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Measles elimination and rubella control

Measles remains a significant cause of morbidity and mortality worldwide, with the South-East Asia Region accounting for about half of the estimated 158 000 global measles deaths in 2011. Measles and rubella can be eliminated, as shown by the WHO Region of the Americas. All other regions, except South-East Asia, have a measles elimination target and some regions have rubella elimination or control targets. Through a regional consultative process, Member States in the South-East Asia Region have agreed that measles elimination and rubella/congenital rubella syndrome (CRS) control are technically, biologically and programmatically feasible by 2020.

Measles and rubella elimination are defined as the absence of indigenous virus transmission in a geographical area (WHO Region/Member State) for at least 12 months in the presence of a well performing surveillance system.

The routine measles immunization coverage or measles-containing vaccine (MCV1) coverage of 79% in 2012, immunization provided through large supplementary campaigns, and improvement in surveillance backed by an accredited laboratory network have resulted in a 63% decline in the measles incidence rate and a 70% decline in measles deaths, India excluded. Seven Member States (and four union territories of India) offer rubella vaccine through routine immunization in combination with measles and/or mumps vaccine.

In 2012, Member States launched intensification of routine immunization in a drive to increase routine immunization coverage. Routine immunization is the foundation for achieving and sustaining measles elimination and rubella/CRS control. The stage is therefore set for the South-East Asia Region to adopt a measles elimination and rubella/CRS control target of 2020. The challenges that must be overcome are significant but well known, and are in various stages of being addressed. Political commitment and adequate financing, national and external, will lead to successful achievement of the target by 2020.

The High-Level Preparatory (HLP) Meeting held in the Regional Office in New Delhi, India, from 1 to 3 July 2013 reviewed the attached working paper and made the following recommendations:

Actions by Member States

- (1) To prepare national plans of action for measles elimination and rubella/CRS control by 2020 integrated into national immunization plans which should ensure that all children, including migrant children, the underserved, marginalized and unreached are included.
- (2) To strengthen the vaccine hub in the Region with WHO technical support for production of measles vaccines to ensure regional self-sufficiency.

Actions by WHO-SEARO

- (1) To develop, in consultation with Member States, a draft resolution on measles elimination and rubella/CRS control by 2020 for the consideration of the Sixty-sixth Session of the Regional Committee.
- (2) To conduct a regional workshop in September 2013 to agree on targets and surveillance standards for measles elimination and rubella/CRS control.
- (3) To provide technical support to Member States in the planning for achieving measles elimination and rubella/CRS control, including support for vaccine development and human resources training.

The working paper and the HLP Meeting recommendations are submitted to the Sixty-sixth Session of the Regional Committee for its consideration.

Introduction

1. Measles remains a significant cause of morbidity and mortality worldwide. Of the estimated 158 000 global measles deaths in 2011, around half occurred in the South-East Asia Region and India alone accounted for more than one third. The importance of measles prevention and control to the achievement of Millennium Development Goal (MDG) 4 is reflected in the key indicator of measles immunization coverage as a measure of progress towards this MDG.

2. Measles elimination is defined as interruption of indigenous measles virus transmission in a geographical area (WHO Region/Member State) for at least 12 months in the presence of a good performing surveillance system (Annex 2). A similar definition is applied to rubella elimination. Measles elimination in all the WHO regions would be equal to global measles eradication. As set in the regional targets, a >95% reduction in the rubella burden (compared to 2008 estimates) through the implementation of integrated measles elimination and rubella/CRS control strategies would constitute rubella/CRS control.

3. The strategies for measles and rubella elimination include: (i) 95% coverage with measles and rubella vaccination; (ii) case-based surveillance with adequate laboratory support; (iii) prevention of outbreaks; (iv) linkages with other child health interventions; and (v) increased public confidence and demand for immunization.

4. Measles and rubella/CRS can be eliminated. The WHO Region of the Americas eliminated indigenous measles in 2002 and rubella in 2010. The Western Pacific Region set a target for measles elimination by 2012, and 32 of 37 Member States are in the process of verifying the achievement of this target. The target year for the European and Eastern Mediterranean Regions is 2015, and for the African Region 2020. The European Region also has a rubella elimination target year of 2015 and the Western Pacific Region has a rubella control goal. The South-East Asia Region is the only region without a target year for measles elimination; nonetheless, three Member States may have eliminated measles and one Member State may have eliminated both measles and rubella.

5. A regional consultation in Delhi in August 2009 agreed on the technical, biological and programmatic feasibility of regional measles elimination by 2020. The Regional Committee in September 2009 encouraged Member States to accelerate measles mortality reduction strategies, and pursue measles elimination; it did not, however, establish a target year for measles elimination (SEA/RC62/R3). The World Health Assembly in 2010 endorsed a series of interim measles control targets for 2015. In September 2012, the Regional Committee decided that it would consider a measles elimination and rubella/CRS control goal for the Region at its Sixty-sixth Session in September 2013. A regional consultation in Kathmandu, in February 2013, reaffirmed the technical and programmatic feasibility of measles elimination and rubella/CRS in the Region by 2020 (Annex 1). The South-East Asia Region Immunization Technical Advisory Group (ITAG) endorsed this target at its meeting in April 2013.

