

AFRICAN REGIONAL GUIDELINES

FOR MEASLES AND RUBELLA

SURVEILLANCE



WHO Regional Office for Africa

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ACRONYMS

AFP	Acute Flaccid Paralysis
AFRO	World Health Organization, Regional Office for Africa
CFR	Case Fatality Ratio
CRI	Congenital Rubella Infection
CRS	Congenital Rubella Syndrome
ELISA	Enzyme linked Immuno-Sorbent Assay
EPI	Expanded Program on Immunization
EPID	Epidemiological identification number
HIV	Human Immunodeficiency Virus
IDS	Integrated Disease Surveillance
IMCI	Integrated Management of Childhood Illnesses
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IST	Inter-country support teams of WHO African Region
MCV1	Measles containing vaccine - first dose
MCV2	Measles containing vaccine - second dose
MR	Measles-Rubella vaccine
MMR	Measles-Mumps-Rubella vaccine
RRL	Regional Reference Laboratory
SIA	Supplementary Immunization Activities
SOPs	Standard Operating Procedures
WHO	World Health Organization
UNICEF	United Nations Children's Fund

I. INTRODUCTION

Measles is one of the vaccine preventable diseases still causing preventable mortality and morbidity in developing countries. Accelerated measles control activities started in 2001 in countries in the World Health Organization (WHO) African Region, aiming to reduce measles deaths by half by 2005. The strategies implemented included improving routine vaccination coverage, providing a second opportunity for measles vaccination through supplementary immunization activities (SIAs), improving measles-case management, and establishing case-based measles surveillance.

By 2008, following the successful implementation of these strategies across the Region, reported measles cases decreased by 93% and estimated measles mortality decreased by 92% in the African Region compared with the reported measles cases and estimated measles respectively for the year 2000. In September 2011, the Regional Committee of the WHO African Region adopted the goals for Regional measles elimination by 2020.

II. MEASLES DISEASE

i. Epidemiology of measles

Measles is an acute, highly infectious viral disease caused by a Morbillivirus and for which humans are the only reservoirs. Transmission is primarily person-to-person via aerosolized droplets or by direct contact with the nasal and throat secretions of infected persons. When measles virus is introduced to a non-immune population, nearly 100% of individuals will become infected and develop clinical illness. The incubation period of measles is about 10 to 12 days (range 7-18 days). Malnourished children are at higher risk of developing complications and mortality from measles infection.

ii. Clinical features of measles

Measles is a systemic infection. In a non-immune person exposed to measles virus, prodromal symptoms of fever, malaise, cough, coryza (runny nose), and conjunctivitis appear after the incubation period. Although there is no rash at disease onset, the patient is shedding virus and is highly contagious. Koplik's spots may be seen on the buccal mucosa in over 80% of cases up to 2 days before rash onset. Within 2 - 4 days of the prodromal symptoms, a rash made up of large, blotchy red spots (maculo-papular rash) appears behind the ears and on the face accompanied with a high fever. (Figure 1) The rash spreads to the trunk and extremities and typically lasts 3 - 7 days. The rash disappears by desquamation in the same order as its appearance. Individuals with measles are infectious 2-4 days before the onset of the rash through to 4 days after rash onset. (Figure 2)

The differential diagnoses of measles are illnesses with fever, rash, and a variety of non-specific symptoms. When examining for measles, it is important to consider rubella, scarlet fever, exanthema subitum (roseola), erythema infectiosum, dengue fever, the early stages of chickenpox, and infectious mononucleosis in the differential diagnosis. Moreover, there are other conditions that may present in a similar form, including erythema infectiosum (fifth disease), enterovirus or adenovirus infections, toxic shock syndrome, rickettsial diseases and drug hypersensitivity reactions.



Figure 1. A child with facial rashes typical of measles.

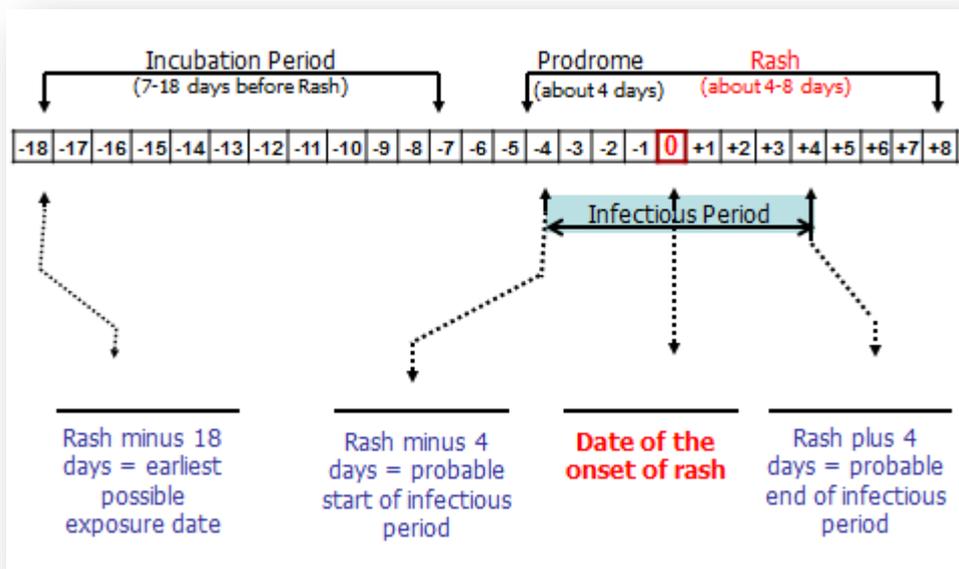


Figure 2. The clinical evolution of measles.

iii. Complications of Measles

In about a third of the cases, measles is followed by at least one complication caused by the disruption of epithelial surfaces and immuno-suppression. These include pneumonia, ear and sinus infections, persistent diarrhea, upper airway obstruction from croup (laryngo-tracheo- bronchitis), and mouth ulcers. Less common complications include corneal drying that could progress to ulceration (keratomalacia) and blindness, protein energy malnutrition, convulsions and brain damage. Complications are more common in young children below 5 years of age. Unless managed early and aggressively, these complications may lead to death within the first month after the onset of rash. The case fatality rate from measles is estimated to be 3 – 5% in developing countries but may reach more than 10% in epidemics, during periods of famine and in certain population groups like refugees and internally displaced people.

As of 2013, it was estimated that, measles caused some 40,000 deaths annually in the African Region. Measles remains among the top causes of death in children less than 5 years of age in many African countries. Before the widespread availability of measles vaccine, virtually all children contracted the disease.

iv. Measles Immunity

A person is naturally immune if he or she has had contact with the measles virus and has developed antibodies against it. Infants born to mothers who have either had measles or have been vaccinated, are protected by trans-placentally acquired maternal antibodies; that is they have **passive immunity**. This protection lasts six to nine months on average, after which the child becomes susceptible to measles infection.

Active immunity may be acquired through natural infection or following vaccination. Persons who have taken measles vaccine and have formed antibodies in response to the vaccine are also immune. Measles vaccines contain live, attenuated viruses. In the African Region, it is recommended that the first dose of measles vaccine (MCV1) be administered at 9 months – the age when most children have lost their maternal antibodies. There is virtually no contra-indication to measles vaccination. When correctly administered at 9 months of age, measles vaccine confers life-long protection to approximately 85% of those vaccinated. Childhood immunization programmes have led to a dramatic decrease in measles morbidity and mortality.

Vaccination coverage levels of 90% or more might be required before a marked reduction in incidence is seen in younger infants through herd immunity. On the other hand, epidemics of measles occur when the number of susceptible individuals in a population reaches a critical threshold. Because the risk of measles outbreaks is determined by the rate of accumulation of susceptible people in the population, programmes should use data on vaccination coverage to monitor the accumulation of susceptible people and conduct follow-up SIAs before the number of susceptible children of pre-school age reaches the size of a birth cohort. This approach has been found to be programmatically useful and sufficiently accurate to prevent large outbreaks.

Outbreaks may occur in pockets of low coverage, which are likely to occur in certain geographic areas, such as urban slums, squatter communities, remote rural areas, border communities, and in certain population groups with habitually low vaccination coverage rates such as nomadic peoples, marginalized population groups, or persons with religious or philosophical objections to immunization.

It is well documented that, as immunization coverage increases, the size of epidemics decreases. In addition, the inter-epidemic period lengthens, and the proportion of cases among older children increases.

III. RUBELLA DISEASE

i. Epidemiology and clinical features:

Rubella is an infectious viral disease characterized by a mild cutaneous maculopapular rash. The rubella rash occurs only in 50%-75% cases and is sometimes misdiagnosed as measles or scarlet fever. Rubella is a benign disease and children usually develop few or no constitutional symptoms. Post auricular and posterior cervical lymphadenopathy is characteristic and precedes the rash by 5-10 days. Arthralgia or arthritis may occur in up to 70% of adult women with rubella. Rare complications include thrombocytopenic purpura and encephalitis.

Rubella is transmitted through direct or droplet contact from nasopharyngeal secretions and has an average incubation period of 17 days. Persons with rubella are most infectious when rash is erupting, but they can shed virus from 7 days before to 7 days after rash onset. There is no specific treatment for rubella but the disease is preventable by vaccination.

ii. Congenital Rubella Syndrome

When rubella infection occurs during pregnancy, especially during the first trimester, serious consequences can result. These include miscarriages, fetal deaths/stillbirths, and a constellation of severe birth defects known as congenital rubella syndrome (CRS). The most common congenital defects are cataracts, congenital heart disease, hearing impairment and developmental delay. (Table 1)

Table 1. Clinical Manifestations of Congenital Rubella Syndrome (CRS) in 376 Children Following Maternal Rubella. Adapted from Nelson Textbook of Pediatrics. 18th Ed.

Clinical Sign	Frequency of occurrence
Deafness	67%
Ocular	71%
Cataracts	29%
Retinopathy	39%
Patent ductus arteriosus (PDA)	78%
Right pulmonary artery stenosis	70%
Left pulmonary artery stenosis	56%
Valvular pulmonic stenosis	40%
Low birthweight	60%
Psychomotor retardation	45%
Neonatal purpura	23%
(Other findings: hepatitis, linear streaking of bone, hazy cornea, congenital glaucoma, delayed growth)	

Rubella and CRS can be prevented by providing a live attenuated rubella vaccine. Rubella vaccines are available in monovalent formulation but are usually given as part of the MR or MMR vaccine (protecting against measles, mumps, and rubella). Rubella vaccination is particularly important for non-immune women who may become pregnant because of the risk for serious birth defects if they acquire the disease during pregnancy. For that reason the combination MR is indicated to be introduced during follow up campaign targeting children aged 9 months to 14 years (or based on the epidemiology for wide age group susceptible population). A single dose of Rubella containing vaccine gives more than 95% long-lasting immunity, which is similar to that induced by natural infection. This will need to be followed by second dose of MR preferably at 18 months of life.

The WHO African Region does not yet have a rubella/ CRS elimination goal as of 2015. However, countries are being supported to introduce rubella vaccine and conduct rubella CRS surveillance alongside efforts to eliminate measles.

IV. MEASLES ELIMINATION IN THE AFRICAN REGION OF THE W.H.O.

Countries in the WHO Africa Region have been implementing the recommended measles control strategies since 2001. By 2011, the Region has adopted the Regional measles elimination goal. The WHO recommended the following strategies for achieving and maintaining measles elimination:

- (1) strengthening routine immunization with a two dose-schedule to protect every child;
 - providing a first dose measles containing vaccine at or shortly after the 9th month of age, ensuring that all children who missed their first dose receive a dose at the earliest possible time irrespective of their age at the time
 - providing a second dose of measles vaccine in the routine immunisation program, at 15 – 18 months of age

- (2) providing an opportunity for measles vaccination through SIAs;
 - at intervals of 2 – 4 years depending on the epidemiological situation and the population immunity as measured by the vaccination coverage levels
 - targeting persons from 6 or 9 months upwards, with the upper target being determined according to the epidemiological data

- (3) conducting case based measles surveillance to enable immunization strategies to be properly adjusted and to document the decline in cases and progress in eliminating the disease;
 - supported by the measles laboratory network to confirm suspected cases as measles and to identify viruses as imported versus indigenous.

- (4) Providing standard case management to measles cases according to the standards set in the Integrated Management of Childhood Illnesses (IMCI) protocols

The African Region of the WHO has developed a strategic plan, which includes a number of targets to be achieved by 2020, as part of the Regional measles elimination goal. These targets and milestones include the following:

By the end of 2015

- Reducing annual regional measles incidence to less than five cases per million and maintain that level in all countries.
- Achieving 90% MCV1 coverage (WHO-UNICEF coverage estimates) nationally in at least 60% of the countries AND exceed 80% vaccination coverage in every district or equivalent administrative unit in all countries.
- Achieving at least 95% coverage with measles vaccines during SIAs nationally and in at least 80% of districts.

By end-2020

- Achieving 95% coverage with the first dose of measles vaccine nationally (WHO UNICEF estimates) and in every district or equivalent administrative unit in all countries.
- Achieving at least 95% coverage with measles vaccines during SIAs nationally and in all districts.
- Achieving a measles incidence of less than one confirmed measles case reported per million population per year (excluding imported cases).
- Achieving the surveillance performance targets with:
 - at least one suspected measles case reported per 100,000 population per year in at least 80% of districts (or equivalent, as used for AFP surveillance);
 - serum samples adequate for detecting measles IgM collected in at least 80% of suspected measles cases (excluding from the denominator cases that are epidemiologically linked to a laboratory-confirmed case);
 - viral isolation obtained from every confirmed chain of transmission (for genotyping to help identify source of virus).

V. PRINCIPLES OF DISEASE SURVEILLANCE

Disease Surveillance is a key component of control programs and serves as the means of monitoring program success. In routine surveillance systems, data on individual patients, which are recorded in patient registers, are used to calculate the number of cases of reportable diseases diagnosed by health facility staff over a certain period of time. These data are periodically reported to district authorities who compile and send them to higher administrative levels. This process of detecting and reporting information on diseases that bring patients to the health facility is known as **passive surveillance**. Passive surveillance yields only limited data because many sick people do not visit a health facility and because those cases may not be correctly classified, recorded, or reported.

