Surveillance Guide for Vaccine-Preventable Diseases in the WHO South-East Asia Region

September 2017
# TABLE OF CONTENT

**Foreword** 4

**Measles and Rubella surveillance** 7

- Introduction 7
- Case/Outbreak detection and reporting 9
- Case investigation 10
- Unique case identification number 10
- Specimen collection and transportation 11
- Case Classification 15
- Case management 17
- Public health intervention 18
- Dealing with large outbreaks (>five suspected cases) 20
- Data management 22
- Surveillance during acute humanitarian emergencies. 25
- Review and Feedback 26

**Annexes** 27

- ANNEX 01- Measles disease 27
- ANNEX 02- Rubella disease 32
- ANNEX 03- Core reporting variables for Measles and Rubella 37
- ANNEX 04- Sample Measles-Rubella Case Investigation Form 40
- ANNEX 05- Outbreak preparedness and response in settings with large outbreaks 42
- ANNEX 06- Key definitions related to measles and rubella 46

**Readings** 47
Foreword

Today, we share a collective vision to have the South-East Asia Region free of vaccine-preventable diseases, where all countries provide equitable access to high-quality, safe, affordable vaccines and immunization services throughout the life-course.

Overwhelming evidence demonstrates the benefits of immunization as one of the most successful and cost-effective health interventions ever known. Over the past several decades, immunization has achieved many milestones, including the eradication of smallpox, an accomplishment that has been called one of humanity’s greatest triumphs. Vaccines have saved countless lives, lowered the global incidence of polio by 99% and reduced illness, disability and death from diphtheria, tetanus, whooping cough, measles, *Haemophilus influenzae type b* disease and epidemic meningococcal A meningitis. We have been able to make the Region free of polio for the last 6 years and eliminate maternal and neonatal tetanus.

We have vaccines against more than 25 diseases in the present day world, and this has increased the need for better surveillance against these diseases to control or eliminate them. As the essence of this subject matter, I would like to highlight that high vaccination coverage may not necessarily indicate the case-load or disease burden in a population. We need to look into the surveillance performance as the key indicators to measure progress towards disease control and/or elimination.
A functional vaccine-preventable disease surveillance system is a key part of public health decision-making in all countries. Thus, there is an urgent need to build on the current efforts to strengthen vaccine-preventable disease surveillance with the latest state-of-the-art technologies at subnational and national levels. This will require a substantial and long-term commitment of human and material resources, usually beginning with a systematic assessment of the national vaccine preventable diseases (VPD) surveillance system by working closely in partnership with all related partners and stakeholders.

I hope that this vaccine-preventable diseases surveillance guide will be well translated into respective national programmes and add to the efforts to have a high-quality surveillance system for priority vaccine-preventable diseases and help accelerate progress towards strengthening vaccine-preventable disease surveillance in our Region.

Finally, every individual in our Region deserves our best work. We all agree that every family, no matter where residing, has the right to all immunization and health services that are provided by the respective government, in the spirit of universal health coverage contributing towards Sustainable Development Goals, especially Goal 3 on health.

Dr Poonam Khetrapal Singh

Regional Director, WHO South-East Asia Region
<table>
<thead>
<tr>
<th>LIST OF ABBREVIATIONS</th>
<th>LIST OF ABBREVIATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACS</td>
<td>active case search</td>
</tr>
<tr>
<td>CCID</td>
<td>cell culture infectious dose</td>
</tr>
<tr>
<td>CFR</td>
<td>case fatality rate</td>
</tr>
<tr>
<td>CHW</td>
<td>community health worker</td>
</tr>
<tr>
<td>CI</td>
<td>confidence interval</td>
</tr>
<tr>
<td>CIF</td>
<td>case investigation form</td>
</tr>
<tr>
<td>CRF</td>
<td>case report form</td>
</tr>
<tr>
<td>EIA</td>
<td>enzyme immune assay</td>
</tr>
<tr>
<td>ELISA</td>
<td>enzymelinked immuno-sorbent assay</td>
</tr>
<tr>
<td>EOC</td>
<td>emergency operations center</td>
</tr>
<tr>
<td>EPI</td>
<td>Expanded Programme on Immunization</td>
</tr>
<tr>
<td>HQ</td>
<td>headquarters (WHO)</td>
</tr>
<tr>
<td>ICD</td>
<td>International Classification of Diseases</td>
</tr>
<tr>
<td>IU</td>
<td>international unit</td>
</tr>
<tr>
<td>ID</td>
<td>identity</td>
</tr>
<tr>
<td>IgG</td>
<td>immunoglobulin G</td>
</tr>
<tr>
<td>IgM</td>
<td>immunoglobulin M</td>
</tr>
<tr>
<td>IHR</td>
<td>International Health Regulation (2005)</td>
</tr>
<tr>
<td>IM</td>
<td>intramuscular</td>
</tr>
<tr>
<td>MCV</td>
<td>measles containing vaccine</td>
</tr>
<tr>
<td>mL</td>
<td>milliliter</td>
</tr>
<tr>
<td>MMR</td>
<td>measles mumps rubella</td>
</tr>
<tr>
<td>MMRV</td>
<td>measles mumps rubella varicella</td>
</tr>
<tr>
<td>MR</td>
<td>measles rubella</td>
</tr>
<tr>
<td>MR-CIF</td>
<td>measles rubella case investigation form</td>
</tr>
<tr>
<td>MRCV1</td>
<td>first dose of measles and rubella containing vaccine</td>
</tr>
<tr>
<td>MRCV2</td>
<td>second dose of measles and rubella containing vaccine</td>
</tr>
</tbody>
</table>
1. Introduction

A sensitive case-based surveillance system is essential to monitor progress toward elimination and to sustain measles elimination and rubella control/elimination. In settings with a measles elimination goal, such as all 11 SEAR countries, the goal of case-based surveillance is to detect, investigate, and classify all suspected cases; and to respond to confirmed outbreaks. For case confirmation, case-based surveillance includes laboratory testing at an accredited laboratory within the Global Measles and Rubella Laboratory Network.

As countries progress from accelerated control toward elimination, surveillance systems need to transition from ‘outbreak surveillance’ to case-based surveillance with individual case investigation and confirmation. This intensification of surveillance will facilitate a better understanding of transmission patterns and guide implementation of rapid outbreak response immunization (ORI) to interrupt the chains of virus transmission. Moreover, case-based surveillance is required to monitor progress toward elimination and the quality of the surveillance is one of the five lines of evidence for the documentation of elimination of measles and rubella. The standard mode of surveillance for elimination strategies is case-based surveillance with detailed case investigation of all suspected cases and the following attributes:

1. **Detect, confirm and classify cases:**
   a. Establish and maintain a network of reporting units and informants with nationwide coverage;
   b. Continuous and comprehensive passive surveillance with weekly reporting;
   c. Periodic active surveillance in reporting units, including hospitals and health facilities;
   d. Close coordination, including monthly meetings of surveillance program manager, EPI manager, and laboratory staff to review and harmonize data, and perform case classification;
   e. Consider each single laboratory-confirmed case as an outbreak, triggering a rapid public health response.

2. **Reporting of suspected cases:**
   a. Report suspected cases immediately (within 24 hours);
   b. Conduct passive zero reporting weekly as part of other VPD surveillance.
3. **Investigating reported cases:**
   
a. Investigate cases within 48 hours of reporting;

b. If rubella is suspected, as part of the investigation, collect pregnancy information on women of childbearing age

c. Collect specimens for confirmation from every case; if outbreak is confirmed to be very large, specimens are to be collected from around 5–10 cases and additional cases are epidemiologically linked;

d. If rubella is suspected, collect specimens on all pregnant women.

e. Establish a pregnancy registry to follow the pregnancy outcome for all pregnant women with lab confirmed rubella,

f. Ensure case management (e.g. vitamin A) as per existing national guidelines with focus on infection prevention.

4. **Laboratory confirmation of cases/outbreaks:**

Cases are confirmed in the lab through detection of IgM in sera (or oral fluid) for measles and rubella in the laboratory by enzyme linked immune-sorbent assay (ELISA). The origin of the virus is determined through nucleotide sequencing of nasopharyngeal/oropharyngeal swabs and molecular epidemiological methods. Cases are classified as lab-confirmed, epidemiologically linked, or clinically confirmed/compatible (or excluded); and further classified according to the source of infection, as imported, import-related, endemic or unknown.

5. **Public health response:**

a. Conduct contact tracing to determine who infected the case in addition to whom the case may have infected; for suspected rubella cases, determine the pregnancy status for the contacts.

b. Enhance case-based surveillance, including community survey for additional cases;

c. Review population immunity/gaps;

d. Enhance population immunity against measles and rubella.

6. **Dealing with large outbreaks**

7. **Surveillance during acute humanitarian emergencies**

8. **Data collection for cases/outbreaks:**

a. Capture core variables data for all reported cases (Annex 3);

b. Collect additional data, including molecular epidemiology to allow for analysis that is more extensive.
9. **Data analysis and interpretation:**
   a. Complete epidemiological analysis: time, place, person (e.g. age, vaccination status); (for rubella: need to include pregnancy status and gestational age)
   b. Identify source of infection;
   c. Identify transmission patterns and effective methods to interrupt transmission chains.

10. **Review and Monitoring surveillance performance indicators**

11. **Reporting / Feed-forward to higher levels:**
   a. Weekly;
   b. Data content (e.g. core variables).

12. **Feedback to peripheral levels:**
   a. Increase frequency and content – e.g. lab results on individual cases should be immediately communicated to lower levels;
   b. Develop weekly/monthly bulletins.

**2. Case/Outbreak detection and reporting**

**Case definition**

**Suspected case of measles and rubella** – A patient with fever and maculopapular (non-vesicular) rash, or a patient whom a health-care worker suspects has measles or rubella irrespective of the age.

**Measles or rubella outbreak** in an elimination setting is defined as laboratory confirmation of any single case and evokes a public health response.

In countries and areas with measles incidence of >five cases per million population, outbreak response could be initiated when a clustering of five suspected cases, or a suspected measles death, within a district or geographical area with population equivalent to 100,000 within a period of four weeks is detected.

**Case reporting**

Health-care workers or other informers should immediately report every suspected case to the local surveillance authority. The channel of this reporting and the information needs to be simple and efficient. All health-care workers – physicians, nurses, allied health personnel, community health workers or personnel maintaining records – should know how to identify and report suspected cases. Private hospitals and practitioners need to be included, as they may be the only health-care providers for many cases. Public health
officials/surveillance officers are responsible for ensuring that health-care workers know how to identify and report cases, to establish a surveillance network and to maintain surveillance of adequate quality.

Public health officials should also regularly conduct active surveillance visits to health facilities to check hospital records, outpatient and inpatient registers and interview health staff to find any missed case of suspected measles or rubella. Such visits also provide an opportunity to sensitize health staff on case reporting and resolve any issues that they may have.