Situation report

6. During 2000 to 2012, regional progress towards measles mortality reduction targets was noteworthy.

- Immunization coverage with the first dose of MCV1 increased from 61% to 79%. Six Member States now have coverage >95%, three have coverage >80% and two have coverage <80%. Nine Member States offer a second dose of measles immunization through routine immunization. Ten Member States conducted wide age-range measles immunization campaigns targeting measles susceptible populations, with Bhutan, Nepal and Sri Lanka conducting campaigns with combination measles and rubella vaccine, and Bangladesh planning to conduct a similar campaign in 2013. Of particular significance, India recently completed a measles immunization campaign targeting 139 million children aged 6 months to 10 years in 14 states and introduced a second dose of measles immunization through routine immunization in another 21 states.
- Surveillance for measles improved. Ten Member States now conduct case-based surveillance with >90% of outbreaks being investigated. With an average rate of 1.8 per 100 000 population, the Region is close to achieving the key surveillance performance indicator of at least 2 discarded non-measles cases per million population, although there was wide variation among the Member States. Surveillance was well supported by a regional network, comprising 23 WHO-accredited measles/rubella laboratories that can isolate virus and perform molecular analysis. Surveillance of rubella was, and continues to be, an integral part of measles surveillance.
- Seven Member States offer rubella vaccine through routine immunization in combination with measles and/or mumps vaccine. Four small states in India also offer rubella vaccine through routine immunization. While the magnitude of the burden of rubella/CRS is not fully known, measles surveillance has “unmasked” a substantial burden in the Region. Estimates indicate that as much as 47% of the global CRS burden is in the South-East Asia Region.
- Reported measles cases decreased by 55%, and the measles incidence rate declined by 63% from 69.9 to 25.0 per million population. There was a 70% decline in measles deaths, India excluded. This is expected to significantly increase once the impact of India’s recent measles campaign is factored in.

The case for measles elimination and rubella/CRS control in the South-East Asia Region

7. Measles and rubella can be eliminated, as demonstrated by the WHO Region of the Americas and the adoption of measles elimination and accelerated rubella/CRS control goals in other regions. Actions and requirements for the South-East Asia Region to adopt a measles elimination and rubella/CRS control target by 2020 are already in place, as follows.

- All Member States launched intensification of routine immunization in 2012 and are in the process of incorporating intensification components in their multi-year immunization plans. Routine immunization will be the key. While supplementary immunization campaigns will be required to prevent outbreaks, unlike polio eradication, these campaigns will be every 2–4 years with the vaccine being delivered through the routine immunization infrastructure.
- Measles and rubella surveillance is supported by a well-established, WHO-accredited regional laboratory network of 23 measles/rubella laboratories, which also have capacity for carrying out more sophisticated analysis such as genetic sequencing.
- The progress made in measles mortality reduction shows that the Region is on the correct trajectory, although it must be noted that unless substantial financial resources are made available, and unless the Region gets out of its “business as usual” mode, the World Health Assembly interim targets of 2015 are unlikely to be reached.
- Commitment from the Measles and Rubella Initiative and the GAVI Alliance will increase external funding for global measles and rubella/CRS efforts. However, in the absence of a measles elimination target, the Region is likely to miss out on its share as these funds will be more readily available to support regions that have elimination targets.
- Just as polio eradication was a “driver” for improving routine immunization, a measles elimination target will continue to “drive and lead” integrated interventions for better child and maternal health and thus contribute to achievement of relevant MDGs.
- The decision on an elimination target will be timely. Considerable effort is going into rejuvenating primary health care by strengthening the basic components of the Alma Ata primary health care framework to provide a package of quality interventions for women and children. Available health system strengthening funds from the GAVI Alliance provide an opportunity for this purpose.
- The Region has been polio-free for more than two and a half years and is on track to achieve polio-free certification by February 2014. The lessons learnt, infrastructure, and the know-how of polio eradication exist and are already being utilized for measles elimination. If the Region was able to eradicate polio, it can eliminate measles.
- Measles elimination is an opportunity for rubella elimination. Because rubella is less infectious than measles, if countries use combined measles-rubella vaccine, then when measles is eliminated, rubella and CRS will also be eliminated. The strategies for both go hand in hand. Rubella vaccine is highly effective (95% with one dose), safe (whether given singly or in combination) and affordable. The effectiveness of integrated measles and rubella/CRS elimination strategies has been amply demonstrated in other regions. Several Member States of the South-East Asia Region have already introduced the combined measles/rubella vaccine in their national immunization schedule with more likely to follow due to an increasing trend towards combination vaccine that is driven by market forces.

- The South-East Asia Region is also a significant global manufacturer of measles vaccine with >70% of the entire UNICEF global supply being sourced from the Region. With some effort, the potential for regional vaccine self-sufficiency exists.

Challenges

8. Once a measles elimination and rubella/CRS control target of 2020 is established, the challenges that the Region must address to achieve it are significant but well known. These challenges are listed below.

