



WORLD HEALTH ORGANIZATION

MEETING OF INTERESTED PARTIES

GENEVA, 18 TO 29 JUNE 2001

Immunization and vaccine development – highlights of 2000

INTRODUCTION

1. The culture of disease prevention gained momentum in the year 2000, particularly through efforts to eradicate poliomyelitis and the entrance on the stage of the Global Alliance for Vaccines and Immunization (GAVI). Reported poliomyelitis cases more than halved in 2000, as accelerated activities successfully cornered the virus. The remaining poliomyelitis-endemic countries on the Asian sub-continent, in West and Central Africa and the Horn of Africa at least doubled the number of rounds on national immunization days (NIDs) and began house-to-house vaccine delivery to reach every child.
2. As the efforts to eradicate poliomyelitis reach a crescendo, there is a sharper focus on strengthening routine immunization and surveillance to secure gains and to systematically build on lessons learned.¹ Measles, *Haemophilus influenzae* type b (Hib) and hepatitis B (hepB) have huge mortality and morbidity in the poorest countries of the world, and effective vaccines against these remain underused. Vaccines still do not exist against various other killer diseases, and research and development (R&D) efforts must be renewed. At the forefront of the movement to make safe quality vaccines and immunization accessible and available to all is the newly launched GAVI initiative.

GAVI

3. GAVI was formally launched on 31 January 2000, as a broad alliance of partners including agencies, foundations, governments, nongovernmental organizations and industry. With a particular focus on the world's poorest children, it aims at strengthening routine immunization services, increasing coverage and introducing new vaccines. Vaccines and Biologicals (VAB), the operational arm of WHO in the Alliance, has played a critical role in the elaboration of the Alliance structure and mechanisms.
4. **Global fund established.** In January, the GAVI partners launched the Global Fund for Children's Vaccines as a new funding mechanism for the poorest countries of the world – those with a GNP per capita of less than US\$ 1000. The Gates Foundation and the Governments of the Netherlands, Norway,

¹ As emphasized in *Global Polio Eradication Initiative Strategic Plan 2001–2005*, WHO/Polio/00.05.

the United Kingdom of Great Britain and Northern Ireland and the United States of America have pledged a total of US\$ 1 billion to the Global Fund over the next five years.

5. **Performance-based programmes.** During 2000, VAB and its partners have assisted countries in their applications to the Global Fund. This has meant focusing on the establishment and strengthening of interagency coordinating committees (ICCs), conducting in-depth assessments and developing multi-year plans. A total of 26 countries made successful applications and are now accessing multi-year grants for the strengthening of immunization services and the introduction of new vaccines. The continuation of the grants is conditional on the yearly achievement of targets set by the ministry of health through consultation with the ICC.

6. **Task forces.** Four task forces were established to ensure broad partnership and elaborate the details of the Alliance workplan in the areas of advocacy, financing, country coordination and R&D. WHO/VAB has appointed representatives in all these groups. In 2000, however, VAB was most particularly involved in Country Coordination (co-chairing with Norway) and R&D (co-chairing with industry and academia) and acted as the secretariat for these task forces. The WHO-led Task Force on Country Coordination outlined a plan of action to coordinate technical assistance to countries, build national capacity and strengthen country-level monitoring and evaluation. It has supported the establishment of regional working groups to further assist the countries in the Global Fund application and implementation process, notably in Africa, the Western Pacific and South-East Asia. The R&D Task Force decided to focus on promoting development of improved vaccines for meningococcal A meningitis, rotaviral diarrhoea and invasive pneumococcal disease, all of which have had priority status in WHO's vaccine R&D portfolio.

STRATEGIC PLANNING

7. *Vaccines, Immunization and Biologicals 2000–2003 Strategy*, published in 2000, maps out what VAB aims to achieve in the areas of innovation in vaccines and vaccine delivery, strengthening of immunization systems and accelerated disease control. The work on these main objectives is presented in terms of targets to be achieved and a detailed discussion of the expected results. Each target and product has well-defined indicators; this ensures that progress can be closely monitored. Among the nine targets in the plan, three have been given extra prominence: poliomyelitis eradication, accelerated vaccine introduction and the safety of immunization. These targets, termed priority projects, draw on the expertise of the five VAB teams.

