Plan of Action for the Documentation and Verification of Measles, Rubella, and Congenital Rubella Syndrome Elimination in the Region of the Americas



Comprehensive Family Immunization Family and Community Health Area

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TAG endorses this Regional Plan of Action for the documentation and verification of measles, rubella, and CRS elimination in the Region of the Americas. The Plan of Action provides an opportunity to place immunization programs as a high-ranking priority on the political agenda of countries as well as strengthen vaccination activities and surveillance systems.

INTRODUCTION

After the global eradication of smallpox in 1979 and the certification of polio eradication in the Americas in 1994, the Region adopted the goal of measles elimination in 1994. The measles elimination goal, to be achieved by 2000, was supported by Resolutions CSP24.R16 (1994), CD38.R6 (1995), and CE118.R14 (1996). Subsequently in 2003 the Directing Council of the Pan American Health Organization/World Health Organization (PAHO/WHO) adopted Resolution CD44.R1 urging countries to eliminate rubella and congenital rubella syndrome (CRS) by 2010. Through the implementation of measles and rubella elimination strategies—recommended by PAHO/WHO,—the interruption of endemic measles virus was achieved in 2002, while the circulation of endemic rubella virus was interrupted in 2009.

After having considered and noted with great satisfaction the tremendous progress in the interruption of endemic rubella virus transmission and recognizing that considerable efforts are required to strengthen and expand partnerships between public and private sectors, the 27th Pan American Sanitary Conference, during its 59th Session of the Regional Committee, adopted Resolution CSP27.R2 in 2007. The Resolution urged PAHO/WHO Member States to begin the process of documentation and verification of the interruption of endemic measles and rubella virus transmission in the Americas. To this end, PAHO/WHO developed this Plan of Action.

The Plan of Action for the documentation and verification of measles, rubella, and CRS elimination was presented in 2009 at the XVIII Meeting of the Technical Advisory Group (TAG) on Vaccine-preventable Diseases for their recommendations. This Plan will guide countries and their national commissions in preparing and providing the necessary evidence to verify that endemic measles and rubella virus transmission has been interrupted based on valid, complete, representative, and consistent data.

The Plan of Action is a "living" document, which must remain flexible to adapt to country realities while also establishing common criteria for documenting and verifying elimination. As the Region of the Americas continues to gain experience in the elimination of vaccine-preventable diseases, the Plan of Action will be updated accordingly.

In addition, PAHO has developed a set of tools to support the documentation of the data required for the verification of measles, rubella, and CRS elimination. These tools are available to the countries of the Region upon request.

1. BACKGROUND

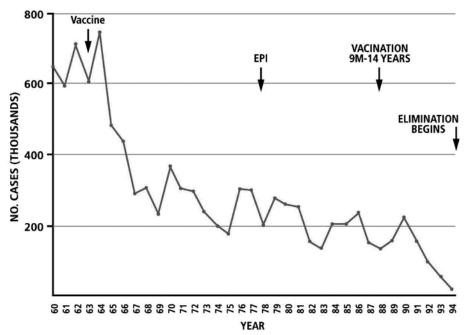
1.1 Burden of Measles, Rubella, and Congenital Rubella Syndrome

Measles and rubella are both viral diseases traditionally regarded as childhood illnesses. Measles is caused by a virus of the genus *Morbillivirus* from the *Paramyxoviridae* family. Rubella is caused by a virus of the genus *Rubivirus* from the *Togaviridae* family. Both diseases are transmitted primarily by infected people during the period of communicability through respiratory droplets or airborne spray to mucous membranes of the upper respiratory tract.

Although the two illnesses present epidemiological similarities in their modes of transmission, there are distinct differences in the burden of disease. According to the World Health Organization (WHO) data, in 1980, prior to the introduction of the vaccine, approximately 2.6 million measles deaths occurred globally due to this disease (1). In the early 2000s, nearly 40 million cases and 733,000 deaths occurred each year, half of which were in Africa (2). During the period of 2000-2008, as a result of immunization activities measles mortality diminished to approximately 164,000 deaths worldwide (a reduction of 78%), which represents 12.7 million deaths prevented during this period (1).

In the Americas more than 600,000 measles cases were reported annually in the early 1960s (3). The introduction of the measles vaccine in the 1960s and the creation of the Expanded Program on Immunization (EPI) in 1977 marked a decrease in the number of reported cases. Between 1982 and 1989 the average number of reported cases was 178,000 per year and the number of deaths was 52,000 (4).

FIGURE 1. NUMBER OF REPORTED MEASLES CASES, REGION OF THE AMERICAS, 1960-1994



Source: Country reports to PAHO/WHO

Rubella, on the other hand, is generally considered a mild rash illness with up to 50% being asymptomatic. However, if a pregnant woman contracts rubella during the first trimester of pregnancy, congenital rubella syndrome (CRS) may occur. In 1996, it was estimated that approximately 110,000 children were born with CRS in developing countries annually (5). Before wide-scale rubella vaccination, it was estimated that 16,000 CRS cases occurred annually (6) and that more than 20,000 children affected by CRS (7) were born each year in Latin America and the Caribbean.

The most concerning effects of rubella occur when the disease is contracted during the early stages of pregnancy. Three studies conducted by Grillner (1969), Peckman (1972), and Miller (1982) indicated that the increased risk of birth defects associated with maternal rubella infection occurs during the first 12 weeks of pregnancy. Furthermore, in one study, 85% (8) of pregnant women with a confirmed rubella diagnosis during the first trimester gave birth to infants with congenital malformations characteristic of CRS. The incidence of fetal disease declines after the first trimester. Several ocular and cardiac problems, as well as deafness, are usually derived from early infection (through the 8th week of gestation). Deafness, however, can result from later infections (up to the 20th week of gestation). Deafness is often diagnosed after 2 years of age (5,8).

With the strengthening of measles surveillance in the early 1990s, the rubella disease burden was evident; approximately 130,653 cases were reported in 1998 (Figure 2).

FIGURE 2. GEOGRAPHICAL DISTRIBUTION OF REPORTED RUBELLA CASES IN THE AMERICAS, 1998



Rubella Cases:130,586

1 dot = 1 case

Source: Country reports to PAHO/WHO

1.2 ELIMINATION INITIATIVES

1.2.1 DEFINITIONS OF ELIMINATION

Measles

Measles elimination in the Americas is defined as:

Interruption of endemic measles virus transmission in all the countries of the Americas for a period greater than or equal to 12 months, in the presence of high-quality surveillance.

Rubella

Rubella elimination in the Americas is defined as:

Interruption of endemic rubella virus transmission in all the countries of the Americas for a period greater than or equal to 12 months without the occurrence of CRS cases associated with endemic transmission, in the presence of high-quality surveillance.

1.2.2 Elimination Strategies

PAHO proposed and recommended the implementation of the following strategies for measles and rubella virus elimination to the countries of the Americas (Table 1). These vaccination strategies are aligned and complement both regional initiatives.

a. Vaccination

- "Catch-up" campaigns targeting children aged less than 15 years. During the first half of
 the 1990s, this type of campaign was carried out only once using measles vaccine. Since
 1998, it has been recommended that countries use measles-rubella (MR) vaccine. Some
 countries also administered rubella-containing vaccine.
- "Keep-up" vaccination in routine programs with the measles-mumps-rubella (MMR) vaccine administered at one year of age to maintain coverage >95%.
- "Follow-up" campaigns targeting preschool-aged children (aged 1 to 4 years) or when the number of susceptibles to measles approaches the size of an average birth cohort for that year. Measles-rubella (MR) vaccines are used in this type of campaign.
- "Speed-up" campaigns targeting adolescents and adults, men and women. These campaigns
 are based on the rubella and CRS elimination initiative and provide a complementary strategy
 to maintain measles elimination. This type of campaign was implemented only once using the
 combined MR vaccine.

b. Integrated Measles and Rubella Surveillance

Given the similarities in the clinical symptoms, epidemiological investigation, and laboratory studies, measles and rubella surveillance were integrated in the Region. Among the strategic and practical reasons for this integration are the following:

- Improve and enhance the detection of measles and rubella cases.
- · Create synergy in surveillance.
- · Save resources through improved efficiency.
- Facilitate supervision.