3. Case investigation

Case investigation is important to confirm the disease and identify the magnitude of public health response required. Epidemiologists or specially trained health staff should be responsible for case investigation within 48 hours of case reporting. Every reported case is investigated using standard Measles Rubella Case Investigation Form (MR-CIF). The MR-CIF should capture certain core variables as given in Annex A11.

If there is clustering of cases with more than five suspected cases of measles and rubella in a population catchment areas of 100 000, the investigation should be conducted as a large outbreak with serology and virology sample collection for the first five to ten cases, with additional cases epidemiologically linked. The exception to this, is suspected rubella in a pregnant woman, sera should be obtained on all pregnant women with suspected rubella.

4. Unique case identification number

It is critical to assign a unique case identification number to each suspected case. This case identification number should begin with one or more three-letter combinations to designate the geographic location, followed by the year and the case number. Forms, specimen labels and all communications related to the case should cite the unique case identification number. The box below gives an example of a unique case identification number:

```
MR-IND-UP-RBL-16-001
MR: indicate disease Measles Rubella,
IND: country code
UP: state code/province code
RBL: district code
16: year of rash onset
001: serial no. of the cases in that year in the same district
```
5. Specimen collection and transportation

For countries that have been verified as measles or rubella eliminated, near elimination or re-established transmission, every case should have a serum sample and a throat, nasal or nasopharyngeal swab for virology.

For countries that are still endemic for measles or rubella, serology remains the gold standard but virology to identify the genotype is expected to be conducted in more than 80% of chains of transmissions.

If the outbreak is large, laboratory specimens should be collected from at least the first five suspected cases, if less than two suspected cases are lab confirmed, laboratory specimen from additional five cases should be collected and tested. If an outbreak continues over a protracted period, another 5-10 samples should be collected every 2 months to ensure that the outbreak is still due to measles or rubella. Genotyping becomes particularly important when the duration of an outbreak is approaching 12 months in a country that was previously eliminated in order to determine whether chains of transmission are part of the same outbreak or due to new importations of a different measles virus strain.

5.1 Serology

Whenever measles/rubella is suspected, designated personnel should secure specimens for laboratory confirmation. Adequate blood sample should be collected on first contact with the patient during the case investigation. A nasopharyngeal swab/throat swab should be obtained for virology along with the serology specimen.

The likelihood of detecting IgM antibodies is high if the blood specimen is collected between 3 and 28 days after onset of rash. Shipment of the sample to a recognized laboratory should take place as soon as possible, maintaining appropriate cold chain (4–8 °C).

Venous blood collection

- Venipuncture in sterile labelled tube (3-5 mL for older children and adults and 1 mL for infants and younger children).
- Whole blood can be stored at 4–8 °C for up to 24 hours before the serum is separated.
- Whole blood should be allowed to clot and then centrifuged at 1000 × g for 10 minutes to separate the serum.
- The serum should be carefully removed with a fine-bore pipette to avoid extracting red cells and transferred aseptically to a sterile labelled vial.

---

Adequate specimens for serology are those collected within 28 days after rash onset that consist of ≥ 0.5 mL serum or ≥ 3 fully filled circles of dried blood on a filter-paper, or oral fluid. For oral fluid samples, the sponge-collection device should be rubbed for at least 1 minute along the gum until the device is thoroughly wet.
- Serum should be stored at 4–8 °C until shipment takes place, but not more than a maximum of 5 days. When kept for longer periods, serum samples must be frozen at a temperature of –20 °C.

**Alternate specimen collection for serology**

Collection of blood samples is the preferred method for specimen collection; however, it is not always achievable where there are challenges to conduct venepuncture, geographical challenges to transportation or maintaining a cold chain when transporting samples to the laboratory. Therefore, the alternative use of dried blood spots and oral fluid samples has been validated in the WHO Measles and Rubella Laboratory Network. Antibody is stable in dried blood spots and so it is particularly valuable where the lack of a cold chain is an issue. Oral fluid samples have a higher sensitivity for viral detection than dried blood samples; however, have cold chain requirements.

a. **Dried blood spot collection**
   - Skin puncture the finger or heel (for young children before they start to walk) using sterile lancet.
   - Up to four full-circles of whole blood are collected on standardized filter paper. For an adequate specimen, ensure that each entire circle is completely filled. One to two drops are collected to completely fill each circle of a filter paper (*whatman protein saver*) properly labelled for each case. (1st circle for Measles IgM, 2nd circle for Rubella IgM, 3rd circle for repeat test if required, 4th circle for quality assurance processes in the lab).
   - Allow the filter paper to dry thoroughly before enclosing in a plastic bag or envelope, and store with a desiccant to keep dry.
   - Samples do not need to be kept refrigerated or frozen during transport; it is advisable to store in a cool, dry place and transport to the laboratory as soon as possible, preferably within 5 days.
   - Thoroughly dried blood spot samples are no longer subject to IATA (International Air Transport Association) dangerous goods regulations.

b. **Oral fluid collection**
   - Use a special swab (such as a toothbrush) to collect crevicular fluid from the gum area of the mouth. The swab should be rubbed along the gum for at least 1 minute until the device is thoroughly wet.
   - Place the wet swab inside a clear plastic tube available for the purpose and label it.
   - Shipment of samples within 48 hours to the lab. Samples should be kept in a refrigerator until shipping to the laboratory with icepacks.
   - The samples are usually not considered biohazardous and can be shipped without special documentation from the site of collection to the laboratory.
   - Specific instructions provided by the device manufacturer should be followed.
5.2 Virology

Data on viral genotypes are critical for identifying the source of cases, whether they are indigenous or imported, and the place of origin if imported. Therefore, specimens for viral detection and isolation should be collected on first contact with the patient for every suspected case and repeated periodically during large outbreaks. Throat swabs should be collected within 5 days of onset of rash for viral detection/isolation for both measles and rubella viruses.

How to collect throat swab or the Nasopharyngeal/oropharyngeal swabs?

- Firmly rub the nasopharyngeal/oropharyngeal passage and back of the throat with sterile cotton swabs to dislodge epithelial cells.
- The swabs are placed in a sterile viral transport medium in labelled screw-capped tubes.
- Nasopharyngeal/oropharyngeal specimens should be refrigerated and shipped to the laboratory with ice packs (4 to 8 °C) to arrive at the testing laboratory within 48 hours.
- If arrangements cannot be made for rapid shipment, swabs should be shaken in the medium to elute the cells and then removed. The medium or nasal aspirate should be centrifuged at 500 × g (approximately 1500 rpm) for 5 minutes, preferably at 4 °C, and the resulting pellet should be re-suspended in cell culture medium. The suspended pellet and the supernatant should be stored separately at –70 °C and shipped to the testing laboratory on wet ice (4 to 8 °C) to arrive within 48 hours or preferably on dry ice in well-sealed screw-capped vials.

Alternate specimen collection for virology

a. Urine samples - the measles virus is present in acute cases of measles in the cells that have been sloughed off in the urinary tract. Urine is collected for virology if throat swab is difficult to obtain. It is preferable to obtain the first urine passed in the morning.

- About 10–50 mL of urine should be collected in a sterile container and held at 4 to 8 °C before centrifugation.
- The virus is concentrated by centrifugation of the urine and the cell pellet re-suspended in a suitable viral transport medium.
- Urine must NOT be frozen before the concentration procedure is carried out.
- Whole urine samples may be shipped in well-sealed containers at 4 °C, but centrifugation within 24 hours after collection is preferable.
- Centrifugation should be performed at 500xg (approximately 1500 rpm) for 5 to 10 minutes, preferably at 4 °C. The supernatant should be discarded and the sediment re-suspended in a 2 to 3 mL sterile transport medium, tissue
culture medium or phosphate-buffered saline.

- The re-suspended pellet may be stored at 4 °C and shipped within 48 hours to a measles reference laboratory. Alternatively, it may be frozen at −70 °C in a viral transport medium and shipped on dry ice in a well-sealed screw-capped vial.

b. Oral fluid - similar to that described earlier for serology.

**Summary of types of sample to be collected for laboratory diagnosis of measles and rubella**

<table>
<thead>
<tr>
<th>Type of Specimen</th>
<th>Test type</th>
<th>Volume to collect</th>
<th>Timing for specimen collection</th>
<th>Storage Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum (venepuncture)</td>
<td>Ig M Antibody detection</td>
<td>5 ml of blood; 1 ml for infants and younger children; 0.5 ml from small infants.</td>
<td>≤28 days post rash onset. Paired sera are normally collected 14-21 days apart. The interval between the two serum samples can be shorter if virus-specific IgG was not detected in the first serum sample.</td>
<td>4-8 °C</td>
</tr>
<tr>
<td>Alternative specimen: Dried blood spot (DBS)</td>
<td>Ig M Antibody detection Detection of viral RNA by RT-PCR</td>
<td>At least 3 fully filled circles on a filter-paper collection device</td>
<td>≤28 days post rash onset.</td>
<td>No cold chain required</td>
</tr>
<tr>
<td>Throat, nasal, or nasopharyngeal (NP) swabs or nasopharyngeal aspirates**</td>
<td>Viral isolation and detection of viral RNA swab or NP aspirate</td>
<td>Within 5 days after rash onset for viral isolation (cell culture). Up to 14 days post rash onset if performing virus detection using RT-PCR</td>
<td>4-8 °C</td>
<td></td>
</tr>
<tr>
<td>Oral Fluid (OF)</td>
<td>IgM antibody detection IgG antibody detection Detection of viral RNA by RT-PCR Using a sponge collection device to collect ~0.5 mL crevicular fluid.</td>
<td>Up to 14 days post rash onset if performing virus detection using RT-PCR up to 28 days if antibody testing</td>
<td>Does not require cold chain if &lt;22 °C ambient temperature</td>
<td></td>
</tr>
<tr>
<td>Type of Specimen</td>
<td>Test type</td>
<td>Volume to collect</td>
<td>Timing for specimen collection</td>
<td>Storage Conditions</td>
</tr>
<tr>
<td>------------------</td>
<td>-----------</td>
<td>-------------------</td>
<td>-------------------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>Urine</td>
<td>Viral isolation by cell culture Detection of viral RNA by RT-PCR</td>
<td>Minimum 10 ml (preference first morning void). Larger volume with higher chance of detection</td>
<td>within 5 days after rash onset</td>
<td>Spin down cell pellet and re-suspend in buffer for storage and transport at 4-8 ºC</td>
</tr>
</tbody>
</table>

6. Case Classification

After investigation, all suspected cases should be classified into one of the following mutually exclusive categories (Figure 1). Case classification is a critical step in using surveillance data for action and requires someone to be in the ‘driver’s seat’ of the system. The responsibility of case classification belongs to the surveillance officer, and must be done in close coordination with the laboratory staff. Case classification of each suspected case is based on laboratory results, and the epidemiological information collected on the CIF.

