



**PACIFIC PUBLIC HEALTH SURVEILLANCE NETWORK  
REFERENCE GUIDE**

**ACUTE FEVER AND RASH SURVEILLANCE  
FOR MEASLES AND RUBELLA ELIMINATION**

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## TABLE OF CONTENTS

1. INTRODUCTION AND OVERVIEW .....	3
2. BASIC DISEASE FACTS .....	4
2.1 Description of disease .....	4
2.2 Agent and infectious doses .....	5
2.3 Epidemiology .....	5
3. ROUTINE SURVEILLANCE.....	8
3.1 Surveillance case definition .....	8
3.2 Recommended surveillance system .....	9
3.3 Urgency of reporting .....	10
3.4 Flow of reports.....	10
3.5 Minimum data set .....	10
3.6 Data analysis and interpretation.....	11
4. INITIAL ACTION AND RESPONSIBILITIES .....	12
4.1 Setting up an outbreak control team .....	13
4.2 Staff responsibilities for the various actions (may be listed in an annex) .....	13
4.3 Clinical assessment of suspected patients.....	14
4.4 Enhanced surveillance .....	14
4.5 Creating and maintaining a line list (and maybe a spot map).....	14
4.6 Searching for a source.....	15
4.7 Communications .....	15
4.8 Laboratory diagnosis.....	15
4.9 Initial community interventions .....	17
4.10 External (international) reporting, requests for support, and coordination among agencies .....	17
5. CASE MANAGEMENT – the clinical response.....	17
6. OUTBREAK INVESTIGATION, PREVENTION AND CONTROL – the public health response....	18
6.1 Individual case .....	18
6.2 Contacts.....	19
6.3 Outbreak.....	20
6.4 Disaster implications.....	21
7. REFERENCES AND FURTHER SOURCES OF INFORMATION .....	21
8. ANNEXES .....	22
9. HISTORY OF GUIDELINE.....	22

## 1. INTRODUCTION AND OVERVIEW

Measles is a serious and highly communicable acute febrile rash illness that can be prevented easily and inexpensively through vaccination, yet still kills hundreds of thousands of children every year. There are global targets for major reductions in the numbers of measles cases and fatalities compared to the 1999 levels, and considerable progress has been made worldwide. Several World Health Organisation (WHO) Regions have gone further and resolved to eliminate measles - including the Western Pacific Region, which made this commitment in September 2003 (with a target date to be set as soon as possible).

Measles elimination is defined as “a dynamic situation in a large and well populated geographical area where endemic measles transmission cannot occur and where sustained transmission does not occur following the reintroduction of measles virus by an imported case. All isolated cases and chains of transmission should be linked to importations. To maintain elimination, regions must sustain high population immunity through vaccination.”<sup>1</sup>

Of the twenty-two Pacific Island countries and territories (PICTs) covered by the Pacific Public Health Surveillance Network (PPHSN), only Papua New Guinea – with 3,863 cases reported in 2003 - is still experiencing intense transmission of measles. Many of the other countries had both measles outbreaks and mass measles immunisation activities in 1997-98, which led to the cessation of endemic transmission of measles. A large outbreak of measles - 828 cases over a period of four months - did occur after an importation in the Marshall Islands in 2003, however this was considered to fall short of a re-establishment of endemicity, which was prevented by a mass immunisation campaign.<sup>2</sup>

Rubella is another communicable acute febrile rash illness which is attracting increasing attention as measles elimination is achieved. Generally a mild illness, rubella can however have serious complications, including devastating effects on unborn babies whose mothers contract it during pregnancy. Prevention of congenital rubella syndrome (CRS) is the main reason for countries to immunise against rubella. Primary rubella illness itself is also not insignificant, as recent outbreaks in Tonga (2002) and Samoa (2003) have shown with much higher rates of rubella encephalitis than previously documented elsewhere. (The rate of encephalitis in these two outbreaks was estimated at 1 in 300 to 1 in 1,500 cases - as compared to previous estimates of 1 in 6,000 cases based on limited information from the USA and Japan)<sup>3</sup>.

In some countries the importance of rubella is only recognised after measles is controlled, as cases of rubella may previously have been mistaken for measles due to their similar symptoms of fever and maculopapular rash. Other countries – including some in the Pacific – may have eliminated rubella at the same time as they eliminated measles, by using a combined vaccine: either measles-rubella (MR) or measles-mumps-rubella (MMR) vaccine. As measles elimination is achieved and maintained, countries still using single measles vaccine have the opportunity to add rubella vaccine to their immunisation schedule and eliminate rubella and CRS as well. This must be done carefully, however, ensuring that all age-groups at risk can be protected and that continued high coverage with a rubella-containing vaccine is sustainable in the long term - as inadequate rubella vaccination programmes can actually increase the risk of congenital rubella syndrome in populations.

Measles and rubella are both acute febrile rash illnesses. Particularly as they become less common due to elimination efforts, it can be difficult to distinguish them clinically from each other or from other febrile rash illnesses. At the same time, as elimination is reached and maintained, it becomes more important to promptly identify any cases of measles or rubella to ensure that widespread local transmission is not re-established. In the late 1990s, WHO and the PPHSN introduced surveillance for “suspected measles” and integrated it into the pre-existing hospital-based active surveillance system for acute flaccid paralysis (AFP) and neonatal tetanus. Within a few years “suspected measles” was replaced with the term “acute rash and fever”, also known as “acute fever and rash” or “acute febrile rash” (AFR), and sometimes more clearly specified as “acute (non-vesicular) rash and fever.” This guideline introduces the operational definition of AFR as any **acute febrile illness with maculopapular rash**. Specifying the character of the rash in this way allows clinicians to be more selective of the cases they report and/or investigate, while at the same time remaining broad enough to catch virtually any case of measles, as well as rubella or dengue cases presenting with rash.

Although attached to the active AFP surveillance system, AFR surveillance is in practice a “stimulated passive” system, since hospital record reviews are not carried out regularly for AFR (as they are for AFP). Clinicians in hospitals are

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<sup>1</sup> Monitoring the interruption of indigenous measles transmission, Cape Town meeting, 14 October 2003. Weekly Epidemiological record 13 February 2004; 79 (7): 70-72.

<sup>2</sup> Western Pacific Regional Guidelines: Introducing Rubella Vaccine (Draft 25 March 2004)

<sup>3</sup> Western Pacific Regional Guidelines: Introducing Rubella Vaccine (Draft 25 March 2004)

required to report cases of AFR promptly to the designated Hospital Coordinator or National Coordinator. The Coordinator reviews the case details, arranges investigation as necessary in collaboration with the clinician, and activates the EpiNet team as appropriate to take rapid public health action. This includes informing neighbouring countries via PacNet. Every month the Hospital Coordinator also has the designated “key clinicians” sign a form (Annex 2) stating whether they have seen any cases of AFR (or AFP or neonatal tetanus) that month. Any new cases picked up in this way are investigated as appropriate at the time, and all the information is forwarded to the National Coordinator, who periodically provides a summary to WHO/ PPHSN.

“Key clinicians” generally include all those responsible for paediatric patients - including both inpatients and outpatients. In many PICTs, hospital outpatient departments are the first point of contact with the health care system, providing primary care (often located outside hospitals in other countries). Thus, cases of AFR need not be admitted to be picked up by the surveillance system.

AFR is primarily intended as a marker for measles, and the system requires that all cases identified that fit this syndromic description be investigated for possible measles; a diagnosis of rubella should also be considered. The first step in investigation is to determine whether the case fits the clinical case definition for either measles or rubella. As laboratory access and capacity increase, the aim is that all cases of suspected measles or rubella - at least in the early stages of an outbreak - will have blood taken and tested for measles and rubella IgM.

AFR is a sensitive marker for measles, as (virtually) all measles cases will be among all AFR cases. Because measles often causes severe illness, it is likely that at least some cases in an outbreak will present to hospital and be picked up through the active surveillance system. The system would be expected to be less sensitive for rubella, as most cases of rubella infection are mild and do not present to hospital, and many do not manifest a rash at all. In recent outbreaks in the Pacific (Tonga, 2002 and Samoa, 2003), however, rubella has caused more severe illness and higher rates of complications than had been documented in previous outbreaks elsewhere. It is thus possible that hospital-based surveillance may be more sensitive for rubella in the Pacific than would otherwise be expected.

Surveillance for measles and rubella is not confined to the hospital-based active AFR surveillance system. All countries maintain passive surveillance systems in which all medical practitioners (or all clinicians) – including those working in primary care - are required to notify public health authorities of designated conditions. These would usually include measles and rubella, notifiable on suspicion, and may also include AFR. Where these systems function well, they can potentially alert authorities to the circulation of rubella or measles before it is picked up by the hospital system. While primary care clinicians may not be expected to investigate or notify all cases of AFR as should happen in hospitals, publicising the fact that AFR can be a marker for measles or rubella increases awareness among clinicians and the public and can lead to improved detection of disease circulation.

As the syndrome of AFR is not unique to measles and rubella, the AFR surveillance system may also help in the identification of cases or outbreaks of other diseases. An important example in the Pacific is dengue fever, which – while it may have a different clinical picture to measles or rubella - also produces a maculopapular rash along with fever, and can often be mistaken for measles – or vice versa – in areas where it occurs. For example, in Puerto Rico in 1985, of 94 cases of rash illness that met the measles case definition, 23% were serologically confirmed as measles, but 34% more were serologically confirmed as dengue<sup>4</sup>. Surveillance for dengue is undertaken separately and covered in another chapter of this manual. The clinical similarity, however, makes it important to ensure that laboratory confirmation is obtained wherever possible; in many PICTs this may mean initial use of the available rapid test for dengue.

The differential diagnosis of AFR is wide and may include human parvovirus, scarlet fever, drug reactions, secondary syphilis, erythema infectiosum, meningococcal disease, dengue hemorrhagic fever and infectious mononucleosis as well as echo-, coxsackie-, and adenovirus infections.)