One way to overcome the limitations of passive surveillance and obtain more reliable and accurate data about the disease burden in the community is for surveillance officers to regularly visit the most utilized health facilities and traditional health care service delivery points. These visits will help to ensure that all cases are notified and reported in time. Surveillance officers can also look for cases of a specific disease at community level. This process is known as **active surveillance**. Since passive surveillance has limitations due to its lack of access to some groups within the population, active surveillance is often used to enhance the completeness of a passive surveillance system.

When there is a suspected case of a disease targeted for eradication/ elimination (such as polio or neonatal tetanus or measles) or during suspected outbreaks of epidemic-prone diseases, health workers conduct case-based investigations to learn more about a specific disease pattern. In such cases, health workers use the epidemiologic case definitions to identify suspected cases, and proceed to record detailed information such as the patient's name, age, vaccination status, district and village of residence, date of disease onset, and to take appropriate specimens for laboratory confirmation if necessary.

VI. INTENSIFIED MEASLES / RUBELLA INTEGRATED SURVEILLANCE

In the drive towards the elimination of measles, intensified surveillance helps to identify and investigate cases and outbreaks, to predict outbreaks through the identification of geographic areas and age groups at risk, and to evaluate vaccination strategies in order to improve measles control efforts.

In the African Region, measles case based surveillance is integrated with the surveillance for other vaccine preventable diseases including Acute Flaccid Paralysis (AFP), yellow fever, and neonatal tetanus. Countries plan and implement this integrated vaccine preventable disease surveillance system using the same mechanisms, opportunities (active surveillance, case reporting, feedback, coordination, etc.), resources and infra-structure.

i. Case definitions

The use of the standard case definition for suspected measles cases is the primary tool in the surveillance system to ensure early detection of any suspected cases.

A suspected measles case is defined as:

- i. Any person with generalized maculo-papular rash and fever plus one of the following: cough or coryza (runny nose) or conjunctivitis (red eyes)
- ii. Any person in whom a clinician suspects measles

Measles suspected cases at community level: A community member should report “any person with *rash* and *fever*” to a health worker and also advise the person to go to a health facility. The definition of suspected case of measles is made simple here to encourage more notification from the community.

A suspected case of measles is reportable and needs to be investigated with a serologic specimen at first contact within the 30 days of the onset of rash. The case definition given above has a high sensitivity for measles. However, suspected cases may not be “true measles cases” particularly in areas of low measles prevalence. As the incidence of measles

decreases individuals meeting the case definition will increasingly have rash illnesses (exanthems) other than measles, such as rubella, roseola infantum, scarlet fever, etc. For these reasons, WHO recommends enhanced measles surveillance based on the serological confirmation of all suspected cases of measles once the case-load has been brought down through the implementation of effective measles control interventions.

For surveillance purposes, a **measles death** is defined as any death from an illness that occurs in a confirmed case of measles within one month of the onset of rash. The immediate and delayed complications of measles (like pneumonias, persistent diarrhea) which are mostly responsible for measles death may manifest and lead to death much later after the disappearance of the rash.

ii. Establishing and strengthening measles surveillance

Many countries already have a system of aggregate summary reporting of notifiable diseases, including measles. The Integrated Disease Surveillance (IDS) monthly surveillance summary report form should be used for regular reporting of cases seen. In this system, health facilities provide routine weekly or monthly summary reporting of measles cases as part of the communicable disease surveillance system. Ideally, this summary reporting system should include the age and vaccination status of reported cases so as to enable basic analysis and interpretation of data. This information should be tallied each month and sent to the district. If no cases were seen, zero cases should be reported. The district level is expected to monitor timeliness and completeness of health facility reporting and to follow-up on late reports.

To complement the reporting through the IDS summary reporting system, all countries in the African Region are expected to set up intensified case-based surveillance for measles. The establishment of case-based surveillance for measles entails that a case investigation form is completed for each case, instead of only relying on the aggregate reporting using a line-list or using summary case counts. In addition, a blood specimen is collected for serologic confirmation of measles infection for every suspected measles case at the first

contact with the case - anytime between the day of onset of rash and the 30th day following the onset of rash. The responsible officers will arrange for transport of the specimen to be sent to the national measles laboratory as soon as possible. Each suspected case reported through the case-based surveillance system should also be reported in the IDS monthly summary reporting system.

The case based surveillance system also requires that all suspected outbreaks be investigated and confirmed by collecting blood specimens from the first five reported cases. Measures should also be taken to isolate viruses and document strains by taking nasopharyngeal (throat) swabs from 5 cases.

Case-based surveillance for measles requires that all suspected measles cases are investigated using an individual case investigation form and that a blood specimen is collected for serologic confirmation of measles infection at the time of initial contact with the case.

iii. Roles and Responsibilities in establishing measles case based surveillance:

In establishing measles surveillance, the roles and responsibilities of health workers and authorities at different levels of the health care system are described below:

Health facility:

- Detect and report suspected measles cases and outbreaks using the standard case definition,
- Investigate suspected cases of measles, and line list outbreak cases as necessary
- Manage all cases of measles appropriately, including the provision of Vitamin A, supportive treatment, and specific treatment of complications
- Collect, consolidate, analyze and interpret surveillance data,

District level:

- Ensure that blood specimens are collected for serologic confirmation from all suspected cases of measles and from the first five cases in suspected measles outbreaks
- Ensure that nasopharyngeal swabs are taken from five suspected measles cases during outbreaks for purposes of determining the circulating viral strains
- Conduct good quality measles outbreak investigation; which includes prompt investigation once the outbreak threshold is reached, conducting active case finding in the community and line listing of all cases with essential variables like date of onset of rash, age, vaccination status and address,
- Analyze disease patterns and trends, interpret data, and produce routine reports,
- Monitoring the epidemiological pattern of measles cases
- Feed data forward to the next level

Provincial level:

- Analyze disease patterns and trends, interpret surveillance data in conjunction with routine immunization coverage data, and produce routine reports
- Monitor the surveillance performance using standard indicators (See Annex)
- Feed data forward to the next level, and provide feedback to peripheral levels and the local staff
- Monitoring the epidemiological pattern of measles cases
- Supervise and provide technical support to district level activities

National level:

- Confirm cases and outbreaks using IgM serologic testing (the National Measles laboratory) and organize possible shipment of specimens for viral isolation.
- Analyze disease patterns and trends, interpret surveillance data in conjunction with the routine immunization coverage data, and produce routine reports
- Monitor the national and subnational level surveillance performance using standard indicators
- Monitoring the epidemiological pattern of measles cases

- Harmonization of data coming to the national level through the different systems- lab, case based surveillance, IDSR...
- Feed data forward and provide feedback (information) to peripheral levels and the local staff
- Supervise and provide technical support to district and provincial level activities
- Use data to evaluate national objectives and to direct the control program
- Review technical and programmatic issues regularly

The conduct of a well structured case based surveillance system for measles includes:

- *Weekly active surveillance visits*
- *Immediate reporting of suspected measles cases*
- *Laboratory confirmation of each suspected measles case in non-epidemic situations*
- *Investigation of outbreaks with lab confirmation*
- *Monthly aggregate reporting of suspected cases (including zero reporting) to the national level*

iv. Identification and notification of suspected measles cases

Every Health facility and hospital should designate one surveillance officer responsible for keeping track of suspected measles or rubella cases and immediately report all new suspected cases. Case-finding through the emergency, outpatient unit, pediatrics and infectious disease wards is critical to the success of a measles surveillance system. The health workers assigned to surveillance will review admission records for suspected measles cases. Reports should be submitted to local and/or state surveillance coordinators. District and provincial officials should, in turn, transmit weekly to the national level the reports they receive from the health facilities in their jurisdictions, and national authorities report weekly to WHO.

Community sources. In addition to all health facilities, a network of community reporters should be organized to report suspected measles cases. At the community level the definition of a suspected case of measles/ rubella is made simple to encourage community to report cases at health center. The community surveillance reporting definition for measles is: “any case of generalized rash and fever.” The community surveillance sources may include community health volunteers, traditional practitioners, pharmacists, private practitioners, village leaders, teachers and students.

Active case-searches. To ensure that all suspected cases are identified and notified, periodic active case-searches should be conducted. These are particularly important in areas that have not yet notified cases (“silent” areas) and high-risk areas. They are mainly conducted in health facilities (clinics and hospitals), but can also be performed in institutions, schools, and in the community. In health facilities, registration records, discharge diagnoses, and hospital charts are reviewed to identify patients with fever and rash illnesses.

v. Case investigation

After notification, investigation of suspected cases should start immediately. A trained health worker should be in charge of the investigation. The three main elements of an adequate investigation are:

- immediate investigation at the health facility following notification
- capture of all relevant epidemiological data in the case investigation form (i.e. date of rash onset, date of notification, date of investigation, date sample taken, type of rash, presence of fever, dates of previous measles /rubella vaccinations);
- and active case-searches.

A unique case identification number should be given to each suspected case investigated. This number is formulated to designate the geographic location and the year of the case under investigation. For example, the case number “CAE–CEN– NSA–2014–006” refers to case number 6, reported in the year 2014 from the Central Region, health district of Nsam in Cameroon. This unique case identification number should be used in all communications and forms related to the case.

Practical steps of the measles case investigation:

- Visit the home or health facility of the reported suspected case to obtain basic demographic, epidemiological and clinical information.
- Interview parents and complete the form for the notification and investigation of suspected measles/rubella cases (see Annex 1).
- Update the line-listing of suspected cases (see Annex 2).
- Collect specimens from suspected measles cases for laboratory confirmation

The countries in the African Region are using serum specimens for lab confirmation purposes. Nasopharyngeal specimens collected using specially made swabs may also be used in some countries.

The procedure for collecting a blood specimen for lab confirmation includes the following :

- Draw just 5 ml of venous blood into a screw capped test-tube labeled with the patient's identification (Name, age, address), and the date of specimen collection. In children with malnutrition or with severe health condition, only 2 to 3 ml of blood may be taken.
- Isolate the serum from the cells by allowing the blood to sit at an angle at room temperature for at least 1 hour (without shaking) or until the clot retracts, or by refrigerating the sample overnight, or by centrifuging the specimen at 2000 rpm for 10-20 minutes, after letting the blood sample stand for about an hour.
- The serum is carefully decanted into another test tube labeled with date of collection and identification.
- The serum is then stored at 4 - 8°C until it is ready for shipment and testing.
- Inform surveillance sites and surveillance coordinators in nearby areas that a suspected case has been identified.
- Evaluate vaccination coverage levels and provide measles vaccination to unvaccinated persons

- Search actively for other suspected cases in the neighborhood, at school/work.

Both natural measles infection and measles vaccine can stimulate an IgM response. If the suspected case has been vaccinated within four weeks before onset of rash, the interpretation of the result may be problematic because of the following reasons:

- 1) Measles vaccine can cause fever and rash
- 2) Vaccinees are expected to have detectable measles IgM after vaccination
- 3) Serological techniques cannot distinguish immunity from natural infection or an immunization
- 4) Other medical conditions (Rubella or dengue) can cause rash and fever in a person who has recently received measles vaccine.

vi. Case classification flow chart for Measles Surveillance

Following the receipt of laboratory confirmation results, the national epidemiologic surveillance unit is expected to classify all cases according to the Regional standard case classification system. For surveillance purposes, WHO AFRO recommends the following scheme for the classification of measles cases. The point of entry into the surveillance system is a suspected case of measles¹. An adequate specimen is one collected upon first contact with a suspected measles case, in the first 30 days of the onset of rash and should be in good condition (adequate volume for serologic testing, no leakage, not turbid from possible contamination, AND not dessicated) upon arrival at the laboratory.² All serum specimens with indeterminate measles IgM results should undergo a second test before being labeled “indeterminate” and being classified as “Compatible”.

¹ Fulfils the measles standard case definition; fever and maculo-papular generalized rash plus cough OR coryza OR conjunctivitis.

² It is always advisable to avoid hemolysis when processing serum specimens in the field. However, hemolysis is not a reason for labeling specimens as being in “bad condition” when they are brought to the laboratory since it is known that hemolysis does not interfere with measles and rubella IgM testing using the Behring test kit.

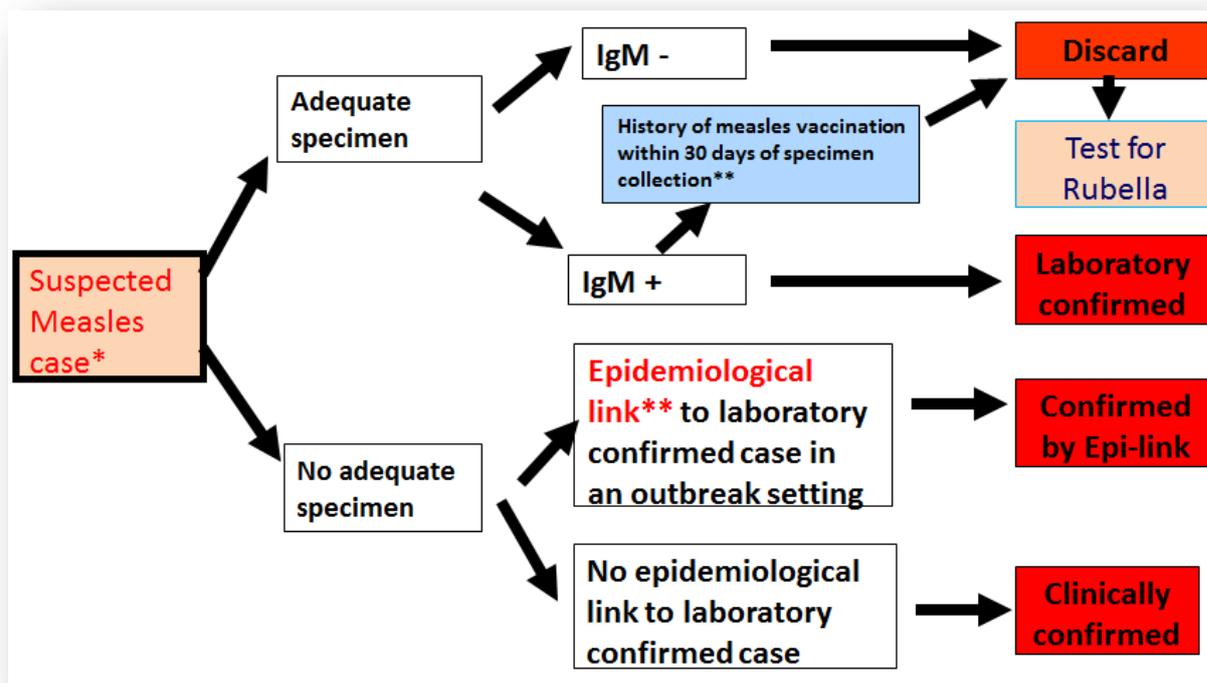


Figure 3. Measles case classification system.

