TAG RECOMMEDATIONS FOR RUBELLA AND CONGENITAL RUBELLA SYNDROME (CRS)

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Contents

1999 Recommendations

Vaccination Strategies

- All countries should incorporate rubella-containing vaccine into childhood vaccination programs, both as part of routine childhood immunization at 12 months, and as part of the follow-up campaigns. Moreover, targeted efforts are needed to reduce the number of rubella susceptible women of childbearing age. Strategies, such as post-partum immunization, immunization in family planning clinics, immunization in schools and the workplace can be used to protect these women.
- There are substantial data available documenting the absence of significant risk of rubella vaccination during pregnancy. However, pregnant women are generally not vaccinated. This is to avoid the risk of the vaccine being implicated should there be an unrelated adverse outcome of the pregnancy. For women who are vaccinated and then subsequently found to be pregnant, abortions are not recommended. Finally, it is not necessary to counsel women to avoid pregnancy for 3 months following rubella vaccination because no known risk of adverse fetal outcomes has been established.
- Countries wishing to prevent and control CRS promptly should conduct a one-time mass campaign to vaccinate all females 5-39 years of age with measles and rubella containing vaccine.
- Countries wishing to prevent and control both rubella and CRS promptly should conduct a one-time mass campaign to vaccinate BOTH males and females 5-39 years of age with measles and rubella containing vaccine.

Surveillance and Laboratory

- Rubella surveillance should be integrated with measles surveillance. The purpose of rubella surveillance is to detect circulation of rubella virus, not to detect every case of rubella. A separate rubella surveillance system is not needed. All sera from suspected measles cases which test negative for measles IgM antibodies should be tested for rubella IgM antibodies and vice versa.
- CRS surveillance should be initiated throughout the Americas. The purpose of CRS surveillance is to detect new or incident CRS cases in infants; efforts should not be routinely made to confirm CRS in older children.
- The following case definitions are recommended for CRS surveillance:
    - **Suspected CRS case:** A suspected CRS case is considered as any infant less than one year of age in whom a healthcare worker suspects CRS. A health care worker at any level of the health care system should suspect CRS in an infant when:
        1. One or more of the following birth outcomes are detected: congenital cataracts, hepatosplenomegaly, patent ductus arteriosus, purpura or hearing impairment.
        2. An infant's mother was known to have had laboratory confirmed rubella infection during pregnancy AND after a thorough physical examination, for any reason, there is clinical suspicion of CRS in the infant. Infants with low birth weight should be specifically targeted for a careful clinical examination for CRS specific birth defects.

- **Laboratory-confirmed CRS case:** A laboratory confirmed CRS case is a patient in whom a healthcare worker initially suspected CRS that is found to have laboratory evidence of rubella virus infection (i.e., rubella IgM positive).
- **Clinically-confirmed CRS case:** A clinically confirmed CRS case is an infant in whom a healthcare worker initially suspected CRS, but laboratory confirmation of rubella infection is not available. This is generally due to the absence of an appropriate clinical specimen. Since presence or absence of rubella infection could not be determined, these cases are considered as failures of the CRS surveillance system.
- **Congenital rubella infection only, without CRS:** This designation is used for an infant born to a woman infected during pregnancy. These infants are IgM positive for rubella, however, there are no clinical findings which are compatible with CRS. These cases should be discarded as not being CRS, and classified as congenital rubella infection (CRI).
- **Discarded CRS case:** A suspected CRS case may be discarded if an adequate serum sample from the infant tests negative for rubella IgM antibodies.

- Similar to measles/rubella surveillance, laboratory confirmation is crucial for the diagnosis of CRS. A blood sample should be collected from every infant with suspected CRS. For surveillance purposes, a single serum specimen is generally considered adequate to either confirm or discard CRS. If, however, the first sample tests negative for rubella IgM and there exists compelling clinical and/or epidemiologic suspicion of CRS, then a second serum specimen may be requested to confirm CRS.
- Little information is available concerning the molecular epidemiology of rubella in the Americas. Similar to measles surveillance, rubella virus surveillance may provide important information concerning the viral sub-types that are currently circulating in the Region. Efforts should be made to collect several appropriate clinical specimens for viral isolation from every documented rubella outbreak. Nasopharyngeal aspirates are the preferred specimens for rubella virus isolation. Specimens should be collected within 4 days of rash onset and forwarded to an appropriate reference laboratory.

