



EUROPE



**SURVEILLANCE
GUIDELINES FOR
MEASLES AND
CONGENITAL
RUBELLA INFECTION
IN THE WHO
EUROPEAN REGION**



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ABSTRACT

Measles and rubella remain important causes of vaccine-preventable disease and death in the European Region of WHO. The *Strategic plan for measles and congenital rubella infection in the European Region of WHO* identifies key strategies to meet the targets for interrupting indigenous measles transmission and preventing congenital rubella infection (< 1 case of congenital rubella syndrome per 100 000 live births) by 2010; strengthening surveillance systems by vigorous case investigation and laboratory confirmation is one of these key strategies. Surveillance indicators identified in these surveillance guidelines will be critical for assessing whether Member States have achieved the disease targets. The *Surveillance guidelines for measles and congenital rubella infection* are intended to provide technical advice on the design and implementation of surveillance programmes for these diseases.

Keywords

Measles
Rubella
Rubella, Congenital
Rubella syndrome, Congenital
Mumps
Immunization
Epidemiologic surveillance

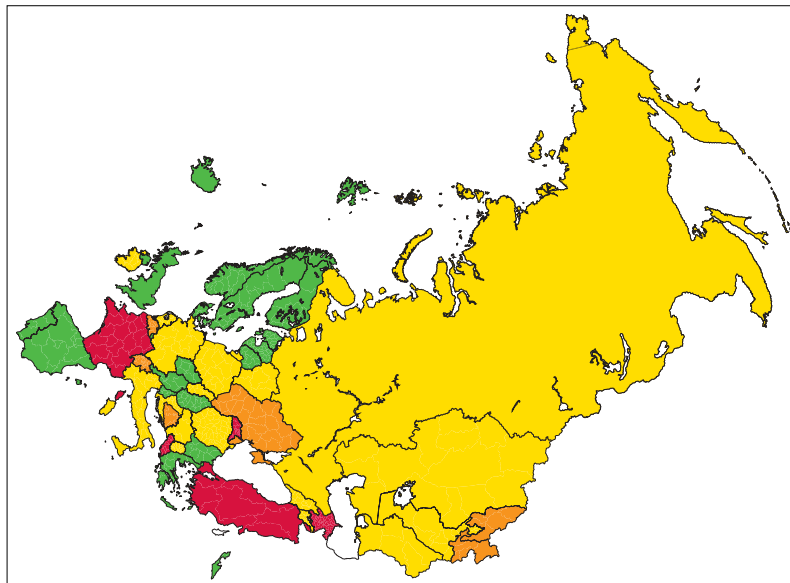
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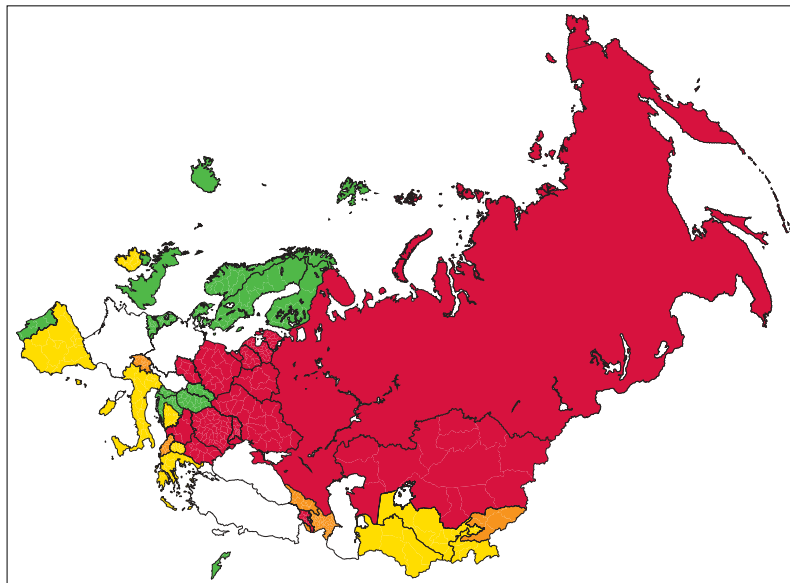
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**Reported measles incidence
WHO/EURO,
1998-2002
(5-year average)**



**Reported rubella incidence
WHO/EURO,
1998-2002
(5-year average)**



The designations and the presentation of material on these maps of the Member States of the WHO European Region do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines represent approximate border lines for which there may not yet be full agreement.

1. INTRODUCTION

Measles and congenital rubella infection (CRI) remain important preventable causes of infectious disease morbidity and mortality (1). As a result of the continuing high level of mortality attributed to measles, a vaccine-preventable disease, WHO and UNICEF developed a strategic plan for 2001–2005 (2). The *Strategic plan for measles and congenital rubella infection in the European Region of WHO* (3) is an integrated immunization approach to achieving measles and rubella control targets while maximizing programme efficiencies. The plan identifies (a) an operational target date of 2010 for interrupting indigenous measles transmission, with a mid-term assessment by 2005 in line with the planned global assessment; and (b) a target date of 2010 for reducing the incidence of congenital rubella infection to <1 case of congenital rubella syndrome per 100 000 live births.

Six key strategies are recommended for meeting these objectives:

- achieving and sustaining very high coverage with two doses of measles vaccine through high-quality routine immunization services;
- providing a second opportunity for measles immunization through supplementary immunization activities to populations susceptible to measles, consistent with national targets for measles control;
- using the opportunity provided by supplementary measles immunization activities to target populations susceptible to rubella, where appropriate;
- ensuring protection to women of childbearing age by achieving high coverage with rubella vaccine;
- strengthening surveillance systems by vigorous case investigation and laboratory confirmation; and
- improving the availability of high-quality, valued information for health professionals and the public on the benefits and risks associated with immunization against measles and rubella.

These surveillance guidelines provide a more in-depth discussion and describe best practices to supplement the strategic plan (3), the *Module on best practices for measles surveillance* (4) and the *Guidelines for surveillance of congenital rubella syndrome and rubella* (5). These guidelines are targeted at programme managers and those responsible for measles and rubella surveillance, to aid them in the development of their country-specific surveillance plans.

2. THE VIRUSES, DISEASES AND VACCINES

2.1 MEASLES

Measles is an acute illness caused by an RNA virus of the genus *Morbillivirus*, a member of the family *Paramyxoviridae*.

Transmission

Measles is one of the most contagious of diseases, with >90% secondary attack rates among susceptible persons. The virus can be transmitted in the air, in respiratory droplets, or by direct contact with the nasal and throat secretions of infected persons. Individuals with measles are considered to be infectious from 2–4 days before to 4 days after the onset of rash. Measles shows a seasonal trend, and in temperate areas occurs mostly in late winter and spring.

Clinical features

After an incubation period that usually lasts 10–12 days (range 7–18 days), prodromal symptoms of fever, malaise, cough, coryza (runny nose) and conjunctivitis (red eye) appear in nonimmune persons exposed to the virus. Koplik spots may occur on the buccal mucosa shortly before the onset of rash and for about 1–2 days after. Nevertheless, the absence of Koplik spots does not rule out measles.

Within 2–4 days after the prodromal symptoms begin, a maculopapular rash of large blotchy red spots appears behind the ears and on the face (Figure 1). At this stage, a high fever develops, the temperature possibly reaching 40.5 °C. Initially the rash blanches with fingertip pressure. The rash spreads to the trunk and extremities, typically lasts for 4–6 days and may be followed by a fine desquamation. The rash fades in the same order in which it appears, from the head to the extremities.

Other symptoms of measles include anorexia, diarrhoea (especially in infants) and generalized lymphadenopathy. A nonproductive cough is present throughout the febrile period, lasting for 1–2 weeks in uncomplicated cases.

Approximately 30% of reported measles cases involve one or more complications. Complication rates from measles in developed countries include otitis media (7–9%), pneumonia (1–6%), diarrhoea (6%), blindness and post-infectious encephalitis (1 per 1000 cases). A less common but serious complication is subacute sclerosing panencephalitis (SSPE) (1 per 100 000 cases).

In developed countries, the case-fatality rate for measles tends to be low, at between 0.1 and 1.0 per 1000 cases. The risk of serious complications is higher in infants and adults. In developing countries, the overall case-fatality rate has been estimated to be 3–6%. The highest case-fatality rates (20–30%) occur in infants under 12 months

of age. Malnutrition and infection with human immunodeficiency virus (HIV) are risk factors for complications and mortality.

Differential diagnosis

Infections with a number of other viruses can present with a rash resembling that of measles, including rubella virus, parvovirus, enterovirus, adenovirus and human herpesvirus 6.

Measles vaccine

Many live attenuated measles virus vaccines are in use. Most of them were derived from the Edmonston or Leningrad 16 strains. Measles antibodies develop in approximately 85% of children vaccinated at 9 months of age, in 95% of children vaccinated at 12 months of age and in 98% of those vaccinated at 15 months of age; those who fail to respond have primary vaccine failure and most will respond to a second dose. Studies indicate that 99% of persons who receive two doses of measles vaccine at ≥ 12 months of age develop serological evidence of measles immunity. Vaccine-induced immunity appears to be long-term, and is probably lifelong in most individuals.

2.2 RUBELLA

Rubella is an acute illness caused by an RNA virus of the family *Togaviridae*.

Transmission

The rubella virus, while less contagious than that of measles, is also transmitted by respiratory droplets and by direct contact with the nasal and throat secretions of infected persons. While individuals with rubella may shed virus from 7 days before to 14 days after the onset of rash, 25% to 50% of infections are asymptomatic.

Clinical features

Rubella symptoms in children and adults are often mild. After an incubation period that usually lasts 14–23 days, a rash may appear (Figure 2). In the second week after exposure, lymphadenopathy may be noted, particularly in the posterior auricular and occipital areas. Later in the second week, there are prodromal symptoms of low-grade fever (<39 °C), malaise and mild conjunctivitis. At the end of this incubation period, a maculopapular rash appears on the face and neck. Rash due to rubella is fainter than measles rash and does not coalesce. During the course of 1–3 days, the rash spreads downwards and begins to fade. However, it is important to remember that it may be difficult to differentiate clinically between measles and rubella.

Arthralgia and arthritis are commonly observed in adults, and chronic arthritis has been reported after rubella infection. Other less common complications are thrombocytopenia and encephalitis (1 per 6000 cases), which may be fatal. There is a rare

late syndrome of progressive rubella panencephalitis. Guillain-Barré syndrome after rubella has also been reported.

Women infected with rubella virus during pregnancy risk having their babies infected with rubella *in utero* (see below).

Rubella vaccination during pregnancy is not an indication for abortion (6).

Rubella vaccine

The two rubella vaccines widely used around the world are based on the live attenuated RA 27/3 strain of the virus (6). Rubella antibody develops in 95% or more of vaccinees 21–28 days after vaccination. One dose of rubella vaccine probably provides lifelong immunity in more than 90% of people immunized.

Paediatric vaccination now often involves a combined measles, mumps and rubella (MMR) vaccine. A large body of safety and immunogenicity data indicates that combining the measles antigen with rubella and mumps antigens is safe and effective. Cases of congenital rubella syndrome (CRS) have not been identified following the administration of rubella vaccine before or early in pregnancy. Nevertheless, if pregnancy is being planned, an interval of 1 month should be observed after rubella immunization (6).



Figure 1.
Clinical measles*



Figure 2.
Rubella rash*

2.3 CONGENITAL RUBELLA INFECTION

Rubella infection during pregnancy can affect all organs in the developing fetus and cause miscarriage, fetal death and congenital abnormalities. The risk for and severity of the effects of rubella virus on the fetus depend largely on the gestation time at which infection occurs. Up to 90% of fetuses born to mothers infected during the first 11 weeks of gestation will develop a pattern of birth defects called CRS. The most common congenital defects include sensorineural deafness, ocular defects, cardiac defects, neurological abnormalities (i.e. mental retardation) and growth retardation (see Annex 1 for a description of clinical signs). Late complications include diabetes mellitus and thyroiditis.

Almost all affected infants will have a positive rubella-specific IgM test in the first 6 months of life, and 60% will be positive in the second 6 months. These infants can shed virus for up to 1 year (sometimes longer) and transmit rubella to others.

* (Source: Health Canada web site:

http://www.hc-sc.gc.ca/pphb-dgspsp/publicat/uvpd-mjmepv/photos_e.html).

3. SURVEILLANCE ACTIVITIES FOR MEASLES AND CRI CONTROL PROGRAMMES

The Member States of the WHO European Region can be placed in one of three stages (I–III) of measles control, based on historical measles vaccine coverage rates and current disease epidemiology (Table 1). The minimum surveillance and outbreak investigation activities needed depend on the stage of control.

Stage	Level of control	Immunization coverage	Epidemiological situation
IIIb	Approaching measles elimination and prevention of CRI	Maintained very high (>95%) coverage with two doses of measles vaccine and Maintained high coverage with at least one dose of rubella vaccine (>90%) among women of childbearing age	<ul style="list-style-type: none"> • Interruption of indigenous measles transmission • Low level of measles susceptibility in the population • CRS incidence < 1 per 100 000 live births • Low levels of rubella susceptibility among women of childbearing age (< 5%)
IIIa	Approaching measles elimination	Maintained, very high (>95%) coverage with two doses of measles vaccine	<ul style="list-style-type: none"> • Interruption of indigenous measles transmission • Low level of measles susceptibility in the population
II	Measles control	Maintained high (>90%) coverage with at least one dose of measles vaccine	<ul style="list-style-type: none"> • Low morbidity with periodic measles outbreaks • Measles inter-epidemic period >5 years
I	Limited measles control	Low to moderate (≤90%) coverage with measles vaccine	<ul style="list-style-type: none"> • Substantial morbidity with frequent outbreaks • Measles inter-epidemic period ≤5 years

Table 1. Stages of control of measles and CRI

3.1 SURVEILLANCE OBJECTIVES

Surveillance systems provide information both for the early detection of and rapid response to health events, including disease outbreaks, and also help to identify disease trends, risk factors and the need for intervention. They provide valuable information for priority-setting, planning, implementation and resource allocation for preventive programmes, and for evaluating control measures.

There are three major objectives related to measles and CRI disease control programmes that are important in all stages:

- monitoring for cases and clusters;
- monitoring vaccination-related events, including coverage and adverse events following immunization; and
- assessing the accumulation of susceptible persons.

Surveillance activities should evolve according to the level of control in the country.

3.2 MONITORING CASES AND CLUSTERS

Effective surveillance systems are necessary at the regional, subregional, national and subnational levels. As the level of measles control increases and countries approach elimination, surveillance systems are required to detect and permit the investigation and laboratory confirmation of suspected cases. Such systems need to be countrywide, sensitive and case-based, and allow one to determine whether cases are linked and whether sustained transmission is occurring. The minimum surveillance expectations at each stage are outlined in Table 2.

The objectives of monitoring for and investigating suspected cases and clusters are to:

- monitor incidence in order to assess progress towards control and elimination targets;
- describe confirmed cases in order to understand the reasons for disease occurrence;
- detect and investigate clusters so as to ensure proper case management and to determine why the cluster has occurred (e.g. failure to vaccinate or vaccine failure);
- strengthen control measures, including active surveillance for rubella infection during pregnancy;
- monitor the status of elimination by determining the proportion of confirmed cases that are imported and whether transmission is sustained following an importation (from the size, nature and duration of clusters and the genotypic diversity of circulating viral strains);
- assess the performance of the surveillance system to identify areas where strengthening activities are necessary through the use of key indicators; and
- provide evidence in countries with low reported incidence that the absence of confirmed cases is attributable to the absence of disease rather than to problems with detection and reporting.