8. At the regional level, a joint strategic plan was developed between the Regional Office for the Western Pacific and UNICEF's Regional Office for East Asia and the Pacific and distributed to WHO and UNICEF country offices. The aim of the plan is to coordinate work for common goals, with aggressive control strategies for such diseases as measles, neonatal tetanus and hepatitis B. Coordination also covers other matters such as staff resources and advocacy. The regional and country ICCs are being expanded beyond poliomyelitis. This will serve as a model for other WHO/UNICEF regional collaboration.

POLIOMYELITIS ERADICATION

9. The Global Polio Eradication Initiative is on track to certify the world poliomyelitis-free in 2005, although key challenges remain access to children in conflict-affected areas, a US\$ 450 million funding gap and maintaining political commitment in the face of a disappearing disease.

10. **Impact of acceleration.** The number of reported cases declined to the lowest levels ever, with less than 3500 cases as compared to 7141 cases in 1999, even with a 25% improvement in the sensitivity of acute flaccid paralysis surveillance. The number of countries with wild poliovirus transmission decreased from 30 at the end of 1999 to 20 at the beginning of 2001. In October 2000, the Western Pacific Region was certified poliomyelitis-free. In November, the European Region completed two poliomyelitis-free years. In poliomyelitis-free areas, laboratory containment of wild polioviruses and the eventual cessation of poliomyelitis immunization have become increasingly important. Staffing in the Initiative was quadrupled to realize accelerated activities. The Governments of the Netherlands and the United Kingdom of Great Britain and Northern Ireland gave unprecedented year-end donations totalling US\$ 90 million.

11. **National immunization days (NIDs).** During 2000, 550 million children were given oral poliomyelitis vaccine in NIDs involving around 10 million volunteers. In October and November 17 West African countries immunized 76 million children during synchronized NIDs. India immunized 152 million children in its December NID round alone. Several war-torn countries negotiated cease-fires or at least improved access for NIDs – Afghanistan vaccinated 5.7 million children and the Democratic Republic of the Congo vaccinated 10.2 million children in 2000.

12. **Strengthening routine immunization services.** Lessons learned from poliomyelitis eradication – on access, interagency coordination, long-term plans of action and micro-planning – are being incorporated in other disease control/elimination strategies. Among strategies are the sustained outreach services (SOS), which focus on reaching the unreached children. SOS is currently being piloted in various countries and will become a key element in strengthening immunization services. In addition, infrastructure created for poliomyelitis eradication is being used more widely, particularly poliomyelitis surveillance and laboratory networks. VAB published two reports analysing the Initiative's impact on health systems, concluding that positive impact requires clear objectives and a process for monitoring progress. As a result, a checklist and indicators were produced to maximize opportunities for strengthening routine immunization.

13. **Vitamin A "bonus".** A known public health problem in 94 countries and a possible one in another 43, vitamin A deficiency is estimated to afflict over 140 million children under five, increasing the risk of death from measles and diarrhoea, and annually causing blindness in 250 000–500 000 children. The distribution of vitamin A during NIDs provides a powerful example of how poliomyelitis eradication can help to address other child health problems. In 2000, over 50 countries gave vitamin A during NIDs, preventing an estimated 240 000 deaths according to the Centers for Disease Control and Prevention (CDC) Atlanta. In March 2000, an expert consultation suggested new guidelines, extending the possibility of linking vitamin A with early infant immunizations, thereby increasing the opportunities for combining two of the most cost-effective child health interventions available.

A GLOBAL PLAN TO REDUCE MEASLES MORTALITY

14. In spite of the availability of an inexpensive and highly effective vaccine, measles still causes 800 000 deaths each year. In May 2000, global experts reviewed the strategies for measles mortality reduction and elimination and recommended that: (i) to reach all children who have not been vaccinated previously or did not respond to the first dose, there should be a second opportunity for measles vaccination in addition to the dose given at nine months; and (ii) campaigns should target large populations (entire nations or large regions) and achieve high coverage (greater than 90%) with quality services. WHO, UNICEF and the CDC incorporated the above recommendations in the Global Measles Strategic Plan developed during the year. Among the goals of the global plan are: (i) to halve annual

global measles-related mortality by the year 2005 (compared with 1999); and (ii) to interrupt transmission of indigenous measles virus in large geographical areas including the Americas, Europe and the Eastern Mediterranean region.

NEW VACCINE DEVELOPMENT AND INTRODUCTION

15. An over-arching programme, the Initiative for Vaccine Research, coordinates the different R&D efforts into a single WHO-wide activity, from pre-clinical to post-licensure issues. The disease focus is broad including tuberculosis, rotaviral diarrhoea and diseases that normally receive low priority – such as dengue and leishmaniasis.