2000 Recommendations

Vaccination Strategies

- All countries should incorporate rubella-containing vaccine (MMR/MR) into childhood vaccination programs, both as part of routine childhood immunization at 12 months, and as part of follow-up campaigns. Moreover, targeted efforts are needed to reduce the number of rubella susceptible women of childbearing age. Immunization strategies, targeting post-partum women, those attending family planning clinics, as well as those in schools and the workplace can be used to protect them.
- Countries wishing to prevent and control both rubella and CRS promptly should conduct a one-time mass campaign to vaccinate both males and females 5-39 years of age with measles and rubella containing vaccine.
- There are substantial data available documenting the absence of any risk of rubella vaccination during pregnancy. For women who are vaccinated and then subsequently found to be pregnant, abortions are not recommended. It is not necessary to counsel women to avoid pregnancy following rubella vaccination because there is no known risk of adverse fetal outcomes.

Surveillance and Laboratory

- Rubella surveillance should be completely integrated with measles surveillance. All sera from suspected measles cases which test negative for measles IgM antibodies should be tested for rubella IgM antibodies and vice versa.
- CRS surveillance should be initiated throughout the Americas in order to detect CRS cases in children under one year of age. Countries should follow the case definitions for CRS surveillance, which were recommended at the 1999 TAG meeting. It is not necessary to routinely confirm CRS in older children.
- A single serum specimen is generally considered adequate to either confirm or discard CRS.
- Countries should improve the collection of samples for virus isolation in outbreak situations. Nasopharyngeal aspirates or swabs are the preferred specimens for rubella virus isolation and should be collected within four days of rash onset. This will provide important information concerning the virus sub-types that are currently circulating in the Region.
- National programs should actively promote the collaboration with the medical sector (especially obstetricians, neonatologists and pediatricians) to enhance rubella/CRS surveillance and vaccination efforts.

2002 Recommendations

Vaccination Strategies

- All countries are encouraged to prevent circulation of rubella virus, which will lead to a reduction in CRS. This is best accomplished by reducing the number of susceptible persons which will result in decreased rubella transmission. Accordingly, countries should conduct a one-time mass campaign vaccinating both males and females. The age group to be vaccinated should be determined based on the country's epidemiology. However, groups to be targeted include children who may not have been vaccinated in the routine program, e.g., children >5 years of age, and adults of both sexes. The upper age limit should be determined from known patterns of fertility and expected susceptibility. Countries conducting successful campaigns have used upper age limits ranging from 29 to 39 years.
- Additional targeted efforts are needed to reduce the number of rubella susceptible women of childbearing age. Immunization strategies, targeting post-partum women, those attending family planning clinics, as well as those in schools and the workplace can be used to protect them.

Surveillance

- Rubella surveillance should be completely integrated with measles surveillance.
- CRS surveillance should be strengthened throughout the Americas through collaboration with the regional Perinatal Information System (SIP 2000) from the Latin American Center for Perinatology and Human Development (CLAP) and the Congenital Malformation Latin-American Collaborative Study (ECLAMC). Special emphasis should be placed on ensuring that thorough investigations of pregnant women with rubella are conducted and that their newborns receive detailed follow-up evaluations.

Measles and Rubella Laboratory Network

- National managers should ensure that the guidelines recommended by PAHO for evaluation of rash illness associated with vaccination are followed to establish the final classification of such cases. Managers should not assume that a rash illness in a recently vaccinated case is always due to the vaccination. All cases that are laboratory positive should carefully be investigated to assure they are not measles or rubella, such as determining whether there are potential source cases with rash and fever, and whether there has been subsequent transmission.
- National laboratories should be commended on their participation in, and the results from, quality control panel testing. All laboratories should continue to participate in these quality control programs. Program managers should ensure that all sera from suspected cases are tested for both measles and rubella antibodies. In addition, special emphasis should be placed on the collection of specimens for viral isolation and the logistics necessary to ensure that adequate specimens are taken and are shipped appropriately.

2004 Recommendations

Surveillance

In 1994, a regional measles eradication surveillance system was developed. This active system targeted the establishment of at least one reporting site per district. Since 1996, suspected measles cases that were IgM negative for measles have been tested for rubella IgM antibodies. In 1999, this active system was expanded into a measles-rubella integrated surveillance system to allow for simultaneous laboratory analysis. The objectives of the rubella component of the integrated surveillance system are to determine where the virus is circulating, to detect rubella cases in a timely manner in order to implement outbreak control measures, and to determine the impact of interventions.