3.3. MONITORING VACCINATION-RELATED EVENTS

Reliable systems for monitoring vaccine coverage, vaccine quality and adverse events following immunization should be in place at national and subnational levels. This document primarily addresses disease surveillance issues. Detailed information on

Surveillance activity for	LEVEL OF CONTROL		
	Stage I	Stage II	Stage III
Measles	<ul style="list-style-type: none"> Aggregate national reporting per month by: <ul style="list-style-type: none"> ✓ age-group ✓ immunization and status ✓ geographical location 	<ul style="list-style-type: none"> Stage I activities plus Move to case-based surveillance at national-level Establishment of capacity for laboratory confirmation 	<ul style="list-style-type: none"> National case-based surveillance Investigation of every suspected measles case, including laboratory diagnostic testing
Outbreaks and clusters	<ul style="list-style-type: none"> Investigation of outbreaks of suspected measles as resources permit 	<ul style="list-style-type: none"> Investigation of all detected outbreaks of suspected measles 	<ul style="list-style-type: none"> Investigation of all detected clusters of febrile-rash illness
Outbreak prediction		<ul style="list-style-type: none"> Undertake outbreak prediction and intervention 	
CRS	<ul style="list-style-type: none"> Conduct CRS burden study 	<ul style="list-style-type: none"> Report total number of CRS cases per year Conduct case-based CRS surveillance in infants 0–11 months of age with laboratory confirmation Monitor rubella susceptibility in women of childbearing age 	
Rubella	<ul style="list-style-type: none"> Report number of suspected rubella cases by age group and immunization status per month (optional for countries with no rubella immunization programme) 	<ul style="list-style-type: none"> Report number of suspected rubella cases by age group and immunization status per month or Conduct national case-based surveillance if a comprehensive rubella immunization strategy is in place 	

Table 2.
Minimum expected surveillance activities for measles and rubella according to stage of control

cold-chain monitoring, injection safety and surveillance for adverse events following immunization can be found in other WHO monographs (7,8).

Monitoring vaccine coverage can be undertaken using administrative methods. These are based on routine reports of the number of children vaccinated at centres responsible for immunization (numerator) together with accurate estimates of the total number of children targeted for immunization (denominator). They permit the identification of pockets of low coverage, which over time indicate the accumulation of susceptible persons in certain areas or populations and thus the need to institute appropriate interventions. Vaccine coverage should be calculated for first- and second-dose measles vaccine coverage, using age-appropriate administrative

data to define the numerator (number of doses administered to children by that age) and the denominator (birth cohort corresponding to the appropriate age group).

Methods used to collect vaccine coverage data and the accuracy of the information produced vary, and priority should be given to improving routine data collection. It is critical that countries using proxy methods (i.e. the number of doses distributed to clinics rather than the number administered) or having inaccurate denominator values (owing to migration, for example) validate their coverage estimates with ad hoc coverage and/or serological survey methods. It is essential, however, that these surveys be undertaken with standardized sampling and laboratory methodology to ensure representativeness and comparability.

3.4 MONITORING THE ACCUMULATION OF SUSCEPTIBLE PERSONS

Elimination requires the achievement and maintenance of low levels of susceptibility in a population at each administrative level. Age-specific targets for the WHO European Region have been established (9), so that sustained transmission does not occur following the introduction of a measles case.

The objective of monitoring susceptibility in the population is (a) to identify possible discrepancies between ideal and estimated levels of susceptibility to measles by age group (“susceptibility gaps”) and thus predict outbreaks, and (b) to plan interventions such as broad supplementary immunization or focal campaigns to address susceptible populations and thus avoid outbreaks.

In addition to the routine monitoring of vaccine coverage, coverage surveys and well standardized and representative serological surveys can be used to assess population susceptibility to measles and/or rubella and to identify susceptibility gaps, particularly in those countries with poor-quality historical coverage data.

4. IMPLEMENTATION AND ENHANCEMENT OF SURVEILLANCE FUNCTIONS: OPERATIONALIZING SURVEILLANCE

The functions of surveillance include:

- detecting and reporting cases and outbreaks
- collecting and collating data
- investigating and confirming cases and outbreaks by laboratory or epidemiological link
- analysing and interpreting data
- producing routine reports
- providing data to the subnational or national level
- providing feedback to more peripheral levels
- providing data to the Regional Office and subregional networks.

These functions are outlined in this section; stage-specific details are described in Section 5.

The general logistics of surveillance are presented and discussed in *Making surveillance work. Module 3: logistics management (10)*.

4.1 DETECTING AND REPORTING CASES AND OUTBREAKS (HEALTH CARE FACILITY)

Health care providers are asked to report and investigate all patients who fulfil the clinical case definitions (Annex 1). Suggested reporting sites include:

- health centres/units/clinics
- hospitals; inpatient and outpatient clinics.

It is important that private medical practitioners and private hospitals are included in the surveillance system, as they may be the first to see suspected cases. In countries where laboratory testing is common, laboratories can be important auxiliary reporting sites.

The use of WHO standard case definitions (Annex 1) (11) is critical at every level to ensure standardized and comparable reporting and to avoid underreporting or overreporting of cases. The reporting site should report all cases meeting the clinical case definition. The basic data required for understanding the causes of cases and the effectiveness of the immunization programme are:

- date of occurrence of cases
- place of occurrence of cases
- age, gender, vital status and vaccination status of patients.

4.2 INVESTIGATING AND CONFIRMING CASES AND OUTBREAKS (ALL LEVELS)

The term “outbreak” is used when the number of cases observed in a given geographical area is greater than normally expected during a given period of time. For this reason it is useful to evaluate trends in recent years (i.e. the mean number of cases or the mean incidence for a defined area during a defined period of time in nonepidemic years).

If previous surveillance data are not available, local health care workers can provide reliable information about an unusual increase in the occurrence of measles in the past month. An increase in the number of cases may reflect an increase in reporting. For instance, a new doctor assigned to a hospital may be more diligent than a predecessor in reporting cases. During the investigation of an outbreak, it is possible to discover whether the observed increase is real or an artefact. An increase in reported suspected measles may also reflect circulation of other viruses such as parvovirus or rubella. If the initial 5–10 samples are negative for measles IgM antibody, it is important always to test them for rubella.

If an epidemic affects a wide geographical area or is nationwide, it is recommended that outbreaks be investigated in a few locations, such as a rural area and an urban area, rather than every outbreak in every town. When an outbreak occurs, it is recommended that:

- district surveillance staff immediately notify other health facilities in their area and make sure serum or oral specimens are collected from 5–10 patients for IgM confirmation (Annex 2);
- blood, urine or nasopharyngeal specimens are collected from 5–10 patients for viral isolation or detection (Annex 2);
- a laboratory form is completed for each specimen, sent to the laboratory, and copied to the district health office (Annex 2); and
- the laboratory ensures that health care staff obtain the results within 7 days of its receiving the specimens.

When the outbreak is confirmed (or before, if circumstances indicate) it is important that:

- the authorities at the national level are notified immediately (Annex 6);
- **in the immediate area:**
 - health care workers and the community are informed at once and given continuous feedback,
 - vaccination efforts continue in the outbreak area and the opportunity is used to increase awareness about the importance of vaccination and increased coverage,
 - the collection and analysis of data continue so that the outbreak is monitored and its cause determined, and
 - persons are treated according to case management guidelines (12).

- **in areas to which the outbreak may spread:**

- assessments are made and efforts to improve vaccination coverage take priority, and
- data collection and data analysis are intensified in order to determine the spread of the outbreak.

In areas with an adequate routine surveillance system, aggregate case and population coverage data may reveal the cause of an outbreak and how it might have been prevented, i.e. whether the outbreak occurred because of vaccine failure, failure to vaccinate or migration of susceptible individuals.

It is very important that data on cases are collected and appropriate analysis undertaken, even if this is not routinely done through the existing surveillance system. The information collected should include data on when patients fell ill, who they are and where transmission occurred.

Data on surveillance and vaccination coverage can help identify where vaccination coverage should be improved. Nevertheless, once an outbreak has begun in an area with low vaccination coverage, vaccination efforts are not usually sufficiently rapid

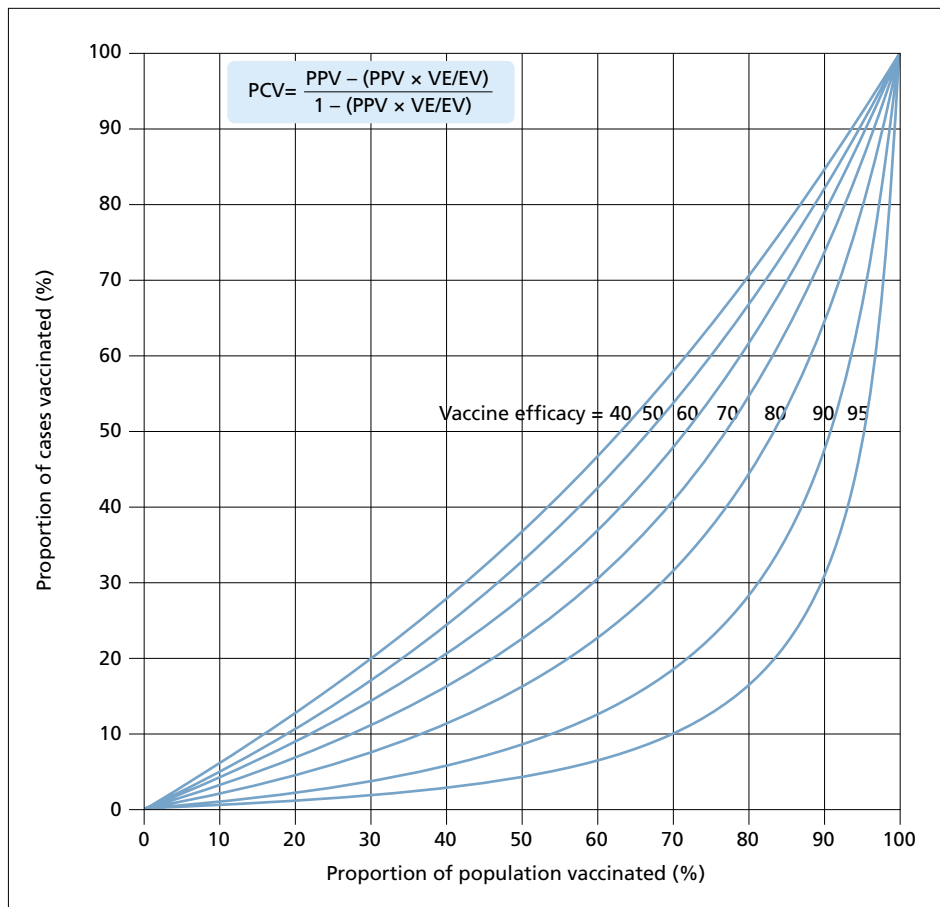


Figure 3. Estimated vaccine efficacy (VE) according to proportion of cases vaccinated (PCV) and proportion of population vaccinated (PPV)

and extensive to control it. Vaccination will be most effective in neighbouring areas not yet involved in the outbreak.

The quality of surveillance during an outbreak is usually enhanced, and thus the age-specific attack rates and estimated vaccine efficacy are the most representative. Vaccine efficacy can be estimated during an outbreak investigation in the same area by plotting the proportion of measles cases in vaccinated individuals against the proportion of the general population vaccinated (Figure 3).

It is important to remember that this field assessment of vaccine efficacy is only a crude estimate and can be confounded by factors such as age, reliability of vaccination history, etc.

Examples of data trends and interpretation

- *High proportion of unvaccinated cases:* poor vaccination coverage.
- *High proportion of vaccinated cases:* high vaccination coverage. Because one dose of measles vaccine provides 85 to 98% immunity depending on the age vaccine was given and two doses provide no more than 99% immunity, it can be expected that cases will occur among individuals who have received vaccine. If the number of vaccinated cases is more than expected, or very high, the effectiveness of the vaccine should be evaluated. For instance, if 60% of measles cases are vaccinated against measles and vaccination coverage in the general population is 95%, the estimated vaccine efficacy is 95%; whereas if 30% of confirmed measles cases are vaccinated against measles and vaccination coverage is 60%, the estimated vaccine efficacy is 70% (13).
- *High proportion of cases among children aged 1–4 years:* poor vaccination coverage.
- *High proportion of cases among school-age children:* low to moderate two-dose vaccination coverage, increased risk of exposure in schools. At moderate levels of coverage, although transmission may be temporarily limited, susceptible individuals accumulate over time and thus measles cases occur in older age groups.
- *High proportion of adult cases:* measles contracted by susceptible persons who have never been exposed to measles virus or vaccine, e.g. workers from isolated rural areas who have recently migrated to urban areas or lived in the area at a time when measles vaccine coverage was low.
- *High incidence in certain areas:* vaccination coverage is poor; cold chain or vaccine handling is a problem, or surveillance is better than elsewhere in these areas.

4.3 COLLECTING AND COLLATING (ALL LEVELS)

District-level staff should combine data collected from all reporting sites. After collation, district-specific data should be made available to the provincial and national levels. If possible, data should be entered into an electronic database at the district or provincial level to facilitate its collation and analysis.

4.4 ANALYSING AND INTERPRETING DATA AND PRODUCING ROUTINE REPORTS (HEALTH CARE FACILITY, DISTRICT HEALTH OFFICE AND NATIONAL HEALTH OFFICE)

Surveillance data should be analysed at each level. Surveillance staff at district health offices should review any areas that do not report cases for extended periods. If there are such areas, it is important to identify at least one reporting site, such as a hospital or large clinic, for a training programme in prompt reporting procedures.

Data analysis can provide insight into the reasons for the occurrence of cases and allow outbreaks to be predicted, thus obtaining guidance for planning and implementing effective outbreak prevention and elimination strategies.

A few simple graphs can present the essential data (i.e. time, place and person):

- number of cases by month of report, comparing two consecutive years (Annex 3);
- number of cases reported by health facility (spot map) (Annex 3); and
- number of cases by age group and vaccination status (cumulative for the year) (Annex 3).

In addition, where information on vital status/death is available, analysis of the number of deaths by age group and vaccination status (cumulative for the year) is recommended (Annex 3).

To monitor the impact of the vaccination system over time, surveillance staff should compare data from previous years with current data:

- number of cases and deaths by year (Annex 4);
- proportion of cases in each age group (Annex 4);
- proportion of vaccinated cases (Annex 4); and
- case-fatality ratio (number of measles deaths divided by the total annual number of cases) (Annex 4).

Calculation of incidence, i.e. the number of new cases divided by the population at risk over a given period, is especially useful at the national level for comparing the occurrence of disease at different places and times and in different age groups (Table 3). To calculate rates accurately, it is important to obtain accurate population figures. Population data can be obtained from the census bureau or can be assessed by special surveys performed by various institutions or by health facilities.

Table 3.
Incidence by district
(place, January–June,
year)

District	Population	No. of cases	Incidence per 100 000
A	50 000	50	100
B	20 000	25	125
C	10 000	100	1 000
D	60 000	30	50
E	100 000	1 500	1 500
F	10 000	10	100
G	15 000	50	333
Total	265 000	1 765	666

Nevertheless, even if population figures are obtained, it may be difficult to determine the area served by reference hospitals. Variations in incidence may also reflect variations in reporting efficiency.

If population data by age group are available, age-specific incidence rates (the number of cases in a certain age group divided by the total number of persons in the age group) can be calculated to identify the age group(s) at highest risk for measles (Table 4).

Table 4.
Age-specific
incidence (place,
January–June, year)

District	Population	No. of cases	Incidence per 100 000
<1	11 141	181	1 625
1–4	44 521	299	671
5–9	55 462	121	218
10–14	55 328	99	179
15–19	55 256	30	54
20–24	61 512	4	7
≥25	10 652	4	38
Total	293 872	738	251

4.5 PROVIDING DATA TO MORE CENTRAL LEVELS (HEALTH CARE FACILITY AND DISTRICT HEALTH OFFICE)

Reports should be submitted to the district or provincial surveillance coordinators. In return, district or provincial staff should promptly report to the state (national) surveillance staff. If there is a sudden increase in cases, health authorities at the more central level should be notified immediately.