- **Securing political commitment:** the Regional Committee's engagement on measles elimination and rubella/CRS control is a sign of political commitment and recognition that measles elimination is an international partnership and requires the Region to show solidarity with neighbouring regions which are at advanced stages of measles elimination. It is also expected that governments will allocate national funds towards meeting their share of the costs.
- **Ensuring adequate funding:** current estimates show that about US\$ 803 million will be required for the Region to achieve measles elimination and rubella/CRS control by 2020 (Annex 1). These costs do not include the additional cost of increasing routine immunization coverage to levels >95%.
- **Establishing quality case-based surveillance for measles and rubella:** Member States have a measles and rubella surveillance system in place that can be strengthened. Surveillance for CRS is a bigger challenge and considerable work needs to be done in this area.
- **Ensuring an adequate supply of quality-assured vaccine:** the Region has a large vaccine-manufacturing base that can be utilized to ensure vaccine security.
- **Other issues:** large countries such as India and Indonesia have a range of challenges including population size and diversity, scale of operations, and issues of decentralization and decision-making.

Conclusions and recommendations

9. In conclusion, there is consensus among all Member States of the South-East Asia Region that measles elimination is technically, biologically and programmatically feasible by 2020. Member States also agree that measles elimination and rubella/CRS control must go hand in hand. Although they recognize that when measles is eliminated, rubella/CRS could also be eliminated, they feel that it may be a little early to adopt a rubella/CRS elimination target. There is agreement that the stage has been set for the Region to adopt a measles elimination and rubella/CRS control goal to be achieved by 2020.

Annex 1

Feasibility of measles elimination and accelerated rubella/CRS control in the South-East Asia Region

A. Background

Five of six WHO Regions have measles elimination goals with established target dates endorsed by their respective Regional Committees. The Western Pacific Region has a 2012 goal, the European and Eastern Mediterranean Regions have 2015 goals, and the Africa Region has a 2020 goal. The Region of the Americas has achieved both measles and rubella elimination.

In August 2009, a regional consultation on measles involving representatives from the 11 Member States of the South-East Asia Region agreed that measles elimination is technically feasible and an elimination goal should be set for the Region for 2020 or sooner. In late 2009, the WHO Regional Committee for South-East Asia passed a resolution that called for the elimination of measles from the Region, but a target year for elimination was not included.

Measles elimination activities present the opportunity to eliminate or accelerate the control of rubella and congenital rubella syndrome (CRS). All regions except the Africa Region and South-East Asia Region have called for the elimination or accelerated control of rubella/CRS.

Measles elimination and rubella/CRS control can only be achieved in the context of a strong routine immunization programme. In 2011, Health Ministers of the South-East Asia Region declared 2012 as the Year of Intensification of Routine Immunization. In 2012, all Member States implemented their action plan for intensification and agreed in a regional meeting in October 2012 that the intensification initiative would be developed into a national multi-year intensification plan. This is work in progress and is occurring at a time when the Region has eradicated polio. The lessons learnt from polio on ways to ensure universal coverage have been applied in the development of the intensification plan. These lessons will also be applicable to measles elimination efforts.

Immunization is one of the eight components of primary health care, which now receives a fresh lease of life with the launch of the Decade of Vaccines and the Global Vaccine Action Plan. Efforts in the South-East Asia Region to rejuvenate primary health care and financial support to countries from the GAVI Alliance for health systems strengthening to sustain high immunization coverage are, therefore, timely. These efforts have contributed to an environment that makes it feasible for the Region to accelerate the implementation of strategies to achieve measles elimination and rubella/CRS prevention and control.

B. Biological feasibility

Measles and rubella/CRS elimination are biologically feasible. These viruses infect only humans and no animal or environmental reservoirs exist. Clinically inapparent and subclinical measles infections are rare. Infection is easily confirmed or discarded through accurate, inexpensive serological tests. Genotypes of both viruses are stable and rarely mutate. A single vaccine prevents infections from all genotypes and is inexpensive. Two doses of measles vaccine (MCV) confer 99% immunity and a single dose of rubella vaccine (RCV) confers 95% immunity. Both immunity to natural infection and vaccine-induced immunity are likely to be lifelong.

Immunosuppression secondary to HIV infection represents a potential biological challenge to measles and rubella/CRS elimination. Vaccinated persons not on highly active anti-retroviral therapy (HAART) may experience waning post-vaccination immunity. Moreover, persons with impaired cell-mediated immunity due to HIV-infection may not present with the characteristic rash following measles infection, thereby delaying case detection. However, experience in sub-Saharan Africa suggests that measles virus transmission may be interrupted after supplementary immunization activities (SIAs) in countries highly endemic for HIV.¹ Additionally, persons on HAART therapy are less likely to become susceptible to measles after vaccination or revaccination.

C. Technical feasibility

Measles and rubella have herd immunity thresholds of 92–94% and 83–85%, respectively,² although large countries may have a higher herd immunity threshold and therefore find elimination more difficult. Nevertheless, it is technically feasible to interrupt measles and rubella virus transmission provided sufficient levels of population immunity are obtained.

WHO-recommended strategies to eliminate measles and rubella/CRS include: (1) achieving high immunization coverage through routine immunization and, when needed, SIAs; (2) utilizing sensitive and timely case-based measles/rubella and CRS surveillance to identify and respond to residual areas of viral transmission; and (3) maintaining an accredited laboratory network capable of confirming or discarding suspected cases and identifying and characterizing measles and rubella virus.