1. The TAG endorses the rubella/CRS definitions based on the deliberations of the Meeting of the Ad-hoc Panel of Experts in Rubella and Measles held in Washington, D.C. in March 2004, cited in PAHO's EPI Newsletter of April 2004 (EPI Newsletter: Meeting of Ad-Hoc Panel of Experts in Rubella and Measles. April 2004, Vol. XXVI (2), <http://www.paho.org/English/AD/FCH/IM/sne2602.pdf>). (Annex 1). The definitions cited in the measles section also apply in full to rubella elimination.
2. For elimination purposes, full integration of measles and rubella surveillance is required; integrated laboratories are an important aspect of this surveillance system. Emphasis must be on active surveillance. Except in an outbreak setting, all specimens must be tested for both measles and rubella.
    - The TAG endorses the indicators currently reported in the PAHO Measles/Rubella Bulletin, with the revisions suggested by the Ad-Hoc Panel of Experts in Rubella and Measles (EPI Newsletter: Meeting of Ad-Hoc Panel of Experts in Rubella and Measles. April 2004, Vol. XXVI, (2), <http://www.paho.org/English/AD/FCH/IM/sne2602.pdf>). (Annex 1). Three indicators are particularly critical: the proportion of suspected cases with an adequate investigation, the proportion of suspected cases with an adequate blood sample, and the proportion of transmission chains with representative samples for virus isolation.
    - An adequate case investigation includes a home visit within 48 hours of notification, completeness of relevant data (i.e., date of notification, date of investigation, date of rash onset, date sample taken, type of rash, presence of fever, dates of previous measles/rubella vaccinations), and active case searches.
    - Efforts should continue to monitor reported measles/rubella cases by age, sex, location, and vaccination status.
3. In the context of CRS elimination, high-quality surveillance requires an active component and a sensitive case definition. The TAG recommends the following definition to guarantee rapid investigation of suspected CRS cases:
    - Suspected CRS case - A health care worker at any level of the health care system should suspect CRS in an infant when: (1) one or more of the following birth outcomes are detected: congenital cataracts, congenital cardiac defects, purpura or deafness; or (2) An infant's mother was known to have had laboratory-confirmed or suspected rubella infection during pregnancy. For diagnosis, a more specific

definition may be appropriate, with laboratory confirmation remaining the gold standard.

- During elimination, all suspected CRS cases should have specimens collected for IgM testing and virus isolation.

4. The TAG recommends that PAHO convene an ad-hoc meeting of experts to determine lessons learned and define good public health practice for establishing CRS surveillance. Issues to consider include review of existing literature and country experience, as well as reaching out to tap the expertise of professionals in various fields who come into contact with CRS-affected children. This includes, but is not limited to, ophthalmologists, cardiac surgeons, schools for the deaf, otorhinolaryngologists, and pediatric infectious disease specialists. This meeting should help to refine surveillance approaches and case detection strategies, for instance the use of low-birth weight as an investigation trigger to narrow the scope of perinatal screening.
5. Collaboration with the regional Perinatology Information System of the Latin American Center for Perinatology and Human Development (CLAP) and the Latin American Collaborative Study of Congenital Malformations (ECLAMC) should help strengthen surveillance.
6. TAG recommends further research on testing algorisms and evaluation of alternative clinical specimens such as oral fluids and dried blood spots. Furthermore, indicators and strategies should be reviewed in the context of country experience with integrated surveillance. The impact of the rubella elimination initiative on strengthening health services, particularly services for women, should also be documented.

Laboratory

The PAHO Measles/Rubella Laboratory Network met to discuss a number of technical and logistical issues. Recommendations emerged relating to IgM kit selection, viral isolation and genotyping, preferred sample types, laboratory accreditation, classification of vaccine-related cases, treatment of false positives, treatment of suspected cases in pregnant women, and laboratory monitoring. The final report and recommendations of the Measles/Rubella Laboratory Network are endorsed by the TAG (Annex 2).