## **2. BASIC DISEASE FACTS**

### **2.1 Description of disease**

#### 2.1.1 Measles

Measles - also known as English measles to distinguish it from German measles or rubella - is an acute, highly communicable viral disease characterized by a generalized maculopapular rash with prodromal fever and respiratory

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<sup>4</sup> Dietz VJ, Nieburg P, Gubler DJ, Gomez I, Diagnosis of measles by clinical case definition in dengue-endemic areas: implications for measles surveillance and control. Bulletin of the WHO 1992; 70(6):745-750

symptoms (coryza, cough), conjunctivitis and/or Koplik spots (small spots with white centres on an erythematous base, found on the buccal mucosa. These are pathognomonic for measles but are not always seen). The illness typically begins, after a 7- to 21-day incubation period, with fever, coryza, hacking cough and conjunctivitis. Koplik's spots may appear 2 to 4 days later, and the characteristic rash usually 1 to 2 days after that, beginning in front of and below the ears and on the sides of the neck and spreading rapidly (within 24 to 48 hours) to the trunk and extremities, as it begins to fade on the face. At the peak of the illness, the temperature may be greater than 40 degrees Celsius (104 degrees Fahrenheit); patients generally appear quite ill. Bacterial superinfections, including pneumonia and otitis media, are common. Less common complications include acute thrombocytopenic purpura, encephalitis (one in 1000-2000 cases of measles) and the rare late manifestation of persistent measles infection, subacute sclerosing panencephalitis. (Although rare world-wide, the highest incidence of SSPE in the world has been reported from the Pacific, with an annual incidence of 98 per million population under twenty years of age observed in Papua New Guinea's Eastern Highlands Province in 1997-1998 - more than ten times higher than the highest incidence in the prevaccine era reported from elsewhere)<sup>5</sup>. Measles and its complications are particularly severe among malnourished or immunocompromised children.

### 2.1.2 Rubella

Rubella - also known as German measles or three-day measles - is a mild febrile viral disease with a diffuse punctate and maculopapular rash which sometimes resembles that of measles, although it is usually less extensive and disappears more quickly. Many cases are misdiagnosed or are mild and go unnoticed. After a 14- to 21-day incubation period, a 1- to 5-day prodrome of low-grade fever, malaise, mild coryza and conjunctivitis and lymphadenopathy may occur, followed by the rash which appears on the face and neck and spreads quickly to the trunk and extremities. Tender swelling of the suboccipital, postauricular, and postcervical glands is characteristic and, with the typical rash, suggests the diagnosis. Arthralgia and occasional transient arthritis may occur; otitis media and encephalitis are rare complications. The public health importance of rubella lies in its ability to produce anomalies in the developing fetus. Congenital rubella syndrome, consisting of malformations of major organ systems, occurs in 80% of infants born to women infected during the first trimester of pregnancy<sup>6</sup> - even where infection has been clinically inapparent.

## **2.2 Agent and infectious doses**

Measles virus is a member of the genus *Morbillivirus* of the family Paramyxoviridae. Measles is one of the most highly communicable diseases of humans, such that people are considered contacts if they have been in an enclosed air space with an infectious measles patient for an hour.

Rubella virus is a member of the genus *Rubivirus* of the family Togaviridae. Rubella is less readily transmitted than measles but still considered moderately to highly infectious.

## **2.3 Epidemiology**

### 2.3.1 Source

Humans are the only reservoir for both measles and rubella viruses.

### 2.3.2 Occurrence

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<sup>5</sup> Takasu T, Mgone JM, Mgone CS, Miki K, Komase K, Namae H, Saito Y, Kokubun Y, Nishimura T, Kawanishi R, Mizutani T, Markus TJ, Kono J, Asuo PG, Alpers MP, A continuing high incidence of subacute sclerosing panencephalitis (SSPE) in the Eastern Highlands of Papua New Guinea. *Epidemiol Infect* 2003 Oct; 131(2):887-98

<sup>6</sup> Chantler J, Wolinsky JS, Tingle A. Rubella Virus. In : Knipe DM, Howley PM, editors. *Fields Virology*. 4th edition. Philadelphia: Lippincott Williams and Wilkins, 2001:963-990

Prior to widespread immunisation, measles circulated worldwide and almost everybody was infected, usually in childhood. In large metropolitan communities it was endemic (circulated constantly), reaching epidemic proportions every other year or so. Isolated communities tended to experience more widely spaced and severe outbreaks in which a large proportion of the population could be infected in a short space of time, with higher case-fatality rates. With effective childhood immunisation programmes, measles incidence declined markedly and endemic transmission has been interrupted in parts of the world.

In the absence of rubella immunisation, rubella is primarily a disease of childhood but occurs more often in adolescents and adults than did measles. Countries that do not vaccinate against rubella generally experience rubella epidemics every 5 to 9 years, with 10-40 cases of CRS per 10,000 births following epidemics and additional cases of rubella (with much lower CRS rates) in between epidemics. An overall estimate of CRS burden (in the absence of rubella immunisation) would be 1-10 cases per 10,000 births<sup>1</sup>. If infant rubella immunisation is introduced in isolation, the median age of those with acute rubella infection will increase. This increasing age of infection may mean that greater numbers of women of child-bearing age are infected, potentially leading to an increase in CRS cases compared to pre-vaccine levels.

### 2.3.3 Mode of transmission

Measles transmission is airborne or by droplet spread, direct contact with nasal or throat secretions of infected persons, or – less commonly – by articles freshly soiled with nose and throat secretions. Measles is one of the most highly communicable infectious diseases.

Rubella transmission is by contact with nasopharyngeal secretions of infected people – by droplet spread or direct contact with patients. Infants with congenital rubella syndrome or infection shed large quantities of virus in their nasopharyngeal secretions and their urine.

### 2.3.4 Period of communicability

Measles is most communicable from four days before rash onset to four days after rash onset.

Rubella is communicable from about one week before until seven days<sup>7</sup> after the onset of the rash. Infants with CRS may remain infectious for several months after birth.

### 2.3.5 Incubation period

The incubation period for measles is usually about ten days but can range from seven to twenty-one days.

The incubation period for rubella ranges from fourteen to twenty-one days.

### 2.3.6 Vulnerable population sub-groups

People who have not been immunised against nor infected with measles remain susceptible to contracting it if they come into contact with an infectious case. The exception is young babies of women immune to measles, who have “passive” protection for the few months of life from maternal antibodies transferred across the placenta before birth. Partly because of this passive immunity in young babies, the effectiveness of vaccination is age-dependent. A single dose of measles-containing vaccine (MCV) produces protective antibodies in about 85% of babies when given at 9 months of age, 90% at 12 months and 95% at 15 months. Most of those who fail to seroconvert (i.e. develop antibodies) with a single dose will do so with a second dose given at least a month later.

When about 95% of the population is immune to measles (through vaccination or infection), any measles virus that enters will be unable to circulate for long or to cause many cases. Many of those who remain susceptible will be protected from contracting measles by the community or “herd” protection that stops circulation of the virus before it can reach them. Vulnerable population subgroups are thus those groups in which population immunity is less than about 95%. Given that a single dose of MCV protects 90% of babies who receive it at 12 months of age, as outlined above, it is clear that a second opportunity for MCV is necessary to reach through immunisation the very high level of population immunity needed to maintain measles elimination. Thus, countries which have not introduced a second MCV opportunity will have vulnerable populations. Young infants and malnourished children – particularly those with clinical or sub-clinical vitamin A deficiency - are most at risk of developing severe complications of measles.

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<sup>7</sup> WHO WPRO, Western Pacific Regional Guidelines: Introducing rubella vaccine. Draft 25 Mar 2004 (NB sources differ – Chin says “at least four days”)

People who have not been immunised against rubella nor infected with rubella virus remain susceptible to contracting it if they come into contact with an infectious case. A single dose of rubella vaccine elicits protective antibodies in 98-99% of susceptibles vaccinated. Most rubella circulation and the highest attack rates are in young children - although compared with measles pre-immunisation, a much higher proportion (10-25%) of people remain susceptible to rubella into adulthood. The most vulnerable population sub-group is foetuses of women who are not immune to rubella. Although available evidence suggests that rubella vaccination during pregnancy is not harmful to the developing foetus, it is recommended that rubella vaccine is not used to vaccinate a pregnant woman and that any woman who has received rubella vaccine avoids pregnancy for at least 3 months.

Where rubella immunisation is in place in the form of MR or MMR vaccination, the level of immunisation activity required for measles elimination is more than enough to maintain elimination of rubella also, since it is less infectious than measles. Rubella vaccine is usually introduced, however, when measles vaccination is already well established. At the time that immunisation programmes introduce rubella vaccine, they must take care that a large proportion of people susceptible to rubella are protected through an introductory vaccination campaign reaching as wide an age range as necessary – at least all primary school and pre-school age children, as these are the most important groups in spreading the virus in the community. People outside the campaign age-range will remain individually susceptible to rubella, but will be protected by the cessation or sharp drop in virus circulation. Inadequately-planned rubella vaccine introduction can actually increase the risk of CRS by leaving many older children, adolescents and adults unprotected without stopping the circulation of the virus, thus pushing the disease into these age groups (which include pregnant women).

### 2.3.7 Risk in the Pacific

Measles was first seen in the Pacific in the mid to late 19<sup>th</sup> century, with devastating results among Fijians and New Zealand Maori<sup>8</sup>. In the pre-vaccine era, there were many large outbreaks of measles every year in the Pacific. After the introduction of measles vaccine from about 1982, the number and size of outbreaks declined, although there continued to be about four measles outbreaks each year Pacific-wide. In 1997-1998 there were both outbreaks and national measles campaigns in several countries; afterwards it became clear that endemic transmission of measles had ceased in these areas (Papua New Guinea being an important exception).

Absence of disease, however, does not guarantee absence of risk. If immunisation coverage is not sustained at very high levels among succeeding cohorts of children, the number of susceptibles accumulates through the birth of babies, and large numbers of people are left vulnerable to contracting measles if an infectious case enters the country. This was illustrated by an outbreak in the Marshall Islands in 2003 in which an importation led to 828 cases of measles, including 100 hospitalisations and 3 deaths over a period of four months, and which required the imposition of travel restrictions and a major vaccination campaign to bring it under control. It is possible for other countries – particularly those without a second opportunity for measles vaccination – unknowingly to accumulate large enough numbers of susceptibles to sustain a large outbreak in the event of an importation, even with relatively high reported immunisation coverage. The late complication of subacute sclerosing panencephalitis (SSPE) could potentially occur at high rates - as reported from Papua New Guinea<sup>9</sup> - in other countries in the Pacific, but these would not necessarily be immediately apparent due to difficulties with diagnosis of SSPE.

The Pacific has experienced recent rubella epidemics in Tonga (2002) and Samoa (2003), which have both now introduced rubella vaccine in response. There was a much higher incidence of rubella encephalitis in each of these epidemics than had previously been documented elsewhere: 1 in 300 to 1 in 1,500 cases, as compared to 1 in 6,000 cases estimated from limited data in Japan and the USA<sup>10</sup>. The CRS burden has not been identified for the Pacific despite many documented rubella epidemics. Several countries and territories in the Pacific do not include rubella in their routine immunisation schedules, leaving their populations vulnerable to epidemics of rubella. In some areas rubella vaccination is available through the private sector or to significant numbers of children through travel to and from neighbouring countries. This has the potential to alter the epidemiology of the disease and eventually lead to more CRS cases.