It is important to note that the purpose of surveillance during the pre-elimination era was to detect where the measles and rubella virus was circulating; during the post-elimination phase surveillance should be case-based for the timely detection of importations as well as to limit secondary transmission.

c. Congenital Rubella Syndrome (CRS) Surveillance

The goal of any rubella vaccination program is the prevention or elimination of CRS. The rationale for CRS surveillance includes:

- Monitor the impact of the rubella elimination initiative.
- Contribute to the documentation of the interruption of endemic virus transmission in the countries of the Region.
- Identify additional CRS cases, considering that up to 50% of infected mothers are asymptomatic.
- Identify reservoirs of viral transmission.
- Serve as an advocacy tool to improve equity and the quality of health services.

PAHO recommends that CRS surveillance focus on the identification of infants aged 0 to 11 months with CRS. Sentinel surveillance should include referral hospitals and primary care services to facilitate the identification of suspected CRS cases. Suspected cases should be investigated using available clinical and laboratory resources. Because the excretion of rubella virus can occur for up to 12 months, virus excretion should be monitored through specimen collection (oropharyngeal swab is the preferred specimen) from all suspected CRS cases, as well from infants with congenital infection only.

d. Serological Diagnosis, Virus Detection and Isolation

Based on elimination strategies (Table 1) and case definitions for measles/rubella suspected cases, the countries of the Americas carry out laboratory confirmation of serum samples collected within 30 days after rash onset. Additionally, virological surveillance is performed through viral detection/isolation and genotypic identification for the detection and monitoring of viral strains that are circulating in the Region. The specimen collection period for measles and/or rubella viral detection begins at first contact with the patient up to 7 days after rash onset. For CRS suspected cases, specimen collection during the first 3 months of life is preferable. Once the case is confirmed, specimen collection should continue until two viral negative cultures, collected at 1-month intervals, are obtained in order to confirm that the case is no longer excreting virus.

TABLE 1. MEASLES AND RUBELLA ELIMINATION STRATEGIES

VACCINATION

- 1. Measles and rubella (alignment of vaccination strategies):
 - · "Catch-up" campaign; children aged 1 to 14 years.
 - · "Keep-up" to maintain coverage ≥95% in the routine program; children aged 1 year.
 - · "Follow-up" campaign; preschool-aged children or when the number of susceptibles to measles approaches the size of an average birth cohort.
 - · Introduction of MMR or MR in routine program; children aged 1 year.
 - "Speed-up" campaign against measles and rubella in adolescents and adults. This type of campaign was conducted only once (the age group of men and women to be vaccinated depends on the year of vaccine introduction, follow-up campaigns, epidemiology, and fertility rates in the country).

SURVEILLANCE

- 1. Integrated measles/rubella surveillance:
 - Reporting, investigation, response capacity, and case classification of suspected measles/rubella cases.
- 2. CRS surveillance:
 - Reporting, investigation, response capacity, and case classification of suspected and confirmed CRS cases.
- 3. Laboratory activities for measles/ rubella and CRS:
 - · Serological diagnosis.
 - Viral detection/isolation and identification and genotyping of measles and rubella virus.

1.3 ECONOMIC ANALYSES OF THE ELIMINATION INITIATIVE

Some of the expected benefits from the elimination of measles, rubella, and CRS include the interruption of endemic virus transmission, prevention of measles- and CRS-associated cases and deaths, and cost savings from a health, family, and societal perspective.

Additional benefits include the impact of follow-up vaccination campaigns in children aged 1-4 years with MR vaccine used for measles elimination, which have most likely reduced rubella virus transmission in this target age group. Vaccination campaigns targeting adolescents and adults (speed-up) have also strengthened and maintained the interruption of endemic measles virus transmission in countries that have used the combined measles-rubella vaccine. Furthermore, the experience of the Region of the Americas is providing an opportunity to document the efficacy and effectiveness of these interventions, which will be useful for WHO Regions that set a target for global measles and rubella/CRS elimination. Lastly, the elimination initiative has strengthened the routine program and developed local capacity for the introduction of new and underutilized vaccines.

The economic benefits of the elimination initiatives are demonstrated through an analysis of direct treatment costs associated with measles and its complications (9,10) and rubella (mainly the costs associated with the prolonged treatment of CRS cases), the costs associated with institutional care and special education required by many CRS survivors (11,12), and the costs of elimination strategies and/or increases in vaccination coverage against measles and rubella (9,10).

It is estimated that the full cost of a measles mass campaign ranges from US\$ 0.50-0.75 per child. When using the measles-rubella vaccine, the cost per child is estimated at US\$ 1.00-1.20. During the period of 2000-2020, the current program would have prevented the occurrence of 3.2 million cases of measles and 16,000 deaths in Latin American and Caribbean countries. Thus, the vaccination strategy has prevented a single case of measles at the cost of US\$ 71.75 and has prevented a death due to measles at the cost of US\$ 15,000. The case fatality rate depends on a well-functioning treatment program for measles cases. The vaccination strategy has saved a total of US\$ 208 million in treatment costs due to reduced incidence of measles (9).

For rubella, several cost analysis studies from the Region estimated that the annual cost to treat a CRS case ranged from US\$ 2,291-US\$ 13,482 (13,14) and lifetime costs to treat a CRS case from US\$ 50,000-US\$ 63,990 (15,16). An analysis of the elimination initiative demonstrated a savings of US\$ 3 billion by preventing an estimated 112,500 CRS cases in Latin American and Caribbean countries over a 15-year period (17). Cost-benefit studies demonstrated a benefit-cost ratio (B:C) of 4.7 in Barbados and 13.3 in the English-speaking Caribbean for elimination initiatives in addition to routine MMR immunization of 1-year-olds (15,18) and a B:C ratio of 38.8 in Guyana for an elimination campaign in addition to routine MMR immunization of 1-year-olds (16). Finally, additional studies have estimated that those countries that have implemented mass rubella vaccination campaigns targeting adolescents and adults aged less than 39 years have saved close to US\$ 3 billion in treatment and special care costs by investing US\$ 272 million in campaign costs to prevent future CRS cases (17).

1.4 STRATEGIC ALLIANCES

The success of the Americas in interrupting endemic measles and rubella virus transmission is evidence that with the commitment of a whole region the goal of elimination can be achieved. This achievement has effectively harnessed the trust of the population in immunization and led to sustained demand for vaccination services for the child and family. Given the increasing credibility of national immunization programs (NIPs), the Region has successfully engaged a wide range of partners to sustain elimination programs.

The overwhelming success of the measles, rubella, and CRS elimination initiatives has been possible through the efforts of the countries of the Americas and through alliances with PAHO strategic partners. Among these partners are the American Red Cross (ARC), the U.S. Department of Health and Human Services Centers for Disease Control and Prevention (CDC), the Canadian International Development Agency (CIDA), the GAVI Alliance, the Inter-American Development Bank (IDB), the International Federation of Red Cross and Red Crescent Societies (IFRC), the Japanese International Cooperation Agency (JICA), the March of Dimes (MOD), the Sabin Vaccine Institute (SVI), the United Nations Children's Fund (UNICEF), the United States Agency for International Development (USAID), and the Church of Jesus Christ of Latter-day Saints (LDS). Large vaccine suppliers have also contributed to the success of these initiatives by donating high-quality vaccines to overcome country vaccine shortfalls and financing gaps (19).

2. PROGRESS TOWARDS MEASLES, RUBELLA, CRS ELIMINATION

2.1 MEASLES

During the 1960s, hundreds of thousands of measles cases were reported annually. Despite generally weak surveillance, Latin American countries reported some 220,000 measles cases each year during 1970-1979, with an annual incidence ranging from 47-116/100,000 population. During 1971-1980, measles mortality ranged from 14-55/100,000 among infants and 8-54/100,000 among children aged 1-4 years. Countries of the Americas noted the impact of measles vaccination during the 1980s as the incidence declined and the interval between outbreaks grew longer (20). Nevertheless, despite improvements in immunization coverage, measles outbreaks continued to occur, particularly in Central America between 1989 and 1991. This occurrence drove Central American authorities to implement catch-up campaigns targeting children aged 1-14 years. Additionally, authorities ratified and made official the decision to eliminate the indigenous transmission of measles by 1997 in this sub-region (20).