Laboratory Confirmed Measles: Laboratory confirmed: A suspected measles case that is investigated, including the collection of blood specimen, has serological confirmation of recent measles virus infection (measles IgM positive) and had not received measles vaccination in the 30 days preceding the specimen collection.

Measles Confirmed by Epidemiological linkage:

A suspected measles case that has not had a specimen taken for serologic confirmation and is linked (in place, person and time) to lab confirmed cases; i.e., living in the same or in an adjacent district with a lab confirmed case where there is a likelihood of transmission; onset of rash of the two cases being within 30 days of each other.

In the case of confirmed measles outbreaks, the national epidemiological surveillance unit should proactively look at the surveillance data on a regular basis, ensure completeness of capture of case based, laboratory and line-listed information, and classify epidemiologically

linked measles cases. The analysis and interpretation of the surveillance data relies on accurate and timely classification of cases.

Clinically confirmed/ Compatible Measles:

A suspected measles case that has not had a blood specimen taken for serologic confirmation and is not linked epidemiologically to any lab confirmed outbreak of measles. Measles cases that have no definite proof of recent infection (measles IgM test indeterminate repeatedly and negative for rubella testing) may also be classified as compatible. WHO AFRO recommends that all measles IgM negative and indeterminate sera undergo rubella IgM testing and that the results be appropriately documented in the database.

Discarded/ not measles :

A suspected measles case that has been completely investigated, including the collection of adequate blood specimen, and lacks serologic evidence of recent measles virus infection (IgM negative) or is considered to have IgM positivity due to measles vaccination within the 30 days preceding the collection of a specimen.

vii. Active search for suspected measles and rubella cases

Active measles and rubella case searches should be implemented to identify suspected cases. Active case search is particularly useful in outbreak situations to identify the primary case, as well as to detect all secondary cases, and contacts that may occur within the corresponding incubation period, and to ensure that virus circulation has been interrupted.

These searches should be conducted in health facilities and in communities. Active searches should also be carried out in high-risk areas (areas with low vaccination coverage, silent areas, refugee camps or areas that do not adhere to weekly reporting standards). Active searches will assess the quality of surveillance by identifying the strengths and weaknesses of the surveillance system.

VII. DETECTING, INVESTIGATING AND RESPONDING TO MEASLES OUTBREAKS

i. Definition of measles outbreaks:

Outbreaks occur when the accumulated number of susceptible individuals is greater than the critical number of susceptible individuals, or epidemic threshold, for a given population to sustain transmission. The epidemic threshold of measles is low because of the high level of communicability of measles. WHO-AFRO defines a suspected outbreak of measles as the occurrence of 5 or more reported suspected cases of measles in a health facility or district in one month, with plausible means of transmission. This threshold value should trigger an outbreak investigation to determine the true size and reason for the outbreak.

A suspected outbreak of measles : the occurrence of 5 or more suspected cases of measles in a health facility or district in one month.

A confirmed outbreak of measles: 3 or more measles IgM positive (laboratory confirmed) cases in a health facility or district in one month.

All confirmed measles outbreaks require proper investigation and appropriate response, including continued efforts in case finding and line listing, improving the case management, strengthening of the overall surveillance system, and reinforcing immunization activities in surrounding districts. The WHO document “Response to measles outbreaks in mortality reduction settings”³ provides updates guidance on the options available for response.

ii. Measles Outbreak preparedness

Preparedness for outbreaks helps to enhance capacity for rapid detection and response to measles outbreaks, and to prevent the spread of measles virus transmission. The following four elements are crucial as part of any outbreak preparedness efforts.

³ World Health Organization 2009. Response to measles outbreaks in measles mortality reduction settings. WHO/IVB/09.03

i. National coordination and prepositioning of inputs

The National outbreak preparedness and response task force plays a key role in coordinating and directing outbreak preparedness activities and mobilized resources and technical assistance for response efforts. The Task Force should be managed by the Ministry of Health with the participation of partners. The National Immunization Programme should develop a measles outbreak preparedness and response plan, to be reviewed and endorsed by the National task force. The plan should identify mechanisms to pre-position supplies, and to rapidly mobilize the resources (human and financial), vaccine supply and the logistics required for response once an outbreak occurs.

ii. Development of communication systems

Communities should be alert to report suspected measles cases rapidly. Clear communication channels should be developed to facilitate the sharing of information amongst districts and health facilities, and also between the health facilities and the community. The dissemination of a lay case definition for reporting suspected cases of measles helps to enhance community active search and reporting. The health center should prepare a guide describing key tasks for engaging community health workers and volunteers.

iii. Regular situation analysis:

As part of the preparedness efforts, the national immunization/ surveillance program should develop a list of high risk areas or populations and update these regularly. A standard measles outbreak risk assessment tool exists to help prioritise the areas at risk, by making use of information from disease surveillance and immunization performance data. Health districts which are silent or have low completeness and timeliness of surveillance reporting should be considered at risk and benefit from supportive supervision.

iv. Setting up Standard operating procedures:

The development and distribution of standard operating procedures (SOPs) for outbreak investigation and response will help countries to take rapid action and to be more efficient in the management of the outbreak. Such SOPs help to structure priority activities, to

define who needs to do what once an outbreak has been confirmed, and to clarify the roles of all levels and stakeholders. The presence of SOPs that are well recognized by all actors helps to mobilise resources faster, and thus to address the situation in a more coordinated and smooth manner.

iii. Investigation of measles outbreaks:

It is important to investigate and document suspected measles outbreaks for the following reasons

- a. To assess the magnitude of the outbreak (severity of illness, potential for further spread).
- b. To develop guidance on control measures needed (to prevent further spread and minimize deaths).
- c. To prevent future outbreaks
- d. To respond to political pressure/ legal obligation, public concern.
- e. As a research opportunity to understand the epidemiological situation better.

The following is a generic list of activities to undertake in the investigation of and response to any outbreaks:

1. Prepare for field work
2. Verify the diagnosis – lab confirmation of cases through IgM testing of blood specimens
3. Collect throat swab specimens from five cases in their early clinical stages (within the first five days of the rash illness) for viral strain characterization
4. Establish the existence of an epidemic – compare trends with the past, and describe clusters against the outbreak definitions
5. Identify and count cases: record reviews, active case search in the community,
6. Notify health facilities and neighbouring districts and intensify surveillance
7. Data analysis: by time, place and person

8. Formulate and test hypothesis regarding the cause of the outbreak; eg., non vaccination vs vaccine failure
9. Assess the local response capacity
10. Set up immediate control measures
11. Address the resource gaps to enable appropriate response to be conducted
12. Report writing
13. Dissemination of findings

A basic epidemiologist's field pack for outbreak investigation may include:

- Calculator & mobile phone
- Log book
- Files: templates, standard questionnaires
- Handbooks
- Specimen collection kits, +/- Laboratory equipment
- List of local contacts
- Maps
- Computer, appropriate software (Epi-Info, Excel, Word, etc.)

At the district level, the investigation of a suspected measles outbreak should include the following:

- The health facility surveillance focal person notifies the district team about the occurrence of clusters of cases using the quickest available means of communication.
- The health facility surveillance focal person or district team completes case forms and takes blood specimen from the first five suspected cases only.
- The district team notifies all clinicians and surveillance coordinators in nearby areas of the outbreak and the need for intensified surveillance.
- The district team creates a line-listing of all subsequent cases to record the age, vaccination status, address, date of rash onset, outcome, EPID number (to be assigned at National level).

- The district team conducts record review in health facilities, and active case searches at health facility and community level (in surrounding villages) to determine the extent of the outbreak.
- The district team analyzes and interprets surveillance data (date of onset of rash, vaccination status, age, geographic location) in order to determine the extent of the outbreak and the reason: whether the outbreak was a result of failure to vaccinate or vaccine failure.
- The district team should then monitor the evolution of the outbreak by keeping track of the number of cases and dates of onset of rash of reported cases using an epidemic curve.
- The district team completes and sends to the National level the 2-page district outbreak investigation report (within 2 weeks of the investigation) summarizing the findings, the response, evaluation and feedback processes. The district team should also complete and send the person analysis, spot map and “epidemic curve” to the national level within 2 weeks.

During a lab confirmed measles outbreak, the line listing of suspected measles cases should be updated regularly until the end of the epidemic. The concerned district should prepare a consolidated line-list from all sources and transmit it to the national surveillance office. The line-list should include the following information:

- Name
- Date of onset of rash;
- Place of occurrence;
- Age;
- Vaccination status;
- Date of last vaccination;
- Outcome: Alive OR Dead

Since line listed cases often are not investigated with a blood specimen, the epidemiological context of the outbreak will be used at national level to classify as measles confirmed by epidemiological linkage. The national level will assign to each case the appropriate identifier

EPID number during the entry of the data into the case based surveillance database. As usual the epid number should be able to capture information on the province, district, year of onset of the rash and the serial number.

A more comprehensive documentation needs to be done at the end of the outbreak. An outbreak of measles in a district is said to have come to an end when there has not been any new case of measles for more than 3 weeks, (which corresponds to the maximum incubation period of measles), and when all neighboring districts have not reported any case for a similar period of time. However, this decision on the end of the outbreak can only be taken if there has been intensive active case search, and notification of all suspected cases from all reporting facilities, including the provision of zero reports when no suspected case is seen.

iv. Response to measles outbreaks:

As soon as an outbreak is suspected, the risk of the outbreak extending into a large one, with high morbidity and mortality, must be assessed. This evaluation is needed to determine susceptibility and potential spread in both affected and neighboring areas as well as the appropriate vaccination response to control the outbreak.

To evaluate the risk of further transmission, morbidity and mortality, the following factors should be taken into consideration:

- Population characteristics such as size, density, movement, and setting;
- Under five mortality rates;
- Nutritional and vitamin-A status;
- HIV prevalence;
- Period of the year: seasonal outbreaks or holidays, festivals and social events that would increase opportunities for spread;
- Cases reported and comparison with previous years; and
- Access to health services.

As soon as a measles outbreak is suspected, the following steps should be taken.

a) Case Management:

The first course of action in an outbreak should be the provision of appropriate and adequate case management to all measles cases. This includes providing supplemental or therapeutic doses of vitamin A, the provision of supportive treatment, and the specific treatment of complications of measles. Vitamin A should be given to all measles cases, irrespective of whether it has previously been done during routine immunization activities. (Table 2). Complicated and severe cases of measles will need to be hospitalized for the purpose of intensive case management and require to be isolated from other patients as much as possible.

Table 2. Recommended vitamin A doses and schedule for treatment of measles cases

Age	Dose to be given	
	Immediately after Diagnosis	Next Day
0 –6 months	50, 000 IU	50, 000 IU
6 –11 months	100,000 IU	100,000 IU
≥12 months	200,000 IU	200,000 IU

b) Reinforcement of routine vaccination.

A measles outbreak provides the opportunity to identify programme weaknesses causing the outbreak and a chance to correct them. As soon as a measles outbreak is suspected, and before laboratory confirmation of the suspected measles cases, the following steps should be taken to reinforce routine vaccination.

- a.** District staff, health-facility staff and partners should rapidly identify priority areas within the affected district (e.g. communities with low vaccination coverage and at high risk of morbidity and mortality).
- b.** Jointly work on strengthening the available district immunization workplans.
- c.** Locate health centres conducting immunization sessions that may need additional staff or vaccine supplies, or repair/ replacement of cold chain equipment.

d. Organize corrective measures such as additional outreach services to communities with a high proportion of unreached children.

c) Appropriate selective vaccination activities

Depending on the epidemiological picture, and the findings of the risk assessment exercise, countries may decide to vaccinate persons within a defined age group, or within a delimited geographic area, or having specific socio-demographic characteristics. Such selective vaccination efforts may take the form of vaccinating within colleges, in-patient populations, health workers, military barracks, populations of migrant workers, etc. In addition, the vaccination of children under five who present to health facilities, but do not have any evidence of having received two doses of measles vaccines in the past is a common example of selective vaccination. The steps to follow to implement selective vaccination activities include:

- a. Enhance social mobilization activities to inform the affected communities about the suspected outbreak, which specific age group of previously unvaccinated children is targeted for measles vaccination, and where parents should bring their at-risk children for vaccination.
- b. Vaccinate all children (six to 59 months of age or determine the target age group according to the local disease epidemiology) presenting to a health facility or an outreach vaccination site without a history of measles vaccination (either written or verbal). Children receiving measles vaccine before the age of nine months must be revaccinated after the age of nine months (with at least a one-month interval between the doses).
- c. Vaccinate hospital staff at risk of exposure who have not been vaccinated.
- d. Ensure sufficient supplies. Use stock management records to determine available quantity and location of vaccine, auto-disable syringes and other supplies (e.g. cold-chain equipment and vitamin A) that are available immediately for use. Estimate and request the additional supplies needed so that activities are not interrupted due to supply stock outs.

d) Non-selective outbreak response vaccination.

As soon as the outbreak is confirmed, and if the risk assessment results indicate that there is a high risk of a large measles outbreak, then the capacity to carry out a high quality, large-scale immunization campaign should be rapidly assessed by:

- Evaluating the availability of staff and financial resources (both internal and external) for the operational and logistical aspects of an outbreak response vaccination campaign; and
- Evaluating if the vaccine and other supplies can be made available at the time needed. If there is sufficient capacity (human and financial resources, vaccine and other supplies), to carry out a safe and timely vaccination campaign, then a mass vaccination campaign should be carried out in the targeted areas (affected and neighbouring areas as determined by the risk assessment). However, if the outcome of the assessment does not indicate the need for a mass vaccination response, then selective immunization of unimmunized children presenting to health facilities as outlined above should be continued and the number of reported cases closely followed to monitor the progression of the outbreak.

