

# Proceedings of the Global Technical Consultation to Assess the Feasibility of Measles Eradication, 28–30 July 2010

World Health Organization<sup>a</sup>

## BACKGROUND

In response to a request by the May 2008 Executive Board (EB) of the World Health Organization (WHO) to assess the feasibility of measles eradication, the WHO Secretariat has performed a detailed and independent technical analysis of the various aspects of the feasibility of eradicating measles. The results of this work were reviewed during the global technical consultation meeting, and the recommendations were made by an independent ad hoc Global Measles Advisory Group. This report summarizes the key meeting findings and the recommendations of the ad hoc Global Measles Advisory Group.

This report will be presented to the WHO Strategic Advisory Group of Experts (SAGE) in November 2010 for their review and recommendations as to the feasibility of measles eradication.

## EXECUTIVE SUMMARY AND ADHOC GLOBAL MEASLES ADVISORY GROUP RECOMMENDATIONS

Although measles mortality has been substantially reduced, measles continues to cause preventable childhood deaths in many countries. Although rapid progress has been made in recent years, there is a real risk that measles will reemerge as a major cause of childhood

mortality unless urgent actions address inadequate implementation of measles mortality reduction strategies in some countries. These include weakness within immunization systems, cross-border transmission of measles virus, and insufficient political will and financial resources.

A comprehensive review of available evidence has established the biological (related to the properties of the disease and the virus) and technical (related to the properties of the vaccine and diagnostic testing) of measles eradication. An operational model has been demonstrated to be effective in the entire American Region and in a number of countries in each remaining WHO Region. In addition, measles elimination has been shown to be cost-effective in the American Region, and global eradication is assessed to be cost-effective. Thus, the ad hoc Global Measles Advisory Group concludes that measles can and should be eradicated.

The interim measles control objectives established by the World Health Assembly (WHA) in 2010 should be actively pursued and will serve as milestones to eradication, while supporting the achievement of Millennium Development Goal 4. They include:

- First-dose measles vaccination coverage of at least 90% at the national level and 80% in all districts
- Reported measles incidence of <5 cases per million population
- At least 95% measles mortality reduction, compared with 2000

Given that the Region of the Americas has achieved and maintained elimination since 2002; that the European and Eastern Mediterranean Regions have target dates for elimination by 2010, which may be postponed to 2015; that the Western Pacific Region has a target date for elimination of 2012; and that the African Region has established a target date of 2020, the ad hoc Global Measles Advisory Group concludes that the WHA should consider establishing a target date for measles

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eradication once the South East Asian Region has established an elimination target. Acceleration of activities and measurable progress towards achieving the 2015 WHA measles targets would make it feasible to accomplish global eradication by 2020.

Building the required political, social and economic platforms for measles eradication is both a disease control opportunity and an important developmental opportunity, requiring a broad multidisciplinary partnership.

The success of measles eradication will depend on strong management, accountability, communication, advocacy, and resource mobilization at all levels. At the country level, measles eradication should be conducted within the context of Expanded Program on Immunization (EPI) activities, with each country taking responsibility for providing the necessary resources for strengthening immunization systems, including robust routine immunization programs and supplemental immunization activities, disease surveillance, program monitoring, and an integrated laboratory network. Responsibilities at the regional level include country coordination, technical support, and special assistance for countries with weak immunization systems. Global-level responsibilities include global leadership and management, coordination of policy and strategies, broad-based partnership facilitation, resource development, and the creation and implementation of a supportive research agenda.

At all levels, linkages should be maximized with other child survival and disease control initiatives. Measles eradication activities should be used to accelerate rubella control and the prevention of congenital rubella syndrome. To this end, all countries that are introducing a second dose of measles vaccine into their routine immunization program should consider the use of measles-rubella (MR) or measles-mumps-rubella (MMR) vaccine.

## MEETING OBJECTIVES

1. To review the outcomes of work done to assess the feasibility and economics of measles eradication
2. To provide recommendations on the timing and nature of the next global goal
3. To provide recommendations on research and additional programmatic work needed to facilitate measles eradication.

The ad hoc Global Measles Advisory Group of experts participating in this Global Technical Consultation addressed the following specific questions:

- Should measles be eradicated?
- If “yes,” when is the appropriate target date? What else needs to be in place before an eradication goal is set?
- If “no,” what level of control should be targeted?
- What are the key areas of work, including research, needed to facilitate eradication?
- What does the group recommend as the best approach and/or strategy for achieving measles eradication?

## SUMMARY REPORT OF MEETING

The WHO invited experts in measles, disease eradication, vaccine and immunization science, public health, health care systems, and economics from a variety of organizations, including ministries of health, the organizations and partners of the Measles Initiative (launched in 2001, the Measles Initiative is an international partnership committed to reducing measles deaths worldwide that is led by the American Red Cross, the Centers for Disease Control and Prevention, the United Nations Children’s Fund [UNICEF], the United Nations Foundation, and the WHO; more information is available at <http://www.measlesinitiative.org>), universities, and nonprofit institutes, as well as independent consultants, to advise the WHO on measles eradication. The meeting was chaired by Professor David Durrheim of the University of Newcastle, Australia. Drs. Okwo Bele and Jon Andrus welcomed participants on behalf of the WHO and the Pan American Health Organization (PAHO), respectively.