Reporting of zero cases should be routine practice at all reporting sites.

In the absence of cases, the reporting of zero cases is a useful mechanism for maintaining an active surveillance system.

Copies of all appropriate reporting forms should be readily available at reporting sites (Annex 5 and 6). The reports can be communicated by mail, fax, courier service or e-mail.

4.6 PROVIDING FEEDBACK TO MORE PERIPHERAL LEVELS (DISTRICT HEALTH OFFICE AND NATIONAL HEALTH OFFICE)

It is important that staff at central levels receive information from peripheral levels on surveillance issues, including:

- the needs of the surveillance system at the peripheral levels, particularly if the central levels have the responsibility of providing equipment, training materials, etc.; and
- whether peripheral-level staff are receiving feedback, or whether corrections are needed to the data in reports.

The provision of feedback to more peripheral levels helps the surveillance system at every level by:

- informing health care workers about current disease epidemiology and surveillance activities and their effectiveness;
- creating a collaborative environment by acknowledging the hard work of data providers and assuring them that their data are being analysed;
- verifying with peripheral levels that data received at more central levels are correct; and
- improving performance by showing national progress towards specific public health goals and making comparisons between regions, provinces, etc.

4.7 PROVIDING DATA TO THE REGIONAL OFFICE AND SUBREGIONAL NETWORKS

It is crucial for the national centre to report to WHO directly or through subregional networks. Reporting to supranational networks can facilitate comparison between countries, encourage improved performance to reach agreed targets, and identify and share good practice (Annex 5 and 6).

5. INTEGRATED SURVEILLANCE ACTIVITIES BY STAGE

5.1 STAGE I

The key components of developing and/or strengthening surveillance at this stage are:

- establishing and maintaining monthly national *aggregate* reporting of clinically confirmed cases of measles and rubella using the WHO case definitions;
- investigating suspected measles or rubella outbreaks in a timely manner to determine the underlying etiology and health impact;
- establishing a laboratory resource with the ability to confirm outbreaks of measles or rubella;
- establishing the capacity to collect detailed case-based information at the peripheral health centres and to manage the data;
- ensuring regular and timely feedback of surveillance data;
- regularly evaluating the surveillance system (timeliness, completeness, etc.); and
- considering the implementation of CRS surveillance or undertaking studies on CRS burden.

5.1.1 Steps to implement and improve surveillance

Monthly national reporting of aggregate data by age group, vaccination status and geographical location is recommended. Case-based reporting might overburden the system and is not essential for decision-making at this stage. The forms used to aggregate data at the district level are illustrated in Annex 5. Aggregated national data should also be reported to WHO and to the relevant subregional network.

Outbreaks of suspected measles should be further investigated. The investigation of each case during an outbreak and laboratory confirmation of the initial 5–10 cases are recommended. Laboratory confirmation of every suspected case is not recommended, as this would overburden the system. The priorities during a measles outbreak are to reduce morbidity by improving case management, strengthening routine immunization practices and undertaking appropriate supplementary activities.

5.1.2 Rubella and CRS surveillance

Rubella surveillance should be undertaken using the same reporting sites as for measles, using *Guidelines for surveillance of congenital rubella syndrome and rubella (5)* (this is optional but strongly encouraged for those countries with no rubella vaccination programme). Countries are requested to report the aggregate number

of cases by age group and vaccination status on at least a yearly basis to the WHO Regional Office for Europe (Annex 5).

Outbreaks of suspected rubella should be investigated (Annex 6). The priority during a rubella outbreak is to alert health care workers to detect cases among pregnant women and subsequent CRS cases; rubella outbreaks may continue over two or more years, and often a smaller outbreak heralds a larger one. Active surveillance for CRS cases should be continued for nine months after the last rubella case is reported. An estimate of the potential burden of CRS disease can be made from age- and female-specific rubella incidence rates and age-specific fertility rates.

Health care workers should be asked to refer all infants aged 0–11 months with birth defects compatible with CRS (Annex 1) to an identified tertiary-care centre, where they will be examined and registered by a qualified paediatrician. The case definitions for a clinically confirmed case, a laboratory-confirmed case and congenital rubella infection are found in Annex 1. Staff at participating sites should receive guidelines and training in CRS surveillance. It is also important to include other potential reporting sites such as:

- midwives and family doctors
- physicians and hospitals specializing in paediatric cardiology and cardiac surgery
- physicians and hospitals specializing in paediatric ophthalmology
- neonatal wards and intensive units
- rehabilitation units.

A serum specimen should be obtained from every infant with suspected or clinically confirmed CRS as soon as possible after birth.

A standard reporting form should be completed for each suspected CRS case and returned to the district health office (Annex 7). Case-based data should be reported to the state (national) level. National staff should combine and evaluate data from all reporting sites. The annual number of CRS cases and the CRS rate per 1000 live births should be calculated.

5.2 STAGE II

On reaching Stage II, there is a need to further strengthen measles surveillance to:

- better define where measles virus is circulating; and
- identify populations where an accumulation of susceptible persons may have occurred, in order to undertake specific interventions.

This is accomplished by:

- introducing case-based investigation of suspected measles cases at the local/district level, and maintaining data in a case-based manner;
- collecting additional information on measles cases;

- implementing national case-based reporting as the number of measles cases decreases;
- implementing laboratory confirmation of suspected measles cases;
- undertaking weekly reporting to the first administrative level and at least monthly reporting to the national level;
- investigating *all* suspected measles outbreaks;
- using outbreak prediction to monitor the possible accumulation of susceptible persons and to thus guide supplementary immunization by using routine coverage data, age-specific disease incidence data, and high quality standardized serological surveillance data; and
- using methods identified in Stage I for rubella and CRS surveillance (Section 5.1.2).

The recommended minimum data to be collected for suspected measles cases at the local level are given in Annex 5.

Laboratory confirmation of suspected measles is needed in order to avoid reporting rash-causing diseases other than measles. As some cases may be lost to follow-up after the first contact, the physician first seeing the patient should be responsible for collecting blood or oral fluid and urine and/or nasopharyngeal samples at the time of the initial examination. When case-based reporting is introduced, in-depth interviewing of patients should also be conducted, including identification of contacts. Examples of forms for reporting to the first and second administrative levels are given in Annex 5. Staff should promptly report to the national level, including reporting of zero cases.

5.2.1 Monitoring the accumulation of susceptible persons

Reviewing trends in reported cases over time can reveal information in the absence of any major interventions or events (such as mass vaccination campaigns, substantial increases in routine vaccination coverage or recent influxes of refugees) as the interval between epidemics changes with the level of immunity in the population. Thus in an area that experiences measles epidemics every three to four years, the timing of the next epidemic can be estimated. To allow for an intervention before an outbreak occurs, it is recommended that a low estimate be made of the inter-epidemic interval.

Outbreaks can also be predicted and prevented by monitoring the population susceptibility profile in order to:

- identify possible susceptibility gaps in the population compared to target susceptibility levels and thus predict potential outbreaks; and
- allow interventions such as supplementary immunization to be undertaken before an outbreak occurs, and to be more cost-effective by addressing susceptible cohorts only.

Three methods can be used to estimate the population susceptibility profile:

- vaccine coverage by birth cohort
- birth-cohort-specific disease incidence
- age-stratified standardized serological survey.

It is important that denominator data include up-to-date information about population dynamics, e.g., migration into and out of the area in question of susceptible groups.

Vaccine coverage data

The proportion susceptible in each birth cohort can be estimated from age- and dose-specific vaccine coverage data:

- first- and second-dose routine measles vaccine coverage by birth cohort from the time of vaccine introduction; and
- coverage achieved during supplementary measures such as campaigns by birth cohort.

In a highly vaccinated cohort (i.e. one with disease transmission reduced or interrupted), vaccine coverage by birth cohort can be used to estimate the population susceptibility levels (Figure 4).

Vaccine efficacy depends on the number of doses administered and the age at which the first dose is given. Using accurate historical, age-specific national coverage data, the proportion of each age cohort that has received 0, 1 or 2 doses of vaccine can be calculated, and the proportion of each age cohort remaining unprotected can be estimated by the following equation, where S_1 is the vaccine efficacy after the first dose and S_2 is the vaccine efficacy after the second dose:

$$\{\% \text{ unvaccinated}\} + \{\% \text{ with 1 dose} \times (1 - S_1)\} + \{\% \text{ with 2 doses} \times (1 - S_2)\}$$

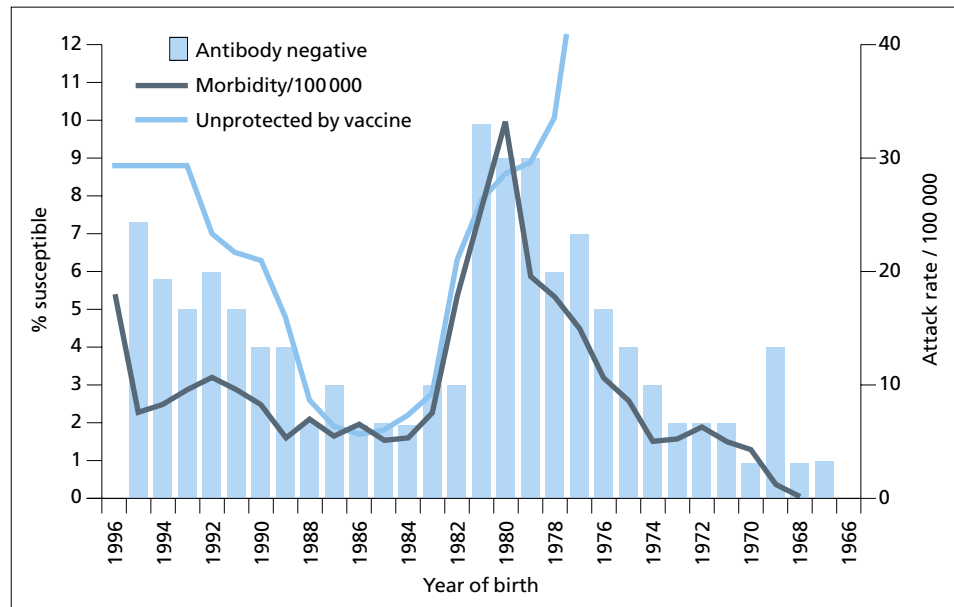
Disease surveillance data

Age-specific disease incidence data can be used to validate vaccine-coverage-derived susceptibility profiles. Although age-specific incidence rates are not a quantitative measure of susceptibility, they provide a qualitative indicator, particularly if data are derived from an epidemic year when their predictive value is higher. Figure 4 shows this relationship.

Age- and sex-stratified serological survey

Serological surveys provide another measure of population susceptibility provided adequate sampling methodology is used (Figure 4). The number of sera collected should be evenly distributed between males and females and sampled from a variety of geographical locations within the country to provide a representative estimate of immunity to measles and rubella in the general population.

Figure 4.
Three indicators
of susceptibility to
measles



To ensure quality control and quantitative comparability with other national serological surveys, standardization using a methodology developed by the European Seroepidemiology Network (ESEN2) project is recommended (14). This involves the distribution and testing of a reference panel of serum samples (including negatives, low positives and positives) before and after main serum bank testing. The national laboratory should test the panels and serum bank with their usual measles and rubella IgG ELISA kit(s). The quantitative results should be standardized using well described methodology involving statistical standardization (15).

A calculation based on vaccine coverage does not account for immunity derived from natural infection and is thus most useful in highly vaccinated cohorts.

Interpretation

Population susceptibility levels should be compared to WHO age-specific susceptibility targets for measles elimination (Figure 5). An appropriate vaccination strategy can then be developed.

5.3 STAGE III

The key elements for strengthening measles surveillance at this stage are:

- identification and investigation of all suspected measles cases at a minimum rate per head of the population (minimum data items are identified in Annex 5);
- active national case-based reporting of suspected measles cases;
- laboratory assessment of all suspected cases and collection of samples for virus isolation from those with suspected measles;
- investigation and identification of clusters of febrile-rash illness, including laboratory confirmation (Annex 6);

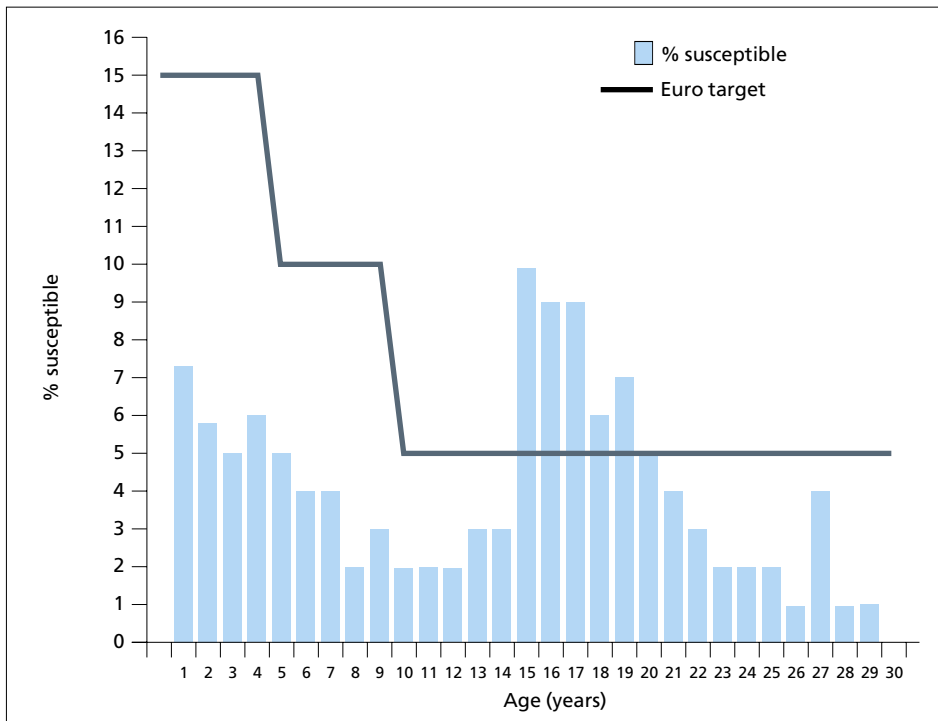


Figure 5.
WHO European
Region age-
specific
susceptibility
targets

- outbreak prediction with timely intervention measures; and
- case-based surveillance for CRS for Stage III.

The maintenance of Stage III, indicating lack of sustained measles transmissions, can be monitored through three indicators:

- age-specific target susceptibility levels for the WHO European Region
- distribution profile of measles outbreak size and duration
- genotypic diversity of circulating measles strains.

5.3.1 Case and cluster detection and investigation

All cases meeting the clinical case definition for suspected measles should be investigated. Furthermore, all clusters of cases meeting the definition for febrile-rash illness (Annex 1) should be investigated.

Laboratory confirmation and in-depth investigation of every suspected measles case or cluster of febrile-rash illness is fundamental. In a highly vaccinated population, only a small proportion of suspected cases will be confirmed as measles (<10%). Other virus infections, such as those with parvovirus, enterovirus, human herpesvirus 6 and adenovirus, will present with measles- or rubella-like illness (16). To ensure the surveillance system is sensitive enough to detect measles transmission, a minimum rate of investigation will need to be undertaken. A rate of at least 1 per 100 000 population in at least 80% of districts and municipalities has been sug-

A single suspected measles case or cluster of rash–fever illness demands immediate investigation to determine the cause and to ensure proper case management.

gested, but this rate needs to be better defined before recommendations can be made for the WHO European Region.