**Laboratory-confirmed case:** A suspected case of measles or rubella that has been confirmed by a proficient laboratory through detection of IgM in sera (or oral fluid) for measles or rubella in the laboratory by ELISA.

During laboratory testing, if a case is found to be equivocal, the laboratory will follow the WHO MR laboratory guidelines for interpreting equivocal cases, including collection of repeat sample when indicated.

A proficient laboratory is one that is WHO-accredited and/or has an established quality assurance programme with oversight by a WHO-accredited laboratory.

**Epidemiologically linked case:** A suspected case of measles, or rubella, that has not been confirmed by a laboratory but was geographically and temporally related, with dates of rash onset occurring 7–21 days apart for measles (or 12–23 days for rubella) to a laboratory-confirmed case or, in the event of a chain of transmission, to another epidemiologically-confirmed measles or rubella case.

**Clinically compatible measles case:** A suspect case with fever and maculopapular (non-vesicular) rash and one of cough, coryza or conjunctivitis, for which no adequate clinical specimen was taken and which has not been linked epidemiologically to a laboratory-confirmed case of measles, rubella, or another laboratory-confirmed communicable disease.

**Clinically compatible rubella case:** A case with maculopapular (non-vesicular) rash and fever (if measured) and one of arthritis/arthritis or lymphadenopathy, for which no
adequate clinical specimen was taken and which has not been linked epidemiologically to a laboratory-confirmed case of rubella, measles or another laboratory-confirmed communicable disease.

**Non-measles non-rubella case:** A suspected case that has been investigated and discarded as non-measles and non-rubella using

- laboratory testing in a proficient laboratory or
- epidemiological linkage to a laboratory-confirmed outbreak of another communicable disease that is neither measles nor rubella.

**Measles vaccine-associated illness:** A suspected case that meets all five of the following criteria:

- the patient had a rash illness, with or without fever, but did not have cough or other respiratory symptoms related to the rash;
- the rash began 7–14 days after vaccination with a measles-containing vaccine;
- the blood specimen, which was positive for measles IgM, was collected 8–56 days after vaccination;
- thorough field investigation did not identify any secondary cases; and
- field and laboratory investigations failed to identify other causes.

\[\text{Suspected case} \rightarrow \text{Laboratory positive} \rightarrow \text{Laboratory confirmed case} \]
\[\text{Suspected case} \rightarrow \text{Laboratory negative} \rightarrow \text{Discarded: Non-measles non-rubella} \]
\[\text{Suspected case} \rightarrow \text{No epidemiological linkage} \rightarrow \text{Discarded: Non-measles non-rubella case} \]

**Figure 1. Flowchart for classification of suspected cases**

Note: Countries that have high burden of other causes of fever and rashes (other rickettsial diseases, Dengue etc.) should consider linking the algorithm to the surveillance of those diseases; if positive for a disease that is neither measles nor rubella, the case should be counted as a discarded case of measles and rubella.
Laboratory or epidemiologically confirmed cases should be further classified according to the source of the infection as imported cases, import-related cases or cases with an unknown source.

**Endemic cases:** Endemic measles transmission is the existence of any continuous indigenous chain or re-established chain of transmission of measles/rubella virus persisting for >1 year in any defined geographic area. An endemic measles case is a laboratory or epidemiologically confirmed measles case resulting from endemic transmission of the measles virus. For rubella, any case that cannot be proved imported is considered endemic.

**Imported cases:** An imported measles case is a confirmed case which, as supported by epidemiologic and/or virologic evidence, was exposed outside the country or region during the 7–21 days prior to rash onset. For rubella, the time frame is 12–23 days. A travel history to an area where measles/rubella occurs and during a plausible time frame must be demonstrated; results of molecular sequencing of the virus isolated from the cases should be compatible with the areas/countries visited. The possibility of local exposure to measles/rubella must be excluded after a careful community investigation.

**Import-related cases:** An import-related case is a confirmed case, which, as supported by epidemiologic and/or virologic evidence, has locally acquired infection as part of a transmission chain related to an imported case. A chain of transmission is two or more confirmed cases that are epidemiologically linked. The investigation should thus demonstrate that the import-related case had direct contact 7–21 days with an imported case or another import-related case (12–23 days before rash onset for rubella). Molecular sequencing data of the isolated virus, if available, could support the link.

**Cases with unknown source of infection:** A confirmed case for which the source of infection was not identified. It is possible that an epidemiological link to an imported case or an import-related case cannot be found even after a thorough investigation, and sporadic cases with unknown source of infection are not necessarily indicative of endemic transmission. However, the identification of sporadic cases might indicate gaps in surveillance. The pattern of occurrence of these cases (e.g. number of transmission chains and number of cases involved, geographical and temporal distribution) is as important as their number.

### 7. Case management

There is currently no specific antiviral treatment for measles or rubella. Administration of vitamin A to children with measles has been shown to decrease both the severity of disease and the case-fatality rate, and WHO recommends that vitamin A be administered to all children with measles: 50 000 I.U. for infants aged less than 6 months, 100 000 I.U. for infants aged 6–11 months and 200 000 I.U. for children aged 12 months of age and older. Administration of vitamin A should be provided at the first health service contact and one dose should be administered the following day. If the child has clinical signs of
vitamin A deficiency (such as Bitot’s spots), a third dose should be given 4–6 weeks later. For children who are being cared at home, public health officers should ensure that they receive vitamin A doses.

Treatment should be provided for a number of measles complications. All cases of measles do not require hospitalization and many can be managed at home. For uncomplicated cases, fluids (such as oral rehydration solution), antipyretics and nutritional therapy are commonly indicated. Many children require 4 to 8 weeks to fully recover their pre-measles nutritional status. All hospitalized cases of measles should be isolated to prevent further transmission inside the hospital. Suspected measles patients should be isolated until 4 days after appearance of rash. Care should be taken in hospital settings to use proper infection control practices (e.g. isolation, negative pressure) as measles is extremely contagious. There is high risk of nosocomial transmission among non-immune health-care workers and other patients, including unimmunized infants. Unless measles patients have complications requiring hospitalization or follow-up, it is recommended for them to be cared for at home.

Other measles complications, such as diarrhoea, pneumonia and otitis media, should be treated following the WHO protocol for Integrated Management of Childhood Illness. (http://apps.who.int/iris/bitstream/10665/42939/1/9241546441.pdf)

For rubella, care is supportive for non-pregnant persons. For pregnant women with suspected rubella, a comprehensive investigation including laboratory testing should be conducted. Pregnant women with confirmed rubella should be followed till the completion of her pregnancy to document the outcome (i.e., normal, CRS, miscarriage, stillbirth, etc). For those pregnancies that go to delivery, the newborn should be placed in contact isolation and evaluated for suspected CRS.

8. Public health intervention

Public health intervention should be initiated for all confirmed cases of measles and/or rubella. In measles elimination settings, a single case is considered an outbreak and evokes public health response.

In countries and areas with measles incidence of >five cases per million population, public health response should be initiated when a clustering of five suspected cases, or a suspected measles death, within a district or geographical area with population equivalent to 100,000 within a period of four weeks is detected. Detailed information and guidelines on large outbreak preparedness and response are available in Annex 5.

The key components of public health response are

a. Contact tracing: Conduct contact tracing to identify the source of infection and determine whether other areas have been exposed or are also experiencing outbreaks.
Identify all people that the case had contact with during the time he/she was contagious (4 days before and until 4 days after the onset of rash for measles and for rubella, 7 days before until 7 days after the onset of rash); make a line-listing of these contacts, including their names and addresses, determine whether they are or were ill and if rubella is suspected, pregnancy status for all women of childbearing age should be obtained.

In large outbreaks, it may not be feasible to identify all contacts due to time, resources, and logistical constraints. In this situation, contact tracing should be deprioritized, and a large public health immunization response should be triggered along with a risk communication and awareness campaign.

The following groups and individuals could be considered priority contacts during outbreaks:

- household contacts
- schools (or other educational centres) contacts, including all school employees and students
- Child care/day care contacts
- workplace contacts
- health care facility: individuals who shared the same room, including waiting room without appropriate protection.

The following actions should be taken to minimize spread.

- Contacts without documented evidence of measles and/or rubella vaccination should be vaccinated and the symptoms of measles and rubella should be explained to them.
- During the second week after exposure, and at the first sign of possible fever and maculopapular rashes the contact should be instructed to stay at home.
- Follow-up should be done to determine if a contact subsequently became ill. If so, laboratory specimens should be collected.
- Pregnant women with suspected rubella should be followed until the completion of her pregnancy to document the outcome especially if the outbreak is labelled as rubella. (i.e., normal, CRS, miscarriage, stillbirth, etc).

- **Enhanced case-based surveillance and active case searches:** In response to confirmed cases of measles or rubella, active case searches should be conducted to detect unreported cases to ensure that all cases are identified and reported. In the community and in schools, active case searches are conducted by asking key people if they know of anyone with fever and rash. This activity can be aided by using pictures of measles/rubella patients with maculopapular rash. Such searches can be conducted in a perimeter of an entire village, cluster of villages, ward of town...
or entire town, etc. depending upon a local epidemiological assessment mostly within the radius of 100–1000 metres from the confirmed case. In addition, health facilities should also be included for active case searches. In health facilities, health staff interviews and review of registration records, discharge diagnoses, hospital charts, etc. should be performed to identify patients with fever and rash illnesses and their final diagnosis. During and following rubella outbreaks, active CRS surveillance should be implemented with special attention to investigation and active follow-up of pregnant women with suspected rash illness in the affected area. Additional measures could include investigation and vaccination of susceptible contacts to reduce the risk of exposure to pregnant women.

c. **Survey of population immunity/gaps:** review of coverage trend for MRCV1 and MRCV2, review coverage of MCV SIA or other Periodic Intensification of Routine Immunization (PIRI) if any in the area, identify any immunity gaps, focus especially on any hard-to-reach populations.

d. **Enhancing population immunity against measles and rubella:** conduct an ORI or SIA based on epidemiological data. All children who were found to be unimmunized and those who cannot produce immunization cards or records during the community survey should be vaccinated with measles- and rubella-containing vaccine according to the national recommendation.

**Isolation of suspected cases:** Children with mild illness may preferably be managed at home without compromising on access to health care and avoiding contact with other vulnerable children. Seriously ill children should preferably be hospitalized for proper management. Since the measles virus is highly infectious, all hospitalized children with suspected measles should be cared for in an isolation facility. School-aged children and working adults should avoid public places and remain confined at home for at least 5 days after the onset of the rashes.

For confirmed rubella infection, persons with rubella should be isolated up to 5 days after rash onset. Emphasis should be placed on preventing exposure of susceptible pregnant women to prevent CRS.