Dr. William Foege, of the Bill and Melinda Gates Foundation, gave the keynote address and noted that eradication contributes to reductions in health inequities and that measles eradication might serve as the “tugboat” that leads to stronger immunization systems. He suggested that measles vaccination coverage be used as an indicator for the allocation of Global Alliance for Vaccines and Immunization (GAVI) funds. In addition, he stressed that we must avoid the paralysis caused by demanding certainty before making worthwhile public health decisions. With smallpox eradication, there were few competing priorities, whereas for measles there are many. The price of not choosing an eradication goal is the eternal risk of importation and outbreaks in all countries.

Dr. Alya Dabbagh of the WHO presented the objectives of the meeting and scope of work undertaken to assess the feasibility of measles eradication. The work has been conducted in a consultative manner with oversight by the WHO SAGE Working Group on Measles and the WHO Quantitative Immunization and Vaccines Related Research Advisory Committee, and it covers the following areas: biological feasibility, programmatic/operational feasibility, vaccine market analysis, impact on health care systems, economic analysis, risk analysis for the post-measles era, and political feasibility in the current global context.

Dr. Peter Strebel of the WHO reviewed global progress towards measles mortality reduction, noting that, as of 2008, the strategies used since 2000 have been effective in reducing mortality from measles by 78%. He identified 3 key innovations followed by worldwide scale-up that have enabled rapid progress in reducing measles morbidity and mortality worldwide: the discovery of measles vaccine in the 1960s and its inclusion in the EPI; the PAHO strategy for delivery of measles vaccine in mass campaigns, which was subsequently taken to scale by the Measles Initiative; and the development of laboratory methods for detection of measles antibody and measles virus now being used by

the Global Measles/Rubella Laboratory Network. He noted that measles mortality reduction accounts for 23% of the overall decrease in mortality among children under 5 years of age between 1990 and 2008 and that this contribution can only be sustained by an ongoing commitment of financial resources. Recent setbacks, such as outbreaks across southern Africa, highlight the need for sustainable financing, improved program performance, better advocacy and communication, and innovation to improve strategies and tools.

## Discussion

- Although supplementary immunization activities (SIAs) have made a major contribution to accelerating measles control, the role of routine immunization, which accounts for two-thirds of all measles deaths averted, should be emphasized. Direct investment in routine vaccination is urgently needed. Financial requirements for routine vaccination related to measles eradication should be estimated as part of an eradication effort.
- The quality and accuracy of data (vaccination coverage, disease surveillance, and mortality estimates) must be improved to monitor program performance and progress towards current and future goals.
- Although the Measles Initiative has generated financial support to achieve its goals to date, including 2 large one-time contributions from American Red Cross tsunami funds and GAVI/International Finance Facility for Immunization, financial uncertainty represents a major concern to sustaining current achievement and progress toward an eradication goal.
- Rinderpest, a severe disease of cattle caused by a virus similar to measles virus, was last seen in Somalia in 2001 following aggressive vaccination efforts that started in the 1970s. The group was informed that an announcement of rinderpest eradication was expected in mid-October 2010, which provides further support for the biological feasibility of eradication of measles-like viruses.

Dr. Bruce Aylward (Global Polio Eradication Program, GPEI; Director, WHO) provided an overview of lessons learned from the polio eradication initiative and noted the importance of operational feasibility. The polio experience suggests that a criterion of proven operational feasibility in all contexts (eg, high population density urban centers, insecure settings, and in settings with very weak health infrastructure) should be added to the feasibility criteria addressed at the meeting (eg, biological feasibility, economic analysis, vaccine market, and programmatic feasibility). This would seem to be of particular importance in the case of measles, given that the prospects for success would be improved with a tightly coordinated, synchronized global effort because of the very high communicability of the virus. The experience of polio eradication is that, although proven eradicability of an organism in the Americas

may be a necessary proof for global feasibility, it may not be sufficient, especially for making the case to move from measles control to eradication with major potential donors and stakeholders. He added that professional management, massive technical assistance, robust communications, effective advocacy mechanisms that reach down to the subnational level, financial support, and ongoing research and tactical innovation will be needed. He suggested examining those countries where the required immunity threshold was highest and routine coverage was lowest as a means of proving operational feasibility of measles eradication in the most difficult areas.