For the non-selective mass vaccination response, the timing, target age group and area for vaccination should be defined by considering key elements including:

- Routine vaccination coverage and coverage during SIAs in each birth cohort;
- Age specific attack rates; and
- Absolute number of cases.

An accelerated micro-planning exercise should be performed to determine the needs for bundled vaccine, logistics, staffing and communication for the response vaccination activity. Existing country or regional guidelines for conducting mass measles vaccination campaigns should be used. Once the decision to intervene has been made, it is critical to act quickly to minimize the number of measles cases and deaths. Choosing the target population depends upon the susceptibility profile of the population.

The response should target both outbreak-affected areas and adjacent areas in which the risk- assessment shows a high risk of spread. As distinct from preventive SIAs (e.g. follow-up

SIAs) that target whole countries, provinces or states, campaigns done in response to outbreaks should be more limited in scale. Health staff should pay particular attention to ensure that groups and areas with a high likelihood of not being reached (i.e., with known low coverage) and at high risk for measles-related complications are reached during the vaccination activities, and any necessary supplemental measures such as the provision of vitamin A are provided.

These vulnerable groups and areas include:

- young children, particularly those under one year of age;
- malnourished and vitamin A-deficient children;
- infants and children of HIV-infected women, and other immunocompromised children;
- certain ethnic and religious groups who may have poor access to immunization;
- populations with poor access to health care;
- staff at hospitals and other health facilities;
- All children above six months of age who are attending hospitals (inpatients and outpatients) or who are visiting the hospital.

Children receiving measles vaccine before the age of nine months during a campaign must be revaccinated after the age of nine months (with at least a one-month interval between the doses), since the efficacy of vaccine administered before nine months of age is likely to be low.

Whenever outbreaks of measles are detected, district health managers should ensure that the IDS outbreak investigation report is filled out and the process of outbreak investigation and response is properly documented and analyzed at country level. The standard WHO AFRO IDS format for outbreak investigation reporting is included in Annex 4. National programs are encouraged to share copies of these reports with their WHO country offices who will in turn share them with the respective ISTs.

VIII. THE ROLE OF THE LABORATORY IN MEASLES/RUBELLA SURVEILLANCE

The laboratory plays a central role in the confirmation of suspected measles cases and outbreaks, and in the identification of circulating strains of measles viruses. The African Region of the WHO has organized a network of national measles laboratories in countries that have started accelerated measles control. The laboratories in the network are supported in terms of supplies, training, and quality assurance.

a. Confirmation of Measles Diagnosis

The most commonly used method for laboratory confirmation of measles is the detection of measles-specific Immuno-globulin M (IgM) antibody. Measles IgM antibodies are markers of recent infection or vaccination. Figure 5 illustrates the antibody response to infection (or vaccination) with a sharp rise in measles IgM and dropping off around 30 days later. The IgG antibody levels increase more gradually in response to infection, remain high throughout life and are hence not useful as markers of recent infection. As both infection and vaccination stimulate an IgM response, the child's vaccination history is important in the interpretation of the test result. Any person with measles IgM positive results who has had history of measles vaccination in the 30 days preceding the collection of the serum sample is not considered to be a laboratory confirmed case of natural measles infection, but IgM positive due to vaccination. Such cases will be discarded during the case classification process according to the classification scheme shown in Figure 3.

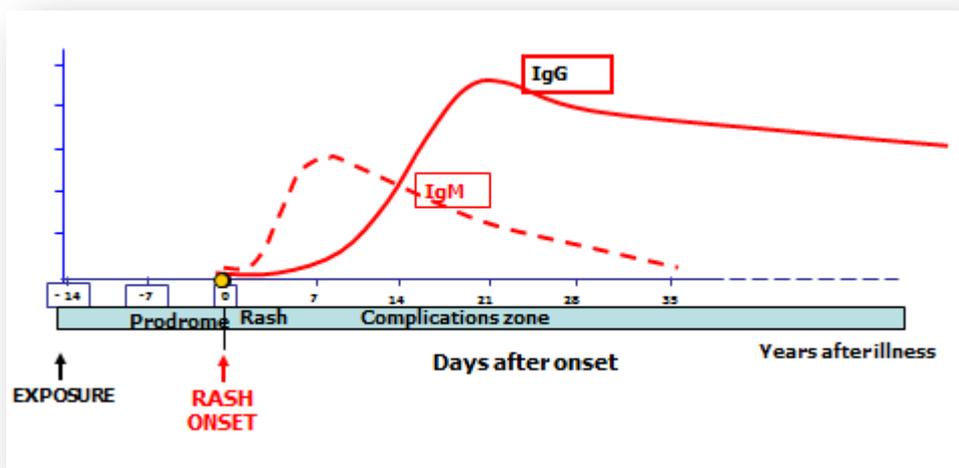


Figure 5. Antibody levels and timing of serological response after measles infection.

WHO currently recommends the IgM indirect ELISA method for rapid confirmation of measles cases. The test can be run in one day so that results can be returned in a timely manner. It is recommended that a single serum specimen be collected from every suspected case or from the first 5 cases in a cluster of suspected measles during the first 30 days following the onset of rash. Obtaining a serum sample is an invasive procedure that can cause distress to an already sick child. Care should be taken to observe injection safety as well as proper handling, storage and shipment of the samples (see Annex 6).

A small proportion of samples may give indeterminate results on IgM testing. All measles laboratories are expected to re-test measles IgM indeterminate samples, and to perform rubella IgM testing on all measles IgM indeterminate and IgM negative specimens.

b. Detection/ Isolation/Identification of viral strains

In the case of suspected outbreaks of measles, the national surveillance unit is expected to organize the collection of nasopharyngeal (throat) or gingival swabs from 5 cases as soon as possible within the first 5 days of the onset of rash. Nasopharyngeal swabs should be taken as early as possible following the suspicion of an outbreak, even before results of confirmation of the outbreak are available. The swabs, which are prepared with transport tubes containing viral transport media, are then refrigerated and transported to the virology

laboratory within 48 hours. The virology lab will process these specimens to isolate viruses in order to document the circulating viral strains following which viral isolates are shipped to the RRL for genotyping. Countries with no viral isolation facilities should ship the swabs to the Regional Reference Laboratory. Information regarding the circulating strains is useful to assess the progress towards measles pre-elimination, identify transmission patterns, and to track importations of measles virus when a country is in the elimination phase. There are 23 genotypes identified by genetic sequencing.

The specimen collection procedures are described in detail in Annex 7.

c. Quality Assurance

Given the importance of the laboratory results when the incidence of measles is low, it is important to ensure that the lab results truly reflect the true status of a suspected case of measles. For this reason, the WHO has established a quality assurance system. This system consists of equipment and performance checks, monitoring of assays with known reference controls, confirmatory re-testing by Regional Reference Laboratories (RRLs) of samples from national labs, annual accreditation exercises and national laboratories performing proficiency panel testing annually. While measles and rubella confirmatory tests are run by national measles laboratories, RRLs re-test 10% of specimens from national laboratories on a quarterly basis. This 10% should be selected from and include a fair representation of the specimens with measles IgM positive, negative and indeterminate results. When national labs have less than 100 specimens, national labs should send at least 10 specimens to the RRL for quality assurance.

IX. MINIMUM MEASLES SURVEILLANCE DATA ANALYSIS

Measles case-based surveillance data is collected using the standard case based investigation form and entered into a standard WHO-AFRO EPI-INFO measles data entry module. Measles laboratory data are also entered into an entry module developed from the customized WHO AFRO data entry program. The standardized database codes for the measles case-based data entry are shown in the annex.

a. Basic epidemiological data analysis

Detailed analysis is recommended looking into all confirmed measles cases: these are cases of measles that are confirmed by laboratory or by epidemiologic linkage, or are clinically compatible. Analyses should aim at understanding the reasons for the occurrence of measles and obtaining clues to guide appropriate control strategies.

The minimum expected data handling and analysis includes:

- i. Monitoring of the timeliness and completeness of surveillance reporting at all levels
- ii. Monitoring the main and supplementary measles surveillance performance indicators at National level disaggregated by province/region.
- iii. Following the trends of measles using the basic epidemiological dimensions:
 - the patterns of occurrence for the person variables like age, vaccination status, outcome (WHO ARE THE CASES AND THE DEATHS??),
 - the epidemic curve (WHEN DID THEY GET ILL?) and
 - spot maps (WHERE DO THE CASES COME FROM?)

The following tools enable such interpretations (Please see Annex 8):

- i. Monthly tabulation of reported suspected cases using the measles specific person analysis table; analysis of age group, vaccination status, outcome (alive/ dead), IgM results of measles cases and deaths. This helps to determine what populations are at risk for the disease according to their host characteristics (age, gender) or exposures (vaccination status, occupation, district of residence, etc). Such analysis is also used

to generate the Attack Rate (by age grouping, by geographic area...) and the Case Fatality Rate (as a measure of the quality of case management).

- ii. Spot map showing those cases classified as confirmed according to their place of residence to be compared with vaccination coverage data and surveillance reporting sites. If the size of the population varies between the areas you are comparing, a spot map (which shows numbers of cases) can be misleading. In such an instance, area-specific attack rates with an area shade map helps to better understand the situation.
- iii. Epidemic curve showing number of cases with rash onset by date, and superimposed display of date of notification, date of investigation, date of specimen collection, and date concrete intervention began. The Epi curve depicts the time course of an epidemic by using a histogram of the number of cases by their date of onset. It provides a simple visual display of the outbreak's magnitude and time trend.

b. Additional epidemiological data analysis during outbreaks

In addition to the standard and basic epidemiological data analysis described above, during an outbreak, it will be important to do detailed data analysis including the determination of the weekly incidence levels, the calculation of the case fatality ratio and the attack rates. Weekly incidence is the number of new cases of the disease by week in a specified population. Attack rates and weekly incidence numbers permit comparison between different geographical areas and monitor the progression of the outbreak over time.

The case fatality ratio (CFR) measures the proportion of deaths among cases. CFR should be calculated for the community and hospitals separately. The CFR is an indicator of the severity of the outbreak. The CFR can be calculated as follows:

$$\text{CFR} = \frac{\text{Number of cases who died of measles} \times 100}{\text{Total number of measles cases}}$$

The Attack rate (AR) expresses the risk of disease in population in a given area since the beginning of the outbreak. If population data by age groups are available, age-specific attack rates can be calculated, which can help identify priority age groups for vaccination. The AR allows the comparison of risk of outbreak between different populations.

$$\text{AR 0-11 months} = \frac{\text{Number of cases in children aged 0 to 11 months} \times 100}{\text{Total number of children aged 0 to 11 months}}$$

X. SURVEILLANCE INFORMATION SHARING

i. Data Feed-forward

National EPI / surveillance/ disease control programmes are expected to share the following datasets and reports with the respective WHO country office **on a weekly basis**, for onward transmission to the WHO IST data manager who will clean, merge and send them to WHO/AFRO **weekly**.

- i. Weekly timeliness and completeness of routine surveillance reporting by districts
- ii. Weekly measles case-based surveillance database (using the AFRO measles EPI-INFO menu)
- iii. Weekly measles lab database (using the AFRO measles EPI-INFO Lab menu)

ii. Feed-back

The feedback process and mechanisms in measles surveillance are identical to the AFP surveillance model. Feedback concerning surveillance performance and results may be given in written form or verbally during on-site supervisory visits and during the periodic surveillance review meetings. At the national level, the EPI program manager/ National epidemiology unit is responsible for producing regular feedback bulletins or newsletters, highlighting any patterns or trends of disease occurrence and describing the possible causes of outbreaks as well as the quality of response following notification.

The WHO-Inter-country support teams (ISTs) and WHO/AFRO produce and disseminate regular written or electronic feedback to countries. This feedback deals with the timeliness/completeness of routine reports, the standard measles surveillance performance monitoring indicators, as well as the incidence and epidemiological pattern of measles cases for countries in their sub-region.

XI. MONITORING SURVEILLANCE QUALITY

National surveillance programmes are encouraged to regularly monitor the performance of their surveillance system to ensure high quality performance and surveillance sensitivity. The monitoring indicators focus on measuring the timeliness of surveillance actions like the speed of notification and investigation as well as specimen collection and submission of results; the sensitivity of case detection across the various geographic-administrative entities within the country; and the quality and promptness of submission of lab results. These indicators are expected to be monitored on a weekly basis, except for the quality control indicators measuring laboratory performance as compared to results from the regional reference lab.