**9. Dealing with large outbreaks (>five suspected cases)**

In some settings, including humanitarian crisis situation, there may be clustering of many suspected cases and in countries and areas with measles incidence of >five cases per million population, public health response could be initiated when a clustering of five suspected cases, or a suspected measles death, within a district or geographical area with population equivalent to 100,000 within a period of four weeks is detected.

In such settings, laboratory specimens should be collected from at least the first 5 suspected cases, if only less than 2 suspected cases are lab confirmed, laboratory specimen from
additional five cases should be collected and tested for measles and rubella IgM. In such situation, outbreaks need to be classified as either measles\textsuperscript{21} outbreak, rubella outbreak or a mixed outbreak.

- If two or more specimen are positive for measles IgM and less than two specimen positive for rubella IgM, or measles virus is isolated/detected from any sample, the outbreak is classified as **Measles outbreak**
- If two or more specimen are positive for rubella IgM and less than two specimen positive for measles IgM, or rubella virus is isolated/detected from any sample the outbreak is classified as **Rubella outbreak**
- If two or more specimen are positive for measles IgM and two or more specimen are positive for rubella IgM, the outbreak is classified as **Mixed Measles and Rubella Outbreak**
- If less than two samples are positive for measles or rubella IgM, the outbreak is **Discarded** and the cases are treated as sporadic cases and public health response initiated accordingly.

When outbreaks become large, the principles of public health response remain the same with some subtle considerations as mentioned below:

1. Contact tracing should be deprioritized, and a large public health immunization response along with risk communication and awareness campaign should be prioritized.

2. Consider moving to line listing cases and decrease the number of variables required to be collected for each individual case. However, it is recommended that unique identifier, name, age, vaccination status, travel history, residence continue to be collected at a minimum. One added element in outbreak settings is to assign an outbreak ID to all cases associated with an outbreak, when possible.

3. Epidemiological linkage should be the primary way that new cases are classified during such confirmed outbreak. However, it is not recommended that all cases in a given area during the particular period be all categorized as epidemiologically linked; all IgM negative cases should be discarded and do better investigations to establish potential relationships between cases to have epidemiological linkage.

4. If epidemiologic linkage is not established, laboratory testing of the suspect case should be done. After initial confirmation of the outbreak, laboratory testing should be conducted among suspected cases that may arise in new locations or in previously unaffected groups.

5. If the outbreak continues over a protracted period, another 5-10 samples should be collected every 2-3 months to ensure that the outbreak is still due to measles. Genotyping becomes particularly important to determine whether chains of transmission are part of the same outbreak or due to new importations of a different measles virus strain.

10. **Data management**

An important aspect of a successful measles elimination and rubella control programme is a well-developed information system that provides programme managers and health workers with the information they need for taking appropriate actions. Information from the surveillance system is used to produce regular summary reports, which are distributed to the personnel responsible for taking actions on identified problems. All surveillance information should be standardized.

**Data collection:** Whether or not the information system is computer-based, it should cover case tracking and site reporting. At the sub-district, district and state levels, there should be a system that is capable of tracking all reported suspected cases until they are either confirmed or excluded. For optimal monitoring and meaningful analysis of surveillance data, systematic and standard collection of critical parameters is essential. These limited numbers of variables are called ‘core variables’ and are required to properly manage such information. Core variables include: unique case identification number; basic demographic data on each case; basic clinical data on each case; data on vaccination status; recording and monitoring of laboratory specimens from collection to final laboratory results; case classification and outcomes. These core variables are incorporated into a standardized form for case investigation.

At the national and subnational levels, a system capable of keeping track of the reporting units should be in place. Reporting units may be a geopolitical jurisdiction, such as a county, district or municipality; or a service unit, such as a hospital, private clinic or private practitioner. Districts should send weekly reports that should reach the national programme. Even if no suspected cases are identified, districts should still send a report once a week, the so-called “zero-case reporting”. The national programme should then forward the collated report to the WHO regional office every week. The timeliness of those reports (on time or late) should be regularly recorded for each unit.

**Data analysis:** Data from the investigation form and line-listings should be analysed to monitor reported suspected, clinically compatible, epidemiologically linked and laboratory-confirmed cases by age, sex, location and vaccination status as well as to determine whether standards for case reporting and investigation are being met.

**Age distribution:** Age distribution of cases permits health authorities to detect any changes in the epidemiology of the disease and to establish which age groups to target for vaccination.
**Geographic location:** Cases should be plotted on a map according to their place of residence, and the map compared with vaccination coverage data and sites reporting in the surveillance system. These maps can be useful for coordinating activities, such as setting up vaccination sites.

**Source of infection:** Surveillance and investigation information will help to identify areas where the measles/rubella virus is still actively circulating or imported.

**Source of reporting:** This information will help to determine whether improvements are needed regarding personnel reporting suspected cases. For example, if cases are being reported only from public health facilities, then additional contacts with private medical doctors, private clinics and informal informants and channels are required.

**Vaccination history of cases:** Accurate information on the vaccination history of confirmed cases is essential for evaluating vaccine coverage, vaccine effectiveness and detecting potential problems with the cold chain.

At the country level, a bulletin, preferably updated on a weekly basis, should be issued with results on suspected and confirmed cases. In addition, this bulletin should indicate the number of units reporting each week (including zero-case reporting). Information about the current epidemiology of acute flaccid paralysis, neonatal tetanus and other EPI target diseases could also be included, and bulletins should be distributed to all health-care providers and other interested health-care personnel on a monthly basis.

**Surveillance Performance Indicators**

Standard indicators of surveillance performance and laboratory accreditation criteria have been described as follows.

- **Timeliness of reporting**
  - Proportion of surveillance units sending measles and rubella reports, including ‘zero-reporting’ to the national level on time (target: ≥80%).

  \[
  \text{Surveillance units reporting measles and rubella data to the national level on time} \times 100
  \]

  \[
  \text{Total number of surveillance units}
  \]

- **Reporting rates of cases discarded as non-measles and non-rubella as a proxy to sensitivity of surveillance**
  - Reporting rate of discarded non-measles non-rubella cases at national level (target: ≥2 per 100 000 total population).

  \[
  \frac{\text{Total number of discarded non-measles non-rubella cases}}{\text{Total population}} \times 100 000
  \]
- **Representativeness of reporting**
  - Proportion of second administrative level units reporting at least two non-measles non-rubella cases per 100,000 population (target: ≥80% of second-level administrative units).

  \[
  \text{Total number of second administrative level units reporting at least two non-measles non-rubella cases per 100,000 population} \times 100
  \]

- **Adequacy of investigation**
  - Proportion of suspected cases with adequate investigation initiated within 48 hours of notification (target: ≥80% of suspected cases).

  \[
  \text{Total number of cases with adequate investigation within 48 hours of notification} \times 100
  \]

  Adequate investigation includes collection of all the following data elements from each suspected case of measles or rubella: Name or identifier; place of residence; place of infection; age or date of birth; sex; date of onset of rash; date of specimen collection; measles-rubella vaccination status; date of last measles-rubella containing vaccination; date of notification; date of investigation and travel history.

- **Laboratory confirmation**
  - Proportion of suspected cases with adequate specimen collection \(^3\) for detecting acute measles and rubella infection collected and tested in a proficient laboratory (target: ≥80% of suspected cases, excluding epidemiologically linked cases).

  \[
  \text{Total number of cases in which adequate serum sample is collected and tested in a proficient laboratory} \times 100
  \]

- **Timeliness of specimen transport**
  - Proportion of serology and virology specimens received at the laboratory within 5 days of collection (target: ≥80%).

  \[
  \text{Total number of specimens received at laboratory within 5 days of collection} \times 100
  \]

---

\(^3\) Adequate specimens for serology are those collected within 28 days after rash onset that consist of ≥0.5 mL serum or ≥3 fully filled circles of dried blood on a filter-paper, or oral fluid. For oral fluid samples, the sponge-collection device should be rubbed for about 1 minute along the gum until the device is thoroughly wet; epidemiologically linked cases should be excluded from the denominator.
11. Surveillance during acute humanitarian emergencies.

The principals of surveillance for fever and maculopapular rashes remain the same during acute humanitarian emergencies with all the components mentioned above. However, vaccination during such situation should be based on the decision tree as mentioned in the “Vaccination in Acute Humanitarian Emergencies: A framework for decision making” (available at http://apps.who.int/iris/bitstream/10665/255575/1/WHO-IVB-17.03-eng.pdf)
12. Review and Feedback

Periodic review of surveillance performance should be conducted through various mechanisms. Some suggested ones are:

- Annual desk review using the WHO Measles Programmatic Risk Assessment Tool
  (http://www.who.int/immunization/monitoring_surveillance/routine/measles_assessment/en/)

- Periodic (every 2-3 years) Joint national and international VPD surveillance review activity

Feedback can be provided effectively by sending monthly measles rubella surveillance bulletins to the reporting sites and to interested parties. If monthly bulletins cover other vaccine-preventable diseases also, then measles rubella surveillance information can be included in it. Informal channels of feedback should also be utilized, such as telephone, personal contacts, visits, common meetings and press releases. If the source of infection is from other states, countries or regions, a feedback mechanism through IHR should be established.
ANNEX 01- Measles disease

Aetiology
Measles virus (genus Morbillivirus, family Paramyxoviridae) is an enveloped, single-stranded RNA virus that has globally retained its monotypic antigenic structure for decades. The genome encodes 8 proteins, including the haemagglutinin (H) and the fusion (F) proteins. WHO recognizes 24 measles virus genotypes; however, following the widespread use of measles vaccine, the number of circulating genotypes is decreasing. Measles virus sequencing, phylogenetic analyses and molecular epidemiology can be used to track measles virus transmission.

Pathogenesis
Measles virus causes systemic infection. The median incubation period is 14 days (range, 7–21 days) from exposure to onset of rash. 2 to 3 days after infection and replication in the respiratory epithelial cells, viruses reach regional lymph nodes and a primary viremia occurs with subsequent spread to the reticuloendothelial system. Following further viral replication in regional and distal reticuloendothelial sites/organs, there is a second wave of viremia, which occurs 5 to 7 days after initial infection. During this secondary viremia, there may be infection of all organs, including the skin, which contributes to the typical rash and the gastrointestinal tract mucosa, which is visible in the oral mucosa as Koplik spots. Measles virus multiplication is more intense now in upper respiratory tract and virus is shed from nasopharynx fluid. Thus, the person is infectious to others from 4 days before rash onset until 4 days after rash onset, the period when the virus spreads into the air as droplets and aerosols). Inhaling such virus results in new hosts getting infected in the community, with the development of immunity, the virus load in the body declines and disappears.