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<sup>8</sup> New Zealand Ministry of Health, Immunisation Handbook 2002

<sup>9</sup> Takasu T, Mgone JM, Mgone CS, Miki K, Komase K, Namae H, Saito Y, Kokubun Y, Nishimura T, Kawanishi R, Mizutani T, Markus TJ, Kono J, Asuo PG, Alpers MP, A continuing high incidence of subacute sclerosing panencephalitis (SSPE) in the Eastern Highlands of Papua New Guinea. *Epidemiol Infect* 2003 Oct; 131(2):887-98

<sup>10</sup> Western Pacific Regional Guidelines: Introducing Rubella Vaccine (Draft 25 March 2004)

### 3. ROUTINE SURVEILLANCE

#### 3.1 Surveillance case definition

3.1.1 “Acute fever and rash” refers to any acute febrile illness with maculopapular rash. This is used as a marker for possible measles or rubella. Cases of AFR should be investigated for measles and rubella – initially using national case definitions but increasingly, because of the difficulties with clinical diagnosis of these diseases, using laboratory tests.

Case definitions of suspected measles and rubella may vary slightly by country but are generally based on the WHO-recommended definitions below.

Laboratory criteria for diagnosing measles and rubella are given below. Eventual case classification depends on laboratory results.

##### 3.1.2 Measles

*Clinical case definition:*

Any person with fever, **and** maculopapular (i.e. non-vesicular) rash, **and** one of the following: cough, coryza (i.e. runny nose) or conjunctivitis (i.e. red eyes)  
- **Or**, any person in whom a clinician suspects measles infection.

*Laboratory criteria for confirmation of diagnosis:*

- Presence of measles-specific IgM antibodies in blood (serum or dried blood spot) taken within 28 days after rash onset *or*
- Demonstration of a four-fold rise in measles-specific IgG between acute and convalescent samples, *or*
- Isolation of measles virus from throat swab, urine or blood (lymphocytes), *or*
- Detection of measles antigen in dried oral secretions by immunofluorescence (IF), *or*
- Detection of measles RNA from throat swab, urine, blood (lymphocytes or dried) or dried oral secretions by reverse transcriptase polymerase chain reaction (RT-PCR)

in the presence of a clinically-compatible illness and in the absence of recent measles immunisation (in the preceding 6 weeks).

##### 3.1.3 Rubella

*Clinical case definition:*

Any patient of any age in whom a health worker suspects rubella. A health worker should suspect rubella when the patient presents with fever, maculopapular rash, and one of the following: cervical, sub-occipital or post-auricular adenopathy; or arthralgia/ arthritis.

*Laboratory criteria for confirmation of diagnosis:*

- Presence of rubella-specific IgM antibodies in blood (serum or dried blood spot) taken within 28 days after rash onset, *or*
- Demonstration of a four-fold rise in rubella-specific IgG between acute and convalescent samples, *or*
- Isolation of rubella virus from throat swab, urine or blood (lymphocytes), *or*
- Detection of rubella antigen in dried oral secretions by immunofluorescence (IF), *or*
- Detection of rubella RNA from throat swab, urine, blood (lymphocytes or dried) or dried oral secretions by reverse transcriptase polymerase chain reaction (RT-PCR)

in the presence of a clinically-compatible illness and in the absence of recent rubella immunisation.

##### 3.1.4 Case classification (generic):

**Suspected case:** A case that meets the clinical case definition but for which laboratory confirmation is not available (or not yet available).

**Laboratory-confirmed case:** A case that meets the clinical case definition and at least one of the laboratory criteria for confirmation of diagnosis.

**Epidemiologically-confirmed case:** A case that meets the clinical case definition and is epidemiologically linked to a laboratory-confirmed case.

Discarded case: A suspected case in which laboratory criteria for confirmation of diagnosis are not met (negative test or tests) and/or an alternative diagnosis is confirmed; or a reported case which, on investigation, is found not to meet the clinical case definition.

### **3.2 Recommended surveillance system**

#### 3.2.1 Acute fever and rash

Recommended AFR surveillance in all PICTs is “active”(strictly speaking, stimulated passive - as explained above) surveillance, in which hospital clinicians should report all AFR cases promptly and selected key clinicians are asked monthly whether they have seen any cases.

Outside hospitals, primary care clinicians are generally not required to report all AFR cases, nor followed up about cases they may have seen. Nevertheless, all clinicians should be made aware that AFR (acute febrile illness with maculopapular rash) can be a marker for measles or rubella, and should notify public health authorities promptly if they are seeing unusually high numbers of AFR cases – particularly if one or more of these is confirmed as measles or rubella (or dengue).

#### 3.2.2 Measles

Recommended surveillance for measles in all Pacific island countries and territories at the present time includes

- (1) active surveillance for AFR in hospitals
- (2) passive surveillance for measles and rubella, or AFR, in primary care
- (3) population immunity surveillance (in the form of ongoing monitoring of measles immunisation coverage at all levels to ensure high two-dose coverage in each birth cohort)

Laboratory testing for measles- and rubella-specific IgM should be carried out on all cases from (1) and (2) meeting the measles (and/or rubella) case definition. Surveillance staff must remember that this definition includes “any person in whom a clinician suspects measles infection.” Clinicians should maintain a high index of suspicion for measles, as cases can present without the classical signs and be difficult to diagnose clinically. Thus the threshold for carrying out laboratory tests should be relatively low: any case that clinicians think could be measles (even if the diagnosis is not strongly suspected) may be tested. Consideration should also be given to testing for measles- and rubella-specific IgG, particularly if the specimen was collected early in the illness and is negative for both measles- and rubella-specific IgM.

Because measles is targeted for elimination, surveillance of population immunity is necessary to ensure that numbers of susceptible children do not increase to the point at which an importation of measles would cause a large epidemic. In every birth cohort (babies born in the same year) at least 95% must be immune by the time they enter school to ensure that overall population immunity remains high enough to stop the spread of measles if it is reintroduced.

The impact of an immunisation programme depends on both the coverage and the age(s) that vaccination is scheduled. The proportion that will be immune due to vaccination in each birth cohort can be calculated using these two pieces of information. For example, 80% coverage with MCV given at 12 months (90% efficacy – see section 2.3.6 above) will protect 72% of the birth cohort against measles. The remaining 28%, consisting of the 20% unvaccinated and 10% of the vaccinated (i.e. 8% of the total) will remain susceptible. A second opportunity in which MCV is given 15 months will protect 95% of susceptible children who receive the vaccine. If coverage is again 80%, randomly distributed between those immune from an earlier dose and those remaining susceptible, 76% of the susceptibles – i.e. a further 21% of the total – will seroconvert. Thus 93% of the birth cohort will be immune to measles (assuming no additional children have become immune through contracting the disease). Annex 1 contains an illustration of these principles using an alternative scenario.

#### 3.2.3 Rubella

Recommended surveillance for rubella includes

- (1) active surveillance for AFR in hospitals
- (2) passive surveillance for rubella and measles, or AFR, in primary care
- (3) (as appropriate) surveillance for congenital rubella syndrome

Laboratory testing for rubella- and measles-specific IgM should be carried out on cases from (1) and (2) that meet the rubella (and/or measles) case definition. Surveillance staff must remember that the case definition for rubella includes “any patient of any age in whom a health worker suspects rubella.” Clinicians should maintain a high index of suspicion

for rubella, as it is extremely difficult to recognise and cannot reliably be diagnosed clinically. Thus the threshold for carrying out laboratory tests should be fairly low: any case that clinicians think could be rubella (even if the diagnosis is not strongly suspected) may be tested. Consideration should also be given to testing for rubella- and measles-specific IgG, particularly if the specimen was collected early in the illness and is negative for both rubella- and measles-specific IgM.

Some form of assessment of the burden of disease due to rubella – via either surveillance for congenital rubella syndrome or other studies - is important for countries considering introducing rubella vaccine, as well as those which already include it in their immunisation schedule. Setting up surveillance or carrying out studies should not, however, delay the introduction of rubella vaccine. CRS surveillance, particularly, requires considerable resources. An indication of the challenges may be seen in the fact that surveillance has not identified the burden of CRS in Tonga or Samoa despite recurrent large rubella epidemics. In the Pacific, countries may wish to use the likely estimated incidence of CRS of 1-10 cases per 10,000 births in the absence of a rubella immunisation programme as a basis for decision making<sup>11</sup>.

### **3.3 Urgency of reporting**

Reporting should be prompt (on the same day) and by the most efficient means available (e.g. telephone, radio or fax) when a case of suspected measles, rubella or AFR is seen in a hospital or primary care.

Monthly reports on cases of AFR seen in hospitals designated active surveillance sites are also elicited via the Monthly EPI Surveillance Form (Annex 2). If any cases had been seen in the previous month, they should already have been reported by clinicians at the time. The monthly report should thus be merely a back-up and a method for “zero reporting” - i.e. confirming no cases had been seen if no reports had been received. (Primary care clinicians are generally not requested to provide “zero reports”).

### **3.4 Flow of reports**

Prompt reporting of suspected measles or rubella, or AFR, by primary care clinicians should be to the person in charge of the nearest health facility (who would then report to the EpiNet team). Prompt reporting of AFR by hospital clinicians should be to the Hospital Coordinator and/or National Coordinator.

If an outbreak of AFR is detected, or measles or rubella is confirmed by laboratory testing, the national EpiNet team (usually the National Coordinator) should report the situation promptly to PacNet to allow neighbouring countries to be alert and prepared for any possible regional transmission of disease – as well as to seek regional support if needed. Prior to confirmation, information on suspected cases or outbreaks can be shared, and support sought from regional colleagues in a confidential forum, via PacNet-restricted.

The Monthly EPI Surveillance Form, once completed and signed by all key clinicians, is forwarded by the Hospital Coordinator to the National Coordinator each month. The National Coordinator provides the aggregated information from all hospitals in the country to WHO/ PPHSN at regular intervals (monthly or quarterly).

### **3.5 Minimum data set**

The principles agreed by the Interagency Meeting on Health Information Requirements in the South Pacific (Noumea 1995) must be observed in collecting, using and sharing data for acute rash and fever (measles and rubella) surveillance. These include:

The data collected for each condition under surveillance should be the minimum required to enable appropriate analysis of the data (i.e. minimal data sets) leading to appropriate public health action.

Data definitions and minimal datasets should be consistently defined (within countries and regionally).

Information sharing at the regional level should reflect the principle of local value. That is, Regional International Agencies should request only a subset of the data being collected at national level.

Data provided to higher levels of governance (e.g. district to country, country to region) should be more highly aggregated than that collected and used at the lower level.

The investigation form(s) used around the Pacific therefore represents the minimum data required to be collected for each case, while data to be shared at higher levels will be derived by aggregating these basic local data. An integrated form for the investigation of acute rash and fever cases has now been developed and is recommended for use around the Pacific (Annex 3).