Over a decade of success using these strategies has demonstrated that it is technically feasible to achieve and maintain measles and rubella elimination. The Region of the Americas has remained measles-free since 2002 despite multiple importations from endemic countries outside the Region every year. The Western Pacific Region has likely interrupted endemic measles virus transmission in 32 of 37 Member States. Immunization coverage and surveillance data suggest that measles may have already been eliminated in 4 of 11 Member States of the South-East Asia Region.

¹Moss WJ, Strebel P. Biological feasibility of measles eradication. *J Infect Dis.* Jul 2011; 204 Suppl 1: S47–53.

²Fine PEM, Mulholland K. Community immunity [in Plotkin S, Orenstein W, Offit P, eds. *Vaccines: Fifth Edition.* 2008]; chapter 71, pp. 1573–92.

Challenges to measles elimination include vaccinating the traditionally hard-to-reach populations (e.g. urban slum dwellers, ethnic minorities, migrants) and children in hard-to-reach areas (e.g. remote villages, conflict areas, border regions). Such challenges are not new and have been successfully addressed by many countries in eliminating both polio and measles.

A potential challenge appears to be that of occurrence of measles and rubella in adults. Adults born during the era of MCV and RCV introduction may be less likely than their predecessors to have natural immunity due to decreased virus circulation and exposure. They also are less likely than those born after them to have been vaccinated. With measles vaccine effectiveness of around 85%, 15% of the birth cohort could remain susceptible to measles into adulthood. This would be less of an issue with rubella, a vaccine that has 95% effectiveness. Nonetheless, in most countries the measles incidence in adults is usually low and few countries have seroprevalence data showing a decrease in immunity against measles in adults.

RCV has been introduced only recently in the South-East Asia Region, in 6 of 11 Member States. Therefore, the susceptible populations are expected to reside primarily among children and adolescents. In this scenario, nationwide age-range targeted SIAs could effectively eliminate rubella virus transmission. To prevent CRS, it is reasonable to additionally target childbearing age women with RCV at appropriate opportunities until rubella is eliminated.

D. Programmatic (operational) feasibility

Strategic and operational progress

Progress and capacity

During the past decade, the South-East Asia Region has made significant improvements in immunization coverage, case-based measles and rubella surveillance, establishing a regional laboratory network, and in outbreak preparedness. The success in implementing these strategies serves as strong evidence for the operational feasibility of measles elimination and rubella/CRS control among the Member States of the Region.

For example, routine coverage with MCV1 has increased from 61% in 2000 to 79% in 2012, and 6 of 11 Member States reported routine MCV1 coverage $\geq 95\%$, 3 countries reported $>80\%$, and India and Timor-Leste reported $<80\%$ coverage. Nine of 11 Member States have incorporated a second dose of MCV (MCV2) into their routine programmes. Ten of 11 Member States have conducted wide-age range SIAs that have reached previously unreached children with two doses of MCV. Eight Member States have conducted follow-up SIAs to reach susceptible children after a prior SIA.

Currently, seven Member States offer rubella vaccine through routine immunization in combination with measles and/or mumps vaccine (MMR). Four small states in India (Delhi, Goa, Puducherry and Sikkim) also offer rubella vaccine through routine immunization. Of the Member States not using RCV, those that are GAVI-eligible have the opportunity to apply for RCV introduction starting with a national wide-age range SIA.

Surveillance capabilities and performance have improved considerably over the past decade. All Member States except India currently conduct case-based surveillance for measles and rubella in health facilities; all Member States conduct case-based surveillance in the setting of outbreaks. Among Member States conducting case-based surveillance in health facilities, the discarded measles rate was 3.3 per 100 000 population in 2011 (target ≥ 2 per 100 000).

Surveillance for CRS within the South-East Asia Region is routinely conducted only in Sri Lanka. However, special studies have been successfully conducted in other Member States including India, the Maldives, Myanmar and Nepal. Additionally, many Member States in the Region have conducted seroprevalence studies to identify susceptibility in women of childbearing age.

The Region's Measles and Rubella Laboratory Network is part of the greater Global Network technically managed by WHO. The network will be crucial in improving the sensitivity and timeliness of case-based measles and rubella surveillance, to rapidly identify and eliminate foci of transmission of measles and rubella viruses in order to accurately measure incidence and determine source of virus. The network has grown to include a total of 23 laboratories (20 WHO-accredited) with at least one national measles laboratory (NML) in each of the Member States and with 3 regional reference laboratories (RRL). Fifteen of the 23 laboratories are capable of virus isolation and genetic sequencing. Thailand has also established a network of 14 subnational measles laboratories guided by the RRL in Bangkok. Twenty of the NMLs are WHO-accredited.

The NMLs and RRLs share serologic data on a weekly or monthly basis with the Regional Office. The Regional Measles and Rubella Laboratory Network tested 17 704 specimens for measles and/or rubella in 2011. To meet a target discarded measles rate of 2 per 100 000 population, the laboratory network will need to evaluate at least 37 500 specimens per year in the absence of measles virus transmission. The network is capable of meeting and exceeding this goal.