Transmission
Measles is a highly infectious (easily transmissible) viral disease spread by direct contact and airborne transmission. If a case of measles is introduced among a group of non-immune subjects, secondary infection may occur in 12 to 18 persons (R₀ = 12–18).

Reservoir
There is no extra human reservoir for measles virus. Infection is self-limited in most individuals, without a chronic carrier state.
Occurrence

In the pre-vaccination period, >90% of individuals were infected by the age of 10 years, the majority with symptoms with significant mortality. Vaccination has now decreased the disease burden, mortality and seasonal pattern. In tropical zones, most cases of measles occur during the dry and cold season; in temperate zones, incidence peaks during late winter and early spring. In SEAR 75 857 suspected cases of measles were reported in 2015. Laboratory tests were conducted on 9737 cases of which 2251 were positive for measles and 1052 for rubella.

Figure 2: Measles cases with MCV1 and MCV2 Coverage estimates SEAR, 2001–2015


Measles elimination

Measles elimination is defined as the absence of endemic measles transmission in a defined geographic area (e.g. region or country) for 12 months in the presence of a well-performing surveillance system. WHO-SEAR has a goal of elimination of measles and rubella and CRS control by 2020. Objectives to achieve this goal are as follows.

1. Achieve and maintain at least 95% population immunity with two doses against measles and rubella within each district of each country in the Region through routine and/or supplementary immunization.

2. Develop and sustain a sensitive and timely case-based measles/rubella and CRS surveillance systems in each country in the Region that fulfil recommended surveillance performance indicators.
3. Develop and maintain an accredited measles and rubella laboratory network that supports every country or area in the Region.

4. Strengthen support and linkages to achieve the above three strategic objectives.

Clinical features and complications
Towards the end of the incubation period, patients develop prodromal symptoms of high fever, cough, coryza and conjunctivitis. The typical maculopapular rash appears after another 3–4 days, often accompanied by a fever that peaks at 39–40 ºC. At the onset of rash, bluish-white Koplik spots, which are pathognomonic of measles, are seen in the oral mucosa. Patients normally improve by the third day after rash onset and are fully recovered 7–10 days after onset of disease.

The severity of measles varies widely, depending on a number of host and environmental factors. Measles tend to be severe in under 5 children, particularly in those below 3 years. Malnourished (especially with vitamin A deficiency) have risk of severe disease and complications consequent to severe vitamin A depletion. In overcrowded situations and in household transmissions the inoculum dose tends to be high contributing to severity of illness. Children with HIV infection are particularly vulnerable to severe measles. Measles mortality is more common with severe measles. In SEAR countries, case-fatality rates among young children may reach 5–10%.

Relatively common complications of measles include otitis media, laryngotracheobronchitis, diarrhoea and pneumonia. In children, otitis media occurs in 5–15% of cases and pneumonia in 5–10%. Diarrhoea and dysentery are also common complications of measles. Persistent diarrhoea with protein-losing enteropathy may ensue, particularly in infants. Post-infectious measles encephalitis occurs in about 1/1000 cases, and subacute sclerosing panencephalitis, a slowly progressing infection of the central nervous system, occurs in about 1/5 000–10 000 cases.

Laboratory Diagnosis
Since clinical diagnosis is not sufficient to confirm measles infection, the laboratory is critical in a measles elimination programme. Measles infection can be confirmed by documenting a measles-specific immune response in the patient and/or by culture and isolation of the measles virus from a clinical specimen.

The most common technique used to confirm the diagnosis of measles is a test for the presence of measles-specific IgM antibodies in sera collected from suspected measles cases. For measles surveillance, a single blood specimen obtained shortly after rash onset may be sufficient to confirm or discard suspected measles cases. All suspected measles cases and outbreaks should be serologically confirmed and differentiated from other fever and rash outbreaks and differential diagnoses.
The ELISA test for the detection of measles-specific IgM antibodies is the recommended standard for the WHO measles laboratory network.

Although technically more difficult than serologic assays, the culture, isolation and genetic analysis of the measles virus obtained from measles outbreaks can provide important information about the circulation of measles virus. Therefore, appropriate clinical specimens for viral culture must be collected from every chain of measles transmission as well as from any sporadic cases.

In order to promote high-quality measles laboratory testing throughout the SEAR, Member States have established WHO supported MR laboratory network. As of 2015, there are 45 laboratories in the MR laboratory network with one Regional Reference Laboratory (RRL) in NIH Bangkok. Each reference laboratory provides technical support and confirmatory measles testing for one or more national measles laboratories. MR lab-network is also critical to establish transmission pathways of measles and rubella virus circulation and document the progress made by the country towards measles elimination and rubella control goal.

Measles and vitamin A

Vitamin A deficiency contributes to delayed recovery and to the high rate of post-measles complications. In addition, measles infection may precipitate acute vitamin A deficiency and xerophthalmia. As a result, measles accounts for a large proportion of preventable childhood blindness. The beneficial impact of two doses of vitamin A during treatment of measles is well established. WHO’s current policy advocates administering vitamin A to all acute cases.

Immunity following measles

Whereas the presence of circulating, neutralizing antibody against the H antigen is sufficient to prevent infection with measles virus, cell-mediated immunity is required to clear virus once infection has occurred. The long-lasting, possibly lifelong, immunological memory of measles virus following natural infection includes both continued production of measles virus-specific antibodies and the circulation of measles virus-specific CD4+ and CD8+ T lymphocytes. Although the levels of anti-measles-virus antibodies may diminish over time, the ability to rapidly mount secondary humoral and cellular immune responses is important in providing protection from infection.

Depending upon the titre of passively acquired maternal antibodies; infants are usually protected against measles for 6–9 months. A large infectious dose may occasionally overcome the protection afforded by maternal antibodies, and measles has also been observed in neonates whose mothers escaped natural infection and had never been vaccinated against measles.
Immunization and immune response

Measles vaccines

Measles vaccine consists of live, attenuated strains of measles virus and is available, either as monovalent measles vaccine or as measles-containing vaccine (MCV) in combination with rubella, mumps or varicella vaccines. When using the combined measles–rubella vaccine, measles–mumps–rubella (MMR) vaccine or measles–mumps–rubella–varicella (MMRV) vaccine, the protective immune responses to each individual vaccine antigen as well as vaccine-associated adverse events remain largely unchanged. However, the rate of febrile seizures occurring 7–10 days after the first dose in children vaccinated with MMRV is about 2 times higher (9/10 000) than in children who receive MMR and varicella vaccines separately at the same visit.

Measles vaccine protects equally well against all wild measles virus genotypes. Although a live vaccine, virus does not spread from vaccinated to the unvaccinated.

Immune responses to MCV

Measles vaccine induces both humoral and cellular immune responses comparable to those following natural infection, although antibody titres are usually lower. Following vaccination, transient measles-specific immunoglobulin (Ig) M antibodies appear in the blood and IgA antibodies appear in mucosal secretions; IgG antibodies, hence protective immunity, persist for decades. Vaccination also induces measles virus-specific CD4+ and CD8+ T lymphocytes.

Vaccinating infants before or at the age of 6 months often fails to induce seroconversion due to the immaturity of the immune system as well as the presence of neutralizing maternal antibodies. The development of a high avidity antibody response is critical to the development of protective immunity to measles virus. Antibody avidity to measles virus is generally lower in children vaccinated at age 6 to 9 months compared with the avidity obtained in children vaccinated at age 12 months or above.

Studies on revaccination in children who failed to respond to their first dose of measles vaccine given at 12 months show that almost all develop immunity after their second dose. Although vaccine-induced antibody concentrations decline over time and may become undetectable, immunological memory persists and, following exposure to measles virus, most people who have been vaccinated produce a protective immune response.

Following vaccination, the long-term persistence of neutralizing measles antibodies (26–33 years) and long-lasting protection against measles have been demonstrated by several investigators.[4] No studies yet have identified declining immunity as an important risk factor.

---

ANNEX 02- Rubella disease

Rubella is an acute, usually mild exanthematous fever affecting susceptible children and young adults worldwide. Its public health importance is due mainly to the teratogenic potential of the virus.

Aetiology

The rubella virus (RV), a togavirus of the genus Rubivirus, is an enveloped single-stranded RNA virus with a single serotype. It is a fragile virus, which is easily inactivated by detergents, heat and extremes of pH. RV contains RNA, which is surrounded by a capsid and a lipoprotein envelope. The capsid is composed of the capsid protein (C), while the envelope contains two glycoproteins E1 and E2. These proteins induce the major immune responses. Although there are no major antigenic differences among RV isolates, a number of different genotypes have been identified. Identification of genotypes is used to trace the origin of outbreaks as countries approach elimination. In 2005, a systematic nomenclature for wild rubella virus genotypes was adopted. The genotypes are divided into two major phylogenetic groups, clade 1 and 2, which differ by 8–10% at the nucleotide level. Currently 3 (1E, 1G, 2B) of the defined 13 genotypes have a wide geographical distribution, whereas the others occur sporadically or are geographically localized.

Pathogenesis

Following respiratory transmission of rubella virus, replication of the virus occurs in the nasopharynx and regional lymph nodes. The incubation period is 18 days (range 12 to 23 days). Viraemia occurs 5–7 days after infection and results in viral spread to different organs. Rubella virus can be found in nasopharyngeal samples from 1 week before the onset of the rash to 2 weeks after, with maximal shedding occurring 1–5 days after rash onset. In pregnant women, transplacental infection of the fetus occurs during viremia. The virus infects the placenta and developing fetus. Fetal damage occurs through destruction of cells as well as mitotic arrest. Infants born with congenital rubella may shed the virus for a year or more in pharyngeal secretions and urine.

Transmission

Humans are the only known host. Rubella virus is transmitted by the respiratory route. The most infectious period is usually 1–5 days after the appearance of the rash.

Reservoir

There is no known animal reservoir. Infants with CRS may shed rubella virus for an extended period. Post-natal infection does not lead to prolonged shedding.

Occurrence

Rubella occurs worldwide. In temperate areas, incidence is usually highest in late winter and early spring. In tropical countries, it is usually highest in the dry cool season.
Clinical features and complications

Apart from congenital rubella syndrome, rubella is a mild self-limited illness that usually occurs during childhood. During the second week after exposure, there may be a prodromal illness consisting of fever usually <39.0 °C, malaise and mild conjunctivitis, which is more common in adults. Post auricular, occipital and posterior cervical lymphadenopathy is characteristic, and typically precedes the rash by 5–10 days. The maculopapular, erythematous and often pruritic rash occurs in 50–80% of rubella-infected persons. The rash, usually lasting 1–3 days, starts on the face and neck before progressing down the body. Serological studies have shown that 20–50% of all rubella infections occur without a rash, or are subclinical. Joint symptoms (arthritis, arthralgia), usually of short duration, may occur in up to 70% of adult women with rubella but are less common in men and children. Post infectious encephalitis occurs in approximately 1/6000 rubella cases, but occasionally incidences have been reported as high as 1/500 and 1/1600. Haemorrhagic manifestations and Guillain–Barré syndrome have been rarely reported.