Below are the standard indicators used to monitor the quality of measles surveillance. These are proposed from the African Regional level for use by the National and provincial levels to monitor the quality of measles case-based surveillance. (Formulas for the calculation of these indicators are given in Annex 9.)

i. Main Measles Surveillance Indicators:

- i. Non measles febrile rash illness rate : (target : at least 2 per 100,000 population)
- ii. Proportion of districts that have reported at least 1 suspected case of measles with a blood specimen per year: (Target: at least 80%)

ii. Supplementary Indicators for Measles Surveillance

- iii. Proportion of reported suspected measles cases from whom blood specimens have been collected (exclude epidemiologically linked cases from the denominator): (Target: at least 80%)
- iv. Timeliness of health facility IDS monthly reporting to the district level within the specified time period. (Target; at least 80% reports received timely at district level) See Annex
- v. Annualized rate of investigation (with blood specimens) of suspected measles cases (Target: > 1 case investigated with blood specimen / 100,000 population per year)

- vi. Proportion of measles outbreaks investigated with blood specimens from the first five cases: (Target: at least 80% measles outbreaks investigated with blood specimens)
- vii. Proportion of measles outbreaks with specimens collected and documentation done on measles viral strains: (Target: at least 80% measles outbreaks with measles viral strains documented)
- viii. Timeliness of suspected measles case investigation: (Target: at least 80% investigated within 3 days following notification)
- ix. Timeliness of serum/ dried blood specimens arriving at lab: (Target; at least 80% specimens arrived at lab within 3 days of being taken)

iii. Laboratory Indicators

- x. Timeliness of feedback of serology results from the laboratory to the national level: (Target: at least 80% results sent out by the lab to the national level within 7 days of receipt of specimens at the lab)
- xi. Proportion of serum specimens arriving at the National measles laboratory in good condition (Target: at least 90% of specimens arriving at the laboratory in good condition; i.e., adequate volume, no leakage, not turbid, not dessicated)
- xii. Proportion of representative serum specimens sent quarterly by the national laboratories to the regional reference labs for re-confirmation as part of quality assurance measures (Target: at least 10% of specimens tested at national lab shared with the RRL)
- xiii. Proportion of concordance of measles IgM results between the national measles lab and the regional reference lab (Target; at least 90% concordance between results of shared specimens between the national lab and the RRL)

iv. Regional Reference Laboratory Indicators

- xiv. Timeliness of feedback of serology results from the Regional Reference lab to the National measles laboratory (Target: at least 80% results sent to the national measles lab within 14 days of receipt of specimens at the RRL)

v. Impact Monitoring Indicators

In addition, the indicator used for the monitoring of impact of the strategies is:

- xv. Incidence rate of confirmed measles: The number of cases confirmed to be measles by lab, epi linkage and clinical compatibility per 1 million total population per year, expressed as a rate

XII. ELIMINATION-STANDARD SURVEILLANCE FOR MEASLES AND RUBELLA

i. Introduction

The measles case-based and lab-supported surveillance system, as described in the sections above, was established when the Region adopted accelerated measles control, and is being implemented by nearly all countries across the African Region since then. This system has served very well to transition countries from a high measles burden state into the period of declining measles burden following the implementation of the strategies to achieve accelerated measles control and measles elimination. The elements of such a case based surveillance system still remain highly relevant across the whole Region, and allow for the monitoring of the impact of the strategies on measles epidemiology, as well as for rubella testing of measles lab-negative specimens. In so doing, the system has allowed countries to better understand the epidemiology of rubella as well, without heavily burdening their surveillance systems to look for every suspected rubella case.

However, as the African Region moves towards the elimination target, and with certain countries having achieved a longer period of sustained low incidence for measles, there is a need to make the surveillance system more sensitive, and more tuned to address the emerging issue of rubella control.

The proposed “elimination-standard measles and rubella surveillance”, will continue to be implemented as a case-based surveillance system, supported by active surveillance visits and integrated with other vaccine preventable diseases. It is expected that all countries will eventually move towards this elimination-standard system once they achieve high population immunity and sustained low measles incidence. The introduction of such an elimination-standard surveillance system will be done gradually, with intensive consultations, capacity building and monitoring support from the WHO Regional and IST level, and prioritizing countries that are already approaching measles elimination.

ii. Key elements of elimination-standard measles/ rubella surveillance

The implementation of elimination-standard measles and rubella surveillance require that countries adopt:

- 1) Broader case definitions for initial recruitment of suspected cases into the surveillance system

The adoption of a broader case definition involves looking for suspected measles or rubella cases, or rather all cases with “fever and generalised rash”. This is expected to bring more cases into the surveillance system, and will require more lab testing of suspected cases.

- 2) Detailed case investigation of every suspected case of measles / rubella

The detailed case investigations of all suspected cases will include taking “travel history” from each case, and conducting active case search around each confirmed case of measles. In addition, for those countries who may have the capacity to do so, it is advised that index finding and contact tracing be included in the surveillance standards.

Finally, this system will require more intensive investigation of all cases and outbreaks. Elimination-standard measles/rubella surveillance makes an emphasis on the completeness of individual case investigation. The case investigation and reporting form has been modified accordingly. See Annex 10. All suspected cases who have been investigated, will need to have adequate documentation of the key demographic and epidemiological variables as part of the high quality investigation. A set of 12 variables have been selected, and these need to be captured in all cases in order to label the case investigation as complete:

- | | |
|---------------------------|--|
| 1) Name, | 7) date of specimen collection |
| 2) Sex | 8) Vaccination status, |
| 3) Age/ Date of birth, | 9) Date of last vaccination, |
| 4) Date of onset of rash, | 10) District of residence, |
| 5) Date of notification, | 11) Reporting District |
| 6) date of investigation, | 12) Travel history 7 - 21 days before date of rash onset |

Detailed investigation of cases requires that, at the very least, active case search is conducted systematically around each confirmed measles case in order to ensure that all cases are detected and reported. While the definition of a suspected and confirmed measles outbreak will remain the same as before, the quality and depth of investigation following each reported case will be more extensive. Countries are expected to amend their Standard Operating Procedures for surveillance in such a way as to accommodate such an aggressive case search around each case.

The definition of epidemiological linkage for measles will be more stringent and requires that actual contact be established with a lab confirmed case during the period of infectivity, rather than applying the broader epidemiological-linkage definition used in the past.

All rubella outbreaks will also need to be investigated and documented, with detailed case finding, specimen collection and epidemiological characterisation.

3) A more refined case classification algorithm

The case classification scheme has been modified to accommodate the above changes. (See Figure 6). The corresponding case definitions are also provided in the section below.

iii. Case definitions in elimination-standard measles / rubella surveillance

The case classification scheme (Figure 6) and case definitions to be utilised in elimination-standard surveillance are indicated below:

The surveillance case definitions are:

- **“Suspected measles/ rubella”:**
 - Any case with Fever + generalised maculopapular rash
 - OR Clinician diagnosed measles/ rubella
- **Epidemiological linkage to a lab confirmed measles case:** suspected case meets surveillance case definition, is directly linked / contact established to a lab confirmed measles case with dates of rash onset occurring 7 – 21 days apart.

- **Confirmed measles case:** All cases of measles that have been lab confirmed or confirmed by epidemiological linkage to a lab confirmed case, or cases that have been labelled as clinically compatible measles cases

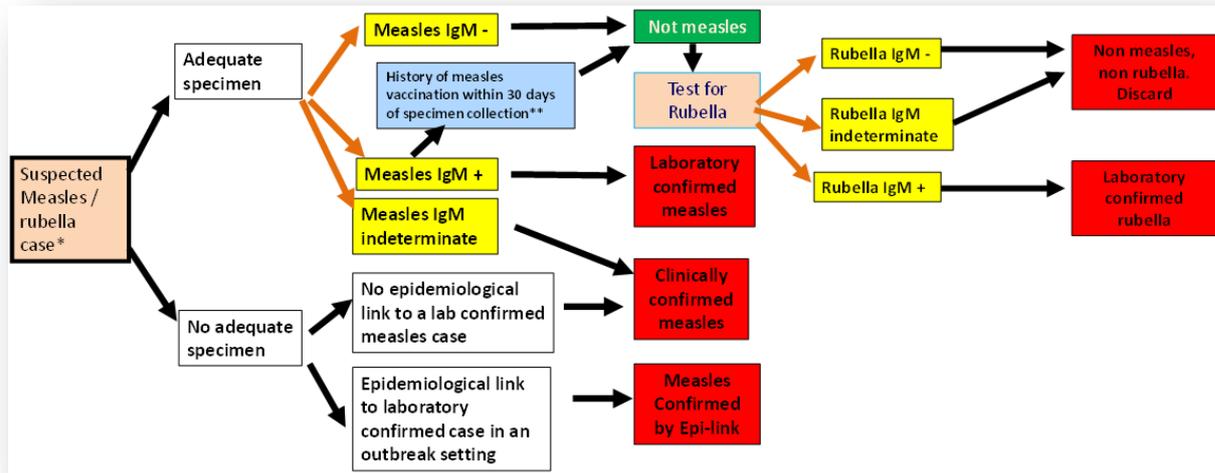


Figure 6. Case classification scheme for elimination standard measles/ rubella surveillance.

- **Rubella outbreaks:** A cluster 5 or more IgM confirmed rubella cases occurring within a month period within a district

In countries that have managed to keep their incidence levels below 1 per million population, and are close to the elimination target, confirmed cases of measles need to be classified further. This classification based on infection source is critical to evaluate whether the endemic circulation of measles virus is still going on in the country or in the region. Based on the infection source, confirmed cases of measles should further be classified into one of the four mutually exclusive categories:

- **An Endemic case of measles is a** confirmed case supported by epidemiological and virological evidence. This indicates that it is part of a chain of endemic transmission, meaning that the isolated virus has been circulating in the country for a period greater than or equal to 12 months.

- **An imported measles case** is a confirmed case which, as supported by epidemiological and / or virologic evidence, was exposed outside of the country during the 7–21 days prior to rash onset.

- **An import-related measles case** is a confirmed case which, as supported by epidemiological and / or virologic evidence, was exposed locally as part of a transmission chain initiated with an imported case.

- **A measles case with unknown source of infection** is a confirmed case for which the source of infection was not identified.

- **Re-establishment of endemic measles 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.

iv. Surveillance performance indicators in elimination-standard surveillance:

The elimination-standard measles and rubella surveillance will make use of the following performance monitoring indicators. The formulas for the calculation of these indicators are given in Annex 11.

1. Main Measles Surveillance Indicators:

- i. NM-NRFRI rate (non-measles, non-rubella febrile rash illness) rate : (target : at least 2 per 100,000 population)
- ii. Proportion of districts reporting ≥ 2 Non Measles-Non Rubella Febrile Rash Illness cases / year (Target: at least 80%)
- iii. Proportion of districts that have reported at least 2 suspected case of measles with a blood specimen per year: (Target: at least 80%)

2. Supplementary Indicators for Measles Surveillance

- iv. Adequacy of individual case investigation: Number of suspected febrile rash illness cases with all 12 epidemiological variables documented in the case reporting forms (target $\geq 80\%$)
- v. Proportion of reported suspected measles/ rubella cases from whom blood specimens have been collected (exclude epidemiologically linked cases of measles from the denominator): (Target: at least 80%)
- vi. Timeliness of health facility IDS monthly reporting to the district level within the specified time period. (Target; at least 80% reports received timely at district level) See Annex
- vii. Annualized rate of investigation (with blood specimens) of suspected measles / rubella cases (Target: > 1 case investigated with blood specimen / 100,000 population per year)
- viii. Proportion of measles outbreaks investigated with blood specimens from the first five cases: (Target: at least 80% measles outbreaks investigated with blood specimens)
- ix. Proportion of measles outbreaks with specimens collected and documentation done on measles viral strains: (Target: at least 80% measles outbreaks with measles viral strains documented)
- x. Timeliness of suspected measles/ rubella case investigation: (Target: at least 80% investigated within 3 days following notification)
- xi. Timeliness of serum/ dried blood specimens arriving at lab: (Target; at least 80% specimens arrived at lab within 3 days of being taken)

3. Laboratory Indicators

- xii. Timeliness of feedback of serology results from the laboratory to the national level: (Target: at least 80% results sent out by the lab to the national level within 7 days of receipt of specimens at the lab)
- xiii. Proportion of serum specimens arriving at the National measles laboratory in good condition (Target: at least 90% of specimens arriving at the laboratory in good condition; i.e., adequate volume, no leakage, not turbid, not dessicated)

- xiv. Proportion of representative serum specimens sent quarterly by the national laboratories to the regional reference labs for re-confirmation as part of quality assurance measures (Target: at least 10% of specimens tested at national lab shared with the RRL)
- xv. Proportion of concordance of measles / rubella IgM results between the national measles lab and the regional reference lab (Target; at least 90% concordance between results of shared specimens between the national lab and the RRL)

4. Regional Reference Laboratory Indicators

- xvi. Timeliness of feedback of serology results from the Regional Reference lab to the National measles laboratory (Target: at least 80% results sent to the national measles lab within 14 days of receipt of specimens at the RRL)

5. Impact Monitoring Indicators

In addition, the indicators used for the monitoring of impact of the strategies are:

- xvii. Incidence rate of confirmed measles: The number of cases confirmed to be measles by lab, epi linkage and clinical compatibility expressed as a rate per 1 million total population per year
- xviii. Incidence of confirmed rubella; The number of cases confirmed to be rubella by lab expressed as a rate per 1 million total population per year,

XIII. CONGENITAL RUBELLA SYNDROME SURVEILLANCE

i. Introduction

In general, rubella presents with a mild rash and fever. The majority of infections occur during childhood resulting in life-long immunity; however, susceptible pregnant women who develop rubella during early pregnancy are likely to experience adverse outcomes of pregnancy like spontaneous abortions, fetal deaths and congenital defects including mental retardation, deafness, heart defects and cataracts (congenital rubella syndrome). For women, the risk of congenital rubella syndrome (CRS) is highest when rubella infection takes place in the first trimester of pregnancy.

A rubella-infected fetus carried to term may be born with congenital rubella syndrome (CRS). Some defects associated with CRS may be recognizable at birth, while others are detected months or even years later. CRS manifestations may be transient (e.g. purpura), permanent structural manifestations (e.g. deafness, central nervous system defects, congenital heart disease, cataract), or late-emerging conditions (e.g. diabetes mellitus). Hearing loss occurs in 70-90% of CRS cases, and in 50% of these children it is the only sign of CRS, although it is often not detected initially. Where there is no rubella vaccination programme, CRS is the most important cause of non-genetic congenital hearing loss. Congenital hearing loss interferes with normal development of speech and language; hearing and vision loss make socialization much more difficult.

In contrast to CRS-associated deafness, most of the CRS eye signs are readily recognized by parents and health care personnel. Health care workers should suspect CRS in an infant under one year of age (a) where there is a maternal history of rubella in pregnancy or (b) when the mother gives a history of one or more of the following: infant not visually fixing on the mother, eyes smaller than normal, rapid oscillation of the baby's eyes, squint, and/or suspicion of hearing difficulty.

ii. Sentinel surveillance for CRS

Congenital rubella syndrome is not a commonly encountered or frequently diagnosed disease entity, and so the surveillance of CRS is best done on a sentinel basis, and over a long term in order to give any meaningful result. Countries are expected to identify and select an appropriate clinical set up with laboratory capabilities to serve as the sentinel surveillance site. CRS sentinel surveillance is done targeting newborns and infants up to 11 months of age.