Vaccination Strategies

1. TAG encourages the implementation of one-time mass vaccination campaigns in both men and women in all remaining endemic countries. The age group to be vaccinated, whether 15-29 years of age, 15-39 years of age, or else, should be determined based on the likely susceptibility of adults. This would depend on the year of introduction of the MMR vaccine in the national schedule, the extent of follow-up MR or MMR vaccination campaigns to maintain measles elimination, and the rubella epidemiology in the country. The TAG commends the countries that have successfully conducted adult mass vaccination campaigns. The countries that have conducted mass vaccination campaigns only in women will need to determine the extent of the virus transmission and susceptibility in men, and develop appropriate strategies to reduce the number of rubella-susceptible men.
2. Substantial evidence has accumulated from many studies, including recent studies in Brazil and Costa Rica, indicating that there is no identifiable link between vaccinating pregnant women and giving birth to a child with CRS. Therefore, there is no reason to

modify the current approach of vaccinating all WCBA during campaigns. Brazil and Costa Rica should be congratulated on their studies and encouraged to submit their findings for publication.

2006 Recommendations

TAG congratulates member countries for the significant progress made toward the goal of rubella and CRS elimination by 2010. Given the countries´ successes, the goal is certainly achievable for the Americas.

Vaccination strategies

- In accordance with previous TAG recommendations, all endemic countries are encouraged to implement a one-time mass vaccination campaign targeting both men and women and achieving >95% coverage.
- TAG recommends that the criteria for high quality campaigns outlined above be included in the design and implementation of rubella mass vaccination campaigns. Those countries that did not vaccinate all susceptibles in the population should analyze their data, in particular to identify the susceptible male population (in which sustained transmission can occur) that should be vaccinated. PAHO should provide support in this process.
- TAG encourages countries to document the experiences, successes, and lessons learned from their adult mass campaigns in order to share them with other countries. These lessons will be useful for the introduction of HPV vaccine and eventually a vaccine against HIV/AIDS.

Surveillance

- Full integration of measles and rubella surveillance is required; integrated laboratories are an important aspect of this surveillance system. Emphasis must be placed on active surveillance. Except in outbreak settings, all specimens must be tested for both measles and rubella.
- Countries should ensure that the seven indicators meet the recommended standards. Special attention should be given to checking clusters of suspect cases as well as "silent areas".
- Countries should review and improve the quality of their surveillance and information systems with PAHO support, as needed.
- TAG endorses the following recommendations reached through consensus by the participants of the *Ad-hoc* meeting of experts on "best practices in CRS surveillance"**:**
    - Sensitivity and quality of surveillance system should be increased by strengthening sentinel site reporting – including secondary and tertiary hospitals, specialty clinics, and the use of TORCHS4 for differential diagnosis as part of CRS surveillance;
    - The use of information should be strengthened, such as the information generated by the perinatal information systems of CLAP5 and ECLAMC6 and national databases related to child and maternal health, in order to increase the capability for CRS case detection.
    - Strong partnerships should be built with professional and academic institutions and societies in order to train professionals and involve them in rubella and CRS surveillance efforts. The modules and field guides published by PAHO should be disseminated with this objective in mind.

- A multidisciplinary team should be formed in each country at national level, similar to the one used for polio eradication, to evaluate and classify suspect cases.

Laboratory

- The number of clinical specimens collected for viral isolation should be increased in order to document the endemic genotypes of rubella and the interruption of endemic transmission of rubella in the Americas.
- In a pregnant woman, IgM should be obtained only when there is a history of rash or contact with a rubella-like rash. IgM is NOT recommended for routine antenatal testing.
- The serological and virological laboratory testing of all suspected CRS cases should be encouraged.
- TAG recommends that PAHO review the laboratory network, with special attention to the subnational networks, to identify the possible bottlenecks and propose corrective actions. [TORCHS stands for Toxoplasma gondii; other viruses (HIV and more); rubella (German measles); cytomegalovirus; herpes simplex; and syphilis. CLAP: Spanish acronym for the Latin American Center for Perinatology and Women and Reproductive Health. ECLAMC: Spanish acronym for the Latin American Collaborative Study on Congenital Malformations.]