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<sup>11</sup> WHO WPRO, Western Pacific Regional Guidelines: introducing rubella vaccine (draft 25 Mar 2004)

Categories of information collected include:

Report/ investigation information

Case identification

Immunisation history

Signs and symptoms

Laboratory investigations

Possible source of infection

Final classification

Investigator details

### **3.6 Data analysis and interpretation**

#### 3.6.1 Monitoring, tabulating, and interpreting raw data, indicators

National Coordinators should monitor the proportion and timeliness of monthly active surveillance forms completed and returned to them, and follow up if forms do not arrive, to ensure that the surveillance system continues to function.

Hospital and national coordinators should maintain line-lists of all reported AFR cases, including identifying data, whether they met case definitions for measles or rubella, whether laboratory testing was carried out and final case classifications. (The suspected measles line-list that has been used is in Annex 4). The numbers of cases reported weekly should be plotted on a chart so that time trends can be observed and (eventually – when enough data has accumulated) compared to any expected seasonal variations. Any clusters of cases closely related in time and space, or rising rates of AFR, warrant further investigation to determine the reason.

The “background” rate of AFR in the absence of measles or rubella circulation is not known for the Pacific. As AFR surveillance in the Pacific matures, countries will start to see patterns in the rates of AFR reported and be better able to recognise increased activity. A study in the United States found an incidence of “measles-like illness” in a large managed-care organisation of 4.5 cases per 100,000 persons per year (of which only a very small proportion were investigated for measles).<sup>12</sup>

Another study found widely varying rates world-wide of measles-like illness investigated and ruled out for measles, and proposed a minimum rate of investigation for measles of one case per 100,000 population per year based on the fact that 90% of areas studied exceeded this rate<sup>13</sup>. The standard of at least one measles investigation per 100,000 population per year is also proposed for use or adaptation by countries in the Western Pacific Region<sup>14</sup>. (With the integration of rubella surveillance into the measles surveillance system via AFR and the testing of all cases for both measles- and rubella-specific IgM, all investigated AFR cases would be counted). Using this minimum rate, the Pacific Island region, with a population of approximately eight million, could expect to investigate at least eighty cases of AFR per year. This may be useful indicator, then, for monitoring investigation rates across the sub-region. It is unlikely to be useful for most countries at a national level as the minimum number of investigations expected would range from about 50 (Papua New Guinea) through several each year (Fiji, Solomon Islands) down to one every few decades (Tokelau, Niue).

Because population immunity is important for measles and rubella elimination, immunisation coverage data should also be monitored carefully and used to estimate the overall immunity and size of the pool of susceptibles that has accumulated over several years. Each birth cohort (babies born in the same year) should be considered separately and its overall immunity to measles calculated from the coverage achieved at each of the two immunisation opportunities, as well as its history of disease, as described in section 3.2.2 above and Annex 1. Results of these calculations are combined for the last several birth cohorts. (If children in these cohorts have received at least one dose of rubella vaccine in combination with measles vaccine, overall rubella immunity will be at least equal to that calculated for measles.) The overall percentage of children remaining susceptible is calculated simply as 100% minus the percentage immune.

The purpose of this exercise is to find any “gaps” – cohorts or sub-groups in which population immunity is less than 95% - so that they can be “filled in.” This can be done, for example, by adding a second immunisation opportunity for measles vaccination if the national schedule does not already include one, or planning a mass immunisation campaign targeting the

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<sup>12</sup> Nordin JD, Harpaz R, Harper P, Rush W, Syndromic surveillance for measleslike illnesses in a managed care setting. *J Infect Dis.* 2004 May 1;189 Suppl 1:S222-6

<sup>13</sup> Harpaz R, Papania MJ, Can a minimum rate of investigation of measleslike illnesses serve as a standard for evaluating measles surveillance? *J Infect Dis.* 2004 May 1;189 Suppl 1:S204-9

<sup>14</sup> WHO WPRO, Field guidelines for measles elimination: field test version 27 Mar 2004

age groups affected.

### 3.6.2 Confirmation

A laboratory-confirmed measles case is a suspected case with a positive blood test for measles-specific IgM (or other laboratory test as outlined in section 3.1.2 above) from a laboratory that is part of (or linked to) the WHO Measles Laboratory Network.

An epidemiologically-confirmed measles case is a suspect case with contact/exposure to a laboratory-confirmed case of measles during the 21 days before rash onset (maximum incubation period) while the source was infectious (four days before to four days after rash onset).

A laboratory-confirmed rubella case is a suspected case with a positive blood test for rubella-specific IgM (or other laboratory test as outlined in section 3.1.3 above) from a laboratory that is part of (or linked to) the Measles Laboratory Network.

An epidemiologically-confirmed rubella case is a suspected case with contact/exposure to a laboratory-confirmed case of rubella during the 21 days before rash onset (maximum incubation period) while the source was infectious (seven days before to seven days after rash onset)<sup>15</sup>.

### 3.6.3 Thresholds for action (recognising an outbreak)

A single confirmed case of measles in any country in the elimination phase of measles control – i.e. in most of the Pacific, with the exception of Papua New Guinea, at the present time - is considered an outbreak. If there is no history of travel outside the country in the incubation period, it must be assumed that transmission occurred within the country, and thus that there has been at least one other case (perhaps unreported). Any confirmed case of measles, whether imported or locally acquired, requires immediate comprehensive investigation.

In any of the PICTs which include rubella vaccine in their immunisation schedules, a single confirmed case of rubella or CRS (other than following a known rubella outbreak) is likewise considered an outbreak and requires immediate investigation. In countries where rubella is endemic, an epidemic is a clear increase in the number of cases reported above the expected rate for the time of year; periodic epidemics of rubella are to be expected and may be followed by CRS epidemics. Countries which would consider responding to an identified epidemic of rubella with an immunisation campaign should consider introducing rubella vaccine before the next epidemic occurs.

Surveillance staff may notice unusually high rates of reporting of AFR or suspected measles or rubella from hospital clinicians or primary care, or may be alerted to outbreaks of AFR before any cases are laboratory tested. As increased AFR may signal an outbreak of measles or rubella even if not initially recognised as such, staff should ensure that laboratory tests are carried out promptly.

### 3.6.4 Feedback

Feedback to the people collecting the information is a very important part of the surveillance cycle. Acknowledging receipt of reports is a minimum requirement; preferably, surveillance staff should inform those reporting cases of any public health action that has resulted from the information they provided, and how this contributes to the achievement of specific public health goals. This can be done generally through presentations at clinical meetings or newsletters, or personally to individual clinicians. Positive feedback encourages more complete and prompt reporting in the future. Surveillance staff should avoid couching feedback about incomplete reporting in overly negative terms, but rather seek constructive solutions in partnership with clinicians.

Summarised data on reports received for the 58 reporting hospitals in the twenty PICTs monitored as a distinct sub-region by WHO are posted periodically on PacNet as a form of feedback to surveillance staff at national and hospital levels.

## **4. INITIAL ACTION AND RESPONSIBILITIES**

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<sup>15</sup> WHO WPRO, Western Pacific Regional Guidelines: Introducing rubella vaccine (draft 25 Mar 2004)

Initial action refers to action taken immediately upon recognition of an outbreak of AFR, measles or rubella – without necessarily waiting for laboratory confirmation. (Remember that one case may define an outbreak).

#### **4.1 Setting up an outbreak control team**

Once an outbreak of AFR, measles or rubella has been recognised, urgent public health action is likely to be required (unless population immunity has recently been reviewed and found to be uniformly high). A core team should be assembled or convened to manage the response to the outbreak. Each PICT should have a national EpiNet team, composed of members with skills in notifiable disease data management, clinical medicine, laboratory, field investigations, environmental health and public health management and supervision<sup>16</sup>, appointed previously and already functioning. All members of this team should be informed immediately when an outbreak of measles or rubella is confirmed. (If confirmation has been preceded by recognising increased rates of AFR, they may already be aware that an outbreak is occurring). Available members should meet urgently - without necessarily requiring a quorum - together with available members of any other official surveillance and response team.

A specific Outbreak Task Force should be designated to deal with the operations to control this particular outbreak. This will usually include all EpiNet team members, and also other relevant key people from different sectors and institutions (e.g. primary care, schools, local authorities) as appropriate for the outbreak and its setting. The Task Force represents a minimum core team fully dedicated to the outbreak for the duration necessary. Other responsibilities and commitments of its members should be re-prioritised, postponed or delegated to others. The Task Force leader – often the previously-appointed EpiNet focal point – should be decided at the first meeting. The purpose of the Task Force is to allocate responsibilities, establish communication channels and implement action. Terms of reference and clear objectives for follow-up should be set at the outset.

#### **4.2 Staff responsibilities for the various actions (may be listed in an annex)**

The Task Force carries out the following tasks, delegating as appropriate within or occasionally outside its ranks:

- Formulates terms of reference
- Recruits key personnel from other agencies
- Convenes timely meetings and keeps a record of these
- Liaises with laboratories and the Ministry of Health
- Decides strategies of control and action
- Nominates a media spokesperson
- Briefs staff who may receive enquiries
- Distributes information at timely intervals
- Defines resources needed and negotiates with relevant manager(s) for these as top priority
- Organises implementation of strategies
- Decides when the outbreak is under control and how activities should be scaled back
- Holds a debriefing / evaluation meeting at the end of the outbreak
- Writes a report with recommendation and distributes it to relevant personnel

One of the first tasks of the Outbreak Task Force will be to review the expected level of population immunity using routinely-collected data available on immunisation coverage and disease history of each birth cohort, as described in section 3.6.1 above, if this has not recently been done. The result of this review will determine the strategies the Task Force adopts to deal with the outbreak.

If population immunity is low, measles particularly (but also rubella) will be able to circulate readily and cause many cases, with attendant high morbidity and perhaps mortality. The urgent need, especially with a laboratory-confirmed case of measles in this situation – but also potentially with a suspected case prior to confirmation - will be to increase population immunity rapidly through mass immunisation of susceptible people or groups. The same will apply with a laboratory-confirmed case of rubella if rubella vaccine is already in, or would be considered for, the national schedule. This type of mass vaccination differs from “ring vaccination” in that it does not attempt to block the transmission of disease from any particular case or cases to those immediately surrounding them, but rather to raise the level of immunity of the wider population to ensure that sustained transmission or re-establishment of endemicity do not occur.

If, on the other hand, population immunity is assessed as being uniformly high (>95% across all birth cohorts, areas and

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<sup>16</sup> PPHSN, Proposed generic terms of reference for PICT EpiNet teams. InformAction 17 Dec 2003

sub-groups), mass immunisation should not be necessary. A cluster of cases is still likely, since not everyone will be immune – but the outbreak should be self-limiting. Close attention to its progress will still be necessary, of course, to ensure that the original assumptions hold true. Rapid effective control measures should also be taken to further limit the extent of the outbreak, but these will clearly be much less intensive than organising a mass immunisation campaign at short notice.