More than 1000 suspected measles or rubella outbreaks were reported and investigated in eight Member States during 2011, demonstrating robust outbreak preparedness and response capacity. Among 551 confirmed outbreaks, 15 628 cases were identified. Though few specimens were collected for virus detection in these outbreaks, extensive training in nasopharyngeal swab collection was conducted during the 2009–2010 H1N1 influenza pandemic; therefore, Member States are likely to have the capacity to collect such specimens. The number of measles and rubella outbreaks in the Region decreased to 225 and 151, respectively, in 2012.

The feasibility of measles elimination and rubella/CRS control is strengthened by WHO human resource support to the Region (currently in five Member States: Bangladesh, India, Indonesia, Myanmar and Nepal). In 2011, over 1400 persons were either contracted or given additional financial support to provide technical and operational assistance to maintain polio-free status and address other immunization initiatives in the Region. This support was critical to achieving polio-free status, and continued support may be crucial to achieving measles elimination and rubella/CRS prevention. However, with decline in polio funding, there is a challenge to continued support for measles/rubella surveillance and vaccine-preventable disease surveillance in general.

Reduction of mortality and disease burden

Measles

The strategic and operational progress over the past decade has resulted in a 70% reduction in the estimated number of measles deaths from 2000–2011 among all countries in the Region except India (36% reduction), which did not begin to conduct measles SIAs until 2010. Between 2000 and 2012, the number of measles cases (including India) as reported in the WHO/UNICEF Joint Reporting Form (JRF) decreased by 55% from 106 419 to 46 945 cases and the measles incidence rate declined by 63% from 69.9 to 25 per million population. The actual decrease in cases is likely to be greater, as measles and rubella surveillance and case detection has improved considerably since 2000.

In 2012, Bhutan, the Democratic People's Republic of Korea, Maldives and Sri Lanka reported very few measles cases and, given the high two-dose immunization coverage in these countries, may have eliminated measles. Member States reporting the most cases included India (18 668), Indonesia (15 489), Thailand (5197), Nepal (3362), Myanmar (2175) and Bangladesh (1986).

The known genotypes currently in circulation are D5 in Myanmar and Thailand, D8 in Bangladesh, India and Nepal, and D9 in Indonesia and Myanmar. In addition, D4 (commonly associated with Europe) has been identified in India and Nepal, D7 in India, G2 in Indonesia and Thailand, and G3 in Indonesia and H1 in the Democratic People's Republic of Korea. It is important to note that specimens for virus detection are collected rarely during measles and rubella outbreaks and the actual genotype distribution remains to be determined.

Rubella

Reporting of rubella in the Region started in 2004 with 1231 cases reported that year. In 2009, the Region reported 17 208 which declined to 6664 cases in 2012. Bangladesh reported 3245, India 1025, Indonesia 1020, Nepal 801 and Thailand 487 cases. The remaining countries did not report rubella.

Achieving measles elimination by 2020 and preventing rubella/CRS

The progress and impacts show that the South-East Asia Region is closer to its measles mortality reduction goal and prepared to engage in measles elimination and rubella/CRS control. As noted above, 4 of 11 Member States (Bhutan, Democratic People's Republic of Korea, Maldives and Sri Lanka) may have already achieved measles elimination. In order to achieve elimination and sustain elimination against the threat of importations, all Member States need to maintain high levels of routine coverage and well-performing measles surveillance that includes a thorough investigation of all cases with specimen collection for virus detection and extensive contact tracing to determine the source of infection as imported, import-related or endemic.

The initiatives to intensify routine immunization in 2012 need to continue so that MCV1 and MCV2 coverage further increases toward elimination levels ($\geq 95\%$) in all Member States. Countries which have not yet done so may wish to introduce MCV2, and countries that provide

MCV2 in late childhood (i.e. Indonesia and Thailand) may wish to adjust their MCV2 schedules so that MCV2 is administered during the second year of life in accordance with WHO recommendations.³ School entry (both pre-school and primary school) should be used to verify or provide missing doses of vaccine. RCV should be included as either MR or MMR in the Democratic People's Republic of Korea, India, Indonesia and Myanmar. School entry (both pre-school and primary school) is a valuable opportunity to review immunization status and should be used to verify or provide missing doses of vaccine.

Depending on the evidence and context, Member States who have not introduced RCV may wish to include this as either MR or MMR. The current cost of vaccine per dose is US\$ 0.243 for measles, US\$ 0.513 for MR and US\$ 0.900 to US\$ 1.950 for MMR. The shortage of DTP experienced by some Member States in the Region in recent years indicates that market forces may result in an increasing supply of MR and MMR vaccines, as compared to stand-alone measles vaccine.

All Member States need to monitor immunization coverage and surveillance performance to define population immunity and identify and or predict susceptible populations. SIAs will generally be required to address immunity gaps in susceptible populations and the need for subsequent follow-up SIAs in a country would be guided by the gaps in population immunity.

For example, Bangladesh has experienced ongoing transmission of measles virus in 2011–2012 despite a follow-up SIA conducted in 2010. In 2011, 43% of cases were <5 years old and another 43% were 5–14 years old. Bangladesh will use GAVI funding to conduct a “catch-up” MR SIA for children and adolescents aged 9 months to 14 years in September 2013; if high coverage is achieved uniformly throughout the country, both measles and rubella virus transmission should be interrupted.