Congenital rubella syndrome

When a woman is infected immediately before conception or during the first trimester, rubella infection of the fetus may cause multiple fetal defects in up to 90% of cases, and may result in abortion or stillbirth. The risk of fetal pathology declines with maternal infection beyond the first trimester; and fetal defects are rarely associated with maternal rubella after the 16th week of pregnancy, although sensorineural hearing deficit may occur up to week 20.
The defects associated with CRS are ophthalmic (e.g. cataracts, microphthalmia, glaucoma, pigmentary retinopathy and chorioretinitis); auditory (e.g. sensorineural deafness); cardiac (e.g. peripheral pulmonary artery stenosis, patent ductus arteriosus or ventricular septal defects); and craniofacial (e.g. microcephaly). CRS can present with neonatal manifestations that include meningoencephalitis, hepatosplenomegaly, hepatitis, thrombocytopenia and radiolucencies in the long bones (a characteristic radiological pattern of CRS). The complications of thrombocytopenia can be fatal. Interstitial pneumonitis may occur in infants with CRS. Those that survive the neonatal period may face severe developmental disabilities (for example, visual and hearing impairments) and have an increased risk for developmental delay, including autism, type 1 diabetes mellitus and thyroiditis. A progressive encephalopathy resembling measles subacute sclerosing panencephalitis has also been observed in patients with CRS.\(^5\)

**Laboratory diagnosis**

Many rash illnesses can mimic rubella infection, and as many as 50% of rubella infections may be subclinical. The only reliable evidence of acute rubella infection is a positive viral culture for rubella or detection of rubella virus by polymerase chain reaction (PCR), the presence of rubella-specific IgM antibody or demonstration of a significant rise in IgG antibody from paired acute- and convalescent-phase sera.

Rubella virus can be isolated from nasal, blood, throat, urine and cerebrospinal fluid specimens from rubella and CRS patients. Virus may be isolated from the pharynx 1 week before and until 2 weeks after rash onset. Although isolation of the virus is diagnostic of rubella infection, viral cultures are labour intensive and therefore not done in many laboratories; they are generally not used for routine diagnosis of rubella. Viral isolation is an extremely valuable epidemiologic tool and should be attempted for all suspected cases of rubella or CRS. Information about rubella virus isolation can be found on the CDC website.

Serology is the most common method of confirming the diagnosis of rubella. Acute rubella infection can be serologically confirmed by a significant rise in rubella antibody titre in acute- and convalescent-phase serum specimens or by the presence of serum rubella IgM. Serum should be collected as early as possible (within 7–10 days) after onset of illness, and again 14–21 days (minimum of 7 days) later.

False-positive serum rubella IgM tests have occurred in persons with parvovirus infections, with a positive heterophile test for infectious mononucleosis, or with a positive rheumatoid factor.

---

The serologic tests available for laboratory confirmation of rubella infections vary among laboratories. The state health department can provide guidance on available laboratory services and preferred tests.

Enzyme-linked immunosorbent assay (ELISA) is sensitive, widely available and relatively easy to perform. It can also be modified to measure IgM antibodies. Most of the diagnostic testing done for rubella antibodies uses some variation of ELISA.

Serological testing is the preferred method for routine laboratory diagnosis of rubella. The presence of rubella IgM or demonstration of a significant rise in rubella IgG from paired acute and convalescent serum samples provides evidence of ongoing or recent rubella infection. On rare occasions, false-positive IgM results may occur when IgM antibody detection kits are used, e.g. enzyme-linked immunosorbent assay (ELISA). Where rubella is rare, false-positive serological results become relatively more common, thereby increasing the need for confirmatory tests. The presence of IgM antibody must always be interpreted with caution if there is no clear clinical context (e.g. when testing is routinely performed during pregnancy). Congenital rubella infection is most commonly diagnosed by detection of rubella IgM in serum or oral fluid sampled during the early months of life. Congenital rubella infections can also be diagnosed by detection of rubella virus using reverse transcriptase–polymerase chain reaction (RT–PCR) and rubella virus isolation.

Currently, ELISA is the most frequently used method for rubella antibody screening and diagnosis because it is sensitive and adaptable and can be readily automated. However, the majority of early studies on rubella vaccines and seroprevalence studies used a haemagglutination inhibition assay. Latex agglutination, single radial haemolysis and plaque neutralization may also be used, mainly for confirmatory purposes. RT–PCR assay is a highly sensitive and specific diagnostic tool. Viral isolation is labour-intensive and costly, and is not routinely used for diagnosis.

**Rubella vaccines**

Rubella vaccine is based on the live attenuated RA 27/3 strain, which is propagated in human diploid cells. There are a few other vaccines based on different strains available in some other regions. Rubella vaccines are available either as monovalent formulations or in combinations with other vaccine viruses, as RCVs. Commonly used RCVs are combinations with vaccines against measles (MR), measles and mumps (MMR) or measles, mumps and varicella (MMRV). Each dose of an RCV contains a defined number of infectious units (≥1000 PFU or CCID50). When stored at +4 °C, most RCVs have a shelf-life of 2–3 years.
Schedules

The high response rate to a single dose of rubella vaccine (≥95%) and the long-term persistence of protection in vaccines do not support a routine requirement for a second dose of rubella vaccine. However, based on the indications for a second dose of measles-containing and mumps-containing vaccines, a second dose of MR or of MMR is now offered in most countries.

An RCV is normally administered as a subcutaneous injection (but may also be given intramuscularly), usually at age 12–15 months, but it can also be administered to children aged 9–11 months and to older children, adolescents and adults. In most countries, rubella vaccine is given as MR or MMR, and the age of administration follows the schedule for measles – that is, the first dose is usually given 9 months or 12–15 months and a second dose at 15–18 months or 4–6 years.

During outbreaks of measles, MR or MMR may be administered to infants as young as 6 months. Because of the possibility of lower seroconversion, the dose administered at 6 months should not be counted as a valid dose, and the child should be vaccinated with subsequent dose(s) of RCVs according to the usual national immunization schedule.

Immunogenicity

Rubella vaccine induces seroconversion rates of approximately 95% or higher after a single dose.

The RA27/3 strain achieves antibody titres that closely resemble those induced by natural infection. In clinical trials, 95–100% of susceptible persons aged 12 months and older developed rubella antibodies after a single dose of the vaccine. It should be noted, however, that the immune response may be relatively slow, and therefore, it is advisable to wait until 6–8 weeks after immunization to assess seroconversion. Up to 5% of all vaccines fail to seroconvert; in part, this may be due to concurrent infection or – in young infants – to preexisting maternal rubella antibodies.

The immune responses to rubella antigens are not affected by the other components of the vaccine in the combinations MR, MMR or MMRV. Also, seroconversion rates are similar among the different formulations of RA 27/3 vaccine when it is given concurrently with other live or inactivated vaccines.
### ANNEX 03- Core reporting variables for Measles and Rubella

<table>
<thead>
<tr>
<th>Variable Name</th>
<th>Description</th>
<th>Field Type</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td>COUNTRY</td>
<td>Country of Report</td>
<td>Text (ISO3 code)</td>
<td>Must be reported</td>
</tr>
<tr>
<td>CaseID</td>
<td>Case identification number</td>
<td>Defined by country</td>
<td>Must be reported</td>
</tr>
<tr>
<td>OutbreakID</td>
<td>Outbreak ID number</td>
<td>Defined by country</td>
<td>Leave blank if case is not part of or linked to an outbreak</td>
</tr>
<tr>
<td>Province</td>
<td>Province</td>
<td>Defined by country</td>
<td>Must be reported</td>
</tr>
<tr>
<td>District</td>
<td>District</td>
<td>Defined by country</td>
<td>Must be reported</td>
</tr>
<tr>
<td>Block</td>
<td>Block</td>
<td>Defined by country</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Sex</td>
<td>Text (option: F; M; U)</td>
<td>Need to add variable for pregnancy</td>
</tr>
<tr>
<td>DOB</td>
<td>Date of birth</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td>Must be reported (if Age year/month is not provided)</td>
</tr>
<tr>
<td>AgeYear</td>
<td>Age in Year (completed)</td>
<td>Number (format: ##)</td>
<td>Must be reported (if DOB is not provided) if &lt;12 months of age, put zero) 99=Unknown age</td>
</tr>
<tr>
<td>DNOT</td>
<td>Date of notification to public health system</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td>DNOT&gt;=DONSET DNOT&gt;=DOB</td>
</tr>
<tr>
<td>DOI</td>
<td>Date of investigation</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td>DOI&gt;=DONSET DOI&gt;=DOB</td>
</tr>
<tr>
<td>DosesMCV</td>
<td>Number of doses measles containing vaccine received</td>
<td>Number (format: ##)</td>
<td>9=Unknown dose</td>
</tr>
<tr>
<td>DateLastMCV</td>
<td>Date of last dose of measles- containing vaccine</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td></td>
</tr>
<tr>
<td>DosesRCV</td>
<td>Number of doses rubella- containing vaccine</td>
<td>Number (format: ##)</td>
<td>9=Unknown dose</td>
</tr>
<tr>
<td>DateLastRCV</td>
<td>Date of last dose of rubella- containing vaccine</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td></td>
</tr>
<tr>
<td>DOOnsetF</td>
<td>Date of onset of fever</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td>Must be reported DONSET&gt;=DOB Cannot be future date</td>
</tr>
<tr>
<td>Variable Name</td>
<td>Description</td>
<td>Field Type</td>
<td>Remark</td>
</tr>
<tr>
<td>---------------</td>
<td>-------------</td>
<td>------------</td>
<td>--------</td>
</tr>
<tr>
<td>DONsetR</td>
<td>Date of onset of rash</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td>Must be reported DONSET &gt;= DOB Cannot be future date</td>
</tr>
<tr>
<td>CCC</td>
<td>Cough or coryza or conjunctivitis</td>
<td>Text (option: 1-Yes; 2-No; 9-Unknown)</td>
<td>Rubella sx include: lymphadenopathy and arthropathy/arthritis</td>
</tr>
<tr>
<td>DateSpecSero</td>
<td>Date of specimen collected for serology</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td></td>
</tr>
<tr>
<td>DateSeroSent</td>
<td>Date serology specimen sent to lab</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td></td>
</tr>
<tr>
<td>DateSeroRec</td>
<td>Date serology specimen received at lab</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td></td>
</tr>
<tr>
<td>SpecIDSero</td>
<td>Unique ID of Serology specimen</td>
<td>Defined by Laboratory</td>
<td></td>
</tr>
<tr>
<td>MeaslesIgM</td>
<td>Measles IgM result</td>
<td>Text (option: 1-Positive; 2-Negative; 3-Equivocal; 4-Pending; 5-Not tested)</td>
<td></td>
</tr>
<tr>
<td>DateMeaIgM-Result</td>
<td>Date serology result reported to the national programme</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td></td>
</tr>
<tr>
<td>RubellaIgM</td>
<td>Rubella IgM result</td>
<td>Text (option: 1-Positive; 2-Negative; 3-Equivocal; 4-Pending; 5-Not tested)</td>
<td></td>
</tr>
<tr>
<td>DateRubIgM-Result</td>
<td>Date serology result reported to the national programme</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td></td>
</tr>
<tr>
<td>TypeViroSpec</td>
<td>Type of virology specimen</td>
<td>1-Urine; 2-Throat Swab; 3-Oral Fluid; 4-Other</td>
<td></td>
</tr>
<tr>
<td>DateViroSpec-Coll</td>
<td>Date specimen collected for virology</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td></td>
</tr>
<tr>
<td>DateViroSent</td>
<td>Date virology specimen sent to lab</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td></td>
</tr>
<tr>
<td>DateViroRec</td>
<td>Date virology specimen received at lab</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td></td>
</tr>
<tr>
<td>SpecIDViro</td>
<td>Unique ID of virology specimen</td>
<td>Defined by Laboratory</td>
<td></td>
</tr>
</tbody>
</table>
### MEASLES AND RUBELLA