### **4.3 Clinical assessment of suspected patients**

Patients suspected of having measles or rubella should be assessed by qualified clinicians. The information in section 2 above may be helpful in this process. In a large outbreak, key messages put out through the mass media by the Outbreak Task Force can inform people of the symptoms and signs of uncomplicated measles or rubella, advise them on how to manage these at home and when to seek medical care, and encourage those eligible to update their immunisations. Suspected cases presenting to health care facilities should be triaged rapidly and, as far as possible, kept isolated from other people during the assessment process - for example by using separate examination rooms in hospitals or clinics. When large numbers of patients are expected at health care facilities, it may be useful to set up a special area to assess them away from others (e.g. in a tent or other space that can be kept separate).

### **4.4 Enhanced surveillance**

#### 4.4.1 Case-finding

The first case of measles or rubella that comes to the attention of surveillance staff may not be the first case to arise in the country, and is unlikely to be the last. A complete investigation will look for

- A possible source of infection for the index case (and each new case for whom the source is not known)
- Potential secondary cases that may have arisen, or may arise after the investigation (contact tracing)
- Other cases without clear epidemiological links to known cases

Search for the first two categories of cases – those which can be linked directly to known cases – will be undertaken as part of the investigation of cases detected through surveillance or contact tracing. A third group of cases may be reported separately as unrelated patients seeking medical care or investigation. Thus, in addition to investigating reported cases, the Outbreak Task Force should communicate with clinicians and/or the public. The occurrence of measles or rubella and the symptoms, signs and case definition of the relevant disease can be publicised to encourage possible cases to seek care appropriately, and clinicians to report suspected cases promptly.

#### 4.4.2 Implementing an outbreak case definition

A specific outbreak case definition should be formulated early in each particular outbreak. This is a list of symptoms and their time of onset which, taken together, suggest that a given person's illness forms part of the outbreak. The outbreak case definition may well need to be developed using the symptoms common among the earliest cases before a definitive diagnosis can be obtained. An outbreak of acute febrile rash illness that could be either measles or rubella might give rise to the outbreak definition “any person in <area, e.g. island or whole country/ territory> presenting after <date> with acute high fever, generalised maculopapular rash and any or all of the following symptoms: cough, runny nose, red eyes, joint pain, body ache and lymphadenopathy.” The start date specified should take into account the range of incubation periods and the degree of certainty around the index case being the first case in the outbreak. The local epidemiological situation – e.g. diseases with similar symptoms that may be prevalent – should also be taken into account.

Once the outbreak organism has been identified through one or more patients being confirmed as having (for example) measles or rubella, cases can be classified as suspected or confirmed based on the results of laboratory tests and epidemiological data – as per the case classification system outlined in section 3.1.4 above.

### **4.5 Creating and maintaining a line list (and maybe a spot map)**

The Outbreak Task Force should create and maintain a central list of all cases meeting the outbreak case definition. The term “line-list” is used to indicate that all vital information about a single case is included in one line, so that each case takes up only one line of the page. The information recorded will include identifying data, vaccination status, possible source, tests taken and final classification.

Wards or clinics where patients may present should also create and maintain their own line-list of suspected cases. (An example of a line-list for suspected measles cases is in Annex 4). These can be used to update and cross-check the central line-list held by the Outbreak Task Force.

“Spot maps” are another useful tool for keeping an overview of the outbreak. Using the patients’ addresses, the locations of suspected and confirmed cases are marked on a map of the island or country/territory. This will clearly show which areas are experiencing intense virus transmission and may be used to direct public health action. Occupational addresses – e.g. schools – should also be mapped if appropriate.

#### **4.6 Searching for a source**

When a country or territory has reached elimination status, a case of measles or rubella arising in a person who has recently (within the incubation period) arrived from an area endemic or epidemic for measles or rubella is most likely have been imported and can be assumed to be the primary case in the country. When, on the other hand, the first case diagnosed with measles or rubella has no history of travel within the time he or she would have contracted the infection, transmission has clearly occurred within the country, and an attempt should be made to identify the source.

The time period within which the patient would have contracted the infection can be determined with reference to a calendar, by using the range of incubation periods together with the date of onset of symptoms. Thus for measles, with an incubation period of 7-21 days, the time period within which the patient would have contracted the infection is from 21 days before the onset of symptoms (usually fever initially) to 7 days before onset of symptoms. For rubella, the patient would have contracted the infection during the period from 21 days before onset of symptoms to 14 days before onset of symptoms. Patients or caregivers should be questioned carefully about the period in question, and whether the case had contact with anyone (particularly a child) who was unwell with respiratory symptoms, fever or rash. (The infectious source may not yet have developed a rash at the time of contact.) Possible sources of infection of the index case should be investigated to the extent possible without hampering the follow-up of susceptible contacts. (Identifying the source of infection is primarily of epidemiological rather than clinical interest. By the time the index case has presented, the source case will no longer be infectious – although secondary cases other than the index case may be).

#### **4.7 Communications**

In an outbreak situation, prompt communication of new developments is vital. All members of the Task Force should be accessible (and available to meet at short notice if necessary). The Task Force should determine at the outset which individuals or groups have an interest in the course of the outbreak, and undertake to keep them informed proactively (i.e. without waiting to be asked each time). Such groups may include hospital clinicians, primary care providers, laboratories, and schools and other institutions where the disease could spread rapidly.

Outbreaks often spark intense public concern, and the community of interest then becomes the general public. Mass media – radio, television, print and electronic media - can be very important in getting key messages across. Again the Task Force should be proactive, appointing a media spokesman at the outset and deciding at each stage what information should be shared and what messages are to be emphasised. Key messages should include signs and symptoms of measles or rubella; that they can be prevented by immunisation; and guidance on symptomatic home management for uncomplicated cases, and when to go to the hospital. Regular press releases or updates on a website can be approved by the Task Force before publication, if appropriate, and should guide the spokesman in any interviews with reporters.

#### **4.8 Laboratory diagnosis**

##### 4.8.1 Field testing/ screening tests

Unfortunately there is no widely available screening test for measles or rubella, and most PICTs will have to send samples overseas for the standard diagnostic tests of measles- or rubella-specific IgM (or alternative tests as outlined in section 3.1 above).

The differential diagnosis for AFR should include dengue fever, particularly in the Pacific where dengue incidence is high. Many PICTs have access to a rapid test for dengue and in some cases it will be appropriate to carry this out on AFR cases before investigating further for measles or rubella. [For further information, see the Dengue chapter in this manual]. A positive rapid test for dengue in an AFR case that is clinically diagnosed as dengue and does not fit either the measles or the rubella case definition will make it unnecessary to carry out further tests. If, however, the presentation is

indeterminate, it may still be appropriate to send samples for measles and rubella testing.

#### 4.8.2 Type of specimens

The standard diagnostic tests (IgM) for measles and rubella are usually carried out on serum, but can also be done using a small amount of dried blood collected on filter paper (“dried venous blood spots”).

Measles or rubella virus can be isolated from throat swabs, urine or blood (lymphocytes).

Measles or rubella RNA can be detected from a throat swab, urine, blood (lymphocytes or dried blood on filter paper) or dried oral secretions on filter paper.

Measles or rubella antigen can be detected by immunofluorescence in dried oral secretions.

#### 4.8.3 When and on whom to collect lab specimens

In the early stages of an outbreak, before the outbreak organism has been definitively determined, all suspected cases presenting (up to a maximum of 10-20 cases) should have specimens taken for diagnosis. Once the cause of the outbreak is established as measles or rubella, cases clearly meeting the outbreak case definition (including arising in the specified geographical area) need not be tested, but can be considered as part of the outbreak. In an ongoing outbreak, occasional cases should be tested to confirm that it is still the same disease and to identify when the outbreak is over. Unusual cases, or those arising sporadically or outside the area originally defined, should be tested in case they represent another disease or outbreak.

Virus isolation should be attempted for every outbreak, but not every patient. Samples for virus isolation must be sent to a regional reference (level 3) laboratory and are usually taken from only a few patients. Virus isolation would only be expected from IgM-positive cases, but these samples must usually be taken before the IgM result is known. Therefore it may be most practical to take these samples from cases epidemiologically linked to the first confirmed cases (who are thus very likely to also be IgM-positive).

Measles IgM antibodies are detectable between about 72 hours and four weeks after the onset of the rash, peaking 1-2 weeks after rash onset. For practical reasons and to ensure the case is not lost to follow-up, the sample may be taken at the first contact with the health system. A specimen is considered adequate if collected within 28 days after rash onset. Measles virus can be isolated from lymphocytes within four days, from urine within five days and from nasopharyngeal samples within seven days of rash onset.

Rubella IgM is detectable from six days to six weeks after the onset of rash<sup>17</sup>. Rubella virus is most easily isolated from pharyngeal specimens, and the viral load is highest within four days of the onset of rash.

#### 4.8.4 Confirmatory testing (PPHSN recommended Tests)

The recommended standard tests for diagnosis of measles or rubella are the detection of specific IgM antibodies in serum or in dried venous blood. Diagnosis can also be made on the basis of a significant rise in specific IgG between the acute and convalescent stages. This approach requires two samples from the same patient, taken at least two weeks apart; it is useful if the initial sample is negative for IgM, and particularly if it was taken early in the course of the illness. Other laboratory tests as outlined above in section 3.1 are not recommended for routine confirmatory use.

#### 4.8.5 Preparing specimens shipping to laboratory

Ideally each national (level 1) laboratory should have an established working relationship – or should work on developing such a relationship - with a level 2 (specialised) laboratory as well as one of the level 3 (regional reference) laboratories within PPHSN’s laboratory network (LabNet). Some PICTs will choose to use laboratories outside the Pacific, for various reasons such as pre-existing connections, airline transport routes or cost. Countries and territories are free to create their own linkages, but should ensure that the laboratories they use are accredited to the WHO Measles Laboratory Network.

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<sup>17</sup> as per draft WPRO rubella guidelines – but note different range quoted elsewhere

For diagnostic measles/ rubella IgM testing, whole blood (3mL) should be taken and kept at room temperature until the clot retracts, then stored at 4 C and the serum separated into a sterile vial within 24 hours. Serum should be frozen (preferably), or at least refrigerated at 0 - 8 C until they are air-freighted to a level 2 laboratory – which should happen as soon as possible. The receiving laboratory should be informed ahead of time that specimens are being sent, and how and when they will arrive. Specimens should be labelled appropriately and accompanied by a request form giving clinical and identifying details of the case. They should be transported packed in cold boxes with ice packs. (See Annexes 5 and 6 for further details).