Indonesia has experienced persistent measles virus transmission despite its rolling follow-up SIAs from 2007–2011. Similar to Bangladesh, 46% of cases were <5 years old and 51% were 5–14 years old in 2011. A high-quality catch-up MR SIA during 2014 targeting an estimated 64.4 million children and adolescents aged 9 months to 14 years in a more concentrated manner (e.g. over several months) should interrupt measles virus transmission and quite possibly eliminate rubella virus transmission.

India has made good progress with its measles mortality reduction strategies. WHO/UNICEF estimates of routine MCV1 coverage increased from 55% in 2000 to 74% in 2012. Routine MCV2 was introduced in Delhi in 1999, Puducherry in 2006, Goa in 2008 and Sikkim in 2009. All other states and union territories are currently introducing MCV2 into the routine schedule for children aged 16–24 months. Measles SIAs conducted in three phases during 2010–2013 targeted 139 million children aged 9 months to 10 years in 14 states believed to have the lowest MCV1 coverage in India. Nine of these completed their SIAs in 2012, with administratively reported coverage ranging from 74–92%. Measles outbreak surveillance with collection of case-based data began in three southern states in 2006 and has expanded to include a total of 14 states in 2013. A measles laboratory network within India has grown to include 10 laboratories in different states and union territories, including two reference laboratories in Chennai and Pune.

³WHO. Measles vaccines: WHO position paper. Weekly Epid Rec 2009; 84:349–60

To achieve measles elimination, India will need to establish case-based surveillance for any suspected measles and rubella case in every state and address immunity gaps. In India, repeated coverage surveys conducted nationwide between 1990–2011 through representative sampling, the National Family Health Survey conducted in 2005–2006, District-level Household Survey by the government in 2007–2008 and seven UNICEF-administered coverage evaluation surveys from 1998–2009 consistently show that administrative MCV1 coverage is often >10% higher than the actual coverage by survey.

Available outbreak surveillance data from 2011 indicate that among the 10 308 cases reported from 11 states, 7% were aged <1 year, 41% were 1–4 years, 36% were 5–9 years, 12% were 10–14 years, 4% were 15 years and older. India's plan to provide a second dose of measles vaccine during the second year of life will increase protection among children previously vaccinated at 9 months of age from approximately 85% to 95%, thereby increasing population immunity among those vaccinated with two doses. However, a state-by-state analysis of administrative and survey routine MCV1 coverage from 1990–2011, supplementary immunization coverage data, and available surveillance data suggests that there are significant gaps in population immunity in most states and union territories which will likely require SIAs targeting the appropriate age-groups and perhaps up to 14 years of age. Therefore, unless tailored strategies for reaching previously unreached children and adolescents are implemented, existing immunity gaps will remain and numbers of susceptible children will accumulate annually.

Myanmar conducted its last follow-up SIA in 2012, targeting children aged 9–59 months. However, among cases in 2011, 27% were <5 years old and 55% were 5–14 years old. Myanmar could apply to GAVI for funding so that an MR SIA in 2015, targeting the 9 months to 14 years age group, could interrupt measles and quite possibly rubella virus transmission.

Nepal concluded a catch-up MR SIA in 2012–2013. To continue high levels of population immunity, Nepal may wish to introduce MCV2 and plan for a follow-up SIA in 2015–2016 if analysis of population susceptibility warrants this.

Thailand has reported high MCV1 and MCV2 coverage for nearly a decade. However, MCV2 is given at 6 years of age, allowing for a constant large pool of susceptible children aged 1–5 years that either were not vaccinated with MCV1 at 9 months of age or who were vaccinated but did not seroconvert. In 2012, among 4 854 cases reported through October, 33% were aged <5 years, 16% were 5–9 years, 8% were 10–14 years, 23% were 15–24 years and 13% were 25–34 years. The age distribution of cases raises concern regarding susceptibility among adults. If good data are available on adult cases and if seroprevalence data are available, Thailand has the opportunity of modelling alternative measles control strategies targeting appropriate sections of the population to achieve elimination.

Timor-Leste has low routine MCV1 coverage (62% in 2011) but reported 92% coverage in a nationwide catch-up SIA in 2011 following an outbreak that affected 763 children, many of which were 5–14 years old. The SIA appears to have interrupted transmission, as only 16 laboratory confirmed cases were reported in 2012. Unless the situation with Timor-Leste's low routine MCV1 coverage improves, more frequent SIAs may be required to prevent the rapid accumulation of susceptible children.

Case-based measles surveillance for all suspected measles and rubella cases should be conducted to identify and characterize areas with residual measles or rubella virus transmission. High-quality case investigations with contact tracing and collection of specimens for virus detection should be the norm so that the source of infection may be identified as imported, import-related or endemic. Standard indicators to monitor surveillance performance have been recommended by WHO⁴ and should be adopted nationally (to monitor subnational surveillance performance) and by the Region (to monitor national surveillance performance). Support staff that focuses currently on maintaining the polio-free status in several Member States likely will be needed to ensure high-quality measles, rubella/CRS surveillance.

The laboratory network is adequate and prepared to handle the increased number of specimens expected as surveillance improves. Care should be taken to avoid the further inclusion of a large number of subnational laboratories when the number of expected specimens per week is manageable by a national laboratory. Additional laboratories incur additional costs, increased kit wastage, and require quality assurance monitoring. Collection of specimens for virus detection is critical to help determine the source of infection and transmission patterns and should be encouraged in all Member States.