Methods of laboratory confirmation based on use of oral fluid have been developed and will soon be approved as WHO-recommended methods. This can improve acceptability of sampling in children and thus increase the rate of investigation and laboratory testing of suspected measles cases.

Virus isolation/detection should be attempted from all clusters of suspected measles and/or rubella cases.

Duties of the health care provider

- Basic information, clinical data and appropriate specimens for laboratory diagnosis and virus detection (e.g. blood, oral fluid and urine) should be obtained during the first contact, as this may be the only contact with the patient (Annex 2). It is therefore important to distribute case investigation forms (Annex 5 and 7) to health facilities in advance and for them to be available at the time of contact with the patient.
- The patient or parent of the patient should be informed that a public health official will visit her or his home, and be informed about measles control and elimination and why the visit is necessary.

Duties of the district health officer/epidemiologist

- The family should be visited immediately with measles investigation forms, measles vaccine and a specimen collection kit.
- The case investigation form should be completed and it should be determined whether the case meets the clinical case definition for measles. It is important to evaluate the presence, date and duration of symptoms (fever, nonvesicular rash, cough, coryza, conjunctivitis).
- If the patient meets the suspected case definition, an active search should be begun for other cases in adjacent homes or in the neighbourhood. A new cases investigation form should be completed on suspect cases.
- All families should be advised to keep the patient at home and to keep the number of visitors to a minimum until the rash disappears.
- Family members should be asked whether they know where the patient contracted the illness, and whether exposure to other persons with rash occurred about 10 days before the onset of rash. Note, however, that the patient may have been exposed to an infectious person during the incubation period before rash developed. Information should be sought on whether the patient had travelled outside her/his area of residence and particularly whether the infection was acquired overseas.

- Homes in the same block or neighbourhood should be visited to inquire as to whether any cases of rash and fever had occurred during the previous month. The vaccination status of all children <15 years of age living in these households should be checked.
- Nurseries, kindergartens, schools, etc. in the area should be visited to find out if any fever and illnesses involving rash have occurred recently.
- Any reports of illnesses involving rash and fever should be investigated. It may be necessary to request staff from other clinics to go to the homes of possible sources to see if there has been an illness involving rash and to investigate cases fully.
- Immediate vaccination should be undertaken of household members and any neighbours, playmates or schoolmates who have been directly exposed to the patient during the illness and who have not received two doses of measles vaccine. An age range (e.g. 6 months to 14 years) may be selected for this vaccination activity, depending on the epidemiology of measles in the area.
- The neighbourhood and schools should be notified about the occurrence of the measles case in the area, with a request that all persons who have not received two doses of measles vaccine be vaccinated.
- Local doctors, laboratories, pharmacies, etc. should be informed about the measles case and asked if they have seen any case of rash and fever.

5.3.2 Reporting network

The establishment of a special “hot line” is recommended to convey information by the fastest means possible (telephone, telegram, fax, e-mail, etc.). A suspected case should be reported to the district within 24–48 hours of detection. Districts should report to the state (national) level within 24–48 hours of confirmation.

5.3.3 Monitoring elimination status

Elimination is a dynamic situation in a large and well populated geographical area in which endemic measles transmission cannot occur and sustained transmission does not occur, following the occurrence of an imported case. All isolated cases and chains of transmission must be linked to an importation. Only by reaching and maintaining a low level of susceptibility throughout the population can measles elimination be achieved. This is related to the effective reproductive number (R), i.e. the number of secondary cases resulting from a case of measles in a population exposed to natural infection and/or vaccination. Using age-structured mathematical models, a susceptibility profile can be summarized by R (17).

The WHO European Region has established age-specific susceptibility targets sufficient to achieve measles elimination (estimated $R = 0.70$) (Figure 5). These targets are set below the threshold of $R = 1$ to allow a safety margin; they nevertheless permit some flexibility.

Figure 6.
Theoretical
distribution of
outbreak size
by effective
reproductive number
(R)

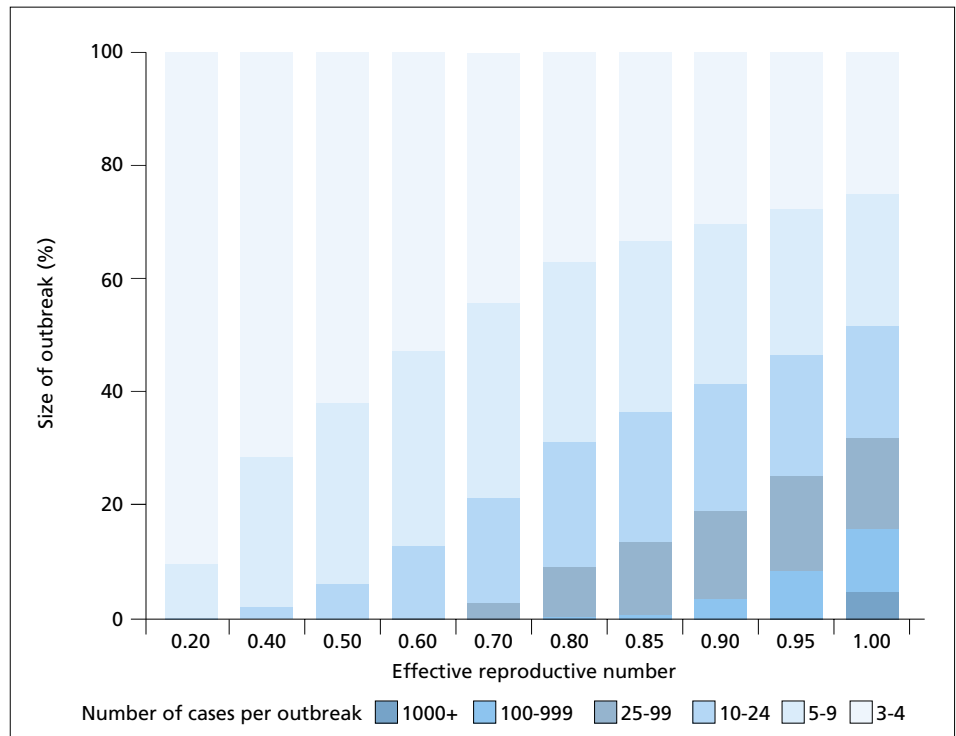
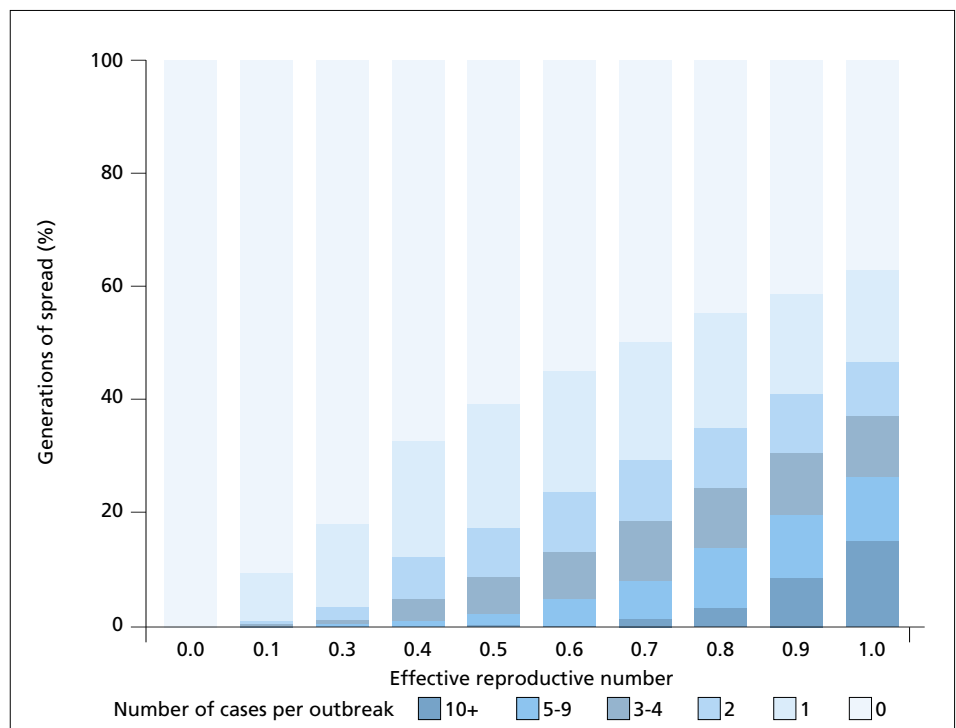


Figure 7.
Theoretical
distribution of
generations of
spread by effective
reproductive number
(R)



The basic reproductive number (R_0) is the number of secondary cases produced by one infectious case in a totally susceptible population. For measles, R_0 is estimated to be between 10 and 20. If $R > 1$, there is a high probability that an introduced case will produce more than one secondary case, i.e. that the number of cases will increase and an outbreak will occur. At low levels of susceptibility ($R < 1$), the number of cases will decrease. To achieve elimination, R must be maintained at < 1 ; this will prevent endemic infection from becoming re-established following the introduction of an imported case, although isolated clusters with lack of sustained domestic transmission will not be prevented.

An estimate of R and the status of measles elimination can be determined from three outcome indicators:

- the distribution of outbreak size (Figure 6) (18);
- the number of generations of spread in an outbreak (Figure 7) (18); and
- the proportion of cases that are imported.

5.3.4 Imported measles cases

Standardized molecular characterization of virus isolates can be used to determine the geographical distribution of genetic variants, to determine the origin of imported viruses and to determine the proportion of viruses that are imported. In Stage III, the virus genotypes detected should reflect the identified sources of imported cases and chains of transmission.

Intra-outbreak variability can be used to differentiate a true outbreak from a cluster of unrelated imported cases. The interruption of virus circulation by mass vaccination campaigns can be demonstrated by comparing the variability of pre-campaign viruses with post-campaign isolates (19).

In Stage III it is critical to detect and investigate (including a laboratory diagnostic assessment) all suspected measles cases, to determine the origin of infection, and to link confirmed cases in chains of transmission.

5.3.5 Steps to improving rubella and CRS surveillance: case detection and reporting

In Stage IIIb, there is a need to further strengthen rubella and CRS surveillance in the following areas:

- introduction of national aggregate or case-based reporting of suspected rubella cases according to the WHO case definition;
- collection of epidemiological information on rubella cases (age, geographical location, vaccination status, gender) (Annex 5);
- introduction of laboratory confirmation for suspected rubella cases for those countries with a comprehensive CRI prevention programme;
- continuation of case-based CRS surveillance in infants 0–11 months of age; and
- monitoring of rubella susceptibility in women of childbearing age to ensure susceptibility targets are achieved.

6. LABORATORY NETWORK

Laboratory confirmation of suspected cases of measles and rubella is a critical activity linked to the *Strategic plan for measles and congenital rubella infection in the European Region of WHO (3)*. The WHO Regional Office for Europe will support the development of a measles and rubella laboratory network. The network will be capable of assisting countries with specific needs at each stage of national programmes for eliminating measles and preventing CRI in the Region (Figure 8).

The network will comprise subnational and national laboratories supported by three regional reference laboratories linked to the global measles network. The number of subnational laboratories in a given country will depend on geography and the population of each Member State.

The national and subnational laboratories will be responsible for confirming suspected measles and rubella cases, using validated assays, and for sending appropriate specimens from measles cases to one of the regional reference laboratories for genotyping.

Laboratory assessment and training will be undertaken to establish and strengthen national and subnational laboratory capacity. Standards for quality assurance will be established and monitored through annual accreditation reviews.

The establishment of the network will be closely linked to the strengthening of surveillance capacity and proposed supplementary campaigns (20).

Subnational laboratory	<p>Confirmation of the diagnosis of clinically suspected cases using validated IgM ELISA kits. Collection and dispatch of samples for virus detection to national or regional reference laboratory.</p> <p>Quality assurance: Performs annual proficiency test; refers selected specimens to national laboratory for validation.</p> <p>Reports to: Country programme manager and national laboratory.</p>
National laboratory	<p>Confirmation of the diagnosis of clinically suspected cases using validated IgM ELISA kits. Collection and dispatch of samples for virus detection to regional reference laboratory.</p> <p>Quality assurance: Performs annual proficiency test; refers selected specimens to reference laboratory for validation.</p> <p>Research: Referral of virus strains to global laboratories and performance of epidemiologically essential serological surveys.</p> <p>Reports to: Country programme manager and WHO Regional Office for Europe.</p>
Regional reference laboratory	<p>Reference: Diagnosis of clinically suspected measles cases; virus isolation and characterization from samples collected by national and subnational laboratories.</p> <p>Quality control: Validation of own and national laboratory results using a “gold standard” test; coordination of proficiency testing of national laboratories.</p> <p>Internal quality assurance: Assessing sensitivity and specificity of own work through proficiency testing.</p> <p>Training: Training and advising national laboratory staff.</p> <p>Research: Referral of virus strains and genetic sequences to global laboratories; collaborating in development and evaluation of new tests.</p> <p>Reports to: Country programme manager and WHO Regional Office for Europe.</p>
Global specialized laboratory	<p>Quality control: Preparation of standards, quality control panels of sera and viruses, and training materials.</p> <p>Technical advice: Providing technical advice, consultation and specialized training to regional and national laboratories.</p> <p>Proficiency testing: Conducting periodic proficiency testing for regional laboratories.</p> <p>Research: Evaluating diagnostic kits and improving diagnostic methods.</p> <p>Reports to: WHO (regional and global) and regional reference laboratories.</p> <p>Strain bank: Genetic characterization, maintenance of genetic sequence database and repository of wild measles virus strains; and provision of information to the system as needed.</p>

Figure 8.
Responsibilities
within the measles
and rubella
laboratory network

7. EVALUATION OF SURVEILLANCE SYSTEM

PERFORMANCE INDICATORS

Stage I

- Validated national coverage for first-dose measles vaccine by age 2 years
- Coverage with second-dose measles vaccine
- Incidence rate reported by month, year, location and immunization status
- Completeness and timeliness of monthly surveillance reports
- Percentage of outbreaks with laboratory confirmation
- Percentage of reported cases with core data (age and immunization status) at the first administrative level

Stage II

TARGETS

The indicators from Stage I plus the following:

- Percentage of districts reporting monthly (completeness) ≥ 80%
- Percentage of reported cases with core data (age, immunization status, outcome and location) ≥ 80%
- Percentage of outbreaks with laboratory confirmation ≥ 80%
- Percentage of districts reporting within a month after the reporting period (timeliness) ≥ 80%
- Validated national coverage of first- and second-dose measles vaccine > 90%
- System for reporting adverse events

Stage III

TARGETS

The indicators from Stage II plus the following:

- Percentage of sites reporting weekly ≥ 80%
- Percentage of cases^a notified ≤ 48 hours after onset of rash ≥ 80%
- Percentage of cases investigated ≤ 48 hours after notification ≥ 80%
- Percentage of cases with adequate specimens^b and laboratory results ≥ 80%
- Percentage of cases with laboratory results within 7 days of detection ≥ 80%

^a All cases meeting the clinical case definition.

^b One specimen collected within 3–28 days of rash onset.

TARGETS

- Percentage of confirmed cases with specimens sent for virus isolation $\geq 80\%$
 - Rate of suspected measles investigated in the general population TBD^c
 - Percentage of confirmed cases with sources of infection identified $\geq 80\%$
 - Percentage of febrile-rash clusters investigated 100%
 - Validated national coverage for first- and second-dose measles vaccine $> 95\%$
 - Coverage of first- and second-dose measles vaccine in all districts $> 90\%$
- ^c TBD: to be decided on the basis of operational research (see 5.3.1).