The sentinel site may be a pediatric specialty hospital or specialty neurology, cardiology, cardiac surgery, ophthalmology or eye clinics or hospitals that serve large populations. Neonatal wards and neonatal intensive care units can also serve as sentinel sites. In these sites, specialists should be provided with written guidelines and trained in order to engage them to report all identified cases of suspected congenital rubella syndrome to the surveillance officer. The sentinel surveillance system can be based on a single reporting site, or on a network of selected sites that can be monitored closely. The choice of sites depends on local conditions and should attempt to maximize both the likelihood and timeliness of identifying a suspected case.

These sites should be visited regularly by the national epidemiology unit, and active case finding and immediate reporting encouraged alongside zero reporting of suspected CRS cases on a monthly basis. Regular training and close supervision are important, as staff turnover may be frequent in many areas.

CRS may be diagnosed by its classic triad of clinical signs: cataract, heart disease, and deafness. However, many infants only have one of these manifestations, or may present earlier with neonatal signs; laboratory confirmation of the diagnosis is therefore recommended. Rubella-specific IgM is readily detected in the first 6 months of life, and among a decreasing proportion of cases up to 1 year of age. Its detection usually indicates prenatal rather than postnatal infection. The persistence of rubella-specific IgG beyond 6 months (the age when maternally derived IgG would usually have waned) can be detected

in 95% of infants with CRS. However, the presence of IgG in a child over 6 months of age may indicate either prenatal or postnatal infection.

The manifestations exhibited by neonates (e.g. purpura, hepatosplenomegaly, low birth weight) or during early infancy (e.g. cataract, congenital heart disease) have been detected most often during investigations that followed rubella outbreaks. Those affecting neonates have also been identified through routine toxoplasmosis, rubella, cytomegalovirus, rubella, cytomegalovirus, herpes simplex, and syphilis (TORCHES) screening programmes. There is special emphasis on investigation of rubella outbreaks. Because rubella outbreaks tend to persist several months or more and because CRS is a late outcome of these outbreaks, there is time to conduct active surveillance for CRS.

CRS surveillance constitutes immediate investigation (including serological testing) of all suspected CRS cases along with appropriate case classification, monthly zero reporting of suspected CRS cases, and generating annual estimates of CRS incidence. A standard case-based reporting format will be used, and specimen testing will be done in a local serology laboratory using rubella IgM testing of cases. The sentinel site is expected to capture the data using a standard database and share the data with the WHO country office on a monthly basis.

Whenever any suspected case of CRS is detected, it is best to immediately initiate clinical and lab investigation. A standard reporting form should be completed for each case of suspected CRS. (See Annex 12). The following information is important:

- Infant's clinical signs and symptoms,
- Infant's date of birth,
- Date of notification,
- Date of case investigation,
- Date of blood specimen collection from the infant,
- Results of IgM test,
- Mother's history of a febrile rash illness or exposure to a febrile rash illness during this pregnancy,
- Mother's address during this pregnancy,
- Mother's history of travel during this pregnancy,

iii. Case definitions for CRS sentinel surveillance

Suspected CRS case

A suspected case of CRS is any infant less than one year of age in whom a health worker suspects CRS. A health worker should suspect CRS where there is a maternal history of suspected or confirmed rubella during pregnancy. In addition, a health worker should suspect CRS when the infant presents with

- heart disease, and/or
- suspicion of deafness, and/or
- one or more of the following eye signs: white pupil (cataract); diminished vision; pendular movement of the eyes (nystagmus); squint; smaller eye ball (microphthalmos); larger eye ball (congenital glaucoma).

Health workers should refer all suspected CRS cases to a qualified physician.

Clinically-confirmed CRS case: A clinically-confirmed case is one in which a qualified physician detects two of the complications in group (a) OR one from group (a) and one from group (b):

- | a) | b) |
|---|---|
| <ul style="list-style-type: none">• <i>Cataract(s) and/or congenital glaucoma;</i>• <i>congenital heart disease;</i>• <i>loss of hearing</i>• <i>pigmentary retinopathy.</i> | <ul style="list-style-type: none">• <i>Purpura;</i>• <i>splenomegaly;</i>• <i>microcephaly;</i>• <i>mental retardation;</i>• <i>meningo-encephalitis;</i>• <i>radiolucent bone disease;</i>• <i>jaundice with onset within 24 hours of birth.</i> |

Laboratory-confirmed CRS case: A laboratory-confirmed CRS case is an infant with a positive blood test for rubella IgM who has clinically-confirmed CRS.

Congenital rubella infection (CRI): An infant with a positive blood test for rubella IgM who does not have clinically confirmed CRS is classified as having congenital rubella infection.

See Figure 7.

iv. Immune response in infants with CRS and the role of the laboratory

At birth, the serum of an infant with CRS contains maternally derived rubella-specific IgG antibodies as well as IgG and IgM antibodies synthesized by the fetus. Maternal rubella-specific IgG is also found in normal infants born to women who are immune to rubella. Therefore, rubella-specific IgM is used to diagnose congenital rubella infection in infants. In infants with CRS, rubella-specific IgM can be detected in nearly 100% at age 0-5 months; about 60% at age 6-12 months; and 40% at age 12-18 months; IgM is rarely detected after age 18 months.

Infants with CRS shed rubella virus for long periods. Rubella virus can be found in the nasopharyngeal secretions of more than 80% of infants with CRS during the first month of life, 62% at age 1-4 months, 33% at age 5-8 months, 11% at age 9-12 months, and only 3% during the second year of life. Infants with CRS who are shedding rubella virus are infectious and appropriate infection control measures should be instituted.

A blood sample (3 ml) should be collected from every infant with suspected CRS as soon after birth as possible. Almost all infants with CRS will have a positive rubella specific IgM test in the first six months of life, and 60% will be positive during the second six months of life. For surveillance purposes, a single blood specimen is generally considered adequate to either confirm or discard CRS. If, however, the first specimen is negative for rubella IgM and there exists a compelling clinical and/ or epidemiological suspicion of CRS, a second blood specimen should be requested.

v. CRS case classification system:

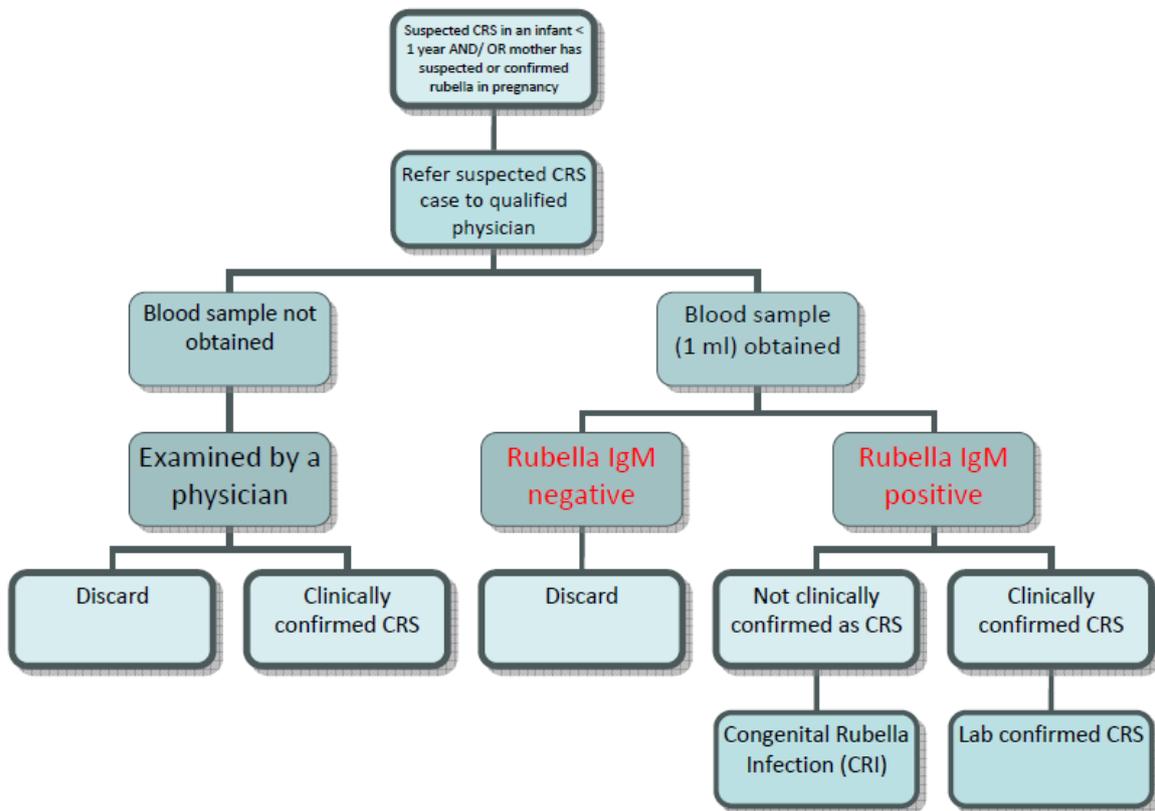


Figure 7. Case classification scheme for CRS.

vi. Retrospective search for CRS cases

Since sentinel surveillance for CRS may take time to produce results given that CRS is an uncommon outcome of rubella infections, it is advised that countries launch a review of past medical records within selected clinical settings in order to accumulate evidence of possible past infections. Retrospective search is the identification of suspected CRS cases through the review of records for diagnoses compatible with the clinical manifestations of the congenital rubella syndrome.

Retrospective record reviews for CRS cases provide an opportunity for countries to be able to understand the extent of occurrence of CRS cases, especially in the face of little pre-existing surveillance information on CRS cases. This exercise is recommended as an initial and inexpensive approach to help understand the extent of the problem, and does not

replace efforts to set up prospective epidemiological studies (eg investigation of rubella outbreaks, setting up sentinel sites for CRS surveillance).

The following steps may be considered to get the retrospective record review started:

- Identify an officer or a local consultant who can dedicate 2 – 3 weeks to conduct retrospective record reviews.
- Do an inventory and a review of existing relevant literature on rubella and CRS cases,
- Review the existing measles case based surveillance / lab data to identify the year when rubella outbreaks occurred in the country
- Identify sites where infants with signs and symptoms consistent with CRS are likely to present:
 - Children’s hospitals
 - Centers for hearing defects and blindness
 - Centers for disabilities
 - Specialty clinics: eg. Cardiology, Ophthalmology, Audiology, Neonatology, developmental clinics
- Consult general physicians, pediatricians, neonatologists, cardiologists, and professionals involved in TORCHES screening programmes in these facilities.
- Start the review of clinical records covering a period of at least two years following the documented onset of the rubella outbreak.
- Review clinical entries to identify cases that may fit the standard WHO clinical case definitions for CRS.
- Review records (if possible) to find out if any history of maternal rash illness was provided during pregnancy, and if any lab confirmation was available for the suspected CRS case
 - Line list by age, district of residence, date / month of birth, clinical description.

XIV. GLOSSARY OF TERMS

CASE: A person who has the particular disease, health disorder, or condition which meets the case definition for surveillance and outbreak investigation purposes. The definition of a case for surveillance and outbreak investigation purpose is not necessarily the same as the ordinary clinical definition.

CASE DEFINITION: A set of diagnostic criteria that must be fulfilled for an individual to be regarded as a case of a particular disease for surveillance and outbreak investigation purposes.

CLUSTER: Aggregation of relatively uncommon events or diseases in space and/or time in numbers that are believed or perceived to be greater than could be expected by chance.

COMPLETENESS OF REPORTING: the proportion of all expected reports that were actually received (usually stated as % completeness as of a certain date).

EPIDEMIOLOGICAL LINKAGE: direct contact with a laboratory-confirmed case

FEEDBACK: The regular process of sending analyses and reports about the surveillance data back through all levels of the surveillance system so that all participants can be informed of trends and performance.

FOLLOW UP SIAs: periodic measles supplemental vaccination campaigns involving all children born since the last catch-up campaigns irrespective of their prior immunization status; often every 2 - 4 years.

PERFORMANCE INDICATORS: Specific agreed measurements of how the surveillance or reporting system is functioning. These indicators may measure both the process of reporting (e.g., completeness, timeliness) and the action taken in response to surveillance information (e.g., the percentage of cases investigated) and the impact of surveillance and control

measures on the disease or syndrome in question (e.g., the percentage of outbreaks detected by the system)

SENSITIVITY: The ability of a surveillance or reporting system to detect true health events i.e. the ratio of the total number of health events detected by the system over the total number of true health events as determined by an independent and more complete means of ascertainment.

SPECIFICITY: A measure of how infrequently a system detects false positive health events i.e. the number of individuals identified by the system as not being diseased or not having a risk factor, divided by the total number of all persons who do not have the disease or risk factor of interest.

ACTIVE SURVEILLANCE : Surveillance where public health officers seek reports from participants in the surveillance system on a regular basis, rather than waiting for the reports (e.g. Regular visits to reporting sites).

SURVEILLANCE, CASE-BASED: Surveillance of a disease by collecting specific data on each case (e.g. collecting details like the age, vaccination status, address, date of onset... on each case of measles).

SPOT MAP: A map that indicates the location of each case of a disease by showing places that are potentially relevant to the health event being investigated.

TIMELINESS OF REPORTING: proportion of all expected reports that were received by a certain due date.

ZERO REPORTING: The reporting of “zero case” when no cases have been detected by the reporting unit. This allows the next level of the reporting system to be sure that the participant has not sent data that have been lost, or that the participant has not forgotten to report.