#### 4.9 Initial community interventions

The main aim of public health action in an outbreak of measles or rubella is to minimise mortality and morbidity through ensuring appropriate treatment of patients and limiting spread of the virus. Initial community interventions will be similar whatever the level of population immunity. These will include ensuring hospitalised patients are nursed in isolation; following up cases and ensuring that they and susceptible contacts are excluded from school, pre-school, day-care and other settings where transmission is likely to occur; and providing timely, appropriate information to clinicians and other key people, as well as to the general public via mass media (e.g. using the key messages outlined in section 4.7 above). Training for nurses and doctors in the specific tasks they need to carry out will be very important.

#### 4.10 External (international) reporting, requests for support, and coordination among agencies

Outbreaks can be reported at the suspected stage to PacNet (or if preferred initially, PacNet-restricted) for advice and support from colleagues within the region. Once an outbreak is confirmed, it should be reported to PacNet both for the support that this can mobilise, and to alert neighbouring countries to possible importations of measles or rubella. A regional EpiNet team will be ready to travel to countries to assist with outbreak control, if needed. The network can also help arrange external assistance from a variety of agencies including WHO. When requesting support, countries should outline the situation as clearly as possible, including information on the extent of the outbreak, resources available in-country, and projected needs - as for any other epidemic. [Further details are available in the generic section of this manual – insert reference]

### 5. CASE MANAGEMENT – the clinical response

There is no specific treatment for either measles or rubella. However, Vitamin A reduces mortality from measles and prevents the blindness that may occur when patients with overt or subclinical vitamin A deficiency contract measles. Patients with confirmed measles, or AFR illness which could be measles, should therefore be given vitamin A orally according to the schedule below:

Age	Vitamin A dosage	
	Immediately on diagnosis	Next day
< 6 months	50,000 IU	50,000 IU
6 – 11 months	100,000 IU	100,000 IU
12 months	200,000 IU	200,000 IU

Management of uncomplicated cases is symptomatic and can be carried out at home. Patients or caregivers should be given clear advice on controlling fever, maintaining hydration and seeking medical care if symptoms or dehydration worsen, or complications develop. Cases should not attend school, pre-school or day care or other public gatherings until the end of the infectious period. This is four days after rash onset in the case of measles, and seven days after rash onset in the case of rubella. If the cause of the outbreak has not yet been determined, the longer period (7 days) should be observed.

Bacterial superinfections of the eyes or ears can be treated in clinics or outpatient departments by cleaning and providing antibiotic ointment or drops. Malnourished children and those with complications such as pneumonia, encephalitis or severe dehydration should be managed appropriately in hospital. Suspected cases should be segregated from other outpatients to the extent practicable, and inpatients kept in respiratory isolation, until the end of the infectious period (four or seven days after rash onset, as above).

In order to prevent nosocomial transmission of measles and/ or rubella, all health care staff should be vaccinated with the available vaccine – preferably one which protects against both diseases e.g. the measles-rubella (MR) vaccine.

## **6. OUTBREAK INVESTIGATION, PREVENTION AND CONTROL – the public health response**

### **6.1 Individual case**

#### 6.1.1 Case investigation (including use of Case Investigation Forms)

Every case of AFR or suspected measles or rubella reported by a clinician to surveillance staff should be investigated within 48 hours. In some countries the initial investigation is carried out by the reporting clinician in consultation with surveillance staff. In other situations surveillance staff visit the case and carry out the investigation themselves. A high degree of collaboration is required in either circumstance.

Case investigation is carried out in a systematic way using the AFR case investigation form (Annex 3), which is filled out for the first 10-20 cases in an outbreak as well as selected cases later in the course of the outbreak. The initial step is to confirm that the case does in fact fit the syndrome of acute fever and non-vesicular rash. Next, the investigator determines whether the case meets the clinical case definition for either measles or rubella (including the broad versions of these: “suspected by a clinician” and maintaining a high index of suspicion for both), or has clinical features that may indicate an alternative diagnosis, such as dengue fever.

Cases meeting the clinical case definition for either measles or rubella should have blood taken for measles IgM (and if this is negative, rubella IgM testing should be carried out on the specimen). Cases meeting the suspected rubella definition should have blood taken for rubella IgM and measles IgM testing to be carried out simultaneously. If an alternative diagnosis can be confirmed more rapidly (e.g. dengue by the rapid PanBio test), measles and rubella testing may not be necessary. It must be borne in mind, however, that measles and rubella can manifest atypically, and so it may be appropriate to carry out measles (+/- rubella) testing even on cases manifesting some signs of different illnesses.

Details of specimens taken and tests requested are recorded on the form, as are the results when available and the final case classification that flows from them. Clear systems of follow-up of results should be established, so that either the investigator or a designated person ensures that they are received and acted on in a timely manner.

Where the source of the illness is not already known (as it may be if the case is a household contact of an earlier confirmed case), an attempt should be made to identify the source - as described in section 4.6 above. The investigation form includes questions about travel and contact with earlier cases or symptomatic people during the time when the case would have contracted the infection.

The investigation should also identify the people with whom the case had contact during his or her infectious period, so that these contacts can be followed up as appropriate (see section 6.2.1 below). The infectious period is considered to be from four days before to four days after rash onset for measles, and from seven days before until seven days after rash onset for rubella. (If the cause of the outbreak has not been definitively established, the longer period should be used.) If the investigation finds that the case is still within the infectious period, he or she should be kept home or in respiratory isolation (if hospitalised) until the end of the infectious period.

#### 6.1.2 Follow-up (including follow-up specimens)

Either the original investigator or another designated person should be responsible for following up with the laboratory to ensure that specimens are received, and later to retrieve the results of the tests if these are not forthcoming. Results must be interpreted appropriately and the final case classification decided, in consultation with other staff if necessary. The results and case classifications should be recorded on the patient’s investigation form as well as the line-list, and all relevant details forwarded promptly to the appropriate levels (e.g. to the Outbreak Task Force).

It is particularly important that the EpiNet team is informed immediately as soon as an outbreak is suspected and immediately when the first case of measles or rubella in an outbreak is confirmed by the laboratory. Laboratories should be given the name of the person or persons to telephone or fax the result to immediately. Surveillance staff should also find out when results are expected and follow up if they are not received by the stated time.

If the initial tests requested are negative, it may be appropriate to ask the laboratory to carry out additional tests. In some cases of negative IgM yet high clinical suspicion of measles or rubella – for example if blood was taken early, perhaps

before IgM would have become detectable - it may be appropriate to take another (convalescent) sample from the same patient to look for a significant rise in IgG. (This is the alternative confirmatory test, not routinely recommended – as per section 4.8.4 above.)

Once an outbreak of measles or rubella is confirmed, an attempt should be made to isolate the virus from a small number of patients chosen for the likelihood of success (as described in section 4.8.3 above).

## **6.2 Contacts**

### 6.2.1 Contact tracing, investigation, and management

Contacts are people who have spent time with a confirmed or suspected case, or had contact with his or her infectious body fluids, during the presumed infectious period. The length of time and amount of contact considered significant varies by disease according to its mode of transmission and infectivity. For measles, contacts include any one who has spent an hour in the same enclosed air space as a case. As rubella is less infectious than measles, contact with a rubella case would likely need to be somewhat more extensive to pose significant risk of transmission. At the beginning of an outbreak of AFR, when the causative organism has not been identified, the more inclusive definition of contacts (i.e. that for measles) should be used.

As part of the investigation of each AFR case, contacts exposed during the case's infectious period should be identified, as described in section 6.1.1 above. Where possible, the immunity or susceptibility of contacts should be determined (e.g. from a school register of children's immunisation status, if available). Young babies and women who may be pregnant should be given highest priority for follow-up as these are the groups at highest risk of severe illness and complications.

Susceptible contacts should be vaccinated (with the vaccine used in the country against measles +/- rubella) as soon as possible – provided that they are old enough, have not received a live virus vaccine within the last month, and are not pregnant. Vaccination will not prevent illness if the contact has already been infected with measles or rubella virus, but it will not make the symptoms worse and may provide protection against measles if given within 72 hours of exposure. Because of theoretical concern about the risk of live virus vaccines (including measles, rubella, MR and MMR) to unborn babies, vaccination is not offered to pregnant women, and women of child-bearing age who receive one of these vaccines are advised to avoid pregnancy for three months after vaccination.

Susceptible contacts who remain unvaccinated should be advised to stay away from school, pre-school or day care as well as other public gatherings, and avoid contact with women who may be pregnant, until three weeks after last contact with the case during his or her infectious period. This is because they may have been infected with measles or rubella virus and may in turn infect others. If they develop symptoms - even after vaccination - they should take similar precautions until seven days after the appearance of the rash (four days if measles is confirmed as the outbreak organism).

A child contact may be considered immune to measles if he or she has received two doses of measles-containing vaccine, at least one of which was after the first birthday, or if he or she has been documented as having confirmed measles in the past. Adult contacts may generally be considered immune to measles if they were born before measles vaccine was introduced into the immunisation schedule (as almost everyone contracted measles as a child in the pre-vaccine era). For most PICTs this means that people born before 1982 (i.e. 23 years or older at the time this chapter is written) may be considered immune to measles. It is prudent nevertheless for pregnant women in this age group to avoid contact with cases of measles as well as of rubella or AFR, and their susceptible contacts. A pregnant woman who is a close contact of a case of measles, has never been vaccinated and is unsure whether she has had measles, may be tested for measles IgG (which would indicate immunity) and IgM (which would indicate infection).

Children or adults may be considered immune to rubella if they have received at least one dose of a rubella-containing vaccine (usually MR or MMR) after the first birthday, or have a documented history of confirmed rubella. Contacts who do not meet these criteria cannot be assumed to be immune to rubella, since before vaccine introduction many people reached adulthood without being infected with rubella. Pregnant women who are contacts of rubella case and are not known to have been vaccinated or had rubella may therefore still be susceptible, and their fetuses thus at risk of CRS, especially if the exposure was during the first trimester of pregnancy. Such contacts should be tested for rubella IgG (which would indicate immunity) and IgM (which would indicate infection), and advised accordingly. WHO WPRO's rubella guidelines state: "The risk of fetal damage depends on timing of the infection: up to 90% at 8 to 10 weeks, declining to about 10% to 20% by about 16 weeks and after this stage of pregnancy, fetal abnormalities are rare"<sup>18</sup>.

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<sup>18</sup> WHO WPRO, Western Pacific Regional Guidelines: Introducing rubella vaccine. Draft 25 March 2004

## 6.3 Outbreak

### 6.3.1 Collecting, tabulating, and interpreting data

When an outbreak has been confirmed and is underway, line lists and spot maps of suspected and confirmed cases (described in section 4.5 above) should be updated regularly and used to monitor the progress of the outbreak. The number of cases with onset of symptoms on each day should also be plotted on a graph to produce an epidemic curve. For each outbreak site, the date of onset of the first case should be recorded and the case-fatality rate should be monitored and compared to expected rates. Rates of serious complications should also be monitored and compared to rates recorded in earlier outbreaks.