<table>
<thead>
<tr>
<th>Variable Name</th>
<th>Description</th>
<th>Field Type</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td>MeaVirDetect</td>
<td>Measles virus detection</td>
<td>Text (option: 1-Positive; 2-Negative; 3-Pending; 4-Not tested)</td>
<td></td>
</tr>
<tr>
<td>GenotypeMea</td>
<td>Genotype of measles virus</td>
<td>Text</td>
<td></td>
</tr>
<tr>
<td>DateMeaGenoResult</td>
<td>Date measles genotyping result reported to national programme</td>
<td>Date: (format: DD-MM-YYYY)</td>
<td></td>
</tr>
<tr>
<td>RubVirDetect</td>
<td>Rubella virus detection</td>
<td>Text (option: 1-Positive; 2-Negative; 3-Pending; 4-Not tested)</td>
<td></td>
</tr>
<tr>
<td>GenotypeRub</td>
<td>Genotype of rubella virus</td>
<td>Text</td>
<td></td>
</tr>
<tr>
<td>DateRubGenoResult</td>
<td>Date rubella genotyping result reported to national programme</td>
<td>Date (format: DD-MM-YYYY)</td>
<td></td>
</tr>
<tr>
<td>Import</td>
<td>Is imported/import related</td>
<td>Text (option: 1-Yes; 2-No; 9-Unknown)</td>
<td></td>
</tr>
<tr>
<td>Class</td>
<td>Final classification for suspected measles</td>
<td>Text (option: 1-Clinically Confirmed Measles; 2-Laboratory Confirmed Measles; 3-Epidemiologically Confirmed Measles; 4-Laboratory Confirmed Rubella; 5-Epidemiologically Confirmed Rubella; 6-Discarded; 7-Pending)</td>
<td></td>
</tr>
<tr>
<td>Comment</td>
<td>Any comments</td>
<td>Text</td>
<td></td>
</tr>
<tr>
<td>LabCode</td>
<td>Laboratory code</td>
<td>Number (format: ##) 99=Unknown</td>
<td></td>
</tr>
<tr>
<td>TravelHistory</td>
<td>History of Travel</td>
<td>Text</td>
<td></td>
</tr>
<tr>
<td>Notes:</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a) Weekly case-based data should be submitted before 10:00 of every Monday (New Delhi time) to: SearEpidata@who.int

b) National dataset may need to recode the variables names and input values to meet the SEARO’s data exchange format

c) Dataset should be exported into “Delimited Text Format Separated by Comma with the double quote of Text Qualifier (e.g. “Field1”, “Field2”) and Field Names included on First Row”.
c) The exported data file to be named as “Country_Disease_WeekNum_Year.txt”, e.g.: Bhutan Measles_Week01_2016.txt
# ANNEX 04- Sample Measles-Rubella Case Investigation Form

## 1. Patient Information

<table>
<thead>
<tr>
<th>Case Identification Number:</th>
<th>Name of Health Facility:-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Name:</td>
<td></td>
</tr>
<tr>
<td>Age in Year: _______ Month: ______</td>
<td>Date of Birth: (<em><strong><strong>/</strong></strong></em>/_____)</td>
</tr>
<tr>
<td>Gender: □ Male □ Female</td>
<td>Date of Onset fever: (<em><strong><strong>/</strong></strong></em>/_____)</td>
</tr>
<tr>
<td>Resident address:</td>
<td>Date of onset of rash: (<em><strong><strong>/</strong></strong></em>/_____)</td>
</tr>
<tr>
<td>District:</td>
<td>Date of notification: (<em><strong><strong>/</strong></strong></em>/_____)</td>
</tr>
<tr>
<td>Contact Number of Patient/Parents Mobile No.:</td>
<td>Date of Investigation: (<em><strong><strong>/</strong></strong></em>/_____)</td>
</tr>
</tbody>
</table>

## 2. Vaccination Status (by card / history)

<table>
<thead>
<tr>
<th>No. of Doses</th>
<th>Date 1st dose</th>
<th>Date 2nd dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles containing vaccine: ______</td>
<td>(<em><strong><strong>/</strong></strong></em>/_____)</td>
<td>(<em><strong><strong>/</strong></strong></em>/_____)</td>
</tr>
<tr>
<td>Rubella containing vaccine: ______</td>
<td>(<em><strong><strong>/</strong></strong></em>/_____)</td>
<td>(<em><strong><strong>/</strong></strong></em>/_____)</td>
</tr>
</tbody>
</table>

## 3. Clinical Information

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maculopapular Rash:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenopathy:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If yes, place........................</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough:</td>
<td></td>
<td></td>
<td>Unknown</td>
</tr>
<tr>
<td>Arthralgia:</td>
<td></td>
<td></td>
<td>Unknown</td>
</tr>
<tr>
<td>If yes, joint......................</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coryza:</td>
<td></td>
<td></td>
<td>Unknown</td>
</tr>
<tr>
<td>Pregnancies:</td>
<td></td>
<td></td>
<td>Unknown</td>
</tr>
<tr>
<td>If yes, weeks........................</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conjunctivitis:</td>
<td></td>
<td></td>
<td>Unknown</td>
</tr>
<tr>
<td>Others:</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## 4. Patient Status

<table>
<thead>
<tr>
<th>Hospitalization?</th>
<th>Yes</th>
<th>No</th>
<th>if yes, Name of Hospital:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of admission: (<em><strong><strong>/</strong></strong></em>/_____)</td>
<td>Date of discharge: (<em><strong><strong>/</strong></strong></em>/_____)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Final status:</td>
<td>Recovered</td>
<td>Referred</td>
<td>Died</td>
</tr>
</tbody>
</table>

## 5. Epidemiological Information

<table>
<thead>
<tr>
<th>Any similar illness in family/community:</th>
<th>Yes</th>
<th>No</th>
<th>If yes, number...........</th>
</tr>
</thead>
<tbody>
<tr>
<td>Travel History (7-21 days before the onset of rash):</td>
<td>Yes</td>
<td>No</td>
<td>If yes, place/country visited:</td>
</tr>
<tr>
<td>Travel dates: From (<em><strong><strong>/</strong></strong></em>/<em><strong><strong>) To (</strong></strong></em>/<em><strong><strong>/</strong></strong></em>)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Name of the Investigator with Designation:</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### 6. Laboratory Information

<table>
<thead>
<tr>
<th>To be filled at specimen collection point</th>
<th>To be filled by the laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Serology Samples and Test Results</strong></td>
<td></td>
</tr>
<tr>
<td>Specimen Collected? ☐ Yes ☐ No</td>
<td>Date of sample received: (<em><strong><strong>/</strong></strong></em>/______)</td>
</tr>
<tr>
<td>If yes, types of Specimen:</td>
<td>Sample received by:</td>
</tr>
<tr>
<td>☐ Serum</td>
<td>Sample status: ☐ Satisfactory ☐ Unsatisfactory</td>
</tr>
<tr>
<td>☐ DBS</td>
<td>If unsatisfactory, give details:</td>
</tr>
<tr>
<td>Date of Collection: (<em><strong><strong>/</strong></strong></em>/______)</td>
<td>Serology Result: Specimen ID:__________</td>
</tr>
<tr>
<td>Specimen Collected By:</td>
<td>Test Done by:</td>
</tr>
<tr>
<td>Sample Shipment date: (<em><strong><strong>/</strong></strong></em>/______)</td>
<td>Date of Test: (<em><strong><strong>/</strong></strong></em>/______)</td>
</tr>
<tr>
<td>Sample sent by:</td>
<td>Date of Report: (<em><strong><strong>/</strong></strong></em>/______)</td>
</tr>
<tr>
<td></td>
<td>Measles:</td>
</tr>
<tr>
<td></td>
<td>☐ Positive ☐ Negative ☐ Equivocal</td>
</tr>
<tr>
<td></td>
<td>☐ Test Not done</td>
</tr>
<tr>
<td></td>
<td>Rubella:</td>
</tr>
<tr>
<td></td>
<td>☐ Positive ☐ Negative ☐ Equivocal</td>
</tr>
<tr>
<td></td>
<td>☐ Test Not done</td>
</tr>
</tbody>
</table>

| **B. Virology samples and Test Results** |                                  |
| SPECIMEN COLLECTED? ☐ Yes ☐ No          | Date of sample received: (_____/_____/______) |
| If yes, types of Specimen:              | Sample received by:                |
| ☐ Throat swab                           | Sample status: ☐ Satisfactory ☐ Unsatisfactory |
| ☐ Urine                                 | If unsatisfactory, give details:    |
| ☐ Other:                                | Virology Result: Specimen ID:__________ |
| Date of Collection: (_____/_____/______) | Test Done by:                      |
| Specimen Collected By:                  | Date of Test: (_____/_____/______) |
| Sample Shipment date: (_____/_____/______) | Date of Report: (_____/_____/______) |
| Sample sent by:                         | ☐ Measles Positive ☐ Rubella Positive |
|                                          | ☐ Negative ☐ Test Not done          |

| **C. Genotyping**                      |                                  |
| Specimen submitted for genotype?      | Genotype results: Measles: ______ Rubella: ______ |
| ☐ Yes ☐ No                             | Results received by National lab: (_____/_____/______) |
| If yes, Date specimen sent: (_____/_____/______) | Date results received by Program: (_____/_____/______) |

### 7. Classification (to be filled by the surveillance program)

**Final Classification:** ☐ Confirmed Measles ☐ Confirmed Rubella ☐ Discarded
**Basis for classification:** ☐ Laboratory ☐ Epidemiological Linked ☐ Clinical
**Source of infection:** ☐ Endemic ☐ Imported ☐ Import-related ☐ Unknown
**Reason for discard:** ..........................................................

