination, a problem which has for too long gone unnoticed. While polio eradication campaigns have delivered vaccine orally with little waste generated, the current mass campaigns against measles generate huge amounts of needles and syringes over a short space of time that need to be disposed of safely. Safer ways of disposing of this material, using various types of incinerator, are now being developed. Meanwhile, a number of new technologies – already developed or in their final stages of testing – are expected to transform immunization over the next decade. The conventional liquid vaccines delivered by needle and syringe are likely to be replaced by safer and more versatile mechanisms such as transdermal patches, powder-jet delivery or oral vaccines. An experimental inhaled measles vaccine has been successfully field tested as a part of a mass campaign in one country.

The revitalization of immunization programmes and the mobilization of commitment and resources are giving vulnerable populations a chance to benefit from safe and effective prevention technologies. The 2002–2003 biennium was marked by a number of developments that signalled further progress in immunization worldwide. The prospects for greater outreach, the expansion of the range of quality-assured vaccines offered to populations at risk, and the attainment of eradication, elimination and disease reduction goals are now brighter than ever. The revitalization of immunization programmes and the mobilization of commitment and resources from governments, funding agencies and other stakeholders are giving vulnerable populations a chance to benefit from safe and effective prevention technologies. The real challenges today are to sustain these commitments in the long term and to ensure that access to immunization is regarded, today and tomorrow, as the right of every child.
The World Health Organization has managed cooperation with its Member States and provided technical support in the field of vaccine-preventable diseases since 1975. In 2003, the office carrying out this function was renamed the WHO Department of Immunization, Vaccines and Biologicals.

The Department’s goal is the achievement of a world in which all people at risk are protected against vaccine-preventable diseases. Work towards this goal can be visualized as occurring along a continuum. The range of activities spans from research, development and evaluation of vaccines to implementation and evaluation of immunization programmes in countries.

WHO facilitates and coordinates research and development on new vaccines and immunization-related technologies for viral, bacterial and parasitic diseases. Existing life-saving vaccines are further improved and new vaccines targeted at public health crises, such as HIV/AIDS and SARS, are discovered and tested (Initiative for Vaccine Research).

The quality and safety of vaccines and other biological medicines is ensured through the development and establishment of global norms and standards (Quality Assurance and Safety of Biologicals).

The evaluation of the impact of vaccine-preventable diseases informs decisions to introduce new vaccines. Optimal strategies and activities for reducing morbidity and mortality through the use of vaccines are implemented (Vaccine Assessment and Monitoring).

Efforts are directed towards reducing financial and technical barriers to the introduction of new and established vaccines and immunization-related technologies (Access to Technologies).

Under the guidance of its Member States, WHO, in conjunction with outside world experts, develops and promotes policies and strategies to maximize the use and delivery of vaccines of public health importance. Countries are supported so that they acquire the technical and managerial skills, competence and infrastructure needed to achieve disease control and/or elimination and eradication objectives (Expanded Programme on Immunization).

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