The pattern of cases - e.g. age, geographical location, birth cohorts with highest attack rates - will give valuable information about population immunity to supplement the estimates made either before or in the early stages of the outbreak (as per sections 3.2.2 and 3.6.1 above). If many more cases occur in certain cohorts than expected, this may indicate that the immunity level was not as high as calculated and should prompt further investigation into the reasons.

One possible reason for unexpectedly high rates of disease in particular groups could be that the vaccine was not as effective as assumed. Vaccine effectiveness can be estimated using the proportion of cases that had been vaccinated together with the proportion of the population vaccinated. (Where two doses of measles-containing vaccine are scheduled, it is easiest to use the proportion of cases and of the population having received two doses. This will give an estimate of the combined effectiveness of two doses, which can be compared to the expected value of at least 98%). The formula is:

$$VE = (PPV - PCV) / PPV (1 - PCV)$$

- where VE is vaccine effectiveness, PPV is the proportion of the population vaccinated and PCV is the proportion of cases vaccinated. Information on vaccination status should be collected for all cases, and the proportion of the population vaccinated is routinely collected as immunisation coverage data.

A high proportion of cases having a history of vaccination should not necessarily cause alarm, as in a highly vaccinated population a higher proportion of cases will be due to vaccine failure than in a population with low vaccination rates. If, however, this “screening” calculation indicates a vaccine effectiveness level much lower than the expected value, there may be problems in the way the vaccine cold chain has been managed.

If it becomes apparent that previous calculations grossly overestimated population immunity, the decision as to whether to carry out mass immunisation should be revisited.

### 6.3.2 Risk factor assessment

Risk factors are factors associated with becoming a case or with developing severe illness or complications from measles or rubella. As the personal characteristics of cases are monitored, it may become apparent that some groups are at higher risk relative to other groups. The relative risk of disease associated with a given factor (e.g. age under one year, residence in a particular area, etc) can be calculated as follows:

$$\text{Relative risk of disease associated with a factor} = \frac{\text{Attack rate among people who have the factor}}{\text{Attack rate among people who do not have factor}}$$

- where attack rate is defined as the proportion of people in the group who develop disease (AFR, measles or rubella)

If an apparent association proves to be a real and significant relative risk – for example, a four-fold difference in rates of disease between people living in neighbouring suburbs – it should be investigated. Is the difference due to different rates of immunisation? Is this because some areas are poorly served by immunisation clinics?

### 6.3.3 Prevention and control measures

#### *6.3.3.1 Individual*

Individuals should ensure that they and their children are up-to-date with all scheduled immunisations. Susceptible people

who cannot be immunised (e.g. due to pregnancy or age) should protect themselves by avoiding contact with large numbers of people, and certainly with any suspected or confirmed cases and their susceptible contacts. Careful attention to hand-washing can reduce the likelihood of becoming infected with measles or rubella, since infection is often via droplets passed from hands to mucous membranes.

#### 6.3.3.2 *Community*

Community prevention and control measures include enforcing the exclusion of suspected or confirmed cases and their susceptible contacts from schools, pre-schools and day-care centres until they are no longer infectious, are immunised or pass the maximum incubation period without developing symptoms; informing and educating the general public about immunisation, symptoms and signs of illness and how to manage uncomplicated cases at home; and providing special assessment facilities for suspected cases. In situations where population immunity is low, mass immunisation for selected groups can increase it rapidly so that sustained or endemic transmission of measles or rubella will not be re-established.

#### 6.3.3.3 *Available options*

School entry checks of immunisation status provide an opportunity to ensure that all children are up-to-date with immunisations or at least have their immunisation status recorded. The records held by schools are invaluable in times of outbreaks as they allow susceptible children to be identified rapidly and (where legislation supports this) excluded temporarily from attending school. Schools can also provide ideal venues for mass immunisation of children, if required.

Many sectors of society are willing to lend their talents, energy and experience to organising large-scale events such as community education or mass immunisation. These may include (but are not limited to) church groups, women's or youth committees, non-governmental organisations, special interest groups and the military.

#### 6.3.4 Special investigations

Occasionally special studies may be required as adjuncts to outbreak control efforts, to identify risk factors for disease, investigate vaccine efficacy (more accurately than via the "screening" method outlined above), examine possible cold chain lapses, etc. Such studies may be time-consuming and resource-intensive, and should not distract from the main aims of outbreak control. If necessary, external advice and assistance can be sought for these special investigations.

### 6.4 Disaster implications

Disasters often disrupt routine immunisation programmes as well as health care services. Introduction of measles, particularly, into displaced or afflicted populations with high proportions of susceptibles can cause devastating epidemics with high case-fatality rates.

## 7. REFERENCES AND FURTHER SOURCES OF INFORMATION

[NB only the most recent/ authoritative references used are cited here]

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## **8. ANNEXES**

1. Calculating population immunity to measles using vaccine efficacy and coverage
2. Monthly Hospital-Based Active Surveillance Form [see HBAS manual annex A – attached]
3. Acute Maculopapular Rash and Fever Case Investigation Form [see HBAS manual annex B2 – attached]
4. Acute maculopapular Rash and Fever line-list
5. Collection and shipment of serum specimens
6. Specimen packing and shipping instructions [see HBAS manual annex D – attached]

## **9. HISTORY OF GUIDELINE**

Date endorsed by PPHSN [to be completed]

Revision date(s) [to be completed]

Review date [to be completed]

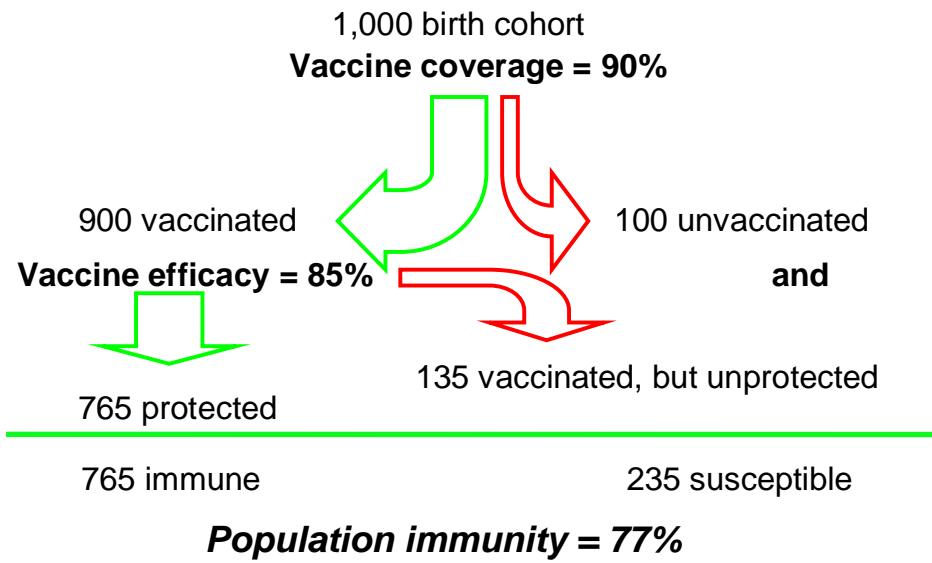
## ANNEXES

### Contents

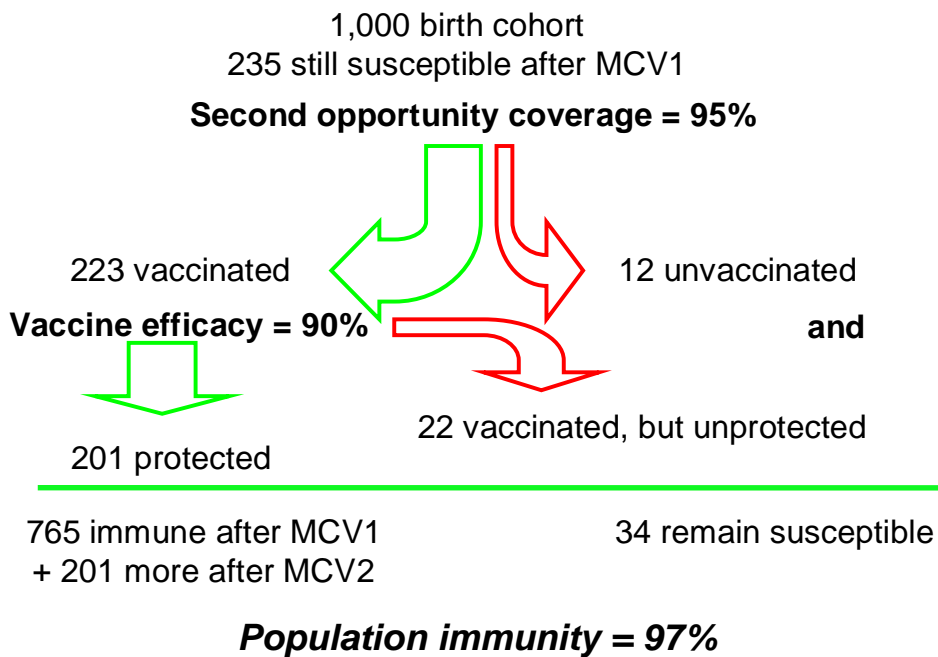
1. Calculating population immunity to measles using vaccine efficacy and coverage
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4. Acute maculopapular Rash and Fever line-list
5. Collection and shipment of serum specimens
6. Specimen packing and shipping instructions [see HBAS manual annex D – attached]

ANNEX 1: Calculating population immunity to measles using vaccine efficacy and coverage

**(a) First vaccination opportunity (MCV1) at 9 months of age: vaccine efficacy 85%**



**(b) Second vaccination opportunity (MCV2) at 12 months of age: vaccine efficacy 90%**





**Acute Fever and Rash (AFR) Case Investigation Form**

Annex 3

Country: \_\_\_\_\_ Hospital / Clinic: \_\_\_\_\_

Examiners Name: \_\_\_\_\_

Today's Date: dd / mmm/ yy

<b>1. Case Identification</b>	Sex: Male      Female
Patient's Name: _____	Date of birth: dd / mmm/ yy
Mother's Name: _____	Age: years ____ months ____
Father's Name: _____	Hospital ID # _____
Permanent Address (for follow-up): _____	Pregnant: <b>Y N U</b> Due: dd / mmm/ yy
Source of notification: Official / hospital / private / laboratory / community / other (specify): _____	

<b>2. Immunization History:</b>	Vaccine received: <b>M MR MMR</b> (circle all that apply)
Date of 1 <sup>st</sup> dose: dd / mmm/ yy	Date of 2 <sup>nd</sup> Dose: dd / mmm/ yy      Supplementary Doses: dd / mmm/ yy
Doses validated by: History (Health Worker/Parent) or Immunization Records (register/card) (circle all that apply)	

