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**FIELD
GUIDELINES
FOR
MEASLES
ELIMINATION**

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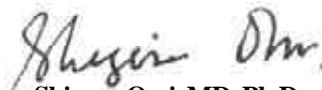
FOREWORD

The Western Pacific Region is now moving towards measles elimination. These guidelines provide guidance for countries to implement the *Western Pacific Regional Plan of Action for Measles Elimination* as urged by the 2003 Regional Committee Meeting resolution (R54.R3).

Countries within the Region are at different stages of, and have variable capacity for measles elimination. Therefore, a target date has not been set yet. An annual review of progress will be undertaken, and a target date will be set as soon as feasible. The annual review will assess progress on the three strategies recommended in the Regional Plan: immunization, surveillance and laboratory diagnosis. These guidelines outline the actions needed for each of these strategies.

The first step is to establish or strengthen the national measles plan, with the input of a coordinating, technical advisory committee. The national plan needs to cover the issues outlined in these guidelines. Most important is achieving and maintaining 95% population immunity to measles through improved routine immunization as well as supplementary immunization activities (SIAs), as needed. To monitor the impact of the activities and accurately track progress towards elimination, surveillance systems need to be of adequate quality. Laboratory diagnosis for confirming measles diagnosis in suspected cases is an essential part of surveillance to achieve elimination. Adding rubella vaccine as part of the measles elimination programme also needs consideration, as well as other opportunities to strengthen health services through measles elimination. The potential of immunization to address broader health issues and alleviate poverty is emphasized through the partnering of measles elimination and hepatitis B control.

These guidelines for developing and implementing national plans are being released as a field test version so that there is opportunity to learn from countries' experiences and to refine the advice at the time that a target date is set for regional measles elimination. Please share your national experiences with the Western Pacific Regional Office so that we can all work together to achieve another historic milestone, building on the Region's poliomyelitis-free status, certified on 29 October 2000.



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GLOSSARY

Measles elimination is a dynamic situation in a large and well-populated geographical area where endemic measles transmission does not occur and where importation of measles virus does not result in sustained transmission. All isolated cases and chains of transmission should be linked to importations. To maintain elimination, high population immunity must be maintained through appropriate measles immunization. (An operational definition is given in Section 3.1.)

Measles importation is the introduction of measles into a country/region as proven by epidemiological (a confirmed case was outside the country/region during the period seven to 18 days before rash onset when measles infection could have been acquired) and/or virological (virus isolated from a case has a genotype not known to circulate in the country/region) evidence.

Measles import-related cases are locally acquired infections originating from an imported case, either directly or through a chain of transmission.

Sustained transmission refers to outbreaks with >100 cases or ongoing transmission for more than three months. Sustained transmission indicates the existence of large numbers of susceptible individuals either in the general population or in some specific high-risk population groups.

Re-establishment of endemicity is a situation in which transmission triggered by an importation continues uninterrupted. The distinction between sustained measles transmission and re-established endemicity remains to be clarified.

1. INTRODUCTION

1.1 Purpose

Measles is a vaccine-preventable disease that remains a leading cause of death among children in the Western Pacific Region. Therefore, the 2003 Regional Committee Meeting (RCM) resolved to eliminate measles. The target date is to be set based on an annual review of progress in implementing the Measles Regional Plan's key strategies: immunization, surveillance, and laboratory diagnosis.¹

This *Field Guide* is to help countries develop and implement **national plans** for these three strategies, implement the RCM resolution, and achieve elimination. It provides health workers, immunization programme managers, public health professionals, and policy-makers at national and subnational levels with advice on what needs to be done and how to do it.

This guide has been released as a 'field test' version. It will be finalized after the Region sets a target date for measles elimination.

1.2 Impact of measles and of immunization

Measles is the most infectious virus that affects humanity. Until the vaccine was introduced in 1963, practically every child got measles. On average (in a completely susceptible population), each infected person infects nearly 20 others. This is why 95% population immunity is needed to interrupt transmission and hence eliminate measles (see *Western Pacific Regional Plan of Action for Measles Elimination*, January 2003).

Without immunization, the Region could expect nearly 25 million measles cases per year – the annual birth cohort of the Region. Measles immunization is already preventing about 95% of the measles disease burden, with the 2002 estimate of 170 000 cases and 32 000 deaths in the Region (see Annex 1 for more details on measles and the vaccine).