Measles/Rubella Laboratory Network

TAG endorses all the recommendations of the pre-TAG meeting of the Measles/Rubella Laboratory Network that took place in Guatemala on the 23 July and highlights the following:

- Laboratory testing is an integral component of measles, rubella, and CRS surveillance and countries are strongly encouraged to incorporate laboratory costs into their surveillance budgets.
- Laboratories should establish a close working relationship with epidemiologic staff to make sure that adequate specimens are collected for serology and virus isolation, and data are recorded and reported in a timely and accurate manner. Laboratory personnel should participate in national committees to discuss final classification of measles/rubella cases.
- A virus genotype should be determined for all chains of transmission of measles and rubella and rigorous efforts should be undertaken to collect specimen accordingly.
- PAHO should continue to advocate with national governments and partner agencies for continued support to the measles/rubella laboratory network as a first line of defense against importations of measles from other regions and to support the elimination of rubella from the Americas

2009 Recommendations

TAG congratulates Member States and their health workers for the tremendous efforts made toward achieving and maintaining measles, rubella, and CRS elimination and for the rapid response to importations to the Americas. TAG also urges other regions to eliminate measles and rubella as a step towards eradication. In addition to the following recommendations, TAG encourages countries to continue to adhere to previous TAG recommendations regarding measles, rubella, and CRS surveillance, vaccination strategies, and laboratory issues.

Immunization Strategies

- Countries should routinely maintain high, homogenous coverage (>95%) by municipality through the administration of the 1st routine dose, monitor the accumulation of susceptibles, and continue the implementation of high quality nationwide *follow-up* campaigns to ensure the vaccination of the entire cohort as a second opportunity to give the first dose to those children that were missed by the routine program.
- In accordance with previous TAG recommendations, any resident of the Americas traveling to areas with reported measles or rubella cases should be immune to measles and rubella and provide proof of vaccination before departure.
- Only where coverage >95% with each of the two routine MMR doses is guaranteed for all municipalities can the *follow-up* campaigns be waived and, before introduction of routine MMR2, countries should determine a suitable age for administration of this dose, define an accurate denominator, implement a nominal registry, monitor coverage, and track defaulters.

Surveillance

- Countries should achieve an adequate level of preparedness by developing national plans for preparation and rapid response to an importation and potential outbreaks.
- Countries should actively involve the private sector in measles, rubella, and CRS surveillance to support the rapid detection of importations and response to outbreaks and to strengthen immunization activities.
- Countries should guarantee the full integration of measles and rubella surveillance systems and ensure the completion and continuous monitoring of the recommended standardized measles/rubella surveillance indicators to attain high-quality surveillance, emphasizing highrisk and “silent” areas.
- Countries that have reported the last rubella and CRS cases should implement activities, such as active case searches and monitoring of virus excretion of identified CRS cases, in order to document and verify the interruption of endemic virus transmission.
- TAG reiterates the previous recommendation to increase sensitivity and quality of the CRS surveillance system by strengthening sentinel site reporting.

Laboratory

Documentation that elimination of measles and rubella has been achieved requires that each national laboratory produces the highest quality surveillance data possible. The final report and recommendations of the Measles/Rubella Laboratory Network Meeting are endorsed by TAG.

- Laboratories must be fully certified according to the current WHO and PAHO LabNet standards.
- Countries should establish priorities for obtaining viral samples with emphasis on, for example, border areas, industrial areas, areas with frequent foreign travel, and contacts with a high likelihood of exposure.
- Laboratory and epidemiologic teams from each country should use the specific PAHO laboratory testing guidelines for classification of sporadic measles and rubella cases according to their needs.
- Measles, rubella, and CRS cases should be classified only after the laboratory and epidemiologic teams have reviewed all laboratory results and epidemiologic data.
- Laboratories should attempt to establish a genetic baseline of rubella and measles viruses through characterization of endemic cases or archival samples (serum, oral fluid, nasopharyngeal swab, and tissue), starting with the year 2000.
- Laboratories/countries should establish the means to support CRS case confirmation and monitoring of virus shedding by CRS cases.

Regional Plan of Action for Documenting and Verifying Elimination

TAG endorses the 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 and strengthen vaccination activities and surveillance systems.

- In accordance with PAHO Resolution CSP27.R2, countries should establish a national commission and develop a plan of action for the documentation and verification of measles, rubella, and CRS elimination, which includes a realistic timetable for goal completion.
- Countries should complete the analysis and evaluation of the following key components of the documentation process as described in the regional plan of action:
    - Analysis of coverage with the measles-rubella vaccine in population cohorts aged <40 years.
    - Epidemiology of measles, rubella, and CRS and the impact of vaccination strategies.
    - Quality and efficiency of integrated measles, rubella, and CRS surveillance.
    - Analysis of virologic epidemiology and verification of the absence of endemic measles and rubella virus strains (through viral detection) in all countries of the Americas.
    - Sustainability of national immunization programs to maintain measles and rubella elimination.
- Countries should prepare and implement a national plan of action for the verification of measles, rubella, and CRS elimination, with technical cooperation from PAHO and the international Expert Committee.