<b>3. Clinical Examination:</b>			
Date of onset of Fever: dd / mmm/ yy and Rash: dd / mmm/ yy			
Rash description (location, spread, macopapular, vesicular etc): _____			
Cough	<b>Y N U</b>	Occipital, cervical &	Nausea/vomiting <b>Y N U</b>
Runny nose	<b>Y N U</b>	auricular lymph nodes <b>Y N U</b>	Muscle Pain <b>Y N U</b>
Conjunctivitis	<b>Y N U</b>	Joint pain/inflammation <b>Y N U</b>	Headache/eye pain <b>Y N U</b>
Koplik's spots	<b>Y N U</b>	Encephalitis <b>Y N U</b>	Spontaneous bleeding <b>Y N</b>
Pneumonia	<b>Y N U</b>	Others: _____	
Hospitalization:	<b>Y N U</b>	Date Admitted: dd / mmm/ yy	Date Discharged: dd / mmm/ yy
Assessment:	Measles <b>Y</b>	Rubella <b>Y</b>	Dengue <b>Y</b> Other <b>Y</b> _____
Place of examination: _____	Examiners Signature: _____		

<b>4. Possible Source of Infection:</b>	
Travel during 7-18 days before rash onset:	<b>Y</b> (where: _____) <b>N U</b>
Contact with other confirmed case of measles/rubella:	<b>Y</b> (who & where: _____) <b>N U</b>

<b>5. Laboratory Investigations</b>			
Antibodies Blood or Dried Blood Spots (DBS)	Date take: dd / mmm/ yy	Date sent: dd / mmm/ yy	
Viral Isolations Urine, throat swab or DBS	Date take: dd / mmm/ yy	Date sent: dd / mmm/ yy	
Type of Test: Measles/Rubella/Dengue: ____	Result _____	Date tested: dd / mmm/ yy	

<b>6. Final Classification:</b>					
<b>Measles</b>	<b>Rubella</b>	<b>Dengue</b>	<b>Parvo B19</b>	<b>Chickenpox</b>	<b>Other: _____ Discard</b>
<b>Confirmation:</b>	<b>Laboratory</b>	<b>Epidemiological</b>	<b>Clinical</b>		
<b>Outcome:</b>	<b>Fully recovered</b>	<b>Morbidity (specify)</b>	<b>Died: date dd / mmm/ yy</b>		



# Annex 5: Measles

## Collection and Shipment of Serum Specimens

meas\_ci/997

### Sampling

**A blood sample should be collected in each of the following instances:**

- Isolated cases of suspected measles.
  - The first 10 - 20 suspected cases in a possible measles outbreak.
  - Unusual cases, or cases in a new geographic area or subpopulation occurring during an outbreak.
  - Occasional samples from outbreak cases when in the midst of an outbreak.
- 1) Three (3) ml of blood should be taken at the first contact opportunity with the suspected case.  
(IgM antibodies are best detected from the 4th day after rash onset, peaking at 1 - 2 weeks, until about 4 weeks (28 days) after rash onset.)
  - 2) Whole blood should be kept at room temperature until the clot retracts, then stored at 4 C and the serum separated into a sterile vial within 24 hours.
  - 3) Serum should be frozen (preferably), or at least refrigerated at 0 - 8 C until shipping.

### Shipping

- 1) Ship specimens by air as soon as possible.
- 2) Place **specimen** in a zip lock bag, labelled with at least:
  - patient's name and medical record number
  - hospital and country where collected
- 3) Place a **form** for each specimen in a separate zip lock bag with at least:
  - patient's name, date of birth, and medical record number
  - date of rash onset
  - date of collection of sample
  - date of last measles vaccination
  - hospital and country where collected
- 4) Specimens and forms should be shipped in approved cold boxes with ice packs.
- 5) Before shipping specimens, make sure the laboratory is capable of and willing to perform such testing.
- 6) **Fax a pre-alert message** to the laboratory and follow with a telephone call giving the **airwaybill number, flight number, and arrival time (ETA)** at the destination.  
Fax a copy to **WHO/ Suva Fax: 679 300 462** ; telephone: 679 304 600.

### Testing

- The standard test is for measles-specific IgM antibodies, indicating acute infection. IgM antibodies may be detected using either indirect or capture EIA testing (ELISA).
  - Alternative testing is for measles IgG antibodies, but this requires two samples collected about two weeks apart, to detect changes in antibody titers.
-

## **ANNEX D - SPECIMEN PACKAGING, MARKING & LABELLING AND DOCUMENTATION INSTRUCTIONS**

### **1. CLASSIFICATION OF INFECTIOUS SUBSTANCES FOR SHIPMENT**

Under the current United Nations Regulations (2003), infectious substances are classified according to two transportation categories based on a detailed, case-by-case, risk assessment of microorganisms known to be pathogens. The new transport categories are:

#### Category A:

An infectious substance which is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease to humans. These substances are given the shipping name of "Infectious substances affecting humans" and the UN Shipping Number: UN 2814. Category A substances are to be packed in accordance with International Air Transport Association (IATA) Dangerous Goods Packaging Instructions PI 602.

#### Category B:

Any infectious substance, which does not meet the criteria for inclusion in category A. Clinical/diagnostic specimens from patients when testing for polio, measles and rubella are classified as Category B under the UN Model Regulations. Category B substances are to be packed in accordance with IATA Dangerous Goods Packaging Instructions PI 650

Category B substances are given the shipping name of "Diagnostic Specimens", "Clinical Specimens", or "Biological substance, category B" and the UN Shipping Number: UN 3373. [Note on 1 January 2007, it is anticipated that the use of the shipping names "diagnostic specimens" and "clinical specimens" will no longer be permitted]

Note that for the US Associated Territories, more stringent packaging instructions may be followed and these countries should be guided by recommendations from their Regional Laboratory Coordinator.

### **2. REDUCING RISK - APPROPRIATE PACKAGING**

Appropriate packaging can reduce the risks to those engaged in the transport of infectious substances, as it provides the necessary and sufficient barriers to prevent leakage of the material to the outside. For the packing of both Category A and B substances, a 3-part (or triple) system of packaging is used, that comprises a primary receptacle, secondary packaging and rigid outer packaging. The use of triple packaging has over the years provided effective containment of infectious substances.

WHO has supplied shipping containers for all Hospital Based Reporting Sites in the Pacific. The smaller containers (HazPak) comply with IATA PI 650 and can only be used to transport Category B substances. The larger containers (Bio-Bottle) comply with IATA PI 602 and can be used to transport both Category A and B substances. WHO recommends that these containers be used for all shipments to laboratories when countries need to test both stool and blood samples for polio, measles or rubella.

### **3. PACKING INSTRUCTION**

#### PI 650 - Category B Substances

When shipping Category B substances [except where local airlines require all specimens to be sent as PI 602], please use the HazPak (or similar) shipping containers supplied by WHO. Shippers of Category B substances must comply with the requirements below and ensure that shipments are prepared in such a manner that they arrive at their destination in good condition and that they present no hazard to persons during shipment. The packing conditions are:

**(a) For liquid substances (e.g. blood or serum specimens for measles/rubella testing)**

- The primary receptacle(s) must be leak-proof and must not contain more than 1 L;
- The secondary packaging must be leak-proof;
- If multiple primary receptacles are placed in a single secondary packaging, they must be either individually wrapped or separated to prevent contact between them;
- Absorbent material must be placed between the primary receptacle and the secondary packaging. The absorbent material, such as cotton wool, must be in sufficient quantity to absorb the entire contents of the primary receptacle(s);

**(b) For solid substances (e.g. Stool samples for AFP testing)**

- The primary receptacle(s) must be sift-proof, to retain the specimen at all times;
- The secondary packaging must be sift-proof to retain the specimen at all times;
- If multiple primary receptacles are placed in a single secondary packaging, they must be either individually wrapped or separated to prevent contact between them;
- If there is any doubt as to whether or not residual liquid may be present in the primary receptacle during transport then a packaging suitable for liquids, including absorbent materials, must be used.

An itemized list of contents must be enclosed between the secondary packaging and the outer packaging for all PI 650 shipments. Seal the list in a plastic bag to avoid the paper becoming wet from condensation.

Wet ice or prefrozen packs when used in a shipment must be placed outside the secondary container packaging(s) or alternatively in an overpack with one or more complete packages

marked in accordance for that type of shipment. If wet ice is used it should be in a leak-proof container and the outer packaging must also be leak-proof.

#### 4. MARKING AND LABELING

Labels and marking on the packaging are an essential source of information to communicate to everyone involved in the transportation process the contents of the package, the nature of the hazard and the applied packaging standards. Most "certified" shipping containers (e.g. Bio-Bottle) already include the appropriate labels and markings as part of the package.

All markings must be placed on the packaging so that they are not covered or obscured by any part of, or attachment to the packaging, or any other labels or markings. All markings must be:

- (a) durable and printed or otherwise marked on, or affixed to, the external surface of the packaging or overpack
- (b) readily visible and legible
- (c) able to withstand open weather exposure without substantial reduction in effectiveness;
- (d) displayed on a background of contrasting colors

##### 4.1 Category B - PI 650

Each package containing diagnostic (or clinical) specimens must be marked, durably and legibly on the outside of the package with each of the following:

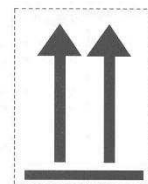
- (a) The UN 3373 label must be displayed on the external surface of the outer packaging. The label must be in the form of a square set an angle of 45° (diamond-shaped) with each side having a length of at least 50 mm, the width of the line must be at least 2 mm, and the letters and numbers must be at least 6 mm high.
- (b) The proper shipping name "Diagnostic specimen" or "Clinical specimen" in letters at least 6mm high must be marked on the outer package adjacent to the diamond-shaped mark.

Example of the UN marking:



Diagnostic Specimen

- (c) Orientation labels are not required for shipments of diagnostic/clinical specimens but their use is recommended
- (d) The full NAME AND ADDRESS of the shipper and the consignee



- (e) Additionally, shipment containers should be marked with "Store at 4°C whenever possible" or similar to identify that the shipping container must be kept cool at all times

## 5. DOCUMENTATION

A Shipper's Declaration for Dangerous Goods is NOT required when shipping Category B substances that have been packaged according to PI 650.

Other documents that are required for specimen shipment, especially when sending to VIDRL in Melbourne, Australia are:

- (a) Customs Declaration (if required) [See Annex E1 & E2 for examples of customs declarations for AFP/AFR samples sent to VIDRL Australia. Please ensure that you are using a valid import permit and samples are addressed to the correct laboratory]
- (b) Import permit (if applicable) [See Annex E3 for a sample import permit]

## 6. EXAMPLES OF PACKAGING AND LABELLING

### PI 650 Category B