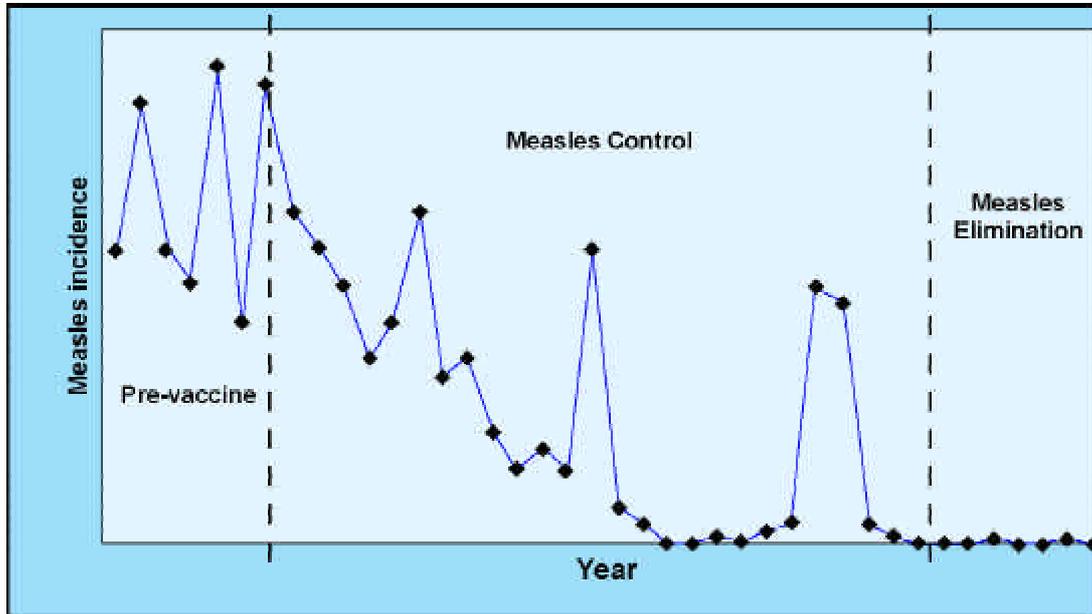
1.3 Public health control options: elimination or epidemics

Measles epidemiology can be broadly categorized in three stages (see Figure 1):

- (1) **Similar to pre-vaccine:** Low immunization coverage (~60% to 70%) means that the epidemiology of measles is similar to that of the pre-vaccine era, with measles constantly present but epidemics of increased activity every two to three years and a reduction in the number of cases proportional to immunization coverage. As coverage increases, so does the time between epidemics.
- (2) **Control:** Moderate-to-high immunization coverage may interrupt measles transmission for a certain length of time, resulting in few cases for some years. However, eventually the number of susceptible persons gradually grows until there are enough to sustain an epidemic.
- (3) **Elimination:** Immunization coverage is sufficient to achieve and maintain 95% population immunity. Not enough susceptibles will accumulate to cause an epidemic. Each importation will only lead to a few secondary cases (unlikely to be more than 100).

¹ World Health Organization. *Western Pacific Regional Plan of Action for Measles Elimination*. 2003, Manila. WHO.

Figure 1. Three stages of measles epidemiology



If moderate immunization coverage results in low numbers of cases, the extra resources to reach elimination may seem hard to justify. However, with only moderate coverage, there will eventually be a large measles epidemic through the build up of susceptibles. Such epidemics are likely to have a disproportionate impact because: (1) health services are no longer used to deal with measles, and there will be many cases; and (2) a greater proportion of cases will be in older children and young adults. It is clear that elimination is the only appropriate option (unless one accepts pre-vaccine measles morbidity and mortality).

1.4 Measles as foundation for other health interventions

Equity is another argument for elimination. Children who are most at risk of disease (the poor and other disadvantaged groups) tend to be insufficiently served by health services. An elimination goal necessarily means that at-risk children will be reached. If the lessons learnt in reaching underserved populations for measles immunization can be used for other basic health services, long-term benefit will accrue. Furthermore, elimination is a 'public good' that benefits the population as a whole, especially the most at-risk members of the community.

Delivering and monitoring immunization is relatively straightforward compared to many other health interventions. As such, it can provide a foundation for delivering other essential health services that need to reach the whole population.

1.5 Regional Committee Meeting (RCM) Resolution R54.R3

In September 2003, the RCM resolved that measles elimination should be a regional goal, and urged Member States to:

- (1) develop or strengthen national plans for measles elimination;
- (2) use measles elimination to strengthen the Expanded Programme on Immunization (EPI) and other public health programmes, such as prevention of congenital rubella syndrome;

- (3) offer all children two doses of measles vaccine, taking into account local situations, so that the 95% population immunity of each birth cohort can be achieved and maintained in every district;
- (4) develop or strengthen measles surveillance systems and laboratory confirmation of cases; and
- (5) improve the quality of routinely reported immunization coverage data and to monitor both immunization and disease data at the district level to improve programme management.