16. Within this context, the VAB priority project on Accelerated Vaccine Introduction seeks to implement a mechanism for accelerating introduction of new and underused vaccines. It involves all VAB teams in activities on efficacy, disease burden and cost-effectiveness studies, vaccine quality, supply, financing and introduction. In 2000, the focus was to accelerate the introduction of hepB and Hib vaccines, and to develop rotavirus vaccine as well as pneumococcal and meningococcal conjugate vaccines.

17. **Hib and hepatitis B vaccines.** HepB vaccine is now used in routine infant programmes in 127 countries, and Hib in 64 countries. A big step forward in 2000 was that the GAVI Global Fund approved support for introduction of hepB and Hib vaccines in 16 countries. Field-testing for a WHO/VAB rapid assessment tool for Hib disease burden was completed, management guidelines for the introduction of Hib and hepB vaccines were distributed and guidelines for economic evaluation of hepB and Hib were drafted.

18. **Meningococcus.** Devastating epidemics of meningococcal disease cause enormous suffering in the African meningitis belt, stretching from Senegal and the Gambia to Ethiopia. The technology to produce the serogroup A/C meningococcal conjugate vaccine has been available for more than 10 years, but the returns on investment were perceived to be too low. Therefore WHO/VAB and the Bill and Melinda Gates Children's Vaccine Program have created a partnership to accelerate the development and introduction of this vaccine at an affordable price.

19. **Pneumococcus.** Pneumococcal vaccine efficacy trials with pneumonia as end point were conducted in the Philippines, South Africa and the United States of America (among the Navajo). A phase III efficacy trial got under way in the Gambia. A protocol for pneumonia burden is ready for field-testing. Because current pneumonia diagnosis techniques are not sufficiently sensitive in identifying cases of pneumococcal (and Hib) pneumonia, a major cause of death in young children, several projects aiming to standardize the measurement of trial outcomes were initiated. One of these, a VAB project to create standards for the interpretation of X-ray readings, is now nearing completion.

QUALITY ASSURANCE AND SAFE BIOLOGICALS

20. The WHO Expert Committee on Biological Standardization plays a key role in reviewing scientific progress and establishing international reference preparations and recommendations on production and control of biological products. New quality control procedures, including the use of transgenic mice as an alternative to the neurovirulence test on primates for all three oral poliomyelitis vaccine serotypes, were accepted in November 2000 at the 51st meeting of the Expert Committee. It also adopted updated recommendations for inactivated poliomyelitis vaccine (IPV). These included stringent standards for that

part of the IPV production process that uses wild polioviruses. In addition, the Expert Committee adopted guidelines for the production and control of live attenuated Japanese encephalitis vaccine.

IMMUNIZATION SAFETY

21. Paradoxically, the success of immunization in removing the scourges of poliomyelitis, diphtheria and measles has led to greater public concern about vaccine safety. The main target of this priority project is to establish a system to ensure the safety of all vaccines given in national immunization programmes.

22. **Auto-disable (AD) syringes.** The use of AD syringes almost doubled in 1999 and this trend accelerated tremendously in 2000. The cost dropped to under US\$ 0.06.

23. **New tool to assess safety.** The availability of a reliable tool to assess safety is of critical importance to develop injection safety policies. Work completed in 2000 on the new injection safety assessment tool showed that it is easily implemented by health workers and sets adequate standards. This VAB project, carried out in collaboration with the Safe Injection Global Network and BASICS, has involved assessments in Burkina Faso, Egypt, Ethiopia, Morocco, Niger and Zimbabwe.

24. **Adverse events.** The Global Vaccine Safety Advisory Committee set up by WHO to advise on technical and scientific matters met twice and proved a great success, facilitating surveillance, evaluation and management of adverse events. Since 1999, the Global Training Network – a network of collaborating centres which proposes courses aimed at strengthening the National Regulatory Authorities – has offered a course on post-marketing surveillance and adverse events following immunization. To date, 42 trainees from 22 countries have successfully completed this course. A media training workshop “partnership building with the media” targeting Expanded Programme on Immunization (EPI) managers has been integrated into the Global Training Network curriculum.

25. **Waste disposal.** In order to deliver a comprehensive set of materials to advise EPI managers on safety and waste management systems, VAB has collaborated with the Environmental Health Department in the production of fact sheets.

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