## Discussion

- Country ownership, government funding and a comprehensive approach are required for successful disease control and eradication programs.
- Upfront commitment of financial support is a requirement. Unless we can be confident that resources will be available when needed, it would be irresponsible to launch an eradication initiative.
- For polio eradication, early cost estimates were overly optimistic, and many countries did not start polio eradication activities until just before the original target date to achieve the goal. We should not underestimate the real costs of measles eradication or the financial impacts of delays.
- Measles is different from polio: with measles, there is 1 virus, not 3; 2 vaccine doses are enough for protection, rather than multiple doses; and if people become reinfected with measles, they do not appear to transmit the infection. In these aspects, measles eradication is likely to be relatively simpler to achieve than was polio eradication.
- At the start of an eradication effort, it should be possible to contribute to health care system strengthening; however, towards the end of the eradication effort, intense vertical activities are likely to be necessary.

## REGIONAL PRESENTATIONS ON PROGRAMMATIC AND OPERATIONAL FEASIBILITY

### American Region

Dr. Carlos Castillo-Solórzano of the PAHO summarized the region's successful efforts to eliminate measles, rubella, and congenital rubella syndrome and stressed how rubella elimination had served as a catalyst to strengthen and sustain measles elimination, especially the implementation of speed-up campaigns (targeting adolescent and adult males and females) and high-quality surveillance, in the face of importations. He documented the effectiveness of the key elimination strategies (vaccination campaigns of catch-up, keep up, follow up, and speed-up) for achieving and maintaining elimination and noted

both cost savings of >\$200 million from regional elimination and a positive impact on health care systems. Until measles is eradicated globally, the Americas face the risk of importation and secondary cases, the cost of outbreak response, and costs associated with continuing high-quality follow-up campaigns with involvement by the private sector. Dr. Ana Morice, Vice-Minister of Health for Costa Rica, stressed that elimination is achievable in relatively less wealthy countries. Common challenges throughout the American Region include maintaining high homogeneous routine immunization coverage with the MR vaccine, sustaining high-quality integrated measles and rubella surveillance, and obtaining adequate political support and financial resources.

### **Discussion**

- There are many lessons from the PAHO experience. The economic benefits of eliminating measles in the Americas should be made more widely known.
- Private sector participation (eg, private practitioners and pediatric associations) was critical to achieving and sustaining elimination, both for reporting cases and providing vaccinations. Alliances with scientific bodies have assisted in rapidly responding to crises related to vaccination and to preserving the integrity of immunization programs.
- MR vaccination of men and women up to 39 years of age has played a key role in maintaining the elimination of measles in the Americas. Before making a decision on global measles eradication, public health leaders and epidemiologists should determine whether this strategy of campaigns to vaccinate older age groups will be required to sustain measles elimination. This policy would have obvious and potentially large implications for the expected financial costs of eradication.
- Although it is important that the commitment of funds should be available up front, not all the money should come from external donors. Country ownership, as evidenced by resources from countries where the disease is endemic, is essential. Intense advocacy efforts are required to ensure political commitment and the mobilization of resources at all levels.

### **African Region**

Dr. Balcha Masresha of the African Regional Office of WHO summarized regional achievements, including a 92% reduction in measles mortality during the period 2000–2008, progress towards the pre-elimination goals for 2012, and the establishment of a regional elimination target of 2020. Although routine immunization coverage increased from 2000 to 2008, progress has slowed since 2006, and measles outbreaks have occurred following measles SIAs due to gaps in routine and SIA coverage, and delayed implementation of follow-up campaigns. He noted that challenges to measles elimination include weakness in country health care systems, funding gaps, competing national priorities, and difficulties managing polio eradication and

measles elimination activities simultaneously. An estimated \$2.6 billion, including \$1.1 billion for routine immunization, will be required to eliminate measles in the African Region. Dr. Nuno Gaspar of the Ministry of Health of Mozambique commented on the importance of high-level government commitment. Key challenges in Mozambique include inadequate access to health services, problems with data quality (especially for the target population), vaccine and cold chain management, case detection and notification, partnership coordination, and funding. A regional strategic plan for achieving measles elimination is being developed that will emphasize routine immunization as the foundation.

### **Discussion**

- The 2012 pre-elimination targets seem quite ambitious and may encourage short-term solutions that overlook system constraints and may not be sustainable.
- Ministers of Health may be eager to sign up for ambitious goals, but they often do not follow-up with the necessary political and financial commitment. This results in shifting target dates for achieving health goals.
- The lack of finances to support follow-up campaigns suggests that measles control has become a lower priority. If governments paid for outbreak response, the preventive campaigns would be seen as cost-saving. Although Malawi used its internal resources for outbreak response, a number of other countries have received external support from United Nations emergency funds.
- During recent outbreaks, most measles cases have occurred in unvaccinated individuals, indicating gaps in both routine and campaign coverage. Routine immunization should be strengthened, and SIAs should be used as an entry point for improving routine services.
- In some African countries, the immunization program only provides measles vaccine to infants between 9 and 11 months of age. This practice must be urgently addressed so that all unvaccinated children who are old enough to receive vaccine are offered measles vaccine through routine child health services.
- The polio infrastructure will have to be in place for another 5–8 years, so waiting for the end of polio eradication does not make sense. If it is well timed, measles eradication can take advantage of the polio infrastructure, and in fact, measles elimination activities already take advantage of the polio infrastructure, with polio field staff currently playing a major role in measles campaigns and measles surveillance.