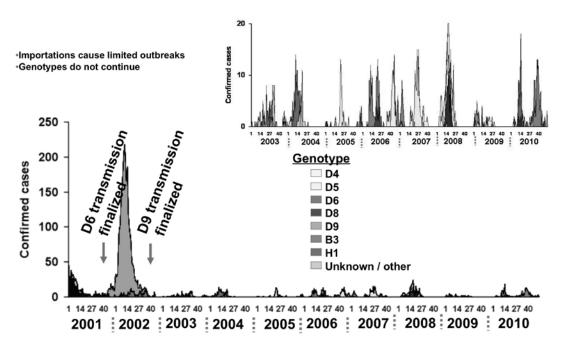
By the early 1990s several countries had employed a different measles immunization strategy and in 1993 the Region reported the lowest number of cases in decades (n=57,400), the incidence rate had fallen to 10 cases per 100,000 population, and regional coverage with the first routine measles-containing vaccine dose was 87% (20).

In 1996, the Americas registered the lowest number of cases in history (2,109 confirmed measles cases); however, the Region experienced a reemergence of the disease in 1997, with 53,683 cases reported and 63 deaths in children aged less than 1 year, mainly due to cases in Brazil (97.4% of reported cases) (20). A main contributing factor for the outbreak was the presence of a large number of susceptibles that were not vaccinated through a follow-up campaign. If a timely follow-up campaign had been conducted, the outbreak may have been prevented or the number of cases would have been reduced significantly. This outbreak extended to the following countries: Argentina, Chile, Costa Rica, Paraguay, Peru, and the United States (20).

The number of confirmed measles cases diminished over the following years to 548 cases in 2001, a 99% reduction compared to 1990. That year, the Dominican Republic and Haiti successfully interrupted measles transmission, effectively ending known endemic transmission of the D6 measles virus genotype, which had been circulating in the Region since 1995 and was associated with large outbreaks in Argentina, Bolivia, and Brazil, as a result of an insufficient routine program and the ensuing accumulation of susceptibles. Also in 2001, a European tourist introduced the D9 measles virus genotype to Venezuela, which spread to neighboring Colombia in January 2002 (20). After intense vaccination campaigns in both countries, D9 virus transmission was interrupted. The last measles case associated with that outbreak occurred in Carabobo, Venezuela, on 16 November 2002, finalizing the interruption of endemic measles virus transmission in the Western Hemisphere.

Since 2003, imported and import-related measles cases have been reported in historically low numbers in the Americas (2): 119 in 2003, 108 in 2004, 85 in 2005, 226 in 2006, 176 in 2007, 207¹ in 2008, 89² in 2009, and 253³ in 2010. In the period 2008-2010, 345 secondary cases resulted from a total of 136 importations, while for 88 cases the source was unknown. Sixty percent of measles importations to the Americas for the same period have come from Europe; these outbreaks occurred in Argentina, Brazil, Canada, Chile, Ecuador, French Guiana, Jamaica, Peru, and the United States. Measles cases reported in the Americas have been isolated and/or sporadic, and outbreaks have resulted in a limited number of cases secondary to importation. The implementation of a rapid response to limit these outbreaks has resulted in intense mobilization of human and financial resources in the countries.

FIGURE 3. MEASLES GENOTYPES IDENTIFIED IN THE AMERICAS, 2001-2010



Source: Country reports to PAHO/WHO and the Global Measles Laboratory

¹ Country reports to PAHO/WHO, 2008

² Country reports to PAHO/WHO, 2009

³ Country reports to PAHO/WHO, 2010

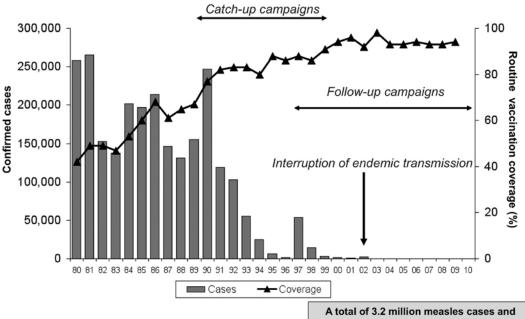


FIGURE 4. MEASLES ELIMINATION, THE AMERICAS, 1980-2010*

Source: Country reports to PAHO/WHO

A total of 3.2 million measles cases and 16,000 deaths would have occurred between 2000-2020 if PAHO strategies were not implemented. This resulted in a savings of US\$ 208 million in treatment costs.1

2.2 RUBELLA AND CRS

Through the implementation of the PAHO-recommended elimination strategies, between 1993 and 2008 nearly 450 million people (children, adolescents, and adults) were protected against measles and rubella during catch-up (140 million people vaccinated mainly with monovalent measles vaccine), follow-up (60 million people vaccinated mainly with MR vaccine) and speed-up campaigns (250 million people vaccinated mainly with MR vaccine). As a result, routine vaccination has also been strengthened.

However, in 2007 the Region experienced a resurgence of rubella cases due to virus importations to countries that initially vaccinated only women during mass vaccination campaigns. The number of confirmed rubella cases increased from 2,919 in 2006 to 13,187 in 2007 as a result of outbreaks in Argentina, Brazil, and Chile in that year. In 2008, a total of 4,536 confirmed rubella cases were reported in the Region, of which 98% were from Argentina and Brazil. These countries intensified vaccination and surveillance activities.

The Region of the Americas has made extraordinary progress in rubella and CRS elimination, interrupting endemic virus circulation in 2009. The last confirmed endemic rubella case was reported in epidemiological week 5 of 2009 in Argentina. During that same year, Canada and the United States reported 4 and 3 import-associated rubella cases (genotype 2B in the United States), respectively. In 2010 the Americas reported a total of 15 rubella cases: in Canada (n=7), the United States (n=7), and French Guiana (n=1).

^{*} Coverage data not available for 2010 ¹ Ref. 9.

As an unfortunate consequence of the rubella outbreaks in 2009, a total of 27 CRS cases were reported in Argentina (n=13) and Brazil (n=14). The dates of birth of the last confirmed CRS cases were 6 July 2009 and 26 August 2009 in Argentina and Brazil, respectively. No CRS cases were reported in 2010.

Despite limited molecular epidemiology information, rubella virus genotype 1C has been identified as endemic in the Americas since it has frequently been found in the Region and has not been identified in other regions of the world. The last occurrence of 1C virus transmission was identified in 2005 in Chile and Peru. Since 2006, the genotype 2B has been isolated during the last rubella outbreaks reported in Argentina, Brazil, and Chile, and is now considered endemic in the Americas.

Finally, taking into account the seasonal pattern of the rubella virus and that CRS cases can excrete virus for up to 12 months, it is essential that countries that reported the last rubella and CRS cases intensify surveillance and monitor virus excretion from CRS cases until two viral negative cultures at least 1 month apart were obtained to verify the interruption of endemic virus circulation in the Western Hemisphere.

24 months with no endemic rubella cases in the Region. Speed-up campaigns 100 140,000 Beginning in 2001, Routine Vaccination Coverage over a 15 year 120,000 Confirmed Rubella Cases period the rubella Follow-up campaigns and CRS initiative 100,000 will have saved an transmission (2B) 1C transmission finalized estimated US \$3 B rubella case 80,000 by preventing more EW 5/2009 than 112,500 CRS 60,000 cases in Latin America and the Caribbean. 40.000 20,000

02 03 04

05 06 07 08

FIGURE 5. RUBELLA ELIMINATION IN THE AMERICAS, 1982-2010*

90

91 92 93 Cases

89

Source: Country reports to PAHO/WHO * Coverage data not available for 2010

3. PLAN OF ACTION

Resolution CSP27.R2 that was adopted during the 27th Pan American Sanitary Conference held in October 2007 in Washington, D.C., authorized the formation of an International Expert Committee responsible for documenting and verifying the interruption of endemic measles and rubella virus in the Region of the Americas. In addition, the Resolution urged PAHO Member States to establish national commissions to collect and analyze the data for the documentation and verification of measles, rubella, and CRS elimination that would be reviewed by the International Expert Committee. This committee will serve as the entity responsible for presenting the regional report to the Directing Council and the Pan American Sanitary Conference, the supreme governing authority of PAHO.

The Region of the Americas has spearheaded the eradication and elimination of smallpox, polio, measles, and rubella/CRS and sustained efforts to eliminate neonatal tetanus as a public health problem. Several lessons can be drawn from the rich experience of the Americas in the eradication and elimination of vaccine-preventable diseases.