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XVI. ANNEXES

ANNEX 1: Integrated disease surveillance - generic case investigation form

Reporting Health Facility	Reporting District
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Generic Reporting Form – from Health Facility to District Health Team

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Cholera	Diarrhoea with Blood/Shigella	Dracunculiasis	Neonatal Tetanus	Measles/	Meningitis	Plague	Viral Hemorrhagic Fever	Yellow Fever	Other

____/____/____ Received form at national level

Name(s) of Patient: _____ Date of Birth: ____/____/____ Age: ____ years ____ months ____ days
 (If DOB unknown) (If <12 months) (NNT only)

Patient's Residence: Village/Neighbourhood _____ Sex: M=Male F=Female
 District of Town/City: _____ residence: _____ U=Urban R=Rural

Urban/Rural _____
 Locating Information: _____
 If applicable, name of mother and father if neonate or child _____

Date Seen at Health Facility: ____/____/____ For cases of Measles, NT (TT in mother), Yellow Fever, and Meningitis:
 Date Health Facility _____ Number of vaccine doses received 9=unknown
 Notified District: ____/____/____ For Measles, TT, YF- documented by card. For Meningitis, by history.

Dates of Onset 6 : ____/____/____ Date of last vaccination: ____/____/____
 (Measles, Neonatal Tetanus (TT in mother), Yellow Fever, and Meningitis only)

Blank variable 7 #1 _____ In/Out patient : 1=In-patient Outcome 1=Alive
 2=Out patient 2=Dead
 Blank variable #2 _____ 9=unknown

Final Classification 8
 1=Confirmed by lab (IgM positive)
 2= Confirmed by epidemiologic link
 3= Compatible/ Clinical
 4= Discarded by lab (IgM negative)
 5= Suspected with lab results pending

Person Completing Name: _____

Form Signature: _____ Date Sent Form to District: ____/____/____

IDS GENERIC CASE INVESTIGATION FORM (reverse side of form)
If Lab Specimen Collected

For Health Facility: If lab specimen is collected, complete the following information. And send a copy of this form to the lab with the specimen.

Date of specimen collection: ____/____/____

Specimen source (Circle): Stool Blood CSF Other: _____

Date Specimen sent to lab: ____/____/____

For the Lab: Complete this section and return the form to district team and clinician

Date lab received specimen: ____/____/____ Specimen condition (Circle): Adequate Not adequate

Disease/Condition	Type of test	Results (P=pending)		Disease / Condition	Type of test	Results*	Virus Detection
Cholera	Culture Direct Exam	+ - P + - P Method used for direct exam: _____		Yellow Fever	IgM	+ - P I	
				Measles	IgM	+ - P I	
Meningitis		Exam		Rubella	IgM	+ - P I	
N. meningitidis	Culture	+ - P		Dengue	IgM	+ - P	+ - P
S. pneumonia	Culture	+ - P		RVF	IgM	+ - P	+ - P
H. influenza	Culture	+ - P		Ebola	IgM	+ - P	+ - P
N. meningitidis	Latex			CCHF	IgM	+ - P	+ - P
S pneumoniae	Latex			Lassa	IgM	+ - P	+ - P
H. influenzae	Latex			Marburg	IgM	+ - P	+ - P
Shigella dysenteriae	Culture	SD type 1: Other Shigellosis: No Shigellosis:					
Plague	Culture IFA ≥ 1/ 64	+ - P + - P					

Other lab results: _____

Date lab sent results to district: ____/____/____

Name of lab sending results: _____

Other pending tests: _____

Date district received lab results: ____/____/____

Date lab results sent to clinician by district: ____/____/____

NOTE: District is responsible for ensuring lab results get to clinicians. Failure to do so will undermine cooperation with clinicians on reporting of cases in the future.

* + Positive, - Negative; P Pending; I Indeterminate

ANNEX 3: The measles case based surveillance database code table

Variable name in EPI - 2002	Case Form Variable/Description	Type		Variable Label (comment Legal)
Datatype	Data type	COMBO	Case-based Line List	
Country	Country Code	TEXT		
IdNumber	ID number	TEXT		
Reporting District	Reporting district	TEXT		
Province	Province of report	TEXT		
ReportingHealthFacility	Reporting health facility	TEXT		
Diseasecondition	Disease/Condition	TEXT		
DateReceivedNational	Date received form at national level			
NamesOfpatient	Name(s) of patient	TEXT		
DateOfBirth	Date of birth	DATE		
AgeInYears	Age in years	NUMBER		
AgeInMonths	Age in months	NUMBER		
PatientsResidence	Patient's residence: village/neighbourhood	TEXT		
Sex	Sex			
Towncity	Town/City	TEXT		
DistrictofResidence	District of Residence	COMBO	Code	
Province	Province	COMBO	Code	
Urbanrural	Urban/Rural	COMBO	R=Rural U=Urban	
DateSeenHealth Facility	Date seen at health facility	DATE		
DateHealthFacilityNotified	Date health facility notified district	DATE		
DateOfOnset	Date of onset	DATE		
NumberOfVaccinedoses	Number of vaccine doses	NUMBER		
DateOfLastvaccination	Date of last vaccination	DATE		
BlankVariable1	Blank variable #1	TEXT		
BlankVariable2	Blank variable #2	TEXT		
Inoutpatient	In/Out patient	COMBO	1 - In_patient 2 – Out_patient	
Outcome	Outcome	COMBO	1-Alive 2-Dead 3-Unknown	
FinalClassification	Final classification			1-Confirmed by Laboratory 2-Confirmed by Epidemiological linkage 3-Compatible/Clinical/ Probable 4-Discarded (IgM negative) 5-Suspected with specimen lab results pending
DateSentFormtoDistrict	Date sent form to district	DATE		
DateRecformdistrict	Date received form at district	DATE		

DateSpecimenCollected	Date specimen collection	DATE		
DateSpecimensentlab1	Date specimen sent to Lab	DATE		
SpecimenSource	Specimen source	TEXT		
Specify	Specify	TEXT		
DateLabReceivespecimen1	Date lab received specimen	DATE		
SpecimenCondition	Specimen condition	COMBO	1-adequate (good) 2-not adequate (not good)	
MeaslesIgM1 Measles IgM		COMBO	1-positive 2-negative 3-indeterminate	
RubellaIgM1 Rubella IgM		COMBO	1-positive 2-negative 3-indeterminate	
OtherLabResults1 Other lab results		TEXT		
DateLabresultdistrict1	Date lab sent results to district	DATE		
DateDistrictrecresults1	Date district received lab results	DATE		

ANNEX 4: Integrated Disease Surveillance district outbreak investigation report format

Title/Description (include disease/condition investigated)	
Period	Place (Villages, Neighborhoods, District, Province)

Executive summary:

I. Introduction:

- Background
- Reasons for investigation (public health significance, threshold met, etc.)
- Investigation and outbreak preparedness

II. Methods:

- Dates of investigation
- Site(s) of investigation (health care facilities, villages, other)
- Case finding (indicate what was done regarding case finding, e.g., register review, contact investigation, alerting other health facilities, other)
- Lab specimens collection
- Description of response and intervention (include dates)
- Data management

III. Results:

- Date and location of first known (index) case
- Date and health facility where first case was seen by the health care system
- Results of additional case finding
- Lab analysis and results
- With text, describe key features of results of time, place, and person analysis
- For detailed results by time (epi curve), place (map), and person characteristics (tables) and line lists
- Results of response and evidence of impact

Evaluation and Feedback:

Indicator	Date 1	Date 2	Interval
Interval between end of the outbreak [date 1] and finalization of outbreak report with case forms/line list sent to national level [date 2] (Target: 2 weeks)			

Indicator	Yes	No
Did the outbreak management committee meet to review investigation results?		
Was feedback given to health facilities and community?		

V. Evaluation of other aspects of the response:**VI. Interpretations, discussion, and conclusions:****VII. Recommended public health actions:**

Comment on following levels: community, health facility, district, partners, provincial, and national

District Epidemic Committee Chairperson:

Name

Signature

District Medical Officer:

Name

Signature

Date reported completed: _____

Evaluation and Feedback:

Indicator	Date 1	Date 2	Interval
Interval between end of the outbreak [date 1] and finalization of outbreak report with case forms/line list sent to national level [date 2] (Target: 2 weeks)			

Indicator	Yes	No
Did the outbreak management committee meet to review investigation results?		
Was feedback given to health facilities and community?		

V. Evaluation of other aspects of the response:**VI. Interpretations, discussion, and conclusions:****VII. Recommended public health actions:**

Comment on following levels: community, health facility, district, partners, provincial, and national

District Epidemic Committee Chairperson:

Name

Signature

ANNEX 5: Sample form for recording timeliness and completeness of IDS monthly reporting to the district

Legend: T = arrived on time L = arrived late W = report not received

Country _____ District _____ Year _____

Name of Health Facility	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Total number of reports expected(N)												
Total reports sent on time (T)												
Total reports sent late (L)												
Total number of reports not received (W)												
Timeliness of the reports =100 * T / N												
Completeness of reporting =100 * (N-W) / N												

NB: Please note that timeliness and completeness are expressed as percentages (%). When the surveillance system is good, the rates for timeliness and completeness should approach 100%. This table allows for monitoring the progress of these two indicators in the district so that action can be taken to improve timeliness for each health facility in the district.

ANNEX 6: Handling and transport of blood specimen for serologic confirmation

Collect 5 ml blood by venepuncture into a sterile tube labeled with patient identification and collection date. To separate the serum from red cells, one of the following three methods described below can be employed. To prevent bacterial over-growth, ensure that the serum is poured into a clean glass test tube. The test tube does not to be sterile—just clean.

- Let the blood sit at an angle for at least 60 minutes (without shaking or being driven in a vehicle), then pour off the serum into a clean glass tube.
- If a refrigerator is available, put the sample in a refrigerator for 4-6 hours until the clot retracts, then pour off the serum the next morning.
- If a centrifuge is available, let the blood sit for 30-60 minutes, then centrifuge the specimen at 2000 RPM for 10-20 minutes and pour off the serum into a clean tube.

Do not freeze whole blood.

Storage and shipment of serum specimens:

Store serum at 4 - 8°C until it is ready for shipment. The serum can be stored in the refrigerator for a maximum of 7 days. Serum must be frozen at -20°C if it is going to be stored for longer periods. Fill in case investigation forms completely. Three dates are very important

- Date of rash onset
- Date of collection of sample.
- Date of last measles vaccination

Specimens must be shipped to the laboratory as soon as possible. Place specimens in plastic bags. Specimens from different patients should never be sealed in the same bag. Place specimen form and investigation form in another plastic bag and tape to inner top of the specimen transport box. If using ice packs (these should be frozen), place ice packs at the bottom of the box and along the sides, place samples in the center, then place more ice packs on top. When shipping arrangements are finalized, inform receiver of time and manner of transport.

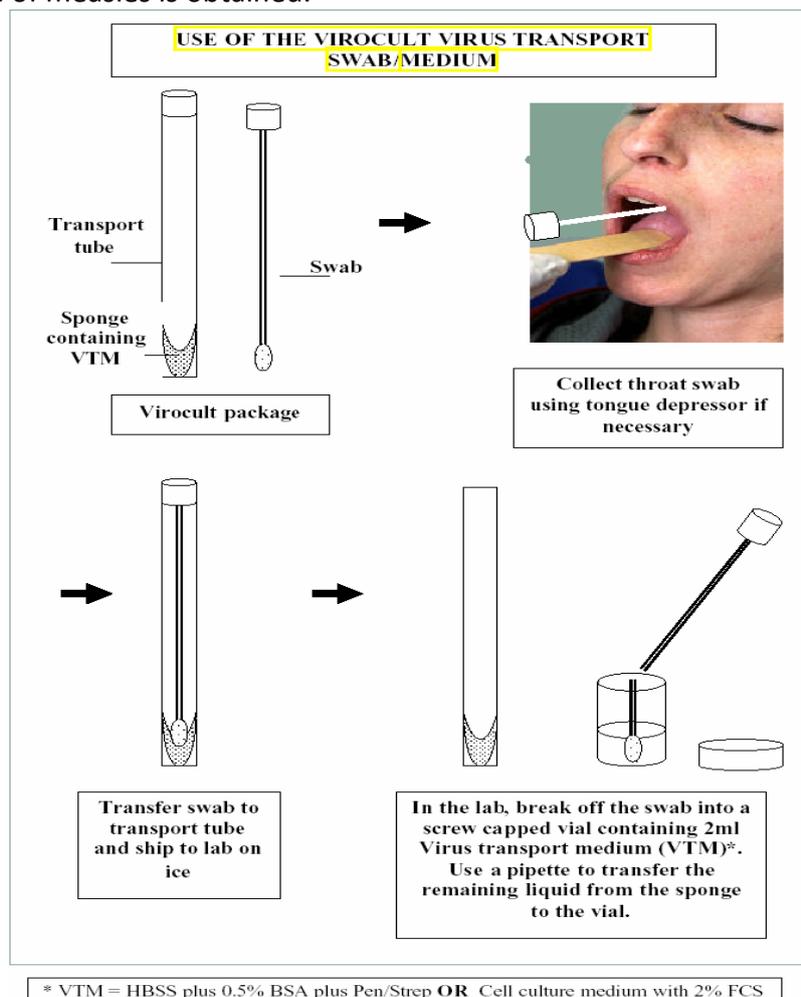
ANNEX 7: Handling and transport of naso-pharyngeal swabs

Nasopharyngeal specimens for virus isolation must be collected as soon as possible after onset and not longer than 5 days after the appearance of the rash, when the virus is present in high concentration. The patient is asked to open the mouth wide and say “aaaahhhh”. The tongue should be depressed with a spatula, and a nasopharyngeal swab is obtained by firmly rubbing the nasopharyngeal passage and throat with sterile cotton swabs to dislodge epithelial cells.

The swab is then placed in a labeled viral transport tube ensuring that the swab is immersed in the sponge containing the viral transport medium. The tube is transported to the laboratory at 4 – 8 °C, using frozen ice packs and appropriate insulated shipping container. (See figure)

Method of collecting and handling throat swabs for viral culture.

NB: Ideally, samples for virus isolation should be collected simultaneously with the blood samples for serological confirmation of measles as the cause of the outbreak. Collection of specimens for virus isolation should not be delayed until laboratory confirmation of a suspected case of measles is obtained.