### **Eastern Mediterranean Region**

Dr. Boubker Naouri of the Eastern Mediterranean Regional Office of WHO noted achievements towards the 2010 measles elimination goal, including increasing routine coverage, establishment of case-based measles surveillance in 19 of 22 countries,



and operational accredited measles laboratories in all countries. He noted the support of the GPEI (polio) staff in implementing measles activities in security-affected areas, including 7 high-burden countries where the challenges include difficult access and high cost due to conflict and weak routine immunization systems. Regional elimination will not be achieved by the end of 2010, and the region currently expects a shortfall of \$34.7 million (out of \$41.2 million) required to reach elimination by 2015. Dr. Shakoor Abdul Waciqi of the WHO/Afghanistan noted the sharp increase in routine measles coverage from 48% in 1997 to 78% in 2009, implementation of measles SIAs since 2002, and establishment of measles surveillance. Special challenges facing Afghanistan included the disruption in health services due to insecurity, problems with data quality and analysis, shortages of trained personnel, weak coordination with nongovernmental organizations (NGOs), and endemic polio.

### **Discussion**

- Although the WHO provides staff to countries affected by conflict, they are not able to access all insecure areas. NGOs may be better able to provide services in these areas, but they remain largely uncoordinated, unaccountable, and a temporary remedy.
- If the population is large enough in a conflict-affected area, measles transmission could be sustained and prevent elimination, as occurs with polio in parts of Afghanistan and Pakistan.
- Opinion is divided as to whether it is appropriate to introduce new vaccines and vaccination goals in conflict-affected countries before securing the basic EPI infrastructure, but clearly with the large immunity gaps that exist in these countries, maximizing protection at every opportunity represents an important consideration while continuing to strengthen routine immunization activities.
- In many developing countries, meeting deadlines is less important than it is in industrialized countries. Achieving disease elimination by a preset date will remain a challenge in these settings.
- Mandatory documentation of immunization is being required by some countries in the Eastern Mediterranean region before children are allowed school enrollment.

### **European Region**

Dr. Rebecca Martin of the European Regional Office of WHO summarized achievements for the region, including reduced measles incidence since 1998, especially in the last 3 years. Measles SIAs have been conducted in 16 countries reaching 57 million children, and rubella vaccine is used in all countries. Enabling factors for measles elimination include strong health care systems, adequate human resources, and good surveillance in most countries. Challenges from the anti-vaccine movement and health system reform efforts that make immunization more

difficult in some countries must be addressed to finish the task of measles elimination. The Regional Committee will likely establish 2015 as a new target date for measles elimination. Dr. Martin also discussed a large outbreak of measles that resulted from an importation in Bulgaria and spread among the largely unvaccinated Roma community.

### **Discussion**

- Anti-vaccine rumors can substantially reduce demand for vaccination. More efforts are needed to counteract vaccine-related rumors. A program at Imperial College, London, has been initiated to track these rumors. Increasing vaccine demand will require better social marketing and more research.
- School entry requirements and even mandatory prior vaccination were suggested as possible ways to address flagging demand for vaccination in Europe.
- Measles eradication should be conducted over a short time-frame. Drawing out measles eradication will allow susceptible individuals to accumulate with recurrent outbreaks. However, all countries that eliminate measles remain at risk for importation, so high levels of population immunity must be maintained while eradication efforts are continued.
- Establishing a target date for measles eradication may require a stepwise approach: first, the political support must be obtained from Prime Ministers of the most difficult countries; then the necessary financial resources must be pledged up front; and only then can a target date be set. In addition, it was argued that we should be sure of polio eradication (eg, interruption of polio virus transmission in India and Nigeria) before setting a target date for measles eradication.
- The year 2020 was proposed as a possible target date for achieving measles eradication.
- Rubella vaccination should be considered in the strategy for measles eradication. For example, all countries that are introducing a second dose of measles vaccine in the routine program should evaluate the inclusion of rubella-containing vaccine, either MR or MMR. Not including rubella would be a missed opportunity for prevention of congenital rubella syndrome (CRS) and for funding, because GAVI is considering including rubella in its portfolio.