In regards to documenting and verifying elimination, the process of certification of smallpox and polio eradication provides lessons learned in five key areas (21,22):

- The periods that must elapse between the last known case and the certification process are 2 years for smallpox and 3 years for polio. However, even when elimination has been certified, it is necessary to continue surveillance efforts until the infectious agent has been eliminated at the global level. As long as the infectious agent continues to circulate in other regions of the world, the risk of importations will continue.
- It is necessary to maintain a surveillance system sensitive enough to detect all cases associated with smallpox or polio, including those diseases that share similar clinical symptoms: fever and rash for smallpox and acute flaccid paralysis in children aged less than 15 years for polio.
- National commissions in countries of the Region must benefit from political backing, and be competent and committed.
- The experience of polio demonstrated the importance of developing a plan of action for the certification process that establishes certification criteria, specifies the functions of the International Expert Committee and the national commissions, and outlines the strategies countries must follow to achieve certification.
- The regional documentation and verification process must be considered within the global context. Discussions have taken place with other WHO Regions regarding the proposal for indicators to monitor the process of global measles eradication.

The draft Plan of Action for the documentation and verification of measles, rubella, and CRS elimination has been piloted in several countries of the Region, including the English-speaking Caribbean. The pilot activities, which began in May 2007 and continued until August 2008, provided an initial test of the utility of the Plan of Action. The regional plan has also been reviewed by numerous international experts in the field of immunization and the eradication and elimination of vaccine-preventable diseases.

The Plan of Action for the documentation and verification of measles, rubella, and CRS elimination is an instrument to guide each NIP program, in collaboration with the national commission, to develop its own plan of action, which will define responsibilities, products, resources, and a timeline of activities.

3.1 Main Objectives of the Plan of Action

- Establish the concepts and criteria, provide methodologies, and identify required data elements to document the interruption of endemic measles and rubella virus transmission in the countries of the Americas.
- Standardize the verification process in countries of the Region to facilitate the collection of required documentation for review by the International Expert Committee.

3.2 BASIC PRINCIPLES

- The area for documenting the interruption of endemic transmission is the Region of the Americas.
- It is recommended that progress in the documentation and verification process be considered by geographic area (e.g., Central America, the Caribbean, Andean and Southern Cone).
- An International Expert Committee will be formed to verify the achievement of the measles, rubella, and CRS elimination goal in the Region.
- The International Expert Committee will provide a standard plan of action to ensure uniformity in the criteria that will be used to verify elimination.
- Each country will establish a national commission with the exception of the Caribbean countries, where a sub-regional commission will be established.
- Each country will prepare a plan of action for the documentation process and a timeline for evaluating the achievement of the verification goal in collaboration with the national commission.
- Documentation will be based mainly on the achievement and sustainability of the components detailed in section 3.4.
- Once the elimination goal is met, countries of the Region will continue surveillance, including virological surveillance, and vaccination strategies to maintain the interruption of endemic transmission, the timely detection of imported and import-related cases, and effective response measures to prevent the re-establishment of endemic measles and rubella virus circulation. They should also monitor indicators for elimination including outbreak size and the incidence of measles, rubella, and CRS cases.
- Given the advances in the Region of the Americas, this experience should be standardized to support the elimination process in other regions of the world.

3.3 ESSENTIAL CRITERIA

The following are the essential criteria for the documentation and verification of measles, rubella, and CRS elimination. Each one of the criteria cannot stand alone but should be evaluated and interrelated to support the argument for elimination.

- Verify the interruption of endemic measles, rubella, and CRS cases in all countries of the Americas for a period of at least 3 years from the last known endemic case, in the presence of high-quality surveillance.
- Maintain a high-quality surveillance system sensitive enough to detect imported and import-related cases.
- Verify the absence of endemic measles and rubella virus strains through viral surveillance in the Region of the Americas.

3.4 DOCUMENTATION AND VERIFICATION COMPONENTS

The documentation and verification process requires the following evidence to support the completion of the essential elimination criteria:

- Epidemiology of measles, rubella, and CRS.
- Quality of measles, rubella, and CRS surveillance.
- Molecular epidemiology of measles and rubella viruses and laboratory activities.
- Measles and rubella vaccinated population cohorts.
- Sustainability of measles, rubella, and CRS elimination.
- Correlation and integration of the evidence for elimination.

3.4.1 EPIDEMIOLOGY OF MEASLES, RUBELLA, AND CRS

Vaccination strategies used in the Americas resulted in rapid decreases in the incidence of measles, rubella, and CRS. These dramatic decreases have led to changes in the demographic characteristics of cases and outbreak patterns. In order to determine that measles and rubella virus circulation has been effectively interrupted and to assess the degree to which the essential criteria are met, an epidemiological analysis should be conducted. This analysis is based on the case definitions for measles, rubella, and CRS (Tables 2 and 3).

TABLE 2. MEASLES AND RUBELLA OPERATIONAL CASE DEFINITIONS (23,24)

Suspected case:

A patient in whom a health care worker suspects measles or rubella infection or a patient with fever and maculopapular rash.

Laboratory-confirmed case or by epidemiological link:

A suspected measles or rubella case that has positive laboratory results* or is epidemiologically linked to a laboratory-confirmed case.

Clinically confirmed case:

A suspected case with inadequate laboratory investigation, and lacking evidence of any other etiology (considered deficiencies in the surveillance system). These cases should be discussed and decided (confirmed or discarded) by the national commission on documentation and verification.

Discarded case:

A suspected case with adequate investigation and with negative laboratory results.*

Endemic case:

A confirmed case which, as supported by epidemiological and virological evidence, indicates that it is part of a chain of endemic transmission, meaning that the isolated virus has been circulating in the Americas for a period greater than or equal to 12 months.

Imported case:

A confirmed case which, as supported by epidemiological and/or virological evidence, was exposed outside of the Americas during the 7 to 21 days prior to rash onset for measles, or from 12 to 23 days for rubella.

Import-related case:

A locally acquired infection occurring as part of a chain of transmission originated by an imported case as supported by epidemiological or virological evidence, or both. (Note: If transmission of measles cases related to importation persists for greater than or equal to 12 months, cases are no longer considered to be import-related, they are considered to be endemic.)

Unknown source case:

A confirmed case for which the source of infection was not identified.

Re-establishment of endemic transmission:

Occurs when epidemiological and laboratory evidence indicates the presence of a chain of transmission of a virus strain that continues uninterrupted for ≥ 12 months in a defined geographical area.

TABLE 3. CONGENITAL RUBELLA SYNDROME OPERATIONAL CASE DEFINITIONS (24)

Suspected case:

An infant aged less than 1 year in whom a health care worker suspects CRS due to:

- 1) One or more of the following birth outcomes detected: congenital cataracts, congenital heart defects, purpura at birth, or hearing impairment, and/or
- 2) History of confirmed or suspected maternal rubella infection during pregnancy.

Laboratory-confirmed case:

A clinically consistent case that has positive laboratory results.*

Clinically confirmed case:

A suspected case that is not laboratory confirmed and lacks evidence of any other etiology. This usually occurs due to a loss of follow-up or inadequate collection of specimens for laboratory diagnosis. This is considered a failure in the surveillance system.

Endemic case:

An infant with confirmed CRS whose mother acquired rubella in the Americas and, as supported by epidemiological and virological evidence, indicates that it is part of a chain of endemic transmission, meaning that the isolated virus has been circulating in the Americas for a period greater than or equal to 12 months.

Imported case:

A confirmed case whose mother acquired the rubella virus infection outside of the Americas or, in the absence of documented rubella infection, the mother was outside the Americas during the period when she may have had exposure to rubella that affected her pregnancy (from 23 days prior to conception or until week 24 of gestation).

Import-related case:

A confirmed case whose mother, as supported by epidemiological and/or virological evidence, was exposed locally as part of a transmission chain that initiated with an imported case.

Congenital rubella infection (CRI):

An infant with ELISA IgM-positive results for rubella at birth who presents with no clinical signs of CRS.

Case requires clinical assessment, including the ruling out of deafness by an adequate procedure.

^{*} Laboratory Results

Positive serologic test for rubella immunoglobulin M (IgM) antibody.

For measles and rubella diagnosis: significant rise between acute and convalescent-phase titers. This is not applicable to CRS.

Isolation of rubella virus.

Detection of virus by reverse transcription polymerase chain reaction (RT-PCR).

Genetic sequencing of measles and rubella virus.

For CRS diagnosis: infant rubella antibody level that persists at a higher level and for a longer period than expected from passive transfer of maternal antibody (i.e., rubella titer that does not drop at the expected rate of a twofold dilution per month).