2011 Recommendations

- TAG encourages countries to continue to adhere to previous TAG recommendations to maintain measles, rubella, and CRS elimination and for the rapid response to importations to the Americas. These recommendations include reaching coverage ≥95% of first and second (routine or in campaign) measles-rubella vaccine doses in all municipalities, strong integrated measles-rubella surveillance, and enhanced CRS sentinel site reporting.
- Countries should continue to ensure that resources are available to support surveillance and laboratory activities.
- TAG urges countries reporting measles cases and outbreaks to conduct detailed epidemiological and virological analysis to fully characterize the cases and outbreaks.
- TAG calls upon the other Regions of the world and the WHO to implement strong measures for the control of current measles outbreaks and to further advance their control and elimination initiatives. TAG also supports country requests to include the topic of a global measles and rubella eradication goal in the discussion at the next World Health Assembly.
- National commissions, in collaboration with ministries of health, should continue to implement a national plan of action for the documentation of measles, rubella, and CRS elimination, with technical cooperation from PAHO and the IEC.
- Countries should complete the analysis and evaluations of key components included in the regional plan of action and submit their final country report to the IEC by December 2011.
- The TAG endorses all of the recommendations that resulted from the annual Meeting of Measles and Rubella Laboratory Network (Annex 1).

Annex 1 (Draft recommendations)

Documentation of elimination of measles, rubella, and CRS in the Region of the Americas

- Laboratories should collect and evaluate laboratory data required for documentation and maintenance of national elimination goals for measles, rubella, and CRS.
    - In the next 6-10 months, national laboratories should seek advice from RRLs and GSLs on case classification when necessary and, after discussions with these laboratories, submit appropriate specimens to RRLs or other network laboratories for additional testing. This should include confirmation of positive IgM results when necessary, and additional testing, such as RT-PCR, avidity, which may not be available in the national laboratory. Laboratories should use the PAHO Laboratory Guidelines and the checklist for sporadic cases (Appendix the Lab Guidelines) for guidance on determining the need for additional testing.
    - A plan of action for testing should be developed which will be used to test samples for sporadic cases and outbreaks and monitor the maintenance of elimination. RRLs and the regional laboratory coordinator will develop a plan of action. It is anticipated that this plan will include establishing molecular diagnostics in most national laboratories and performing specialized testing in specific network laboratories through a defined referral system.

- Develop strategies to strengthen communication between the measles and rubella laboratory and public health epidemiology units. Laboratories should take appropriate steps to develop organizational arrangements necessary for the documentation and maintenance of national elimination goals for measles, rubella, and CRS. These include coordinated case classification using all available epidemiologic and laboratory data through direct discussions between epidemiology and laboratory teams regarding all available data. Laboratory and epidemiological staff should meet at least once a month to reconcile data, identify data omissions and decide on any further specimen collection and testing required for the classification of cases.
- In order to verify measles, rubella and CRS elimination every lab in the network should monitor all the indicators referring to the lab as described in the components of the Plan of Action for the documentation and verification of the elimination.

Laboratory Management

- PAHO headquarters should work with RRLs and GSL to manage the laboratory network in the Americas. PAHO will continue to manage kit distribution and other essential organizational activities, and facilitate and support essential technical activities in RRLs and GSL such as accreditation of laboratories and development and evaluation of testing protocols.
- Because of the demand for laboratory support for regional documentation and verification of measles, rubella and CRS, and because of the compressed timeline that network laboratories will require to receive the additional training and support needed to establish new testing procedures and strategies, PAHO should support a laboratory coordinator dedicated to measles, rubella and CRS for at least a period of 2 years.
- PAHO, the GSL and RRLs should work to improve communications between the network laboratories and develop methods to rapidly disseminate information regarding new methods, recent outbreaks, and changes in testing procedures. PAHO should consider developing a newsletter that can be distributed to the laboratories. In addition, periodic web based meetings should be held with laboratory staff, epidemiologists, RRLs, CDC, and PAHO to discuss case classification. Ad hoc meetings should be also be considered for consultation on complex case classifications.
- A meeting of the regional and sub-regional reference laboratories should take place in 2011.