ANNEX 8: Person analysis tables for case-based measles surveillance data

Data for the month/year of _____

Data from (district / province / country) _____

Table 1. Age distribution (Measles confirmed cases only; lab, Epi link, and compatible clinical cases)

Age	Number(#)	Percentage (%)
< 9 months		
9 – 11 months		
1 – 4 years		
5 - 9 years		
10 – 14 years		
15 - 19 years		
20 + years		
Missing		
Total confirmed		

Table 2. Vaccination status Measles confirmed cases only; lab, Epi link, and compatible clinical cases)

Number of vaccine doses taken	Number (#)	Percentage (%)
0 (not vaccinated)		
1		
2 or more		
Unknown		
Missing		
Total confirmed		

Table 4. Measles IgM Lab results (Only for cases with blood specimen)

Lab result	Number (#)	Percentage (%)
IgM positive		
IgM negative		
Indeterminate		
Pending results		
Total with specimen taken		

Table 5. Final classification (All reported cases)

Final classification	Number (#)	Percentage (%)
Lab confirmed (IgM +ve)		
Confirmed by epidemiologic linkage		
Confirmed clinically/ Compatible		
Discarded (IgM –ve)		
Lab result pending		
Missing		
Total reported		

Table 6. Outcome Measles confirmed cases only; lab, Epi link, and compatible clinical cases)

Final outcome	Number (#)	Percentage (%)
Alive		
Dead		
Unknown		
Total confirmed		

ANNEX 9 : Formulas for the calculation of measles surveillance performance monitoring indicators

The formulas for the calculation of the surveillance indicators are shown below. All the formulas are calculated as percentage points except indicator number four, which is a rate calculated as indicated.

- i. Non measles febrile rash illness rate: **(target : at least 2 per 100,000 population)**

$$\frac{\text{Discarded cases following lab serological testing of blood specimens} \times 100,000}{\text{Total population in area (country/ province)}}$$

- ii. Proportion of reported measles cases from whom blood specimens have been collected (excluding epidemiologically linked cases from the denominator): **(Target; = / >80%)**

$$\frac{\text{Reported suspected measles cases with blood specimen}}{\text{Total reported suspected measles cases - measles cases confirmed by epidemiological linkage}}$$

- iii. Proportion of districts that have reported at least 1 case of measles with a blood specimen per year: **(Target; = / >80%)**

$$\frac{\text{Number of districts that have reported at least 1 measles case with a blood specimen}}{\text{Total number of districts in the area covered by case-based surveillance}}$$

- iv. Timeliness of health facility surveillance reporting to the district level within the specified time period. **(Target >80% reports submitted timely to next level)**

$$\frac{\text{Total number of weekly reports that have reached on time to the district level}}{\text{Total number of reports expected for the period under consideration}}$$

- v. Annualized rate of investigation (with blood specimens) of suspected measles cases **(Target: > 1 case investigated with blood specimen / 100,000 population per year)**

$$\frac{\text{Total number of suspected measles cases investigated with blood specimen in the area} \times 100,000}{\text{Total population in area (country/ province)}}$$

NB: To annualize, multiply figure by 12/ month (eg 12/2 for February, 12/8 for August.)

- vi. Proportion of measles outbreaks investigated with blood specimens from the first five cases: **(Target; =/ > 80% outbreaks investigated with blood specimen)**

$$\frac{\text{Number of measles outbreaks investigated with blood specimens from the first five cases}}{\text{Total number of measles outbreaks in the area in the time period under consideration}}$$

- vii. Timeliness of suspected measles case investigation: **(Target: >80% investigated within 3 days following notification)**

$$\frac{\text{Number of measles outbreaks investigated within 3 days of notification}}{\text{Total number of measles outbreaks in the area in the time period under consideration}}$$

- viii. Timeliness of serum/ dried blood specimens arriving at lab (**Target > 80% arriving at lab <3 days of being taken**)

Number of serum / dried blood specimens that arrived at National lab within 3 days of collection
total specimens received at National lab

- ix. Timeliness of feedback of serology results from the laboratory: (**Target: = / > 80% results received at National level within 7 days of specimen receipt at lab**)

Number of results sent out by laboratory to the National level within 7 days of receipt of specimens
Total number of specimens received by lab

- x. Proportion of serum specimens arriving at the National measles laboratory in good condition (**Target: at least 90% of specimens arriving at the laboratory in good condition; i.e., adequate volume, no leakage, not turbid, not dessicated**)

Number of serum specimens that arrived at National lab in good condition
total specimens received at National lab

- xi. Proportion of lab confirmed measles cases (**Target: < 10% of investigated cases confirmed to be measles by serological investigation**)

Number of lab confirmed measles cases
Total number of serologically investigated suspected measles cases with lab results available

- xii. Proportion of representative serum specimens sent quarterly by the national laboratories to the regional reference labs for re-confirmation as part of quality assurance measures (**Target: at least 10% of specimens received at national lab shared with the RRL**)

Number of serum or dried blood specimens sent to the RRL by the national measles lab
Total number of serum and dried blood specimens received at National laboratory in the quarter

- xiii. Proportion of concordance of measles IgM results between the national measles lab and the regional reference lab (**Target; at least 90% concordance**)

Number of serologic results concordant with the National lab when re-tested at RRL
Total number of serum and dried blood specimens shared by the National laboratory with the RRL since the beginning of the year

- xiv. Incidence rate of confirmed measles per million population:

cases confirmed to be measles by lab, epi linkage and clinical compatibility x 1 million
total population

ANNEX 10: Reporting form for measles/ rubella suspected cases in countries implementing elimination-standard surveillance.

MEASLES/ RUBELLA SUSPECTED CASE REPORTING FORM - PAGE 1

**Measles/ rubella suspected case investigation form for immediate reporting:
from health facility / district to the national level**

For Official Use Only (to be completed by the district / national team) **EPID Number:** _____ - _____ - _____ - _____
Country Province District year onset case #

Reporting Health Facility _____ Reporting District _____

Date the form was received at national level: ____/____/____ (dd/ mm/ yy)

IDENTIFICATION:

1. Name of Patient: _____
 2. Date of birth: ____/____/____ (dd/ mm/ yy) 3. Age: ____ yrs ____ months
 4. Sex: _____ M=Male F=Female

ADDRESS:

5. Patient's Residence: Village/ Neighborhood _____
 6. Town/City: _____ 7. District of residence: _____
 8. Urban/Rural ____ U=Urban R=Rural

VACCINATION STATUS:

9. Number of measles containing vaccine doses received in routine EPI and/or SIAs (valid values: 1 – 4 doses) _____ 9=unknown
 10. Type of vaccine received (circle one) M MR MMR
 11. Date of last vaccination: ____/____/____ (dd/ mm/ yy)

CASE INVESTIGATION: (dd/ mm/ yy)

12. Date case was notified to the district: ____/____/____ 13. Date of case investigation: ____/____/____
 14. Date of onset of rash: ____/____/____

CLINICAL HISTORY:

15. Clinical symptoms (tick as appropriate)

- Fever Generalized rash Cough Running nose Red Eyes
 Swollen lymph nodes behind ears Joint pain/ swelling

16. History of travel outside the village/ town/ district in last 7 – 21 days before onset of rash _____ 1. Yes 2. No
 17. Most probable place of exposure to measles/ rubella: _____ district
 18. In/out-patient : _____ 1=In-patient 2=Out-patient
 19. Outcome : _____ 1=Alive 2=Dead 9=unknown

FINAL CLASSIFICATION:

20. Final Classification: _____
 1=Confirmed measles by lab (IgM positive measles)
 2= Confirmed measles by epidemiologic link
 3= Compatible/ clinical measles
 4= Discarded non-measles, non-rubella by lab (IgM negative for both)
 5= Confirmed rubella by lab (IgM positive rubella)
 9= Suspected measles/ rubella with lab results and or case classification pending

21. Person Completing the form: Name _____ Signature: _____
 22. Date Form Sent to next higher level: ____/____/____ (dd/ mm/ yy)

MEASLES/ RUBELLA SUSPECTED CASE REPORTING FORM -PAGE 2

FOR SUSPECTED MEASLES/ RUBELLA CASES WITH LAB SPECIMENS

For Health Facility: If lab specimen is collected, complete the following information. And send a copy of this form to the lab with the specimen.

23. Specimen source (Circle): Blood, gingival fluid, throat swab, urine, other: _____

24. Date of specimen collection: ____/____/____ (dd/ mm/ yy)

25. Date Specimen sent to lab: ____/____/____(dd/ mm/ yy)

For the Lab: Complete this section and return the form to the national epidemiology/ surveillance team

26. Date lab received specimen: ____/____/____ (dd/ mm/ yy)

27. Specimen condition: Adequate Not adequate

Disease Condition	Type of test	Results (circle one)	Virus Detection (Genotype)	Remarks
28. Measles	IgM	Positive / Negative/ Indeterminate		
29. Rubella	IgM	Positive / Negative / Indeterminate		

30. Name of the national/ subnational lab processing and sending results: _____

31. Date lab sent results to national epidemiology or surveillance team: ____/____/____ (dd/ mm/ yy)

32. Date national level sent results to the district: ____/____/____ (dd/ mm/ yy)

NB: District is responsible for ensuring lab results get to clinicians. Failure to do so will undermine cooperation with clinicians on reporting of cases in the future.

ANNEX 11 : Formulas for the calculation of surveillance performance indicators – for countries implementing elimination-standard measles / rubella surveillance

- i. Non-measles non-rubella febrile rash illness rate: **(target : at least 2 per 100,000 population)**

$$\frac{\text{Discarded cases (measles AND rubella IgM negative) with lab testing of blood specimens X 100,000}}{\text{Total population in area (country/ province)}}$$

- ii. Proportion of districts reporting ≥ 2 Non Measles-Non Rubella Febrile Rash Illness cases / year **(Target; = / >80%)**

$$\frac{\text{Number of districts reporting } > 2 \text{ Non Measles-Non Rubella Febrile Rash Illness cases X 100}}{\text{Total number of districts in the country}}$$

- iii. Adequacy of individual case investigation: **(Target; = / >80%)**

$$\frac{\text{Number of suspected febrile rash illness cases with all 12 variables captured in case forms x 100}}{\text{all reported suspected cases (target > 80%)}}$$

- iv. Proportion of reported measles cases from whom blood specimens have been collected (excluding epidemiologically linked cases from the denominator): **(Target; = / >80%)**

$$\frac{\text{Reported suspected measles cases with blood specimen}}{\text{Total reported suspected measles cases - measles cases confirmed by epidemiological linkage}}$$

- v. Proportion of districts that have reported at least 1 case of measles with a blood specimen per year: **(Target; = / >80%)**

$$\frac{\text{Number of districts that have reported at least 1 measles case with a blood specimen}}{\text{Total number of districts in the area covered by case-based surveillance}}$$

- vi. Timeliness of health facility surveillance reporting to the district level within the specified time period. **(Target >80% reports submitted timely to next level)**

$$\frac{\text{Total number of weekly reports that have reached on time to the district level}}{\text{Total number of reports expected for the period under consideration}}$$

- vii. Annualized⁶ rate of investigation (with blood specimens) of suspected measles/ rubella cases **(Target: > 1 case investigated with blood specimen / 100,000 population per year)**

$$\frac{\text{Total number of suspected measles cases investigated with blood specimen in the area X 100,000}}{\text{Total population in area (country/ province)}}$$

- viii. Proportion of measles outbreaks investigated with blood specimens from the first five cases: **(Target; =/ > 80% outbreaks investigated with blood specimen)**

$$\frac{\text{Number of measles outbreaks investigated with blood specimens from the first five cases}}{\text{Total number of measles outbreaks in the area in the time period under consideration}}$$

⁶ NB: To annualize, multiply figure by 12/ month (eg 12/2 for February, 12/8 for August.)

- ix. Proportion of measles outbreaks with specimens collected and documentation done on measles viral strains: **(Target: at least 80% measles outbreaks with measles viral strains documented)**

<u>Number of measles outbreaks with viral strain documentation</u> <u>Total number of measles outbreaks in the area in the time period under consideration</u>

- x. Timeliness of suspected measles / rubella case investigation: **(Target: >80% investigated within 3 days following notification)**

<u>Number of measles outbreaks investigated within 3 days of notification</u> <u>Total number of measles outbreaks in the area in the time period under consideration</u>
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- xi. Timeliness of serum/ dried blood specimens arriving at lab **(Target > 80% arriving at lab <3 days of being taken)**

<u>Number of serum / dried blood specimens that arrived at National lab within 3 days of collection</u> <u>total specimens received at National lab</u>
--

- xii. Timeliness of feedback of serology results from the laboratory: **(Target: = / > 80% results received at National level within 7 days of specimen receipt at lab)**

<u>Number of results sent out by laboratory to the National level within 7 days of receipt of specimens</u> <u>Total number of specimens received by lab</u>

- xiii. Proportion of serum specimens arriving at the National measles laboratory in good condition **(Target: at least 90% of specimens arriving at the laboratory in good condition; i.e., adequate volume, no leakage, not turbid, not dessicated)**

<u>Number of serum specimens that arrived at National lab in good condition</u> <u>total specimens received at National lab</u>
--

- xiv. Proportion of representative serum specimens sent quarterly by the national laboratories to the regional reference labs for re-confirmation as part of quality assurance measures **(Target: at least 10% of specimens received at national lab shared with the RRL)**

<u>Number of serum or dried blood specimens sent to the RRL by the national measles lab</u> <u>Total number of serum and dried blood specimens received at National laboratory in the quarter</u>
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- xv. Proportion of concordance of measles / rubella IgM results between the national measles lab and the regional reference lab **(Target; ≥ 90% concordance between results of shared specimens)**

<u>Number of serologic results concordant with the National lab when re-tested at RRL</u> <u>Total number of serum and dried blood specimens shared by the National laboratory with the RRL since the beginning of the year</u>
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xvi. Timeliness of feedback of serology results from the Regional Reference lab to the National measles laboratory (**Target: at least 80% results sent to the national measles lab within 14 days of receipt of specimens at the RRL**)

xvii. Incidence rate of confirmed measles per million population:

$$\frac{\text{cases confirmed to be measles by lab, epi linkage and clinical compatibility} \times 1 \text{ million}}{\text{total population}}$$

xviii. Incidence rate of confirmed rubella per million population;

$$\frac{\text{cases confirmed to be rubella by lab} \times 1 \text{ million}}{\text{total population}}$$