### **Southeast Asia Region**

Dr. Jayantha Liyanage of the South East Asian Regional Office of WHO summarized achievements towards measles mortality reduction, including the conduct of SIAs reaching 140 million children. Measles incidence rates have decreased by nearly 50% from 2000 to 2009, and case-based surveillance has been established in 7 of 11 countries. However, in countries that have fully implemented measles control strategies (all countries except India and Thailand), measles incidence rates decreased by 61%–98%. Enabling factors for measles elimination include political and financial support in most countries, community

acceptance of vaccine, and a strong laboratory infrastructure. Challenges include reaching and sustaining high routine coverage in all countries; engendering stronger political support in India; the large populations of India, Indonesia, and Bangladesh; establishing a system to monitor and respond to adverse events following immunization (AEFI); and funding (an estimated \$2 billion is needed for measles elimination). During the Regional Consultation in August 2009, country representatives agreed that 9 of 11 countries could achieve measles elimination by 2015; India and Timor-Leste could achieve it by 2020. However, the Regional Committee has not yet established a target date for measles elimination. Up-front funding commitments from member states and partners would be important to advance measles elimination when there are several competing health priorities in member states. Dr. Pradeep Halder, Assistant Commissioner of the Ministry of Health and Family Welfare, India, noted that, although national-level coverage with measles vaccine is 69%, 21 Indian states have reached 80% first-dose coverage, and 4 states have implemented second-dose strategies through the routine immunization program. In the remaining 17 states with >80% coverage, a second dose of measles vaccine will be introduced through routine services. In the 14 states with measles coverage <80%, SIAs targeting 134 million children 9 months through 10 years of age are being planned.

#### **Discussion**

- The opportunity of measles SIAs in northern India should be used deliberately to strengthen routine immunization. This should be measured using appropriate indicators.
- Bangladesh provides evidence of the success of measles elimination strategies in Southeast Asia. Factors enabling success included support from the Prime Minister, interagency collaboration, integration of EPI with other programs, extended clinic hours for working women, and strong program management.
- Thailand has high coverage with 2 routine doses of measles vaccine. Measles elimination is not among the highest health priorities in Thailand, and outbreaks continue to occur in border areas and among adults.
- India is making progress. Polio eradication is very close, and emphasis is being placed on developing the human resources to support child health services through the National Rural Health Mission.

#### **Western Pacific Region**

Dr. David Sniadack of the Western Pacific Regional Office of WHO summarized progress towards the 2012 elimination goal. All countries in the region, except China, reported a 92% reduction in measles incidence between 2000 and 2009, and most of the island countries are at or near elimination. Political commitment and high routine coverage are enabling factors for elimination. Challenges to elimination included gaps in routine

immunization coverage, delayed follow-up campaigns, cases in infants <6 months of age and in young adults (eg, Vietnam and China), and importations (eg, Australia). There is a funding gap of \$23 million for achieving elimination by 2012. Dr. An Zhijie of the WHO/China reported that a 2-dose MR schedule was introduced in China in 2007, and China conducted measles SIAs in 27 provinces from 2004 through 2009. China anticipates a national measles SIA targeting 95 million children in September 2010. Challenges to elimination in China include high population density in urban areas, difficulty reaching high routine coverage among the mobile population, susceptibility in young babies and older age groups, uneven implementation of school entry requirements, and adequate funding for SIAs. China plans to adopt MMR vaccine universally, expand its vaccination registration system, and create a National Measles Elimination Office.

#### **Discussion**

- Aerosol measles vaccine may be useful in large countries, such as China and India.
- In Japan, measles incidence has decreased and a problem of measles importations and false-positive measles immunoglobulin M results has emerged. This is not unexpected, given a false-positive rate of ~4% for this test. As incidence decreases, virus identification and characterization become more important.
- Papua New Guinea (PNG) and Laos may pose major challenges to elimination because of difficulties in achieving high coverage through periodic outreach services (eg, PNG) and during SIAs (Laos).
- China provides an example of a systematic approach to measles elimination through a combination of high 2-dose routine coverage, national SIAs, and laboratory-supported case-based surveillance. Concerns about vaccine safety and improved information and communication for parents and providers need to be addressed.
- Most countries in the Western Pacific Region use rubella vaccine in their routine program, and the Regional Technical Advisory Group recommends that countries reduce CRS to <1 case per 100,000 live births by 2015.
- The regional measles elimination plan reflected the costs for SIAs, surveillance and laboratory support, but it did not reflect those costs of the routine immunization program directly related to measles elimination. These costs should be included.

#### **OTHER PRESENTATIONS**

##### **Financial Feasibility**

Ms. Charlotte Obidairo of Coxswain Social Investment Plus summarized a pilot survey to assess stakeholder political will and financial capacity to support a measles eradication initiative. The survey had a very low response rate (22%). Among organizations

and agencies, the survey found an association between the self-assessed level of knowledge of measles eradication strategies and its implications and the agencies' willingness to support a measles eradication target. Key success factors identified that would support measles eradication included the strength and support of the Measles Initiative and the political and financial commitments made towards measles elimination in 5 of the 6 WHO regions. Specific challenges identified for establishing an eradication goal included the need for more support from donor organizations and development agencies, finding "space" for measles eradication given the ongoing polio eradication initiative, and strengthening communication and advocacy efforts.