2. DEVELOPING A NATIONAL PLAN FOR MEASLES ELIMINATION

The RCM urged all Member States to develop or strengthen their national plans for measles elimination. Each country/area should establish a national Measles Elimination Coordinating Committee, or use an existing body for this task. The Committee needs to include technical experts and representatives of all stakeholder groups. For example, representatives from the education sector should be included to ensure effective implementation of school-based immunization activities.

Important issues to be addressed by the plan are discussed in this section (to supplement the outline provided in Annex 2 of the Regional Plan); details about immunization strategies, and surveillance methods and laboratory support appear in Section 5. The Measles Elimination Coordinating Committee should provide the strategic and technical guidance to the National Immunization Programme in developing the national plan, as well as assistance in its implementation. The national Committee should consider the value of establishing subnational bodies to help planning and implementation.

2.1 History of measles control

The plan should provide a historical context to aid understanding and planning for measles elimination strategies. Useful information includes estimates of annual incidence, identification of outbreak years, and the timeline, target groups and coverage attained in previous measles immunization activities.

2.2 Estimating needed vaccine and minimizing wastage

The global supply of measles vaccine is barely adequate to meet current demand, and demand is likely to increase. Each country/area should estimate its vaccine requirements in five-year blocks (updated annually) so that global efforts can be coordinated to ensure that each country's needs are met. As needed, updated estimates should be communicated to vaccine suppliers and the WHO Western Pacific Regional Office.

The key issues for planning vaccine requirements relate to the introduction of a second dose, SIAs, and efforts to improve routine coverage. Wastage will also have important consequences for demand. Countries need to develop strategies to minimize wastage in a way that does not impact on coverage.

2.3 Groups with less than 95% population immunity

Groups likely to have less than 95% population immunity should be defined by age and geographic location. Grouping by other characteristics such as ethnicity or religious affiliation may be needed in some settings.

2.4 Immunization strategies

Each country should devise strategies to: (1) achieve 95% immunity in each cohort of children born after the adoption of the elimination goal; and (2) 'fill in' gaps in immunity among groups identified in the population immunity profile.

Every newborn child needs to be protected through routine immunization. Periodic SIAs for children in cohorts born after the adoption of the elimination goal will be needed as long as routine immunization coverage is less than 95%, even for routine programmes that include two doses of a measles-containing vaccine.

SIAs for identified groups with less than 95% immunity are needed to prevent future outbreaks. There is an immediate need to immunize these cohorts while still of school age, as mass immunizations in older groups are more challenging.

Special strategies may be needed in high-risk areas, which include areas with crowded populations, with a large number of 'unregistered' or migrant children, with ethnic populations, and that are physically remote.

2.5 Case-based measles surveillance system

Each country should assess its current surveillance system and plan needed improvements for surveillance of adequate quality to achieve elimination (case-based measles surveillance). At levels of incidence approaching elimination a case-based system should already be in place and fully functional.

Case-based means that the surveillance system collects a minimum data set at national level on each case, including but not limited to information on age, gender, vaccination status, place of residence, travel history, date of rash onset, disease outcome, etc. Case-based measles surveillance in elimination settings implies laboratory support for confirmation at appropriate levels (5-10 per outbreak, all cases when approaching elimination) of the clinical diagnosis via identification of measles-specific IgM-antibodies and/or identification of measles virus in appropriate clinical specimens.

Case-based surveillance allows for analysis of measles epidemiology to guide control efforts. As countries approach elimination status it becomes important for every suspect case of measles to be reported and included in the national database.

2.6 Laboratory confirmation of suspected measles cases

As disease prevalence decreases, the positive predictive value of clinical diagnosis decreases too – this is of course true for all diseases, not only for measles. Therefore, laboratory confirmation of suspected measles cases becomes increasingly important.

Each country needs to establish a system and procedures for collecting and testing blood samples from cases of acute fever and rash (AFR) and to develop that system so that eventually any suspected measles or AFR case has a laboratory test undertaken.

2.7 School entry check of immunization status

Measles can spread rapidly in schools because of the large number of children in close contact to each other. Checking immunization status at the time of school entry can prevent this spread while also ensuring high population immunity – if most children attend school.

A school entry requirement of two doses of measles vaccine has proven very effective in attaining extremely high coverage. It effectively places a maximum age a child can attain without receiving the recommended two doses – and stipulates all children should have done so by then.