OUTCOME INDICATORS AND TARGETS

Stages I and II

- Disease incidence reported by month and year

Stage III

TARGETS

- Incidence of measles < 1 per 1 000 000 population
- Susceptibility profile needed for interruption of indigenous measles transmission see section 5.3.3
- Size of measles outbreaks and number of generations see section 5.3.3
- Measles virus genotype distribution see section 5.3.4

Stage IIIb

- Annual reported incidence of laboratory-confirmed rubella in countries with a comprehensive rubella immunization programme < 1 per 100 000 population
- Rubella susceptibility level among women of childbearing age $< 5\%$
- Annual reported incidence of laboratory-confirmed CRS < 1 per 100 000 live births

ANNEX 1 CASE DEFINITIONS RECOMMENDED BY WHO

Clinical measles

- Any person in whom a clinician suspects measles infection
- or*
- Any person with fever *and* maculopapular rash (non-vesicular) and cough, coryza (runny nose) or conjunctivitis (red eyes)

Suspected rubella

- Any patient of any age in whom a health worker suspects rubella. A health worker should suspect rubella when a patient presents with: fever, maculopapular rash; and cervical, suboccipital or postauricular adenopathy or arthralgia/arthritis; however, **rubella cannot be confirmed clinically: laboratory confirmation is required.**

Febrile-rash illness

- Any person with fever and maculopapular rash

Laboratory criteria for diagnosis

- Presence of measles- or rubella-specific IgM antibodies

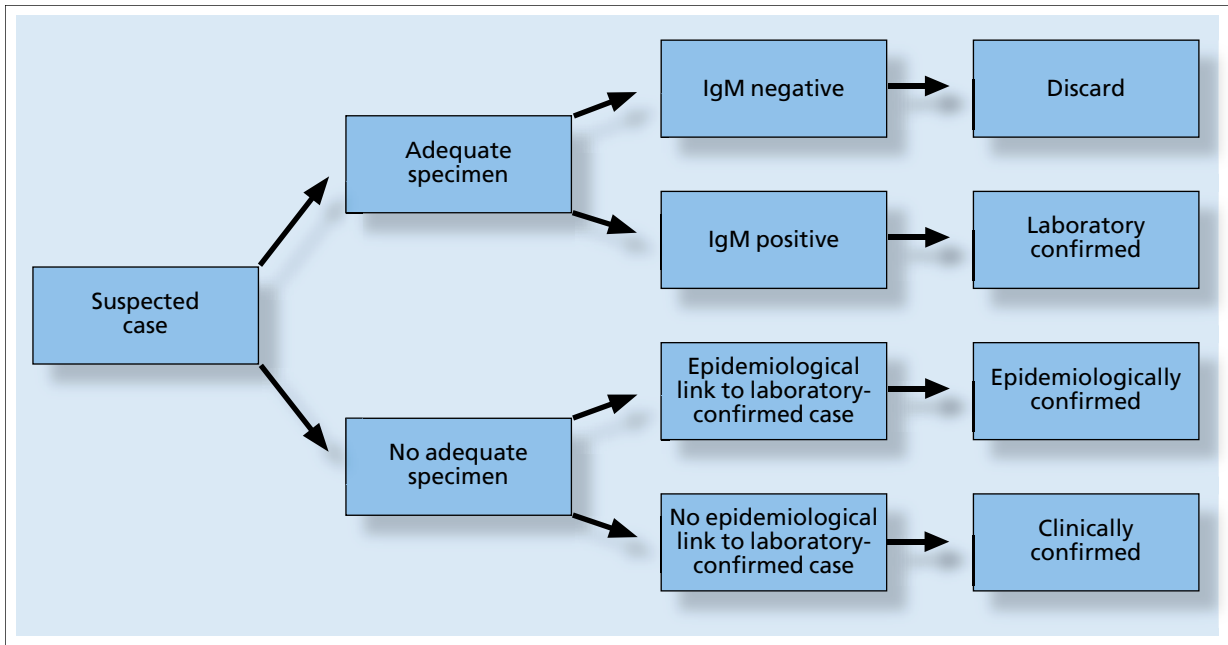
FINAL CASE CLASSIFICATION

Clinically confirmed	A measles case that meets the clinical case definition.
Laboratory confirmed	A case that meets the clinical measles case definition or suspected rubella case definition and is laboratory-confirmed.
Epidemiologically confirmed	A case meeting the clinical measles case definition or the criteria for a suspected rubella case, and who is linked epidemiologically to a laboratory-confirmed case of the corresponding disease.
Discarded	A suspected case that does not meet the clinical or the laboratory definition.

Suspected case of CRS

Suspected case of CRS: Any infant less than one year of age in whom a health worker suspect CRS. A health worker should suspect CRS when an infant aged 0-11 months

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 (microphthalmus), or larger eye ball (congenital glaucoma); **or** when an infant's mother has a history of suspected or confirmed rubella during pregnancy, even when the infant show no signs of CRS.



Clinically confirmed CRS case

An infant in whom a qualified physician detects two of the complications in section A or one from section A and one from section B:

- A) cataracts(s), congenital glaucoma, congenital heart disease, hearing impairment, pigmentary retinopathy.
- B) purpura, splenomegaly, microcephaly, mental retardation, meningoencephalitis, radiolucent bone disease, jaundice with onset within 24 hours after birth.

Laboratory-confirmed CRS case

An infant with anti-rubella IgM antibody and who has clinically confirmed CRS.

Congenital rubella infection

An infant with anti-rubella IgM antibody and who does not have clinically confirmed CRS.

Algorithm for evaluating suspected cases of measles and rubella

ANNEX 2 COLLECTION, STORAGE AND SHIPMENT OF SPECIMENS FOR MEASLES DIAGNOSIS AND OUTBREAK INVESTIGATION*

* Most of the content of this Annex has been taken from *Manual for the laboratory diagnosis of measles viral infection* [20]

The correct timing of sampling with respect to the clinical signs is important for interpreting results and arriving at an accurate conclusion. Samples for measles IgM antibody diagnosis and virus detection should be collected in accordance with the stage of measles control and elimination in which a country is classified (Table A2.1).

Appropriate laboratory and epidemiological staff should agree in advance on the number and type of specimens and the best locations for collection of samples for virus detection. Ideally, samples for virus detection should be collected simultaneously with samples for serological diagnosis and confirmation of measles virus as the cause of the outbreak. Since each type of sample has different requirements, the decision on the type of sample depends on the local resources and facilities for transportation and storage.

Because virus is more likely to be isolated when specimens are collected within three days of the onset of rash, the collection of specimens for virus detection should not be delayed until laboratory confirmation of a suspected case of measles is obtained.

SPECIMENS FOR MEASLES AND RUBELLA DIAGNOSIS

Timing of single blood specimen sampling for IgM

While IgM ELISA tests are more sensitive between days 4 and 28 after the onset of rash (measles and rubella), a single serum sample obtained at the first contact with the health care system at any time within 28 days after onset is considered adequate for measles surveillance. Depending on the specific conditions of the country, alternative sampling methods could be used. These include use of oral fluid or dried capillary bloodspots on filter paper.

Collection and handling procedures

- Blood should be collected by venipuncture in a sterile tube (5 ml for older children and adults and 1 ml for infants and younger children) or if applicable, by finger prick onto filter paper and labelled with the patient's identification and the collection date.

Stage	Function of laboratory	Epidemiological situation	Sample for measles IgM antibody detection	Sample: specimen for virus detection
I and II	To confirm initial cases during outbreaks To analyse wild virus strains from selected cases in order to facilitate genetic characterization of circulating measles viruses	Isolated case	No	No
		Outbreak	Yes From initial 5–10 cases to confirm outbreak	Yes 5–10 specimens
III	To confirm clinical diagnosis of all suspected cases for early detection of virus circulation To analyse wild virus strains and monitor their distribution and circulation for assessing the impact of immunization strategies	Isolated case	Yes From all suspected measles cases	Yes From suspected measles cases
		Cluster of febrile-rash illness	Yes From initial 5-10 cases to confirm outbreak	Yes 5–10 specimens; more may be collected in newly infected districts

Table A2.1.
Minimum requirements for measles serology and measles virus isolation according to control stage

- Whole blood can be stored at 4–8 °C for up to 24 hours before the serum is separated, but it must not be frozen.
- Whole blood should be allowed to clot and then centrifuged at 1000 × g for 10 minutes to separate the serum.
- If there is no centrifuge, the blood should be kept in a refrigerator until there is complete retraction of the clot from the serum (no longer than 24 hours).
- The serum should be carefully removed with a fine-bore pipette to avoid extracting red cells, and transferred aseptically to a sterile labelled vial with the patient’s name or identifier, date of collection and specimen type.
- The measles and rubella laboratory request and result form (Figure A2.1) and the case investigation form (for Stage II or III; Annex 7) should be filled in completely.
Three dates are very important:
 - date of last measles vaccination
 - date of onset of rash
 - date of collection of sample.

The ELISA test for the detection of measles- and rubella-specific IgM antibodies is recommended for the WHO measles and rubella laboratory network.

Storage and shipment of specimens

- Serum should be stored at 4–8 °C until shipment takes place or for a maximum of 7 days.
- When kept for longer periods, serum samples must be frozen at –20 °C and transported to the testing laboratory on frozen ice packs. Repeated freezing and thawing can have detrimental effects on the stability of IgM antibodies.
- Dried blood specimens can be stored and transported at room temperature in sealed plastic bags.
- Specimens should be shipped to the laboratory as soon as possible. One should not wait to collect additional specimens before shipping.

Alternative sampling methods will soon be available for detection of measles-specific IgM antibodies and/or measles virus genomic RNA. These include the use of oral fluid and dried blood spots on filter paper. Protocols for both techniques will be available in the revised WHO laboratory manual to be published in 2004.

- Specimens should be placed in Ziplock® or similar sealable plastic bags.
- Styrofoam boxes or a Thermos® insulating(vacuum) flask should be used.
- The specimen form and investigation form for each specimen should be placed in a plastic bag and taped to the inner surface of the top of a Styrofoam box.
- If using ice packs (which should be frozen), these should be placed at the bottom and along the sides of the box. The samples should then be placed in the centre and more ice packs placed on top.
- A shipping date should be arranged.
- When the arrangements have been finalized, the receiver should be informed of the time and manner of transportation.
- More details on how to package and ship samples are given in the *Manual for laboratory diagnosis of measles viral infection (20)*.

Urine for measles virus isolation

Samples of 10–50 ml urine are adequate for this purpose. It is preferable to obtain the first urine passed in the morning. Most of the measles virus excreted in the urine is located in epithelial cells. The virus is concentrated by centrifugation of the urine and resuspension of the pelleted cells in a suitable viral transport medium. Urine should NOT be frozen before the concentration procedure is carried out.

Timing

The isolation of measles virus is most successful if the specimens are collected as soon as possible after the onset of rash, and at least within 7 days after onset.

Collection and handling procedures

- Urine should be collected in a sterile container.
- It should be held at 4–8 °C before centrifugation.
- Centrifugation should be performed within a few hours (see below).

Storage and shipment of urine samples

- Whole urine samples may be shipped in well sealed containers at 4 °C, but centrifugation within 24 hours after collection is preferable.
- Centrifugation should be performed at 500 × g (approximately 1500 rpm) and 4 °C for 5 minutes.
- The supernatant should be discarded and the sediment resuspended in 1 ml viral transport medium or tissue culture medium.
- DO NOT FREEZE the sediment if shipment is possible within 48 hours. DO NOT FREEZE urine before the concentration procedure has been carried out.
- The resuspended pellet may be stored at 4 °C and shipped within 48 hours to a measles reference laboratory. Alternatively, it may be frozen at –70 °C in viral transport medium and shipped on dry ice in a well sealed screw-capped vial to protect against CO₂ contamination.

Nasopharyngeal specimens for measles virus isolation

Timing

Nasopharyngeal specimens for virus isolation must be collected as soon as possible (not later than 7 days) after the appearance of the rash, when the virus is present in high concentration.

Collection and handling procedures

Nasopharyngeal specimens can be taken as follows (in order of increasing yield of virus):

- nasal aspiration
- throat washing
- nasopharyngeal swabbing.

Nasal aspirates are collected by introducing a few ml of sterile saline into the nose with a syringe fitted with fine rubber tubing and collecting the fluid in a screw-capped centrifuge tube containing viral transport medium*.

Throat washes are obtained by asking the patient to gargle with a small volume of sterile saline and collecting the fluid in viral transport medium*.

* If viral transport medium is not available, isotonic saline solution, tissue culture medium or phosphate-buffered saline may be used.

*If viral transport medium is not available, isotonic saline solution, tissue culture medium or phosphate-buffered saline may be used.

Nasopharyngeal swabs are obtained by firmly rubbing the nasopharyngeal passage and throat with sterile cotton swabs to dislodge epithelial cells. The swabs are placed in sterile viral transport medium* in labelled screw-capped tubes.

Storage and shipment of nasopharyngeal specimens

- Nasopharyngeal specimens should be refrigerated and shipped on wet ice (4–8 °C) to arrive at the testing laboratory within 48 hours.
- If arrangements cannot be made for rapid shipment, swabs should be shaken in the medium to elute the cells and then removed.
- The medium or nasal aspirate should be centrifuged at 500 × g (approximately 1500 rpm) and 4 °C for 5 minutes, and the resulting pellet should be resuspended in cell culture medium.
- The suspended pellet and the supernatant are stored separately at –70 °C and shipped to the testing laboratory on dry ice in well-sealed screw-capped vials to protect against CO₂ contamination.

Whole blood for virus isolation

A detailed protocol for virus isolation from whole blood will be available in the revised WHO laboratory manual to be published in 2004.

Collection and handling procedures

- For isolation of peripheral blood mononuclear cells (PBMC) for subsequent virus isolation, blood should be collected by venipuncture in a sterile tube supplemented with EDTA. A minimum blood volume of 5 mL is recommended.
- The plasma fraction can be used to determine the measles-specific IgM antibodies.
- The tube should be labelled with the patient's identification number and the date of collection.

Storage and shipment of whole blood

- Whole blood samples may be shipped in well-sealed tubes at 4°C.
- EDTA supplemented whole blood should be processed for virus isolation within 48 hours after collection and must not be frozen at any time prior to processing.

Specimen kit for measles diagnosis

The components required in a specimen collection kit for measles diagnosis have been established. They are suitable for distribution to facilities collecting samples from suspected cases in countries at the stage of measles elimination.

The basic kit for blood collection consists of:

- a 5-ml vacutainer tube (non-heparinized) with a 23 gauge needle

- a tourniquet
- sterilizing swabs
- serum storage vials
- specimen labels
- band aids
- Ziplock® or similar sealable plastic bags
- a specimen referral form
- a cold box with ice packs.

Final classification	Vaccination history	Epidemiological findings
Vaccinated	Measles vaccination within six weeks before onset of rash	Active search in community does not reveal evidence of measles transmission No history of travelling to areas where measles virus is known to be circulating
Confirmed	Measles vaccination within six weeks before onset of rash	Active search in community reveals other laboratory-confirmed measles cases

Table A2.2.
Classification of cases with IgM-positive result and recent history of measles vaccination

Interpreting laboratory results

Final classification of suspected measles cases for countries in Stage III

- Only patients that have a positive result with a validated IgM ELISA assay are considered to have laboratory-confirmed measles.
- Patients with a positive assay result obtained by other methods are considered as suspected pending final laboratory testing.

If for any reason an approved IgM ELISA assay is not performed on samples positive by other methods, such cases are considered “clinically confirmed” for surveillance purposes.

Interpretation of results in recently vaccinated patients

Natural measles infection and measles vaccination can stimulate an IgM response in the host. If the person with suspected measles has been vaccinated **within six weeks before onset of rash** the interpretation of the results may be difficult because:

- measles vaccine can cause fever in 5% and rash in approximately 20% of vaccinees;
- first-time vaccinees are expected to have detectable measles IgM after vaccination;

- a mild rash lasting 1–3 days may occur approximately a week after vaccination;
- serological techniques cannot distinguish between immune responses to natural infection and immunization (this can only be done by viral isolation and characterization); and
- other medical conditions, such as rubella and dengue, can cause rash and fever in persons who have recently received measles vaccine.