It is recommended that the following data elements be evaluated in the epidemiological analysis of measles, rubella, and CRS. This analysis should aim to compare and contrast the pre-interruption and post-interruption epidemiological periods to support the identification of a "breaking point" or a point at which endemic virus interruption was achieved.

• Morbidity rates:

- Analysis of cases reported annually, including the mean/median (as appropriate) and range.
- Incidence: X case(s) per 1,000,000 population (highlight incidence over last 3 years).
- Analysis of cases per geographic location (e.g., municipality, department/state).
- Analysis by case classification (confirmed [laboratory versus epi-linked], imported, import related, endemic, unknown source, special cases).
 - Analysis of importation status by year and predetermined time period.
- The number of suspected cases lost to follow-up (include the geographic area where these cases were reported).
- Analysis of special cases (for example, false positives, false negatives, indeterminate, post-vaccination, etc.).
- Analysis of cases that are sporadic and difficult to classify. These cases require immediate and complementary investigation and specimen processing using other methods.

• Temporal and spatial characteristics:

- The number of weeks with reported cases per year or over a certain time period.
 - Examine total cases and unknown source cases.
 - Assess time intervals between cases.
 - Assess the maximum number of cases reported weekly.
 - Include rash onset dates of the last endemic cases.
- Analysis of the number of geographic areas that reported cases. This can be done per time period (pre-interruption, post-interruption) or annually.

Seasonality:

 Assess seasonality over predetermined time periods (verify the loss of cyclical and seasonal patterns characteristic of endemic transmission).

• Demographic characteristics:

- Incidence by age, sex, race/ethnicity, specific area (e.g., urban, tourist area).
- Follow-up of pregnant women exposed to rubella and their infants.
- Analysis by country of birth/origin (if appropriate).

• Outbreaks:

- Epidemiological description of outbreaks includes:
 - Distribution by age, sex, race/ethnicity, specific area (e.g., urban, tourist area).
 Number of outbreaks per X time period.

- Size (e.g., number of chains of transmission or outbreaks and number of cases in each chain or outbreak).
- Duration of outbreaks (e.g., number of weeks).
- Types of outbreaks (schools, communities, etc).
- Risk factors or groups most affected.
- Source of outbreak.

Investigation:

- Procedures used for the investigation, follow-up, and confirmation of outbreaks.
- Follow-up of contacts.
- Results of active search in the population and health units.
- Response or strategy used to control the outbreak.
- Vaccine efficacy (field effectiveness), if needed.
- Laboratory results: serological and virus detection/isolation.
- Final case classification.

• CRS specific:

- Number of CRS cases over time period of evaluation.
- Annual: incidence per 10,000 live births.
- Final case classification: confirmed, clinically confirmed.
- Demographic characteristics of mother (age, race/ethnicity, country of birth, if appropriate).
- Number of cases by year of birth.
- Import status of cases.
- Molecular epidemiology and laboratory activities:
 - Number of adequate specimens obtained and analyzed over time periods.
 - Genotypes identified during time periods (import versus endemic).
 - Sporadic cases versus outbreak-associated cases.

Additional sources of information may include MESS, ISIS, other surveillance software (developed by some countries), case studies, outbreak reports, etc.

3.4.2 QUALITY OF SURVEILLANCE

In order to verify measles, rubella, and CRS elimination it is necessary to determine whether the surveillance system provides timely and sufficient information based on pre-established quality criteria. The following indicators (tables 4 and 5) should be monitored by the countries of the Region in order to assess the quality of surveillance and monitor elimination. In addition, for the national epidemiological analysis the countries should include data collected from the private sector, which demonstrates continued collaboration with that sector.

The indicators are the following:

TABLE 4. MEASLES AND RUBELLA SURVEILLANCE INDICATORS

CRITERIA		INDICATOR	MINIMUM THRESHOLD
Reporting Rate		Annual rate of suspected measles and rubella cases at the national and subnational level (state, province, or equivalent level).	≥2 per 100,000 population
Adequate Suspected Investigation		% suspected cases with household visit within 48 hours following reporting. % of suspected cases with the following 11 data points completed: name and/ or identifier, place of residence, sex, age or date of birth, date of reporting, date of investigation, date of rash onset, date of specimen collection, presence of fever, date of prior MR vaccination and travel history.	≥80%
Confirmed Cases		% confirmed cases with follow-up of contacts for 30 days.	≥80%
Laboratory Confirmation		% suspected cases with adequate blood specimen.	≥80%
Viral Detection		% outbreaks with adequate specimens and genotype information available from at least one viral specimen.	≥80%

TABLE 5. INDICATORS OF CRS SURVEILLANCE QUALITY

CRITERIA	INDICATOR	MINIMUM THRESHOLD	
Reporting Rate	Annual rate of suspected CRS cases by country.	≥1 per 10,000 live births	
Adequate Investigation	% suspected CRS cases with the following 8 data points completed: name and/or identifier, place of residence, sex, date of birth, date of reporting, date of investigation, date of specimen collection, and vaccination history of mother; also clinical examinations for deafness, blindness, and congenital cardiopathy.	≥80%	
Laboratory Confirmation	% suspected cases with adequate blood specimen.	≥80%	
Viral Detection	% confirmed cases with adequate specimen analyzed for virus detection/isolation.	≥80%	
Monitoring of Virus Excretion	% confirmed cases with at least 2 negative tests for virus detection/isolation, after 3 months of age, with 1-month lapse between tests.	≥80%	

Active search for suspected measles and rubella cases

Active measles and rubella case searches should be implemented to identify suspected cases as well as document the absence of cases. Active case searches are particularly useful in outbreak situations to identify the primary case, secondary cases, and contacts that may occur within the corresponding incubation period (detection of recent circulation within the past month), as well as to ensure that virus circulation has been interrupted. These searches should be conducted in health centers or other appropriate medical facilities and in communities. Active searches should also be carried out in high-risk areas, which include silent areas, or areas that do not adhere to weekly reporting standards, tourist areas, and areas of high migration, etc. Areas with low vaccination coverage (<95% per municipality) should also be included. Active searches will assess the quality of surveillance by identifying the strengths and weaknesses of the surveillance system and by monitoring the integrity of epidemiological reports.

Retrospective search for CRS cases

To document the absence of CRS cases it is necessary to complement routine reporting systems with the retrospective search for suspected CRS cases using various sources of information, for at least 3 years (2008, 2009, and 2010). This methodology will assess the quality of reporting by identifying cases that were not reported to the surveillance system, identify reservoirs of viral transmission, evaluate the impact of elimination strategies, and contribute to the documentation of the interruption of endemic rubella virus transmission in the Region. Some countries have conducted retrospective searches during the pre- and post-vaccine introduction phase and pre- and post-campaign implementation.

Retrospective search is defined as the identification of suspected CRS cases through the review of records with diagnoses compatible with the clinical manifestations of this disease. This search can be performed in both health and special care institutions. Records from the ICD-9 and ICD-10 databases (if available), records from congenital cataract surgery, and congenital disease registries are considered additional sources for identifying cases.

Coordination with dengue surveillance

Countries are encouraged to process a percentage of dengue samples with negative laboratory results for measles and rubella from cases presenting fever and rash and identified in high-risk areas (i.e., silent municipalities and areas where dengue circulation has been detected).

3.4.3 Molecular Epidemiology and Laboratory Activities

Molecular epidemiologic data are essential components of laboratory surveillance for measles and rubella, especially in an elimination setting. The genetic information provides a tool for documenting the transmission patterns of circulating strains of measles and rubella. This information is used to identify endemic viruses, as well as the potential sources of imported virus. The molecular data can help to verify that elimination has been achieved by documenting the interruption of transmission of endemic viruses.

The success of molecular epidemiologic studies depends on the collection of suitable samples; shipment of the samples to network laboratories that can perform viral isolation, RT-PCR, and genetic characterization; and the timely and accurate reporting of the results. Application of molecular epidemiologic techniques depends on the availability of a robust global sequence database. Laboratories are encouraged to report genotype information to the global database at WHO and GenBank.