### **Discussion**

- The low response rate to the survey may represent a lack of interest in measles eradication, especially among partners interested in health systems development. Alternatively, because the survey was conducted near the time of the WHA, some prospective respondents may have felt that their interventions at the Assembly adequately expressed their views.
- Stakeholders are not sufficiently engaged. The issue may be that the case has not been adequately made for people to invest in measles eradication.
- The Millennium Development Goals represent an opportunity that should continue to be pursued to accelerate the measles agenda.
- Donors strongly expressed the need for an ambitious goal, such as a target date for measles eradication, and stated that the lack of a target date was inhibiting fundraising.
- More communication and advocacy efforts were needed to strengthen and expand the Measles Initiative.
- The operational requirements of a global eradication effort should not be underestimated. The global management apparatus of polio eradication is both expensive and human resource intensive. A similar supportive structure would most likely be needed for measles eradication. The Measles Initiative does not currently have the management capacity required to track progress, oversee resource mobilization, and support program operations.
- The key stakeholders in an eradication decision are not only the Health Ministers but also subnational and community leaders. Local ownership is necessary for the success of an eradication program.
- Large civic organizations could play a very important role in supporting measles eradication.

### **Comparison With Previous Eradication Programs**

Mr. Robert Keegan, a WHO consultant, compared measles eradication with previous eradication programs from technical (eg, the properties of the agent, surveillance factors, and the quality of intervention tools), political (eg, wars and armed conflicts and population displacement or migration), social

(eg, the perception of disease burden and risk, motivation and acceptance of intervention, and competition from other health programs) and economic perspectives. He noted that a measles eradication program would be easier than some prior eradication programs, based on some technical and social factors and due to the progress towards elimination already made in the Americas and other regions. It would likely be cheaper than polio eradication and the failed malaria eradication effort. Factors that will make measles eradication more difficult include the high infectiousness of the virus, population growth and urbanization, and war and civil conflicts, including terrorism.

### **Discussion**

- Efforts should begin immediately in the countries where eradication will be most difficult, rather than leaving those countries until last, as occurred with previous eradication programs. Strengthening routine immunization should be a major component of these efforts.
- The high infectiousness of measles will require high routine immunization coverage. Efforts should be made to ensure that routine immunization programs are strengthened to the greatest extent possible before embarking on eradication.
- At least 10 years will be needed for measles eradication. We should avoid the lengthy delays that occurred at the beginning of most previous eradication programs. Significant financial and political commitments should be made before measles eradication is launched, although not all resources would be required beforehand.

### **Biologic Feasibility**

Dr. William Moss concluded that measles eradication is biologically feasible, because humans are the only reservoir, accurate diagnostic tests are available, and the measles vaccine is highly effective. His assessment was that human immunodeficiency virus (HIV) infections, waning immunity, and possible rare long-term shedders of measles virus RNA are not likely to present significant obstacles to eradication. A seroconversion study in Zambia found a more rapid decrease of measles antibodies after measles vaccination among HIV-infected versus noninfected infants. However, in the absence of antiretroviral therapy, these children do not constitute a sufficiently large cohort of susceptible individuals because of their high mortality rate. As highly active antiretroviral therapy (HAART) becomes more widespread, it may be necessary to revaccinate HIV-infected children against measles.

### **Discussion**

- No evidence currently exists to support the hypothesis that a single dose of high-titer measles vaccine given at 12 months of age achieves the same population immunity level as does a 2-dose standard regime. Because it may not be possible to obtain data on vaccine effectiveness in HIV-infected

children, consideration should be given to updating measles immunization policy to revaccinate children receiving HAART based on immunogenicity studies. The problem is made more complex because decreasing antibody titers do not necessarily mean loss of protection.

- The importance of the second opportunity for measles immunization through SIAs is both to immunize those who fail to respond to the first dose and to vaccinate those who missed the first dose.
- We do not have enough experience to say that measles vaccination confers life-long immunity, but the vaccine offers “long-lasting” immunity.
- The current window of opportunity to eradicate measles provided by the sizeable proportion of the population with natural immunity suggests that, with respect to eradication efforts, faster may be better. There is evidence that mothers with vaccine-induced immunity transfer less anti-measles virus antibodies through the placenta, and hence, their infants become susceptible at an earlier age, and uncertainty exists about the durability of measles vaccine-induced immunity, particularly among the elderly population.
- Additional research is required to better understand the reported nonspecific effects of measles vaccination on reducing childhood mortality.
- Measles virus, perhaps genetically modified, should not be discounted as a potential biological weapon in the post-eradication era.

### **Health Systems Impact**

Dr. Piya Hanvoragonchai concluded that the impact of measles activities on immunization and health systems in 6 study countries is mixed, based on a qualitative assessment. Overall, the benefits outweighed the negative impacts in Bangladesh, Brazil, Tajikistan, and Vietnam, but this was less apparent in resource-poor countries, such as Cameroon and Ethiopia, with multiple SIAs of different disease initiatives (including polio, yellow fever, and maternal and neonatal tetanus). Measles activities contributed to EPI strengthening, but no evidence of specific activities aimed at removing health care systems bottlenecks was reported. Benefits in some countries included staff development and training; strengthening of surveillance, cold chain, and logistics; improved data on target populations; and serving as a platform for delivery of other health interventions. Problems identified in some countries included interruption of health care services during SIAs, fragmentation of logistics and information systems, and reduced emphasis on strengthening routine immunization and health care systems. In addition, donor restrictions on financial support (earmarking of funds) was reported to undermine national governance capacity in resource allocation decision-making.