Outbreak preparedness and rapid response will be important to eliminate any residual areas of virus transmission. Countries will need to have budgeted plans in place following future SIAs. Outbreak response immunization (ORI) will be needed to eliminate residual areas of endemic or import-related measles and rubella virus transmission in the final years of elimination.

Social mobilization and communication will be critical factors for success of measles elimination and rubella/CRS control to ensure acceptance by the public and by health staff, and to generate demand for services.

Programmatic and operational research may be useful to identify better and more efficient ways to prevent measles and rubella transmission.

E. Financial feasibility

Projected costs

Total estimated costs to eliminate measles and prevent rubella/CRS for the Region by cost category and year are summarized in Table 1. Estimated costs during 2013–2020 are based on assumptions regarding the need for SIAs, ORI, and measles and rubella surveillance including laboratory support in every country of the Region. These costs do not include current costs for SIAs in India that are being completed in 2013, and also assume that India and Indonesia will conduct future SIAs and ORI using MR.

⁴WHO. Monitoring progress towards measles elimination. *Weekly Epid Rec* 2010; 85:490–5

Table 1: Summary of estimated costs to eliminate measles and prevent rubella/CRS, South-East Asia Region 2013–2020 (amount in US\$)

2012–2015	2013	2014	2015	Total
SIA	62 708 959	121 463 489	196 918 757	381 091 204
Outbreak response	0	0	0	0
MR surveillance	14 191 491	14 275 401	21 208 767	49 675 659
CRS surveillance	160 000	192 000	230 400	582 400
Communication	50 000	50 000	50 000	150 000
Research	50 000	50 000	50 000	150 000
Technical support	50 000	50 000	150 000	250 000
Verification	0	200 000	100 000	300 000
Total	77 210 450	136 280 890	218 707 924	432 199 263

2016–2020	2016	2017	2018	2019	2020	Total
SIA	41 408 263	305 091	68 056 778	51 736 846	30 180 143	191 687 122
Outbreak response	2 585 761	3 721 898	3 803 613	6 064 527	9 838 730	26 014 530
MR surveillance	20 159 351	27 129 298	34 018 336	34 339 400	34 188 736	149 835 121
CRS surveillance	276 480	331 776	398 131	477 757	573 309	2 057 454
Communication	50 000	50 000	50 000	50 000	50 000	250 000
Research	50 000	50 000	50 000	50 000	50 000	250 000
Technical support	50 000	0	100 000	100 000	100 000	350 000
Verification	50 000	50 000	50 000	100 000	200 000	450 000
Total	64 629 856	31 638 064	106 526 858	92 918 530	75 180 919	370 894 227

Summary	2013–2015	2016–2020	2013–2020
SIA	381 091 204	191 687 122	572 778 327
Outbreak response	0	26 014 530	26 014 530
MR surveillance	49 675 659	149 835 121	199 510 780
CRS surveillance	582 400	2 057 454	2 639 854
Communication	150 000	250 000	400 000
Research	150 000	250 000	400 000
Technical support	250 000	350 000	600 000
Verification	300 000	450 000	750 000
Total	432 199 263	370 894 227	803 093 490

Total costs are estimated to be US\$ 803.1 million, of which US\$ 572.8 million (71%) is for SIAs, US\$ 199.5 million (25%) is for MR surveillance including laboratory support, and US\$ 26.0 million (3%) is for ORI. Costs for the other budget components are estimated to be US\$ 4.8 million (1%). These estimates do not include direct support to strengthen routine immunization services. Detailed budget breakdowns and methodologies are provided in the strategic plan.

Financing

Eliminating measles from the Region will have substantial health and economic benefits for all countries. These benefits need to be brought out and used to build country commitment and a multi-year financing mechanism. Country ownership is essential to ensure that whatever activities are required to achieve the goal are provided adequate human, material and financial resources. Existing external financial support structures (e.g. MRI, GAVI and pandemic preparedness resources) may be useful, especially in regard to fulfilling common objectives of strengthening health and immunization services and improving the surveillance infrastructure.

GAVI is expected to finance approximately US\$ 79.1 million for catch-up SIAs in Bangladesh (2013), Myanmar (2015) and Timor-Leste (2015). This accounts for approximately 14% of the total SIA cost of US\$ 572.8 million. Additional funding for priority countries and areas with relatively limited economic resources such as Bangladesh, Myanmar, Nepal and Timor-Leste will be needed to help finance special interventions for measles elimination and prevention of rubella/CRS, such as follow-up SIAs and surveillance. The Measles Rubella Initiative (MRI) and its core partners the American Red Cross, United Nations Foundation, UNICEF, United States Centers for Disease Control and Prevention, and WHO, also will continue to contribute both financial and technical support. Efforts to expand the donor-partner landscape are needed to complement government contributions. In addition to immunization activities, additional resources will be required to improve sensitivity and timeliness of case-based measles surveillance and the measles laboratory network so that foci of residual or new transmission of measles virus are quickly identified and eliminated, incidence is accurately measured, source of virus as imported, import-related or endemic is accurately determined and standard indicator targets of surveillance performance are achieved.