### 8. Follow-up

**Active case search done?** ☐ Yes ☐ No If yes, number of additional suspected cases detected: ______
**Outcome at 30 days follow-up:** ☐ Alive ☐ Died ☐ Lost to follow-up
ANNEX 05- Outbreak preparedness and response in settings with large outbreaks

MEASLES/RUBELLA OUTBREAK PREPAREDNESS

To ensure measles/rubella outbreak preparedness and implementation of a rapid, effective response to outbreaks, a national plan for outbreak preparedness and response should be established in the context of measles elimination and rubella /CRS control. The outbreak preparedness and response plan should provide guidance for local, state, and national level so that plans can be put in place prior to an outbreak, and followed immediately when an outbreak is detected, to avoid any delays in the response.

Logistics and Vaccine Supply

Logistics planning should account for the current capacity of the public health infrastructure, and focus on establishing mechanisms for a surge capacity that might be needed during an outbreak. The surge capacity needs should focus on staff, as well as supplies. A sufficient vaccine supply is essential for outbreak response immunization activities. The national vaccine stockpile should be continuously monitored to ensure there is enough vaccine to continue routine immunization as well as surge resources to respond to an outbreak. When estimating vaccine needs, in addition to the routine immunization schedule, account for the estimated number of measles-susceptible persons in the population. Vaccine procurement is often a lengthy process due to the time needed for financial approval; therefore, funds should be pre-allocated for potential emergency vaccine requests. Additionally, a streamlined mechanism for the release of funds should be established by the national outbreak preparedness and response plan. These measures will decrease delays in vaccine acquisition, which is essential for timely measles outbreak response activities. Additionally, memorandums of understanding could be established with partner organizations, such as WHO, UNICEF, and vaccine manufacturers, regarding the procurement, management and distribution of the vaccine to establish communication channels for streamlined requests during an outbreak.

Health System

Health care systems can become quickly overwhelmed by measles and rubella outbreaks, especially if there are delays in response measures. All aspects of the public health infrastructure, from staff in EOCs to front-line care healthcare providers and vaccinators. Health care facilities should have established emergency response plans to address needs for staff surge capacities, implementation of measures to prevent nosocomial transmission, including ensuring vaccination of staff, and implementation of infection prevention and
control guidelines. These plans should include specific guidance for measles/rubella case isolation, patient flow from triage, designated areas for care, and tertiary care referral processes.

The availability of resources required for clinical case management must be ensured, including vitamin A, antibiotics, rehydration fluids, facemasks, isolation rooms, and mechanical ventilators. Procurement and distribution plans of these resources during an outbreak should be done during the preparedness phase.

Preparedness plans should establish mechanisms to recruit additional staff to participate during measles outbreaks. This can be done by pre-identifying personnel who can be activated or repurposed during an outbreak, including epidemiologists, healthcare professionals, paediatric specialists, nurses, and vaccinators. In addition, volunteers can fill a number of roles such as, community health workers, community advocates, and risk communication focal points. Once staff and volunteers have been identified, they should be trained in outbreak response activities appropriate for their professional background, SOPs should be established for activating the roster, deployments, incentives, and incorporation of emergency response should all be described in preparedness plans.

Contingency planning for health care facilities to expand beyond normal operating capacity should be considered in the planning phase. For example, one alternative to expand workspace, may include using temporary medical tents on the hospital campus that can operate as triage centres for all rash-fever patients prior to entering the hospital and as treatment areas serving as isolation wards. This solution may decrease the risk of virus transmission in waiting areas and treatment areas. Additionally, to limit potential virus exposures of unvaccinated persons in health-care settings, mobile and/or temporary vaccination points outside of healthcare facilities can be used to ensure access to vaccination without risk of nosocomial transmission. These alternative scenarios should be addressed in the planning phase and SOPs developed for implementation of contingency plans.

**Measles outbreak response**

a. Case management
b. Contact Tracing
c. Enhanced case-based surveillance and active case search
d. Risk communication and awareness campaign
e. Survey of population immunity/gap
f. Enhancing population immunity against measles and rubella
g. Outbreak Response Immunization
**Rubella outbreak response**

The rubella outbreak response would follow the same steps as of measles outbreak response and in addition would focus on pregnant women who would have potentially been exposed to rubella virus during the period and follow them until the outcome of the pregnancy is known and investigate the child for CRS or enrol into the CRS surveillance system.

**Prevention of nosocomial transmission of measles and rubella during outbreaks**

In countries that have made considerable progress with measles elimination, a significant means of transmission of measles can be nosocomial (acquired at hospitals and other health facilities). In such situations, measles may be relatively rare, and health staff may not immediately recognize measles. In addition to direct contact between children attending hospitals, measles can be transmitted from patients to health care workers and then to other patients. Since measles can be highly infectious in the three days before the onset of rash, there can be considerable difficulties in separating suspected measles cases from other patients who, for example, may be attending a crowded hospital outpatients unit. The following control measures should be considered:

- Ensure awareness of measles transmission and provide measles vaccination of health facility staff, especially those newly employed.
- Maintain high population immunity among health workers and other hospital employees.
- Reduce missed vaccination opportunities by checking the immunization status of children attending hospitals and offering measles immunization.
- Reduce vaccination age to six months in outbreak situations.

Isolate individuals with fever and rash. If possible, patients attending with fever and rash should be taken directly to a separate room in waiting and treatment areas, where feasible.

Another intervention that is most likely to reduce nosocomial measles is to enforce the measles immunization requirement for all staff who work in a healthcare facility. Only staff who have two documented MCV doses or evidence of immunity (through serologic testing) should be allowed to interact with patients. Healthcare facilities should plan to develop and maintain records of their staff measles immunity status, and proactively identify their staff that need MCV doses and provide it.
Improved triage and referral practices can minimize the number of persons exposed in healthcare facilities. The guidance for triage and referral of suspected measles patients should emphasize the need to identify patients that can be managed with supportive care measures at home, and do not require additional medical care delivered by a healthcare professional.

- Ensure all health workers are immune to measles and rubella (e.g. vaccination of health workers)
- Develop national guidelines for preventing the nosocomial transmission of measles and rubella viruses, including infection from CRS cases. Guidelines should include appropriate triage, patient placement and airborne isolation precautions
- Ensure all health facilities are provided with the national guidelines
- Conduct regular training for national, provincial and district staff to ensure all health staff are familiar with the guidelines
- Ensure that all health care associated cases are promptly investigated, including contact tracing with appropriate post-exposure measles prophylaxis to exposed patients, family members, and health workers
- Develop public messages on the isolation of suspected cases and care of uncomplicated cases at home
- Furlough all HCW who have suspected or confirmed measles or rubella, from the first day of symptoms until 4 days after rash onset. Furlough all susceptible health workers who have been exposed to a suspected or confirmed measles or rubella case, from 5 days until 21 days following exposure, regardless of symptoms, and regardless of post-exposure prophylaxis

Standard precautions (All body fluids, except sweat, are regarded as potentially infectious.) and universal precautions on infection prevention should be followed as per the national guidelines while measles and rubella cases.

Place the patient in a negative-pressure isolation room. If no negative-pressure room is available, a private room with good external ventilation (open windows) may be used; keep people away from the window. When not available or not feasible, place the patient in a room with a patient(s) who has active infection with the same microorganism but with no other infection. Limit the movement and transport of the patient from the room to essential purposes only and then place an appropriate mask (for example P2 or N95 mask) on the patient.
ANNEX 06- Key definitions related to measles and rubella

1. **Measles, or rubella, eradication**: worldwide interruption of measles, or rubella, virus transmission in the presence of a surveillance system that has been verified to be performing well.

2. **Measles elimination**: the absence of endemic measles transmission in a defined geographical area (e.g. region or country) for ≥ 12 months in the presence of a well-performing surveillance system. However, verification of measles elimination takes place after 36 months of interrupted endemic measles virus transmission.

3. **Rubella and CRS elimination**: the absence of endemic rubella virus transmission in a defined geographical area (e.g. region or country) for >12 months and the absence of CRS cases associated with endemic transmission in the presence of a well-performing surveillance system. However, verification takes place after 36 months of interrupted endemic virus transmission.

4. **Rubella and CRS control**: a 95% reduction of rubella and CRS as compared with the 2008 baseline nationally and for the Region.

5. **Endemic measles, or rubella, virus transmission**: the existence of continuous transmission of indigenous or imported measles virus, or rubella virus, that persists for ≥ 12 months in any defined geographical area.

6. **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 where measles or rubella had previously been eliminated.
Readings


Acknowledgement

The document was produced under the strategic guidance of the Regional Director, Dr Poonam Khetrapal Singh, Director, Programme Management, Dr Arun Thapa, and Dr Pem Namgyal, Director FGL WHO SEARO. The entire process was overseen by Dr Nihal Abeysinghe and Dr Sunil Bahl.

Dr Sudhir Khanal, WHO SEARO, coordinated the development of the technical document in collaboration with a team of international experts, Dr Jacob T John from India, Dr Naresh Pratap KC from Nepal, Dr Sujeeka Amarasena from Sri Lanka and Dr Kumnuan Ungchusak from Thailand along with WHO Consultant Dr Sudhir Joshi who were crucial in the conceptualizing and initial drafting of the document.

This document also benefited from the dedication, support and expertise of all the participants of the regional workshop on surveillance standards for measles, rubella and priority vaccine-preventable diseases in September 2016 at Kathmandu, Nepal, which included National EPI Programme Managers from Member States as well as a number of WHO and UNICEF country office staff and external collaborators.

The IVD SEARO team wishes to thank all mentioned above, including the following contributors whose expert review and guidance made this document possible:

WHO HQ staff: Dr. Minal Patel and Mr. Antoni Sebastien reviewed the draft surveillance standard document and provided technical inputs.

WHO-SEARO: Dr. Jayantha Liyanage, Dr. Sigrun Roesel, Ms. Sirima Pattamadilok, Dr. Pushpa Ranjan Wijesinghe, Ms. Uttara Aggarwal, Mr. Tika Sedai and Dr. Aarti Garg reviewed the draft and provided necessary inputs, including drafting of selected sections.

US CDC: Dr. Jim Goodson, Dr. Heather Scobie and Dr. Susan Wang provided inputs to the various sections of the document and final draft of the surveillance standard document.

The IVD team would also like to acknowledge the support provided by the entire IVD team for the administrative work, the R-DOC team, the building management, ICT services, travel unit and all related staff who played a crucial role at the hind side in the smooth preparation of this report.