Dr. Ulla Griffiths recommended that measles eradication strengthen immunization and health care services by supporting

the Reaching Every District (RED) strategy, introduction of a second dose of measles vaccine through the routine system, and integration of measles activities with other child health interventions. She further encouraged donors to fund strengthening of routine systems and not just SIAs. She suggested that any eradication initiative needed to be held accountable for its impacts beyond the disease targeted for eradication (eg, its impact on immunization systems) and that a measles eradication initiative should seek to use indicators to track improvements in routine immunization services.

### **Discussion**

- Numerous studies have explored the potential impacts of disease eradication efforts on health care systems, and they generally concluded that targeting interventions in the right way can yield positive impacts.
- Steps should be taken before measles eradication is launched to ensure that strategies to strengthen routine immunizations and health care systems, particularly in countries with weak health care systems, are built into the eradication initiative.
- Specific indicators, such as RED indicators, should be measured as a critical component of evaluating progress towards measles eradication. Eradication staff must be held accountable for these indicators and not just for those for measles eradication. Measles eradication programs at all levels should be part of routine EPI programs. Separate vertical programs should be avoided if possible.
- Donors should avoid incentive payments for measles activities. Measles elimination plans should estimate the costs of the routine immunization program that directly relate to measles eradication.
- Part of debt relief money is for social services. This money should be used for building health services with evaluation of the health services in place to demonstrate the effect of this funding in yielding measurable health improvements.
- Measles eradication cannot fix the health care system, but we should ensure that eradication does not detrimentally affect the health care system.
- Specific efforts to support routine immunization services, including funding, have been made by the Measles Initiative, and this should be recognized.
- A measles eradication program should not be the sole program responsible for strengthening routine immunization services, because routine immunization depends on other partners, especially GAVI and national governments, which should also be held accountable.

### **Economic Analysis**

Dr. Alya Dabbagh introduced the session on economic analysis by indicating that 2 independent groups performed cost-effectiveness analyses using dynamic measles transmission models.



The groups focused on 6 selected countries and also provided global estimates. Both groups shared programmatic assumptions and primary data from the 6 countries, but they used different transmission models and applied some different costing methodologies. Both groups used the same 2 time horizons for the analysis, 2010–2030 and 2010–2050. The key questions for the economic analyses included:

- Is measles elimination cost-effective in 6 countries (Brazil, Colombia, Bangladesh, Ethiopia, Tajikistan, and Uganda), and is eradication cost-effective globally?
- How does eradication by 2020 compare with alternative goals?
- How much will it cost to eradicate measles?
- What are the impacts on cost and cost-effectiveness of (1) a 5-year delay, (2) inclusion of rubella-containing vaccine, and (3) several different post-eradication vaccination strategies?
- How does measles eradication compare with other public health interventions?

Dr. David Bishai reported the results of economic modeling by the Johns Hopkins Bloomberg School of Public Health. Measles elimination would be highly cost-effective in all 6 countries, but especially in low- and middle-income countries. Globally, measles eradication is cost-effective in all of the different income group countries. In countries that have already eliminated measles, measles eradication provides financial savings. Furthermore, health ministries around the world have few health investments that can parallel the disability-adjusted life-year (DALY) impact per dollar spent on measles eradication. Depending on the scenario adopted, the estimates suggested that eradicating measles would cost between \$7.7 and \$13.9 billion additional US\$ and avert between 465 and 488 million discounted DALYs between 2010 and 2050. Including rubella offered societal savings that equaled 50%–100% of the measles program, regardless of strategy. Measles eradication is cost-effective regardless of the post-eradication vaccination strategy used (eg, even if vaccination with 2 routine MCV doses plus SIAs continues after eradication has been certified).

Dr. Ann Levin, an independent health economics consultant, reported similar findings. Measles eradication would be cost-effective in all countries and globally and would be more cost-effective than measles mortality reduction and other health interventions. Eradicating measles by 2020 is projected to cost an additional discounted \$7.8 billion and avert a discounted 346 million DALYs between 2010 and 2050. If measles eradication were delayed to 2025, the projected costs would be higher and avert fewer DALYs, but eradication would still be cost-effective.

### **Discussion**

- Patterns and rates of importations have a large impact on the study results. In calculating cost-effectiveness, assumptions about importation represent a key factor and highlight the

importance of coordinated eradication efforts. If the WHO cannot get countries to coordinate efforts, then eradication is unlikely.