While efforts are made to increase partner support, Member States must be prepared to shoulder much of the costs required to eliminate measles and prevent rubella/CRS by 2020. Trends in national economic indicators suggest that countries are increasingly able to finance proposed measles elimination and rubella/CRS prevention activities.

F. Using measles elimination to achieve MDG 4 and strengthen immunization and health systems

An investment in measles elimination provides multiple benefits to child survival in addition to decreased morbidity and mortality from measles. The WHO/UNICEF Regional Child Survival Strategy: accelerated and sustained action towards MDG 4 identifies measles immunization coverage as one of the core indicators to track progress in child survival, and integrated management of childhood illness protocols seek to utilize opportunities to provide MCV and

other vaccines to children presenting to health facilities. Measles elimination contributes to achieving MDG 4: "Reduce by two-thirds, between 1990 and 2015, the under-five mortality rate." One of the three indicators for monitoring progress towards achieving MDG 4 is the "proportion of 1-year-old children immunized against measles."

Benefits provided by measles elimination are many. First, prevention of measles infection prevents the increased susceptibility to and mortality from pneumonia and diarrhoea that lasts for months following infection. At a global level, diarrhoea and pneumonia cause 36% of deaths among children aged under 5 years. Second, the need to achieve 95% coverage with two doses of MCV requires programme managers at every level to re-focus efforts on strengthening routine immunization service coverage and quality using strategies recommended in the Global Vaccine Action Plan. Third, measles and rubella SIAs can and should be used to strengthen routine immunization services by identifying and developing strategies for reaching high-risk areas and populations, strengthening vaccine and cold chain management, providing additional training on important immunization and health system components, including routine immunization monitoring together with SIA coverage monitoring, and other areas. Fourth, administering a second dose of measles vaccine at 15–24 months of age creates a platform for other interventions such as DTP4, OPV4, vitamin A, de-worming medicine, and growth monitoring. Fifth, provision of nutritional supplements such as vitamin A with routine MCV1 and during SIAs provides additional protection of children against disease. Sixth, establishing school entry requirements provides an opportunity to ensure fully immunized status of children with all antigens, decreases child absenteeism from school and parental absenteeism from work, and strengthens collaboration between health and education ministries, establishing relationships that will help promote school health overall. Finally, use of standardized monitoring indicators and requirements to report, analyse, interpret and feed back data builds capacity to strengthen monitoring and surveillance systems and data management overall, thereby strengthening health systems.

In conclusion, over the next eight years, the South-East Asia Region has a unique opportunity to establish and achieve elimination of measles combined with prevention of rubella/CRS, which will not only have direct health and financial benefits but also serve to strengthen national immunization and disease surveillance systems.

31 May 2013

Annex 2

Measles elimination and rubella/CRS control, South-East Asia Region, 2020 (proposed targets)

	2010 ⁵	2015	2020
Disease burden reduction targets			
Measles	Reduce measles mortality by 90% compared to 2000 estimates	<ul style="list-style-type: none"> Reduce measles incidence to <5 cases per million population Reduce measles mortality by 95%, compared to 2000 estimates 	<ul style="list-style-type: none"> Absence of endemic measles transmission for ≥ 12 months in a defined geographical area (e.g. region or country) in the presence of well performing surveillance system '0' [zero] mortality due to measles
Rubella/CRS	No target set	50% reduction in rubella/CRS cases compared to 2008 estimates ⁶	>95% reduction in rubella/CRS cases compared to 2008 estimates
Immunization targets			
First routine dose of measles and rubella vaccine	At least 90% coverage at national level and 80% at the district level with measles vaccine	At least 90% coverage at national level and 80% at the district level with a first dose of measles and rubella vaccines	>95% coverage both at the national and district level with a first dose of measles and rubella vaccines
Second routine dose of measles and rubella vaccine	Measles immunization to eligible children in all Member States ensuring >90% coverage	At least 90% coverage at national level and 80% at the district level with a second dose of measles and rubella vaccines	>95% coverage at national and district level with a second dose of measles and rubella vaccines
Surveillance targets			
Measles and rubella	No target set	<ul style="list-style-type: none"> Achieve reporting rate of discarded non-measles cases of ≥ 2 per 100 000 population per year nationally Achieve at least 80% of suspected measles cases tested for measles and rubella in a proficient laboratory 	<ul style="list-style-type: none"> Achieve reporting rate of discarded non-measles non-rubella cases of >2 per 100 000 population per year nationally Achieve 100% of suspected measles cases tested for measles and rubella in a proficient laboratory
Suspected measles outbreak Investigation	All outbreaks fully investigated ⁷ (100%)	All outbreaks fully investigated (100%)	Even single measles case will be considered as an outbreak and investigated

⁵ In 2010, there was only measles mortality target.

⁶ 2008 estimate for CRS burden: South-East Asia 52 643 (Unpublished, Adems E. Vynnycky E).

⁷ Measles outbreak is fully investigated if: a) a house-to-house survey is conducted in the affected area; b) At least five suspected cases are serologically tested for measles/rubella IgM; and c) case investigation form or line list with basic epidemiologic data-geographic location, age, vaccination status for measles, date of last vaccination, date of rash onset and outcome of illness is compared.