Each national laboratory should produce surveillance information of the highest possible quality in order to document that measles and rubella elimination has been achieved. To this end countries should report the following:

- Quality Control:
 - Laboratories are fully certified according to the current WHO and PAHO LabNet standards and conducting proficiency tests.
- Case Classification and Laboratory Testing for Sporadic Cases:
 - Countries collected a second specimen for all special cases (such as when false-positive/false-negative IgM results are suspected, in cases involving pregnant women, and in instances of cross reactions and vaccine-related cases), and used the specific laboratory testing algorithm guidelines from PAHO for classification of measles and rubella cases.
 Some countries may use a sample for virus detection/isolation as a second specimen.
- Molecular Epidemiology:
 - Laboratories established a genetic baseline of rubella and measles viruses through the characterization of endemic cases or archival samples (serum, oral fluid, nasopharyngeal swab, and tissue) starting with the year 2000.
- Laboratory Surveillance for Congenital Rubella Syndrome:
 - Virus detection from CRS cases was used to confirm the infection.
 - Laboratories/countries established the means to support CRS case confirmation and monitoring of virus shedding by CRS cases through serological and virological testing.

• Appropriate Sample:

Adequate receipt of the samples according to the following criteria:

- Labeling: name, identification number, legible collection date that corresponds with the relevant form.
- Quantity: minimum established quantity for the process(es).
- Quality: The serum should not be hemolyzed or contaminated.
- Timeliness: should be collected within the periods established by the process(es).
- Shipment to the laboratory with the previous shipment report, taking into account transportation considerations previously established.

Resources:

Countries have included laboratory costs in their surveillance budgets.

Virus Containment

The definition of eradication implies that the etiologic agent is no longer a threat to humans. For measles virus, and those agents which may be replicated *in vitro*, eradication in the absence of extinction requires sufficiently stringent laboratory containment policies and facilities to prevent deliberate or accidental human infection and subsequent reintroduction of the disease.

For the laboratories participating in the PAHO Measles/Rubella Laboratory Network aspects related to biosafety and biosecurity are very relevant. Measles and rubella are still endemic in other regions and importations of virus will continue until these regions achieve their elimination goals. Therefore, a stringent containment policy such as the one currently in place for containment of wild-type polio viruses is not necessary for measles and rubella at this time.

An important recommendation from the last TAG meeting in August 2009 was that all of the laboratories in the PAHO LabNet be accredited according to current WHO standards. Accreditation requires that adequate biosafety and biosecurity measures be implemented in the laboratory. Once these measures are fully implemented, measles and rubella virus containment strategy will be reviewed. These measures include limiting access to laboratory areas to authorized personnel only, documentation that staff who are handling potentially infectious material have proof of immunity to measles and rubella or at least two doses of MR vaccine, use of adequate personal protective equipment, handling all potentially infectious material in a certified class-II biosafety cabin enclosure, storing all potentially infectious material in a -70 °C freezer that has access limited only to authorized laboratory staff, and maintaining a database of all clinical samples and viral isolates.

Another recommendation of the TAG was for increased virological surveillance to identify the sources and track the transmission pathways of measles and rubella viruses. The data from the molecular epidemiologic studies will be an important component of the documentation needed to verify elimination. Fulfilling the WHO accreditation requirements and strict adherence to regulations for shipping infectious materials will ensure that all of the laboratories in the PAHO network are operating as safely as possible even as virological surveillance activities are increased.

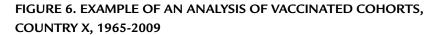
3.4.4 VACCINATED POPULATION COHORTS

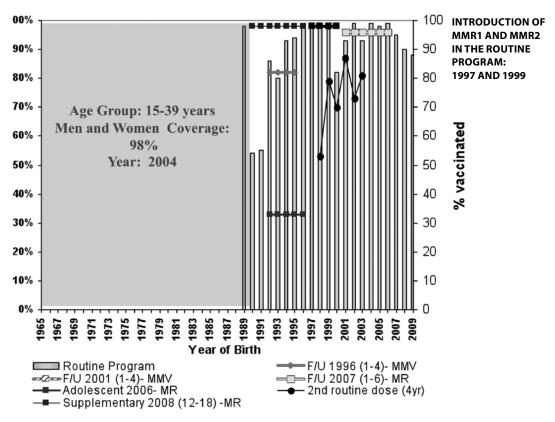
To support the evidence for measles, rubella, and CRS elimination, vaccination strategies and resulting coverage should indicate that all population cohorts aged less than 40 years, as well as those cohorts which correspond to the year of campaign implementation, should be protected against measles and rubella.

Administrative reports of vaccinated persons, results from rapid coverage monitoring (RCM), and coverage surveys (when applicable) should be analyzed to provide a realistic picture of the coverage achieved (ideally reaching ≥95%). The analysis will also allow countries to determine if high coverage has been sustained over time at the municipality, department/state, and national levels, as well as among population cohorts and age groups targeted in routine and supplementary vaccination activities. Special emphasis should be given to the following:

- Coverage in children aged 1 year with combined MR or MMR vaccine in the routine program.
- Coverage from catch-up and follow-up campaigns by target population, year of campaign implementation, and type of vaccine used (measles, MR, or MMR).
- Vaccination coverage from the second opportunity (i.e., second measles/rubella-containing vaccine dose administered through a follow-up campaign) or booster dose (i.e., second measles/rubella-containing vaccine dose administered through the routine program) and the age of administration established in the routine program (if this strategy is used); any changes in the age of administration in the immunization schedule should be documented.
- Year, coverage, and target age group of the MR speed-up campaign in men and women (adolescents and adults) to eliminate rubella and CRS.
- MR/MMR vaccination in the post-partum and/or post-abortion period.

The analysis should begin with the year of vaccine introduction in the country, the interventions implemented, and corresponding target age groups, taking into account the different vaccination strategies used. This information will allow for the estimation of population cohorts vaccinated against measles and rubella. An example of an analysis of vaccinated cohorts is provided on the opposite page (Figure 6):





Source: Country reports to PAHO/WHO

A review of different information sources should be completed to verify consistency in reported vaccination data, such as:

- Annual doses administered since the introduction of the measles/rubella-containing vaccine.
- Percentage of coverage obtained in vaccination campaigns by age group (stratified by municipality and department/state to ensure that there are no gaps in coverage).
- Results of RCM, surveys, and evaluation of MMR and MR vaccination coverage in different geographic strata.
- Review of dropout rates for DPT and routine measles-containing vaccine.
- Percentage of accumulation of susceptibles (continuous monitoring).

- Population size by municipality and by established range of coverage in each of the country's departments/states (e.g., 50%-79%, 80%-89%, 90%-94%, ≥95%), allowing for the identification of poor performing municipalities and/or areas at risk of transmission.
- Correlation of this information with the impact on the epidemiology of measles, rubella, and CRS.

Seroprevalence studies will only be used if they are available and are useful for assessing consistency with other information sources.

3.4.5 Sustainability of Measles, Rubella, and CRS Elimination

Political commitment at all levels, an efficient organization, and a favorable economic and legal environment have been fundamental conditions to ensure that national immunization programs (NIPs) of the Americas are considered successful over time. It is also important to include continued improvements to the existing capacity of vaccination services, to epidemiological surveillance systems, and to laboratories. These conditions have enabled the measles, rubella, and CRS elimination initiatives to achieve expected outcomes and have contributed to the overall strengthening of the NIPs.

The level of excellence achieved by the NIPs, the surveillance systems, as well as laboratories should be maintained over time to ensure that immunization services are considered a public good. This will facilitate the work of strategic partners and key actors to continue supporting and managing the effective mobilization of resources.

Different from the constant challenges that NIPs are subjected to, such as the permanent risk of measles and rubella virus importations, sustaining the elimination of these diseases is an essential component of the documentation and verification process. This sustainability refers to the following:

- 1. Sustained and homogeneous vaccination coverage, equal to or greater than 95%, with strategies and tactics in place to assure two MMR vaccine opportunities.
- 2. A sensitive and efficient surveillance system that detects, reports, and investigates all measles and rubella cases in a rapid and timely manner. The participation of the private sector is fundamental and implies continued collaboration with this sector.
- An efficient laboratory with the capacity to conduct serological diagnosis and virus detection and isolation when facing imported and sporadic cases.

The following evidence is required in order to properly document the capacity of NIPs to sustain elimination over time, beginning with the last measles and rubella cases:

 Recent reports that demonstrate that the three activities mentioned above have been sustained satisfactorily.