- The real world has a habit of not behaving exactly as predicted by mathematical models. Programmatic realities that may not be predicted by models include late release of funds, changes in age ranges for SIAs, unsynchronized SIAs, and decreased routine measles coverage.
- The 2 studies with different models came up with similar results, showing that eradication by 2020 will be cost-effective or highly cost-effective, and they both suggest that measles eradication represents a good investment.
- Economic analyses need to do a better job of capturing the full benefits of disease prevention, including greater participation and economic productivity of women due to less time spent caring for sick children and cost-saving associated with less funerals and mourning.
- Governments should not fool themselves that they save money by failing to treat a case of measles, because disease prevention has a real value.

### **Measles-containing Vaccine Supply**

Mr. Graeger Smith of Oliver Wyman addressed the question: if a 2020 eradication goal is set, will there be sufficient vaccine supply to meet the projected demand of measles containing vaccines (M, MR and MMR)? Based on expert consultations and subsequent analysis, he reported that projected near-term M, MR, and MMR vaccine capacity would be sufficient to meet the projected range of demand for a 2020 eradication goal. The primary supply risk is the concentration of production capacity, which poses risks to both supply certainty and long-term price stability. These risks might be mitigated by stockpiling inventory, entering into supply contracts, or developing new supply sources. The supply and demand situation is a dynamic process that could change in the future as suppliers modify their production capacity and respond to local and global changes in demand. Therefore, it is important that this analysis is revisited if an eradication target is set and specific risk mitigation measures are needed. Furthermore, it would be important to engage current and potential manufacturers, encouraging them to be active participants in the eradication process.

### **Discussion**

- GAVI is encouraging countries to introduce some relatively expensive new vaccines. Many countries need to introduce less costly rubella vaccine, which is considered for support by GAVI.
- For UNICEF, stockpiling means making funds available to purchase vaccines on short notice; the vaccines remain in the factory. Measles vaccine availability has not been an issue, and UNICEF continues to seek to bring more prequalified suppliers on board, which impacts price (ie, more suppliers means more competition).

### **Risk of Measles Reintroduction**

Dr. Ray Sanders explained the risks of reintroduction of measles virus after transmission is stopped. He characterized the risks from vaccine-derived virus, persistent infections, and non-human primates, and he noted that the risks qualitatively appear to be very low. Risks from laboratory-associated measles virus will require mitigation with proper containment procedures. A bioterrorism threat might not be very effective as long as population immunity is maintained.

#### **Discussion**

- Deciding to eradicate measles does not mean that countries will stop vaccination after eradication is certified. Many or most countries will continue to use measles-containing vaccines.
- Measles vaccine virus is different from polio vaccine viruses in that it does not appear to revert to a virulent form or circulate among vaccinated individuals.

### **Research Needs**

Dr. Amra Uzicanin discussed the need for research related to measles epidemiology, vaccine and immunization strategies, interactions with health care systems, diagnostics and surveillance, economics, and risk reduction in the post-certification era. Within these categories, she identified some important topics for research, including measles epidemiology and vaccine efficacy in different states in India; the role of <9-month-old babies, adolescents, and adults in measles transmission; the interaction between measles epidemiology and HIV/AIDS in areas of increasing HAART coverage; needle-free vaccination technology; and social behavior and social marketing.

#### **Discussion**

- Carefully designed serological surveys will be necessary to monitor the age spectrum of susceptibility to infection.
- Serological tests that distinguish between vaccine-derived and natural immunity would be useful.
- Research is needed about post-eradication communication, aerosol vaccines, and other technologies. Research activities need to be comprehensive, and the WHO should seek to develop a complete list of research areas and specific questions before prioritizing.
- Many countries appear to be stuck at 80% coverage, and drivers for achieving higher coverage need to be explored.
- We need to understand the effect on CRS (in terms of increasing risk and incidence) of rubella vaccination with low coverage. There is a burden of proof required prior to encouraging rubella vaccination in underperforming countries.

- Sociological research is very important to preempt negative societal reactions.
- More research is needed on adverse events and on methodology for strengthening AEFI monitoring.
- Although many important research questions were identified throughout the meeting and this session, a separate meeting dedicated to identifying critical research that is needed to achieve measles eradication should be conducted. During this meeting, research should be prioritized with respect to criticality for completion prior to setting an eradication target. The meeting should include explicit consideration of the reality that some research may become difficult or impossible as the number of areas with circulating measles decreases to zero and as laboratories must adopt additional containment measures.

### **CONCLUSION**

Prof. Durrheim, the meeting chair, requested a reading of the Draft Recommendations of the ad hoc Global Measles Advisory Group (see the Executive Summary) by the Rapporteur. These draft recommendations were generally well received. Prof. Durrheim provided closing comments and expressed gratitude to the participants for their valuable contributions. On behalf of the PAHO, Dr. Andrus expressed the sentiment that the meeting had met the set objectives, and he congratulated participants on their work and the outcome. Dr. Okwo-bele explained that the recommendations would be finalized and then forwarded to the WHO SAGE for recommendation and endorsement. He also expressed appreciation to all participants.

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