Consequently, an operational definition is required to facilitate the final classification of suspected measles cases with an IgM-positive result (Table A2.2). Nevertheless, all IgM-positive individuals should be reported.

Measles and rubella laboratory request and result form. For date please use: dd-mm-yyyy (like 20-10-2002)

Country: _____ Date: - - Patient ID: _____

Patient name: _____ M F Date of birth: - -

Age in months: _____ Name of parent or guardian: _____

Address: _____ Date of onset of rash: - -

Specimen ID	Specimen type	Date of collection	Date of shipment	Date received at laboratory	Condition	Date of result	Measles test IgM	Other*	Rubella test IgM	Other*
1)	_____	- -	- -	- -	_____	- -	_____	_____	_____	_____
2)	_____	- -	- -	- -	_____	- -	_____	_____	_____	_____
2)	_____	- -	- -	- -	_____	- -	_____	_____	_____	_____

Comment: _____ *Other methodology (specify): _____

Name of person to whom laboratory results should be sent: _____

Address: _____

Telephone number: _____ Fax number: _____

For use by the receiving laboratory

Name of laboratory: _____ Name of person receiving the specimen: _____

Figure A2.1. Measles and rubella laboratory request and result form

ANNEX 3 CASE-BASED ANALYSES OF SURVEILLANCE DATA

Figure A3.1.
Number of cases and deaths reported by month (place, year 1 and year 2)

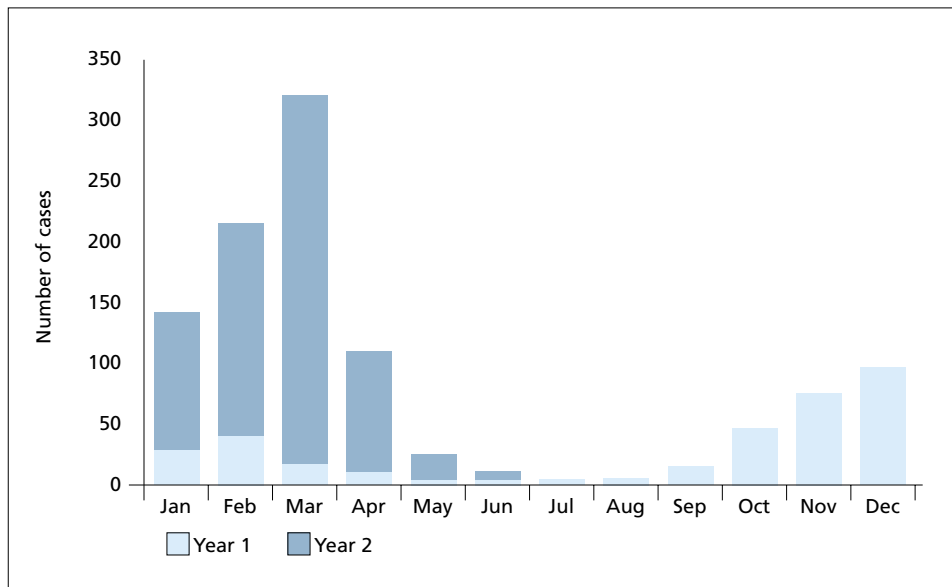
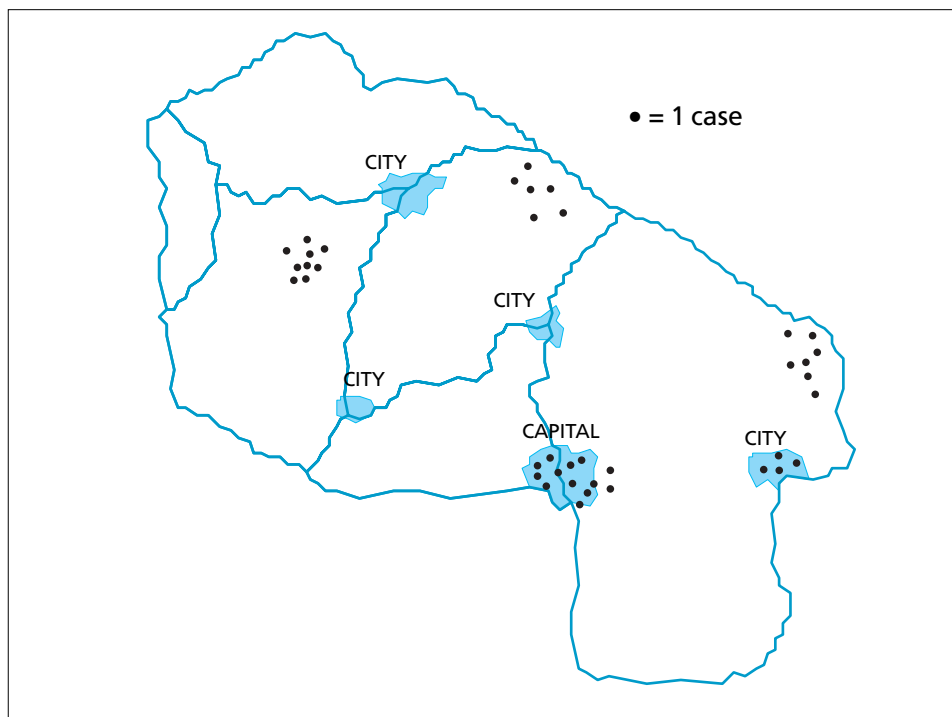


Figure A3.2.
Spot map of cases (place, year)



Note:
Areas with no measles cases may indicate poor surveillance and lack of reporting.

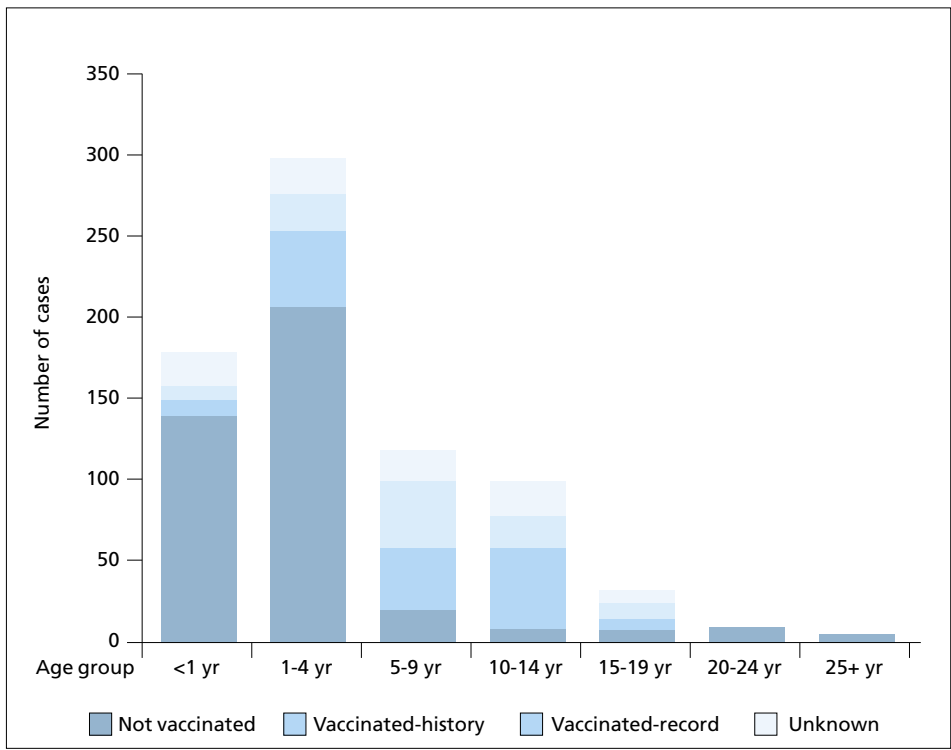


Figure A3.3.
Number of cases
by age group and
vaccination status
(place, January–
June, year)

Note:
 Adult age groups
 can be grouped
 together if few cases
 are occurring in these
 groups

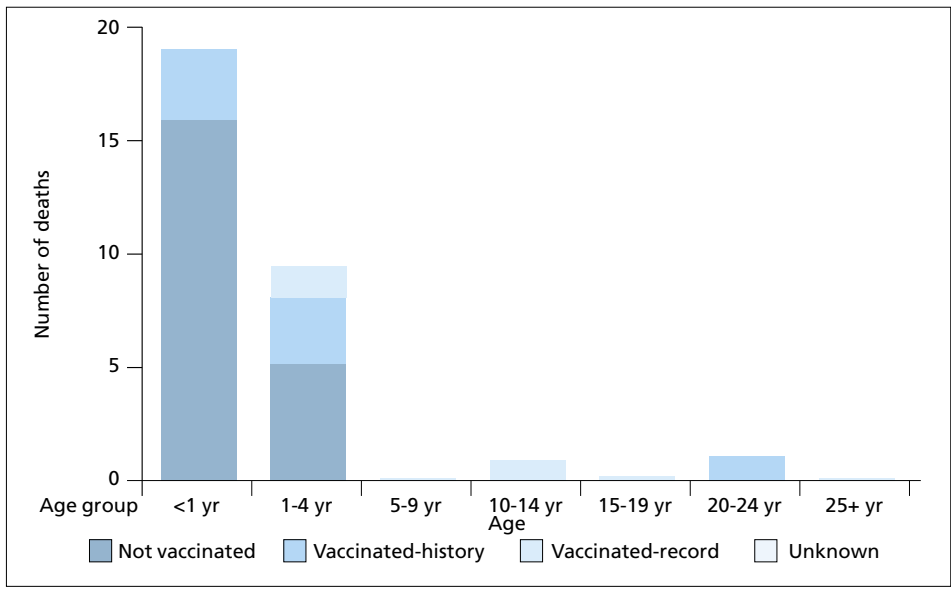


Figure A3.4.
Number of deaths
by age group and
vaccination status
(place, January–
June, year)

ANNEX 4 HISTORICAL TREND ANALYSES OF CASES

Figure A4.1.
Number of cases
by year (place,
1994–2000)

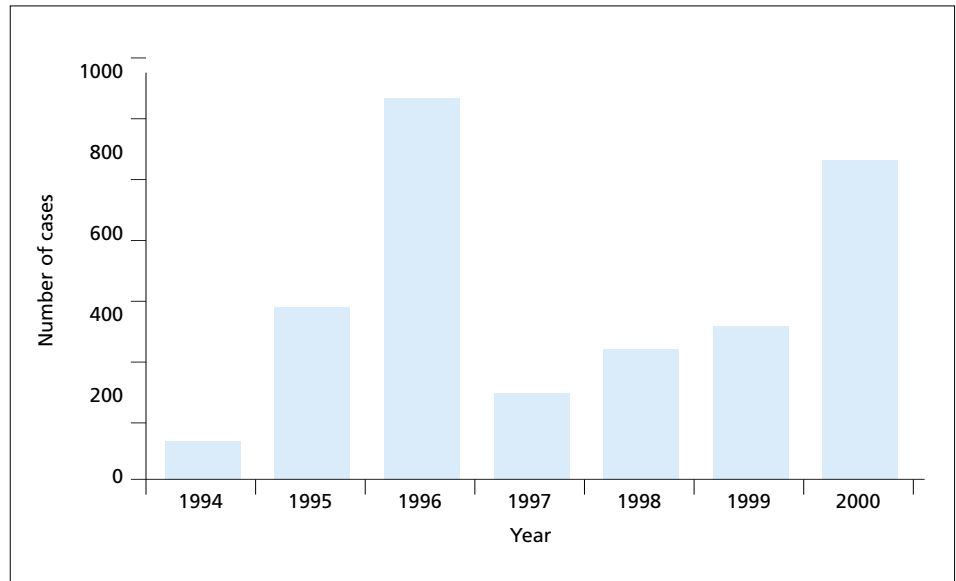
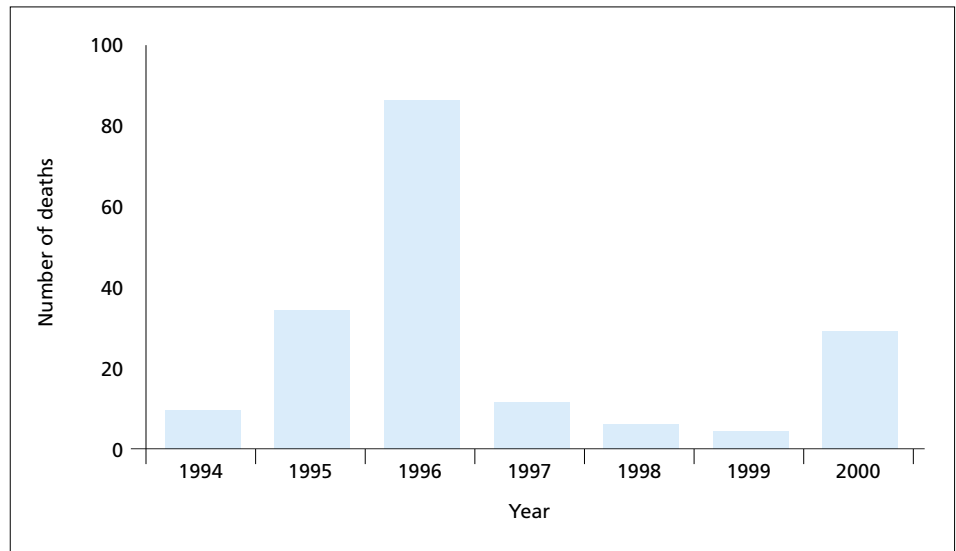


Figure A4.2.
Number of deaths
by year (place,
1994–2000)



The comparative evolution of vaccine coverage can also be included.