Challenges for the diagnosis of measles, rubella, and CRS in low incidence settings

- Laboratories should be aware of important information on case classification other than the results of laboratory testing, including timing of the use of various diagnostic tests and the effectiveness of diagnostic tests in specific situations (e.g. PPV of 1 and multiple defect suspected CRS cases). Laboratories should bring this type of information to discussions with epidemiologic teams concerning case classification.
- Laboratories should achieve and maintain the level of technical expertise necessary to maintain laboratory surveillance capacity to monitor measles, rubella, and CRS elimination. This expertise should include molecular testing. To facilitate this, PAHO will support a regional laboratory training workshop at FIOCRUZ in August 2011 and another workshop at a location to be determined in the first quarter of 2012.

- National laboratories with sufficient capacity are encouraged to use molecular tests, especially real time RT-PCR for measles and rubella to aid in case confirmation.
- The validated avidity test for measles IgG that is performed at the CDC is not available in commercial format. Laboratories should send samples requiring measles avidity testing to CDC after consultation with PAHO and CDC. To facilitate this process, laboratories should use the checklist developed by CDC to help determinate the need for avidity testing. The CDC avidity test will be transferred to other RRLs if there is an increased demand for testing or to improve turnaround time.
- The avidity test for rubella IgG is commercially available, and PAHO, the RRLs and GSLs should conduct a workshop or meeting to standardize the methods and the interpretations of results and to develop a specimen referral protocol as well as a quality control program for the laboratories that are performing avidity testing.
- Recognizing that laboratory confirmation of CRS cases requires an understanding of the timing of various diagnostic tests relative to the appearance of markers of disease; laboratories should become familiar with this timing and with managing receipt of specimens from sources outside the rash and fever surveillance network such as neonatologists and pediatricians. Laboratories need to report findings to the epidemiologic teams in the country.

Molecular epidemiology

- Laboratories should encourage collection of samples for virus detection in an attempt to obtain genetic information from at least 80% of confirmed outbreaks of measles and rubella.
- Timely reporting of genotype information and sequence data are essential for rapid confirmation of viral importation. NLs that are performing sequencing should report measles sequences to and rubella genotype information to the WHO database. RRLs performing sequence analysis for NLs should submit the sequence information to MeaNS and the WHO database after obtaining permission from the NL. It is important that all relevant epidemiological data be included with the sequence information so that the submitting laboratory can submit complete reports. Laboratories are reminded of the need to share sequence data within at least 2 months of sample collection and that this performance indicator is monitored in the WHO accreditation process.
- Future training workshops should include activities to increase the regional capacity for sequencing and sequence analysis in addition to molecular diagnostic techniques.
- Molecular epidemiologic data are often limited for countries in the region, especially for rubella viruses. Nevertheless, laboratories must seek to use such data to the extent possible in support of documentation of elimination of measles, rubella, and CRS as required by the Plan of Action.

Quality Control

- Laboratories should continue to perform quality control for serologic testing as required for WHO accreditation. National labs are strongly encouraged to provide a proficiency testing program for any sub national labs in their country.
- The WHO accreditation process is an important component of the quality control process and laboratory results to support documentation of elimination must be provided by an accredited laboratory. Laboratories should be accredited on an annual basis either by

paper accreditation or by a site visit. PAHO should conduct site visits to the NLs and RRLs on a rotating basis so that all laboratories are visited once every 3 years. A priority list of laboratories to be reviewed should be developed in consultation with PAHO, RRLs and GSLs. PAHO will conduct site visits in 4 countries by the end of 2011.

- Sub-national laboratory (SNL) proficiency testing is a critical measure of the quality of the laboratory surveillance program in countries which have SNLs, but identifying sufficient volumes of IgM positive samples has been a challenge in many countries. Efforts should be made globally to collect large volumes of IgM positive measles and rubella serum for use in the SNL LabNet in the region and support RRLs in the region to produce a SNL proficiency testing panel.
- In many countries, the SNLs perform a critical role in surveillance for measles and rubella by conducting a large volume of the primary serologic testing. However, successfully, managing a network of SNLs requires a substantial effort from the NL. To document these management activities, the WHO accreditation checklist for NLs should be modified to include a summary of the performance of each SNL and a description of the management activities performed by the NL.
- Laboratories in the PAHO network should work with the LabNet laboratories in other regions to develop a quality control program for molecular testing.
- Laboratories are strongly encouraged to use the standard PCR controls and standardized kits provided by CDC for molecular testing and confirmation of viral isolation.
- Laboratories should document any suspected problems with the performance of the Siemens kits for detection of IgM to measles and rubella. The laboratory coordinator, in consultation with the GSL and RRLs, will develop a protocol to assist laboratories with monitoring assays performance. Problems with assay performance should also be reported to WHO/HQ and CDC.