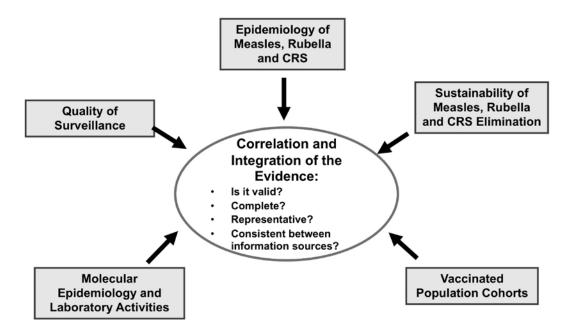
- Legal basis of the NIP and other documents that demonstrate the political commitment for the sustainability of elimination.
- A 5-year plan (or similar) and an annual plan of action of the NIP, where the three activities mentioned previously are clearly reflected and with sufficient financing.
- Sufficient human and financial resources that guarantee a high level of implementation of the annual and 5-year plan.
- Plan of action for low-coverage municipalities.
- Periodic evaluations of the different components of the NIP.
 - · Coverage analysis to monitor susceptibles.
 - · Monitor the completion of surveillance indicators.
 - · Monitor cold chain operations.
 - Data quality and assessing if the information system of the NIP is efficient and integrates all management levels, including the private sector.
- Periodic institutional active search for suspected measles, rubella, and CRS cases.
- Accredited laboratories and fulfillment of established proficiency controls.
- Algorithm that presents the coordination of the NIP with other key actors, such as the Interagency Coordinating Committee (ICC), the Immunization Advisory Committee, and/ or the Operational-Technical Committee.

3.4.6 CORRELATION AND INTEGRATION OF THE EVIDENCE

The documentation and verification components—namely the epidemiology of measles, rubella, and CRS; the quality of surveillance; molecular epidemiology; the analysis of vaccinated population cohorts; and the sustainability of measles, rubella, and CRS elimination—should be evaluated to identify the relationships that exist between the different data elements of each component and how they complement each other to support the verification of the interruption of endemic measles and rubella virus transmission. The process of correlating and integrating the evidence from the various sources of information will allow countries to determine whether the available data is valid, complete, representative, and consistent.

The results from this process should be incorporated into the final country report on the documentation and verification of measles, rubella, and CRS elimination. The report will be reviewed by the International Expert Committee, which will determine if the country meets the verification criteria for elimination.

FIGURE 7. ESSENTIAL COMPONENTS OF THE PLAN OF ACTION TO DOCUMENT AND **VERIFY MEASLES AND RUBELLA ELIMINATION IN THE AMERICAS**



4. STRUCTURE AND FUNCTION OF THE INTERNATIONAL EXPERT COMMITTEE AND THE NATIONAL COMMISSIONS

Both the International Expert Committee and the national commissions will be external and independent entities whose members will not be involved in the managerial or operational aspects of the national immunization program. In addition, these entities will not be involved in vaccination, surveillance, or laboratory aspects, nor will they have a direct responsibility in the achievement of the goal at the regional or national level.

4.1 International Expert Committee

The International Expert Committee will evaluate the documentation submitted by the national commissions to verify elimination at the regional level. The scope of work of the International Expert Committee includes verification that sub-regions/countries have been free from endemic measles and rubella virus transmission for at least 3 continuous years.

The International Expert Committee will be comprised of experts in the field of immunization, epidemiologists, clinicians, virologists, and molecular biologists. Its members will not be involved in managerial and operational aspects of elimination activities in the Region of the Americas. The organization of the committee will include a president, a secretary, and five to six additional members.

- The functions of this committee are as follows:
- Convene two meetings or more annually, if necessary, of the International Expert Committee.
- Oversee the process for documenting and verifying the achievement of elimination in the Region.
- Advise the national commissions on the process for collecting and analyzing the data for verification in the country.
- Receive and review the final reports submitted by the national commissions in each country.
- Prepare and submit the final report for the Region of the Americas to the Pan American Sanitary Conference or Directing Council.
- For each of the seven areas of the Americas listed below, one or two members of the International Expert Committee will have the responsibility to supervise the documentation and verification procedures. These areas are: 1) Southern Cone countries (excluding Brazil); 2) Brazil; 3) Andean countries; 4) Central American countries; 5) Caribbean countries (as a sub-region); 6) Mexico; and 7) Canada and the United States.
- Conduct field visits to the countries of the Region.

4.2 National Commissions

The national commissions and the subregional commission for the Caribbean countries will participate in and monitor the documentation and verification process in the countries. The commissions will be responsible for reviewing and observing the verification activities at the country level, following standardized operational procedures, and for preparing a national report to be reviewed by the International Expert Committee.

The national commission will be an external and independent entity, whose members will not be involved in managerial or operational aspects of the immunization program. In addition, this entity will not be involved in vaccination, surveillance, or laboratory issues, nor will the commission have direct responsibility in the achievement of the goal at the country level.

Each national commission will be comprised of four to five members: a president, a secretary, and two to three additional members. Recognized specialists from various fields (clinicians, laboratory experts, epidemiologists, etc.) will participate on a voluntary basis. Its members will be designated by the Minister of Health through the official procedures of each country.

The functions of the national commissions are as follows:

- Convene two meetings or more annually, if advice and follow-up activities to the country are requested or if officials assigned to the elimination process request it.
- In collaboration with the national immunization program, prepare the work plan for the
 documentation and verification of measles, rubella, and CRS elimination in the country,
 defining responsibilities, products, resources, and a timeline of activities, with technical
 cooperation from PAHO/WHO and the International Expert Committee.
- Approve the country work plan to be submitted to health authorities and present the plan to the International Expert Committee.
- Compile and analyze the information required to verify that the country has eliminated measles, rubella, and CRS, in accordance with the established criteria and procedures.
- Propose alternative solutions if the available country data is not sufficient or presents inconsistencies.
- Participate in the work sessions and visits of the International Expert Committee to the country at the different stages of the documentation process.
- Advise national surveillance, laboratory, and immunization teams on the activities related
 to the documentation and verification process of the interruption of endemic measles and
 rubella virus transmission in the country, including the classification of special cases (i.e.,
 sporadic cases, false-positive/false-negative results suspected, pregnant women, cross
 reactions, and vaccine-related cases).
- Review and approve the final country report and submit the report to the national health authorities who will then officially present the documentation to the PAHO/WHO Representation in the respective country.

The documentation process of each national commission will be as follows:

- Once the national commission is established and authorized, the commission will receive
 all information related to the concepts, criteria, methodologies, and practical guidelines for
 developing each component of the documentation for measles, rubella, and CRS elimination.
 In addition, the president and each one of the members of the commission will receive a
 certificate of membership, presented by the International Expert Committee and PAHO/WHO.
- The work plan, developed by the national commission in collaboration with the national immunization program, should include the necessary activities for collecting and integrating the required data, also defining responsible parties, products, resources, and relevant time periods. The technical surveillance and immunization teams should compile and provide all the information required to the national commission, according to the established terms. The identification of various sources of data, both official and unofficial, will provide the information needed to determine consistency with the data reported by the official surveillance system.
- The evidence documented by the national commission, and overseen by the International Expert Committee, will assess whether the data is valid, complete, representative, and consistent among the different sources of information. Based on this analysis it will be determined whether the country successfully interrupted endemic measles and rubella virus transmission.

5. TIMELINE

	YEAR				
ACTIVITY	2009	2010	2011	2012	
Presentation of the Plan of Action at the XVIII Meeting of the Technical Advisory Group on Vaccine-preventable Diseases	x				
Formation of the International Expert Committee		x			
Establishment of the National Commissions in the Countries of the Americas	x	→			
Data Collection and Analysis by the Ministry of Health in Collaboration with the National Commissions	x				
Implementation of Follow-up Campaigns	x —			~	
Continuous Monitoring of Surveillance Indicators	x —				
Processing of Specimens for Serological Diagnosis and Virus Detection	x —				
Active Case Search for Suspected Measles and Rubella Cases and Retrospective Search for CRS Cases	x —			→	
Preparation of Preliminary Report	х —				
Visit of International Expert Committee to Countries			х	х	
Review of Evidence by International Expert Committee			х	х	
Presentation of the Final Report to the Pan American Sanitary Conference/Directing Council				х	