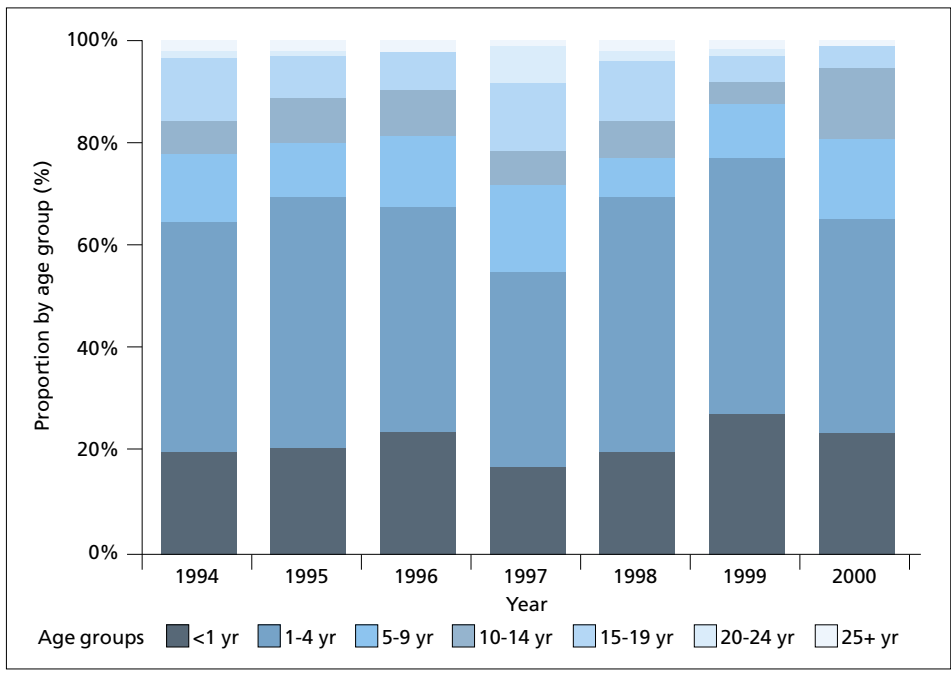


Figure A4.3.
Proportion of cases
by age group
and year
(place, 1994–2000)

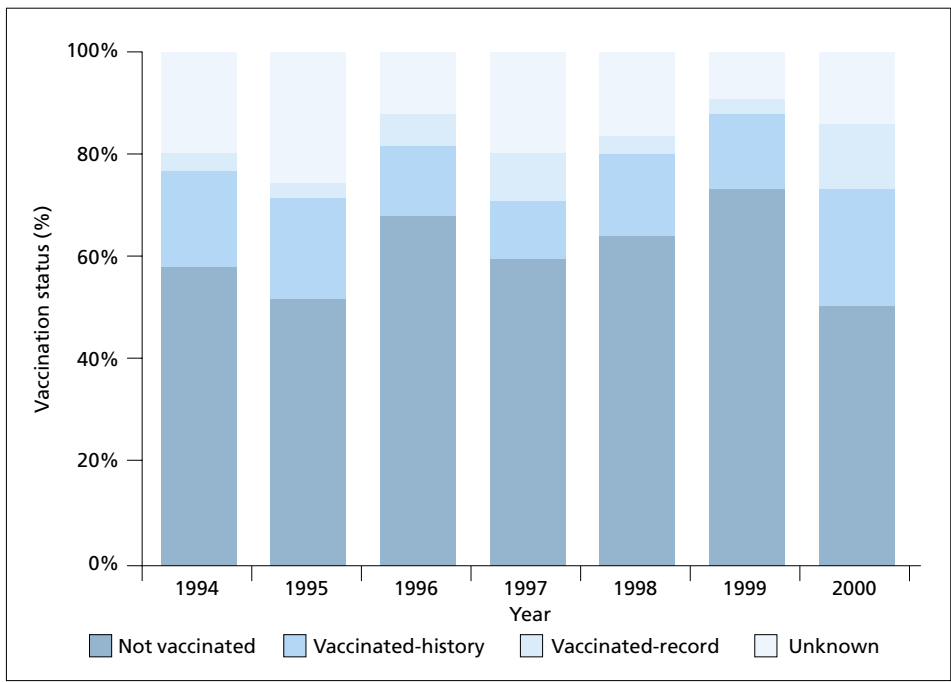
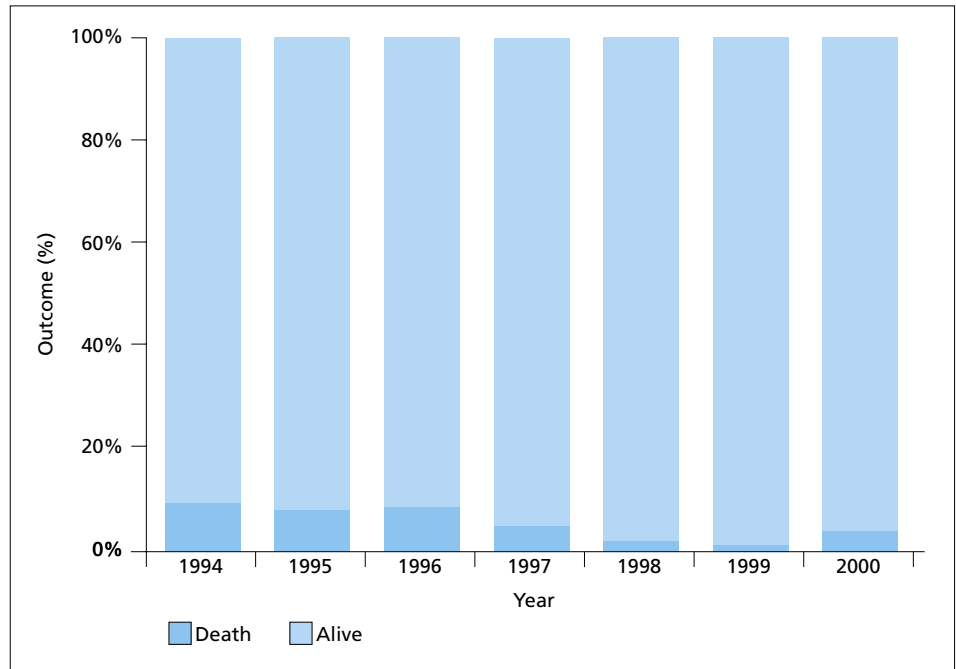


Figure A4.2.
Proportion of cases
by vaccination status
and year (place,
1994–2000)

Figure A4.5.
Proportion of
cases by outcome
and year (place,
1994–2000)



MEASLES AND RUBELLA AGGREGATE AND CASE-BASED SURVEILLANCE

ANNEX 5

- The frequency of reporting to WHO Regional Office for Europe is monthly
- The deadline to submit data on the previous month is the 25th of each month

THIS SURVEILLANCE MONITORS FOR EVERY MEMBER STATE:

- Timeliness and completeness of reporting to WHO
- Number of new cases (measles and/or rubella) for that month
- Number of districts who reported to the national authority the status of measles and/or rubella (0 case or notification of cases) for that month

ACCORDING TO THE PHASE OF ELIMINATION IN THE MEMBER STATE, REPORTING TO WHO CONSISTS OF AGGREGATED DATA OR CASE-BASE DATA

Aggregated data

- **How to aggregate data?**

A report for a month includes all measles cases that were first reported to national authorities in that month.

These reports have to be completed every month and previous months' reports also need to be updated to take into account the information that arrives at the national authority with some delay (especially death). This will enable the sum of monthly reports to accurately represent the total number of cases over a given period (quarter or year).

- **Measles**

Member States in Stage I should use the measles aggregated reporting form.

Reporting includes clinically, epidemiologically linked and laboratory-confirmed cases of measles only.

Distribution by age and measles vaccine status is required as well as the number of laboratory confirmed cases, hospitalised cases and number of deaths related to measles infection (defined as death due to measles or its complications within 2 months of onset of measles)

- **Rubella**

Member States in Stage I or II for measles control AND who have a rubella vaccination programme should use the rubella aggregated form, although countries in Stage II are strongly encouraged to move to case-by-case reporting for rubella.

Member States who are in Stage I or II without a rubella vaccination programme are strongly encouraged to move to aggregate reporting of rubella cases.

Distribution by age and rubella vaccine status is required as well as the number of laboratory-confirmed cases, hospitalised cases and number of deaths related to rubella infection.

Case-based data

- **How to report case-based data?**

The fields used for case based reporting of measles and/or rubella are in Table A5.4 with the name of the variable, the label, the definition, the possible answers and the rules that would ensure data quality.

A case report must at least include information on (mandatory fields):

- Unique identifier
- Country
- First administrative level
- Date of onset of the rash
- Date of birth OR age at rash onset
- Gender

Final classification of the case should be provided for every case when available but with a target of having all cases classified 30 days after the date of onset of the rash.

- **Measles**

Member States in Stage III must report case-based measles data.

Member States in Stage II should report case-based measles data.

Measles reporting includes suspected, clinical, epidemiologically linked and laboratory confirmed cases of measles as well as vaccine-associated cases.

- **Rubella**

Member States in Stage III for measles control who have introduced rubella vaccination must report case-based data on measles and rubella.

Member States in Stage II for measles control with a comprehensive rubella vaccination program (3) should report case-based data on measles and rubella

Reporting includes suspected clinical, epidemiologically linked and laboratory-confirmed cases of measles *and* rubella as well as vaccine-associated cases.

HOW TO REPORT?

The WHO Regional Office for Europe has developed an online entry tool and would strongly encourage Member States to use this mode of reporting. To have an account set up on the server please contact measles@euro.who.int

This website enables secure connection (each Member State can only edit its own information) to:

- Fill in and update completeness of reporting
- Enter and update aggregated reports if the Member State falls under the aggregated report category
- Enter and update case-based data if the Member State falls under the case-based report category. Cases can either be entered one by one in an online entry form or uploaded with a tab delimited text file complying with the specifications of Table A5.4 which can contain information on many cases.

If Member States are not able to report online, the WHO Regional Office for Europe would like to be aware of the technical difficulties Member States encounter (contact measles@euro.who.int) and offers the possibility to email (measles@euro.who.int) or fax (+45 39 17 18 63) the corresponding forms (completeness + aggregated report OR completeness + case-based report).

Table A5.1.
Data fields and definitions for timeliness completeness

Field Name in the database	Label	Definition	Possible answers	Rules
AreaID	Reporting entity	Code of the reporting entity		
Year	Year of report	Year of report	YYYY	
Month	Month of report	Month of report	1 to 12	
Newcases	New cases reported	number of new cases (measles and/or rubella) for that month	positive integer	
ReportReceived	Number of districts reporting	number of districts who reported to the national authority the status of measles and/or rubella (0 case or notification of cases) for that month	positive integer	ReportReceived<=ReportTotal
ReportTotal	Total number of districts	Total number of districts in the country	positive integer	Modification of this field can be made by submitting to measles@euro.who.int a comprehensive list of 1st and 2nd administrative levels

Table A5.2.
Measles aggregated reporting. Monthly reporting to the WHO Regional Office for Europe.
measles@euro.who.int or fax to +45 39 17 18 63

Identification		Reporting	
Country		Year of report	
Name of the responsible person		Month of report	
Email		New cases reported	
Tel		Number of districts reporting	
Current date		Total number of districts in the country	

	Age Group						
	<1 year	1 - 4yrs	5 - 9yrs	10 - 14yrs	15-19yrs	20-29 yrs	30+ age unknown
Vaccination status							
0 doses							
1 dose							
2+ doses							
Unknown No. vaccines							

Nr Laboratory confirmed	
Nr Hospitalised	
Nr died	

Table A5.3.
Rubella aggregated reporting. Monthly reporting to the WHO Regional Office for Europe.
measles@euro.who.int or fax to +45 39 17 18 63

Identification		Reporting				
Country		Year of report				
Name of the responsible person		Month of report				
Email		New cases reported				
Tel		Number of districts reporting				
Current date		Total number of districts in the country				

Vaccination status	Age Group						age unknown
	<1 year	1 - 4yrs	5 - 9yrs	10 - 14yrs	15-19yrs	20-29 yrs	
0 doses							
1 dose							
2+ doses							
Unknown No. vaccines							

Nr Laboratory confirmed	
Nr Hospitalised	
Nr died	

Table A5.4.
Data fields and definitions for case-based reporting.

Field Name in the database	Label	Definition	Possible answers	Rules
CaseID	CaseID	Unique identifier for the case	Free text (limit of 50 characters)	must be reported at first report and unique; recommended naming convention: 2 letter code of the country + arealD + sequential number ; ex RU20460003 (Russian Federation, St Petersburg city, case number 3)
AreaID	Country 1st administrative level 2nd administrative level	one code defines country and 1st and 2nd administrative level of residence of the case when the illness was contracted.	Updated information can also be obtained in the "area code reference" function of the EURO website	A code defining at least the 1st administrative level must be provided
DRash	Date of rash onset	Date of rash onset	dd/mm/yyyy	must be reported at first report cannot be a future date DRash>= DBirth
GenderID	Gender	Gender	1 Male 2 Female 4 unknown	must be reported at first report
DBirth	Date of birth	Date of birth	dd/mm/yyyy	must be reported at first report if the age at rash onset is not provided cannot be a future date DRash>= DBirth
AgeAtRashOnset	Age at rash onset	Age at rash onset	Positive integer Child is zero years until first birthday, one year until second birthday, etc	must be reported at first report if the date of birth is not provided
NumOfVaccines	Number of vaccines	Number of measles vaccines (any measles containing vaccine) from vaccination card or by verbal history	Positive integer use -2222 if the number vaccines received is unknown	

Field Name in the database	Label	Definition	Possible answers	Rules
Dvaccine	Date of the last vaccination	Date of the last measles vaccination (any measles containing vaccine)	dd/mm/yyyy	Dvaccine>=Dbirth cannot be a future date
DNotification	Date of notification	Date when the case is first reported or notified to public health authorities	dd/mm/yyyy	DNotification>=DBirth DNotification>=DRash cannot be a future date
DInvestigation	Date of investigation	Date of epidemiologic investigation of the case by public health authorities	dd/mm/yyyy	DInvestigation>=DBirth DInvestigation>=DRash cannot be a future date
ClinFever	Fever	Presence of fever	1 Yes 2 No 9 Unknown	
ClinCCC	Cough or Coryza or Conjunctivitis	Presence of one or more of the following symptoms; cough, coryza, conjunctivitis	1 Yes 2 No 9 Unknown	
ClinRashDuration	Duration of rash	number of days when the rash is present	Positive integer use -2222 if duration of rash is unknown	
ClinOutcome	Outcome	Outcome of the case death is defined as death due to measles or its complications within 2 months of onset of measles	1 Death 2 Alive 3 Lost to follow up or unknown	
ClinHospitalisation	Hospitalisation	The case was hospitalised	1 Yes 2 No 9 Unknown	
SrcImportRelated	Import related	The case is part of a chain of transmission originating with an imported case	1 Yes 2 No 9 Unknown	
SrcOutbreakRelated	Outbreak related	The case part of an outbreak	1 Yes 2 No 9 Unknown	

Field Name in the database	Label	Definition	Possible answers	Rules
SrcOutbreakID	Outbreak ID	Unique identifier for that outbreak	Free text (limit of 50 characters)	can only be filled in if the Srcoutbreakrelated=1 when a case is part of an outbreak, the outbreak should be reported in the measles outbreak section Unique identifier for that outbreak
CompComplications	Complications	The case had complications	1 Yes 2 No 9 Unknown	
CompEncephalitis	Encephalitis	The case suffered from encephalitis	1 Yes 2 No 9 Unknown	answer is only possible if Compcomplication=1
CompPneumoniae	Pneumoniae	The case suffered from pneumoniae	1 Yes 2 No 9 Unknown	answer is only possible if Compcomplication=1
CompMalnutrition	Malnutrition	The case suffered from malnutrition	1 Yes 2 No 9 Unknown	answer is only possible if Compcomplication=1
CompDiarrhoea	Diarrhoea	the case suffered from diarrhoea	1 Yes 2 No 9 Unknown	answer is only possible if Compcomplication=1
CompOther	Other	the case suffered from other complications	1 Yes 2 No 9 Unknown	answer is only possible if Compcomplication=1

Field Name in the database	Label	Definition	Possible answers	Rules
FinalClassification	Final classification	Final classification of the case	<ul style="list-style-type: none"> 0 Discarded, not a measles case 1 Measles Laboratory confirmed 2 Measles Epidemiologically linked 3 Measles Clinically confirmed 4 Measles Vaccine related 5 Discarded, not Rubella or Measles case 6 Rubella Laboratory confirmed 7 Rubella Epidemiologically linked 8 Rubella Clinically confirmed 9 Rubella Vaccine related 	<p>It should be provided 30 days after the date of onset of the rash</p> <p>Final classification can only be measles laboratory confirmed if MeaslesIgM=1 or MeaslesVirusDetection=1 or both</p> <p>Final classification can only be rubella laboratory confirmed if RubellaIgM=1 or RubellaVirusDetection=1 or both</p>
DSpecimen	Date of collection	Date when the first specimen was collected from the patient regardless of the test results	dd/mm/yyyy	<p>DSpecimen>=DBirth</p> <p>DSpecimen+4days>=DRash</p> <p>cannot be a future date</p>
Specimens	Type of specimen	Type of specimen collected	<ul style="list-style-type: none"> 1 Serum 2 Saliva/Oral fluid 3 Nasopharyngeal swab 4 Dry blood spot 5 Urine 6 EDTA whole blood 7 Other specimen 	<p>several type of specimens can be specified separated by a comma</p> <p>ex 1,2 means that a serum sample and a saliva sample have been taken</p>
DLabResult	Date of laboratory result	Date when laboratory results become available (first validated result)	dd/mm/yyyy	<p>DLabResult>=DBirth</p> <p>DLabResult>=DSpecimen</p> <p>cannot be a future date</p>
MeaslesIgM	Measles IgM	Validated result of measles IgM testing whether on serum or oral fluid or other at the patient level	<ul style="list-style-type: none"> 0 Not tested 1 Positive 2 Negative 3 In process 4 Inconclusive 	
MeaslesVirusDetection	Measles Virus detection	Validated result of measles isolation or detection by for example RT-PCR at the patient level	<ul style="list-style-type: none"> 0 Not tested 1 Positive 2 Negative 3 In process 	

Field Name in the database	Label	Definition	Possible answers	Rules
RubellaIgm	Rubella IgM	Validated result of Rubella IgM testing whether on serum or oral fluid or other at the patient level	0 Not tested 1 Positive 2 Negative 3 In process 4 Inconclusive	
RubellaVirus Detection	Rubella Virus detection	Validated result of Rubella isolation or detection by for example RT-PCR at the patient level	0 Not tested 1 Positive 2 Negative 3 In process	
CommentsEpi	Comments	Comments	Free text, should contain if relevant: if the case is the index case of an outbreak, the name of the country where the imported case acquired the disease; the rubella vaccination status for rubella cases; the presence of SSPE (Subacute Sclerosis Pan Encephalitis)	

ANNEX 6 MEASLES AND RUBELLA OUTBREAK SURVEILLANCE

Documentation of the outbreaks will allow the evaluation of the size and duration (number of generations) of outbreaks, which will give an insight into the control of measles

The outbreak reporting offers the possibility to give a more comprehensive picture of the activity of measles and/or rubella in areas where it is not yet feasible to investigate every case and have every case laboratory confirmed and reported through the case-based surveillance.