2012 Recommendation

1. The TAG endorses and urges countries to implement the Emergency Plan of Action to maintain the elimination of measles, rubella and CRS in the Americas, as stated in Resolution CSP28.R14 of the Pan American Sanitary Conference 2012.

2013 Recommendations

- The TAG commends countries for their efforts in maintaining measles and rubella elimination and encourages countries to continue implementing its previous recommendations in order to maintain the elimination of measles, rubella and CRS.
- TAG endorses the IEC recommendations, made at the fourth joint meeting with representatives of the national commissions, and urges countries to implement them and to submit their final verification reports by 01 December 2013.
- With the goal of achieving the highest MMR2 coverage possible, administration of the MMR2 vaccine is recommended at 15-18 months, and can be given simultaneously with other vaccines, such as the first DPT booster.
- Countries should continue to verify vaccination status at school entry and immunize children who have not been vaccinated with MMR2.
- Countries should continue with high-quality follow-up vaccination campaigns in order to guarantee a high level of immunity, while the Region continues with the verification process and vaccination coverage >95% has been achieved with two doses of MMR or MR in the routine program.
- PAHO Governing Bodies and Member States should continue advocating for measles and rubella elimination in global forums such as the World Health Assembly considering that importations of the virus pose a challenge for maintaining elimination in the Americas.
- PAHO should support country efforts to systematize the lessons learned from the recent measles outbreaks and to share them with other countries of the Americas as well as with the rest of the world.

2014 Recommendations

- TAG recommends that the PAHO Secretariat review, with the Brazilian authorities, the epidemiological data and the outbreak response in order to identify opportunities to halt the epidemic as soon as possible.
- To this end, TAG urges Brazilian authorities to present the most updated data and outbreak response to both the TAG and IEC members.
- TAG suggests the Brazilian government consider PAHO's availability and readiness to provide any type of assistance to interrupt the measles virus transmission in the country.
- PAHO Secretariat should lead a further in-depth examination of the epidemiology of and response to recent outbreaks to better understand transmission patterns and age-distribution of cases, use of MR vs. MMR vaccines in outbreak response, the usefulness of dose 0 at 6 months of age in addition MMR1 at 12 months of age and MMR2 at 18 months of age during outbreaks.
- All countries need to maintain their capacity to respond rapidly and decisively to outbreaks. In order to anticipate the spread of an outbreak, thorough outbreak investigation is critical in order to define geographical areas and age ranges to be targeted. Outbreak responses must be aggressive and timely to halt secondary transmission.
- All countries should also review their measles/rubella surveillance performance and vaccination coverage levels to identify areas of vulnerability. Specifically and within the context of the 2014 FIFA World Cup, countries should implement additional surveillance actions (i.e., active searches) to document the absence of measles and rubella cases.
- TAG reemphasizes previous recommendations that coverage of at least 95% with 2 doses of measles-containing vaccines in all districts and in all countries is needed to maintain elimination. If 95% coverage is not reached with two doses, countries should continue to conduct periodic follow-up campaigns.
- TAG reissues its 2013 recommendation to lower the age for the second MR-containing vaccine dose to 18 months and use school entry requirements as a platform to monitor MR-containing vaccine vaccination status.

2015 Recommendations

- TAG recognizes the efforts of Brazil in the face of the ongoing outbreak of measles. Nonetheless, TAG urgently calls on the Government to take decisive measures to end the outbreak of measles in Ceara. Following the last confirmed measles case in Ceara, the government will need to document the interruption of measles virus circulation in the affected areas, in accordance with the verification criteria established by PAHO.
- TAG urges countries to fully implement the currently recommended surveillance indicators, in order to have a sensitive and timely surveillance system, which produces reliable and consistent data.
- TAG recommends vaccinating infants 6-11 months of age in outbreak situations. (This dose will be considered to be a "zero dose"). These infants should then receive the first dose of measles-rubella-mumps (MMR) containing vaccine when they reach 1 year of age, and a second dose according to the country's national schedule, preferably at 18 months of age.
- TAG strongly recommends that WHO-Geneva raise progress towards the global elimination of measles as a resolution at the next World Health Assembly (WHA), to strengthen the commitment of the other regions in achieving the goals of the Global Vaccine Action Plan (GVAP).