6. REFERENCES

- 1. WHO/UNICEF Joint Annual Measles Report 2009. Strengthening Immunization Services Through Measles Control, PHASE X (unpublished).
- De Quadros C, Andrus J, Danovaro C, Castillo-Solorzano, C. Feasibility of global measles eradication after interruption of transmission in the Americas. Expert Review of Vaccines 2008;7(3):355-362.
- 3. Olivé JM, de Quadros CA, Castillo-Solorzano C. Measles in the Americas. Review of the last 30 years. 8th EPI TAG, 1990.
- 4. Global Burden of Disease, 1999.
- 5. Robertson SE, Featherstone DA, Gacic-Dobo M, Hersh BS. Rubella and congenital rubella syndrome: global update. *Pan American Journal of Public Health* 2003;14:306-315.
- 6. Cutts FT, Vynnycky E. Modeling the incidence of congenital rubella syndrome in developing countries. *International Journal of Epidemiology* 1999;28:1176-1184.
- 7. Pan American Health Organization. Final report: XII Meeting of the Technical Advisory Group on Vaccine-preventable Diseases, Guatemala, Guatemala, 8-12 September 1997. Washington, DC: Pan American Health Organization; 1997.
- 8. Miller E, Cradock-Watson JE, Pollok TM. Consequences of confirmed maternal rubella at successive stages of pregnancy. *Lancet* 1982;2:781-784.
- 9. Acharya A, Diaz-Ortega JL, Tambini G, de Quadros C, Arita I. Cost-effectiveness of measles elimination in Latin America and the Caribbean: a prospective analysis. *Vaccine* 2002;20:3332-3341.
- 10. Zwanzinger J, Szilagny PG, Kaul P. Evaluating the benefits of increasing measles immunization rates. Health Services Research 2001;36:885-909.
- 11. Irons B, Lewis MJ, Dahl-Regis M, Castillo-Solorzano C, Carrasco PA, de Quadros CA. Strategies to eradicate rubella in the English-speaking Caribbean. *American Journal of Public Health*. 2000;90:1545-1549.
- 12. Castillo-Solórzano C, Carrasco P, Tambini G, Reef S, Brana M, de Quadros CA. New horizons in the control of rubella and prevention of congenital rubella syndrome in the Americas. *Journal of Infectious Diseases* 2003;187(suppl 1):S146-S152.
- 13. Saad de Owens C, Tristan de Espino R. Rubella in Panama: still a problem. *Pediatric Infectious Diseases Journal* 1989;8:110-115.
- 14. Robinson M. CRS unit costing in Jamaica. In: Final Report, Fourteenth Meeting of the English-speaking Caribbean EPI Managers, Castries, Saint Lucia, 18-20 November 1997. Washington, DC: Pan American Health Organization; 1998.
- 15. Kommu R, Chase H. Follow-up of rubella issues and costing of CRS in Barbados. In: Final Report, Fourteenth Meeting of the English-speaking Caribbean EPI Managers, Castries, Saint Lucia, 18-20 November 1997. Washington, DC: Pan American Health Organization; 1998.
- Kandola K. CRS cost burden analysis for Guyana. In: Final Report, Fourteenth Meeting of the English-speaking Caribbean EPI Managers, Castries, Saint Lucia, 18-20 November 1997. Washington, DC: Pan American Health Organization; 1998.

- 17. Castillo-Solórzano C, Morice A, Marsigli C, Andrus A. Burden of disease of congenital rubella syndrome and an estimation of cost-benefit of interventions in the Region of the Americas. Poster Session. XVII Meeting of the Technical Advisory Group on Vaccine-preventable Diseases. Guatemala, 2006.
- 18. Irons B. Rubella eradication: the countdown begins. West Indian Medical Journal 1998;47(3):75-76.
- Pan American Health Organization. Resolution CSP27.R2. Elimination of Rubella and Congenital Rubella Syndrome in the Americas. 14th Executive Committee Session. Washington, DC, June 2007.
- 20. Castillo-Solórzano C, Ruiz Matus C, ed. Compendium of Measles Articles. Washington, DC: PAHO; 2009.
- 21. World Health Organization. Report of the 1st meeting of the Global Commission for the Certification of the Eradication of Poliomyelitis. WHO/EPI/GEN/95.6.
- 22. Pan American Health Organization. Plan of Action for Certification of the Eradication of Indigenous Transmission of Wild Poliovirus in the Americas. Technical Publication No. 39. Washington, DC, 1994.
- 23. Pan American Health Organization. Measles Elimination Field Guide. 2nd ed. Technical and Scientific Publication No. 605. Washington, DC, 2007.
- 24. Pan American Health Organization. Rubella and Congenital Rubella Syndrome Elimination. Field Guide (draft).

7. LIST OF ADDITIONAL TOOLS

Guideline 1: Analysis of Epidemiology of Measles, Rubella, and CRS

Guideline 2: Evaluation of the Quality of Surveillance

Guideline 3: Active Search of Measles and Rubella Cases

Guideline 4: Retrospective Search of CRS Cases

Guideline 5: Molecular Epidemiology and Laboratory Activities

Guideline 6: Analysis of Vaccinated Population Cohorts

Guideline 7: Sustainability of Elimination

Guideline 8: Recommendations for the Final Report

Guideline 9: Rapid Coverage Monitoring

Guideline 10: CRS Surveillance at the Primary Care Level: "Suspecting the Suspected"

ANNEX 1: RESOLUTION CE140.R10: ELIMINATION OF RUBELLA AND CONGENITAL RUBELLA SYNDROME IN THE AMERICAS



140th SESSION OF THE EXECUTIVE COMMITTEE

Washington, D.C., USA, 25-29 June 2007

CSP27/7 (Eng.) Annex I

RESOLUTION

CE140.R10

ELIMINATION OF RUBELLA AND CONGENITAL RUBELLA SYNDROME IN THE AMERICAS

THE 140th SESSION OF THE EXECUTIVE COMMITTEE,

Having considered the progress report presented by the Director on the elimination of rubella and congenital rubella syndrome (CRS) in the Americas (Document CE140/8);

Noting with satisfaction that tremendous progress has been achieved in obtaining the interruption of endemic rubella virus transmission, thus reducing the number of rubella cases in the Region by 98%, and that incidence is at its lowest to date in the Americas; and

Recognizing that considerable efforts will be needed to support and reach the elimination goal by 2010, requiring further commitment on the part of governments and the partner organizations that are collaborating on the elimination initiative, and the strengthening of ties between public and private sectors,

RESOLVES:

To recommend to the 27th Pan American Sanitary Conference the adoption of a resolution along the following lines:

CE140.R10 (Eng.) Page 2

THE 27th PAN AMERICAN SANITARY CONFERENCE.

Having considered the progress report presented by the Director on the elimination of rubella and congenital rubella syndrome (CRS) in the Americas (Document CSP27/7);

Noting with satisfaction that tremendous progress has been achieved in obtaining the interruption of endemic rubella virus transmission, thus reducing the number of rubella cases in the Region by 98%, and that incidence is at its lowest to date in the Americas; and

Recognizing that considerable efforts will be needed to support and reach the elimination goal by 2010, requiring further commitment on the part of governments and the partner organizations that are collaborating on the elimination initiative, and the strengthening of ties between public and private sectors,

RESOLVES:

- 1. To congratulate all Member States and their health workers on the progress achieved to date in the elimination of rubella and congenital rubella syndrome (CRS) in the Americas, which demonstrates their level of commitment to the health of the population of the Western Hemisphere.
- 2. To express appreciation and request continued support from the various organizations that, together with PAHO, have offered crucial support to national immunization programs and national endeavors to eliminate rubella and CRS, including the U.S. Department of Health and Human Services Centers for Disease Control and Prevention, the Canadian International Development Agency, the Global Alliance for Vaccines and Immunization, the Inter-American Development Bank, the International Federation of Red Cross and Red Crescent Societies, the Japanese International Cooperation Agency, the March of Dimes, the Sabin Vaccine Institute, the United Nations Children's Fund, the United States Agency for International Development, and the Church of Jesus Christ of Latter-day Saints.
- 3. To urge all Member States to:
- (a) Achieve the elimination of rubella and CRS in the Americas by finalizing the implementation of vaccination strategies, intensifying integrated measles/rubella surveillance, and strengthening CRS surveillance;
- (b) Establish national commissions to compile and analyze data to document and verify measles, rubella and CRS elimination, for review by an expert committee.

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- 4. To request the Director to:
- (a) Continue efforts to mobilize additional resources necessary to surmount the challenges described in the progress report;
- (b) Form an Expert Committee responsible for documenting and verifying the interruption of transmission of endemic measles virus and rubella virus.

(Seventh meeting, 28 June 2007)