However, Member States must report in the case-based system all cases that died as a result of measles or had encephalitis.

Case-based reporting and outbreak reporting are linked through the unique outbreak ID.

Reporting of outbreaks should be made as soon as possible when national authorities are notified. Subsequently outbreak records should be updated on a monthly basis.

Member States should report to the WHO Regional Office for Europe outbreaks where at least one case has been laboratory confirmed (measles or rubella)

One outbreak record must be created for each outbreak. If an outbreak extends over several geographical areas (1st administrative level), one record must be created for each area (indicating the date of onset of the first and last case in that specific area).

If after laboratory confirmation, it appears that some cases are measles and others are rubella laboratory-confirmed cases, all efforts should be made to classify clinical or epidemiologically linked cases as measles OR rubella and therefore report the event as 2 separate outbreaks.

HOW TO REPORT?

The WHO Regional Office for Europe has developed an online entry tool and would strongly encourage Member States to use this mode of reporting. To have an account set up on the server please contact measles@euro.who.int

This website enables secure connection (each member State can only edit its own information) to enter and update outbreak reports annex

If Member States are not able to report online, the WHO Regional Office for Europe would like to be aware of the technical difficulties Member States encounter (contact measles@euro.who.int) and offers the possibility to email (measles@euro.who.int) or fax (+45 39 17 18 63) the corresponding outbreak report.

Table A6.1.
Data fields and definitions for reporting of outbreaks

Label	Definition	Possible answers	Rules
Outbreak nr	Outbreak nr	Text	unique mandatory
country	one code defines country and 1st and 2nd administrative level of residence of the case when the illness was contracted.	Updated information can also be obtained in the "area code reference" function of the website	A code defining at least the 1st administrative level must be provided Only one code can be provided
1st administrative level			
2nd administrative level			
Date of onset of the first case	Date of onset of the first case in that area	dd/mm/yyyy	mandatory Dstart<=Dend No future date
Date of onset of the last case	Date of onset of the last case in that area	dd/mm/yyyy	Dstart<=Dend
Date of notification	Date the outbreak was first reported to national authorities	dd/mm/yyyy	mandatory Dreport>=Dstart No future date
Nr Cases	Total number of clinical, epidemiologically linked, laboratory confirmed cases of measles OR rubella	positive integer	
Nr Death	Number of measles cases that resulted in a death defined as death due to measles or its complications within 2 months of onset of measles	positive integer	Death<=Cases
Nr Encephalitis	Number of measles cases that resulted in encephalitis	positive integer	Encephalitis<=Cases

Label	Definition	Possible answers	Rules
Nr hospitalised	Number of cases hospitalised	positive integer	Hospitalised<=Cases
Nr CBAW	Number of child bearing age women (15-49 years old) who are cases	int	CBAW<=cases
Nr Pregnant women	Number of pregnant women who are cases	int	pregnant<=cases
importation	The index case was an imported case, (case outside the country during the period in which infection could have occurred (7-18 days prior to rash onset OR case with positive virus characterization not known to circulate in the country or region)	1 Yes 2 No 9 Unknown	
Nr cases with specimen	Number of cases with specimens sent for laboratory confirmation	int	caselab<=cases
Nr measles laboratory confirmed cases	Number of measles laboratory confirmed cases	int	mealabconf<=caselab
Nr rubella laboratory confirmed cases	Number of rubella laboratory confirmed cases	int	rublabconf<=caselab
Genotype	Genotype of the strains of measles or rubella involved in the outbreak		there can be more than one genotype notified
Description	Age and vaccination status distribution (see form)		
Description	Description of the outbreak, such as source of outbreak, description of the index case, number of chains of transmissions...	Text	
Measures taken	Measures taken such as coverage survey	text	

Table A6.2. Measles Rubella Outbreak Reporting, Monthly reporting to the WHO Regional Office for Europe. measles@euro.who.int or fax to +45 39 17 18 63

Name of the responsible person	Email	Tel	Current date
--------------------------------	-------	-----	--------------

Identification	Cases	Laboratory
Outbreak Nr	Nr Cases	Nr cases with specimen
Country	Nr Death	Nr of measles laboratory confirmed cases
1st administrative level	Nr Encephalitis	Nr of rubella laboratory confirmed cases
2nd administrative level	Nr Hospitalised	Genotype(s)
Date of onset of first case	Nr CBAW	
Date of onset of last case	Nr Pregnant Women*	
Date of notification		
Importation (Yes/No/Unknown)		

*Child Bearing Age Women

	Age Group						
	<1 year	1 - 4yrs	5 - 9yrs	10 - 14yrs	15-19yrs	20-29 yrs	30+ age unknown
Vaccination status							
0 doses							
1 dose							
2+ doses							
Unknown No. vaccines							

Description	
Measures taken	

ANNEX 7 CASE INVESTIGATION FORMS

Table A7.1.
Congenital rubella
syndrome case
investigation form

Page 1

Case ID: _____ Date of report: - - Date of investigation: - -
Country: _____ Region: _____ District: _____

Infant's identification

Name of child: _____ Date of birth: - - City/town/Village: _____
Sex: Male Female Place infant delivered: _____ Nationality: _____

Notification

Date of notification: - - Telephone: _____ City/town/Village: _____
Name of referring health worker: _____ Place of work: _____

Clinical signs and symptoms

Gestational age (weeks): _____ Birth weight (gms): _____

Group A (please complete all)			Group B (please complete all)		
Congenital heart disease	Yes <input type="checkbox"/>	No <input type="checkbox"/> Nk <input type="checkbox"/>	Purpura	Yes <input type="checkbox"/>	No <input type="checkbox"/> Nk <input type="checkbox"/>
If yes describe:			Microcephaly	Yes <input type="checkbox"/>	No <input type="checkbox"/> Nk <input type="checkbox"/>
Cataracts	Yes <input type="checkbox"/>	No <input type="checkbox"/> Nk <input type="checkbox"/>	Meningoencephalitis	Yes <input type="checkbox"/>	No <input type="checkbox"/> Nk <input type="checkbox"/>
Glaucoma	Yes <input type="checkbox"/>	No <input type="checkbox"/> Nk <input type="checkbox"/>	Jaundice	Yes <input type="checkbox"/>	No <input type="checkbox"/> Nk <input type="checkbox"/>
Pigmentary retinopathy	Yes <input type="checkbox"/>	No <input type="checkbox"/> Nk <input type="checkbox"/>	Splenomegaly	Yes <input type="checkbox"/>	No <input type="checkbox"/> Nk <input type="checkbox"/>
Hearing impairment	Yes <input type="checkbox"/>	No <input type="checkbox"/> Nk <input type="checkbox"/>	Developmental delay	Yes <input type="checkbox"/>	No <input type="checkbox"/> Nk <input type="checkbox"/>
			Radiolucent bone disease	Yes <input type="checkbox"/>	No <input type="checkbox"/> Nk <input type="checkbox"/>
Other abnormalities	Yes <input type="checkbox"/>	No <input type="checkbox"/> If yes please describe: _____			
Name of physician who examined infant: _____					
City/town/Village: _____			Telephone: _____		
Present status of infant: alive <input type="checkbox"/> dead <input type="checkbox"/> .					
If not living, cause of death (please describe): _____					
Autopsy conducted: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>					
Autopsy findings: _____			Autopsy date: - -		
City/town/Village: _____			Telephone: _____		

**Table A7.1.
Congenital rubella syndrome
case investigation form
(continued)**

Maternal history/Antenatal care

Number of previous pregnancies: _____	Mother's age (years): _____
Vaccinated against rubella: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	If yes, give date: - - _____
Conjunctivitis: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	If yes, date of onset: - - _____
Coryza: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	If yes, date of onset: - - _____
Cough: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	If yes, date of onset: - - _____
Maculopapular rash: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	If yes, date of onset: - - _____
Lymph nodes swollen: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	If yes, date of onset: - - _____
Arthralgia/arthritis: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	If yes, date of onset: - - _____
Other complications: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	If yes, date of onset: - - _____
Was rubella laboratory confirmed in the mother: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	If yes, by: _____
Exposed during pregnancy to any person (any age) with maculopapular (e.g. not vesicular) rash illness with fever: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	Travel during pregnancy: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>
	If yes, give month _____
	Describe where _____

Maternal history/Antenatal care

Date blood collected _____	Name of reference _____
Date serum sent to referency _____	City/Town/Village _____
Telephone _____	Type of IgM test/name of: _____
Test results: IgM Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	Virus isolation Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>
	PCR Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>
	Genotyping Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>
Date results received: - - _____	Date family informed of results: - - _____
By: _____	By: _____

Final classification of case

No laboratory tests, but clinically confirmed CRS	<input type="checkbox"/>
Positive Lab. tests + clinically confirmed CRS = Laboratory confirmed CRS	<input type="checkbox"/>
Positive Lab. tests + no clinically confirmed CRS manifestation = Congenital rubella infection (CRI)	<input type="checkbox"/>

Investigator

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Table A7.2.
Case investigation
form for suspected
measles or rubella

Page 1

Fill in this form for case investigation and reporting of suspected measles or rubella

Report date: - -	Region: _____	District: _____
Date of investigation: - -		Date of notification: _____
Initial classification (please check): Measles <input type="checkbox"/> Rubella <input type="checkbox"/> Rash fever <input type="checkbox"/>		
Outbreak associated: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>		Outbreak ID: _____

A. Identification

Name: _____	Case number: _____	Sex: Male <input type="checkbox"/> Female <input type="checkbox"/>
Age: Years _____ Months _____	Date of birth: - -	Address: _____
Source of notification: Public <input type="checkbox"/> Laboratory <input type="checkbox"/> Community <input type="checkbox"/> Active search <input type="checkbox"/>		
Contact to suspect case <input type="checkbox"/> Other <input type="checkbox"/>		
Name of mother: _____		
Vaccination; number of doses received: Last vaccination date: _____		
Measles 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> >2 <input type="checkbox"/> Nk <input type="checkbox"/>	- -	Written record: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>
Rubella 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> >2 <input type="checkbox"/> Nk <input type="checkbox"/>	- -	Written record: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>
Pregnancy: Yes <input type="checkbox"/> No <input type="checkbox"/> Due date: - -		

B. Clinical information

Rash: Yes <input type="checkbox"/> No <input type="checkbox"/> If yes: Date of onset - -		Duration (days): _____
Site of initial rash: Retroauricular <input type="checkbox"/> Face <input type="checkbox"/> Neck <input type="checkbox"/> Thorax <input type="checkbox"/> Other <input type="checkbox"/> , specify: _____		
Type of rash: Maculopapular <input type="checkbox"/> Vesicular <input type="checkbox"/> Other <input type="checkbox"/> , specify: _____		
Other symptoms:		Presence of complications? Yes <input type="checkbox"/> No <input type="checkbox"/>
Fever: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	Pneumonia: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	
Coryza: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	Malnutrition: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	
Cough: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	Diarrhoea: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	
Conjunctivitis: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	Encephalitis: Yes <input type="checkbox"/> No <input type="checkbox"/> Nk <input type="checkbox"/>	
Outcome:	Other: Yes No Nk	
Hospitalized: Yes <input type="checkbox"/> No <input type="checkbox"/> Name of hospital: _____		
Death: Yes <input type="checkbox"/> No <input type="checkbox"/> Lost to follow up <input type="checkbox"/> Date of death: - - Cause of death: _____		

Table A7.2.
Case investigation form for
suspected measles or rubella
(continued)

C. Possible source of infection

Did the case have contact with another suspected case of measles 7–23 days before onset of rash?
 Yes No Nk If yes, who? _____ Where? _____

Was there any suspected case of measles in the area before this case?
 Yes No Nk

Did the case travel 7–23 days before onset of rash?
 Yes No Nk If yes, where? _____

Does the case work in tourism or in area with a large flow of international tourists/persons?
 Yes No Nk

Is the case epidemiologically linked to an imported case?
 Yes No Nk If yes, who? _____ Where? _____

D. Final classification

Measles Rubella Vaccine reaction Other Not known

Confirmed by: Laboratory Epidemiological link Clinical diagnosis Not done

Vaccine related Discarded

Imported: Yes No Nk If yes, from? _____ Date of final classification: - - -

Investigated by

Name: _____ Position: _____

Date of investigation: - - - Observations: _____

Signature: _____

GLOSSARY

Congenital rubella infection (CRI) Fetal infection with the rubella virus that can lead to miscarriage, fetal death or the birth of a normal infant or one with some or all of the manifestations of CRS.

Congenital rubella syndrome (CRS) One of the possible outcomes of rubella infection *in utero*, particularly during the first trimester. The birth defects associated with CRS include heart disease, blindness, hearing impairment, and developmental delay or mental retardation.

Measles control The routine, regular and ongoing use of measles vaccine to reduce measles morbidity and mortality, carried out in accordance with targets.

Measles elimination A dynamic situation in a large and well populated geographical area in which endemic measles transmission cannot occur and sustained transmission does not occur, following the occurrence of an imported case. All isolated cases and chains of transmission must be linked to an importation.

Health care facility A hospital, private clinic, pharmacy or public health clinic where health surveillance activities (e.g. detection, investigation, analysis and reporting) can take place.

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Measles and rubella remain important causes of vaccine-preventable disease and death in the European Region of WHO. The *Strategic plan for measles and congenital rubella infection in the European Region of WHO* identifies key strategies to meet the targets for interrupting indigenous measles transmission and preventing congenital rubella infection (< 1 case of congenital rubella syndrome per 100 000 live births) by 2010; strengthening surveillance systems by vigorous case investigation and laboratory confirmation is one of these key strategies. Surveillance indicators identified in these surveillance guidelines will be critical for assessing whether Member States have achieved the disease targets. The *Surveillance guidelines for measles and congenital rubella infection* are intended to provide technical advice on the design and implementation of surveillance programmes for these diseases.