The plan should include developing/strengthening a system, in collaboration with the education sector, for checking and bringing up to date a child's immunization status at the time of entering pre-school and school. In some countries, the check/requirement for immunization may be more effective if legally required. **The key point is to have systems that ensure that every child who starts school has received the recommended two doses of measles-containing vaccine.**

2.8 Potential to add rubella elimination to measles elimination

If a country is able to eliminate measles by achieving and maintaining very high immunization coverage, rubella could be eliminated at the same time by substituting measles-rubella vaccine (MR) or measles-mumps-rubella vaccine (MMR). For countries moving to measles elimination, the considerations for adding rubella are:

- added cost of MR compared to measles (approximately US\$ 0.35 per dose at 2003 United Nations Children's Fund [UNICEF] prices);
- need to conduct an initial wide-age-range immunization campaign with MR to ensure high immunization levels among childbearing age women (CBAW); and
- commitment to continue rubella immunization to prevent risk of an increase in congenital rubella syndrome (CRS).

2.9 Opportunities for vitamin A and other health interventions

In countries with vitamin A deficiency problems, the provision of high-dose vitamin A supplements every four to six months protects against blindness and death. Vitamin A supplementation has been shown to reduce all-cause mortality by 23%–30%, possibly due to amplification of a nonspecific effect of immunization.²

Vitamin A supplementation can take place during any immunization activity and is the standard of care in measles case management. Incorporating vitamin A in measles SIAs as well as the routine programme needs to be considered as a strategy for improving child health.

Other health interventions (such as anti-helminthic treatment [deworming], delivery of bed nets [malaria prevention], and other vaccines) also need to be considered as possible interventions to be incorporated in the routine programme or regular SIAs. However, if any addition compromises achievement of high coverage with measles-containing vaccine, it should not be included.

² Benn CS, Bale C, Sommerfelt H, Frils H, Aaby P. *Hypothesis: Vitamin A supplementation and childhood mortality: amplification of the non-specific effects of vaccines?* Int J Epidemiol 2003;32: 822-8

3. OPERATIONAL ASPECTS OF IMPLEMENTING THE PLAN

3.1 Operational definition and indicators for 'elimination'

Interim criteria are proposed for an operational definition that a country or area has achieved elimination (see Glossary). Regional experience may lead to modifications of these definitions when the target date for regional elimination is set. The following interim criteria are proposed:

- (1) less than one confirmed measles case reported per million population per year (excluding imported cases) – not applicable in countries with less than one million population;
- (2) excellent surveillance with comprehensive reporting and investigation of all fever and rash cases and chains of transmission, as demonstrated by:
 - (a) at least one suspected measles case reported per 100 000 population per year in at least 80% of districts (or equivalent, as used for AFP surveillance);
 - (b) serum samples adequate for detecting measles IgM collected in at least 80% of suspected measles cases (excluding from the denominator cases that are epidemiologically linked to a laboratory-confirmed case); and
 - (c) viral isolate obtained from every confirmed chain of transmission (for genotyping to help identify source of virus); and
- (3) maintaining 95% immunity to measles in each cohort in every district, as demonstrated by:
 - (a) at least 95% coverage with two doses of measles-containing vaccine; and
 - (b) importations lead only to small outbreaks (< 100 cases, < three months duration).

The key issue is having adequate quality surveillance, as otherwise measles transmission may not be detected (see *Surveillance*, Section 5).

3.2 Estimating population immunity profile

Historical data on measles cases and coverage can be used to construct the population's measles immunity profile. Immunity can only arise from immunization or infection.

- Immunity from immunization = coverage multiplied by vaccine efficacy
- Immunity from infection = incidence of measles (estimated from reported cases)

Each birth cohort's immunity profile can be modelled by estimating the percentage of the cohort that gains immunity each year through infection or immunization (see Annex 2 for more details).

In some countries, data quality on cases and coverage will be too poor to enable modelling of the immunity profile. The option, successfully used in the Americas, is to assume that all cohorts born in the vaccine era will have gaps in immunity and to target all those up to age 15 years (or school-leaving age) as being the upper age that can be effectively reached.

3.3 Validating population immunity profile

If the immunity profile estimated by the method introduced above (and in Annex 2) is to be used to determine the target population for SIAs, it is worth considering validating the result. It can be validated in two ways: disease data or serological survey.

When measles transmission is still relatively common, the age distribution and age-specific incidence rate of routinely reported cases over the past year can be used to validate the immunity profile – assuming that surveillance quality is adequate. An important bias in reported data, if primarily from hospitals, is the lower hospitalization rate in children aged five to 14 years than in younger children.

Although a serosurvey requires additional resources, it provides the only direct measure of a population's immunity profile. The required sample size (in simple random sampling) depends on the expected prevalence. A serosurvey is ideally done using a representative sample; a convenience sample of blood taken for other purposes is likely to be adequate for this purpose, as has been validated in Australia,³ and is routinely used in the United Kingdom of Great Britain and Northern Ireland.⁴ In the United Kingdom, regular convenience serosurveys are part of the routine surveillance system for measles, and could be considered in countries with sufficient resources. Such serosurveys must be designed and conducted carefully, and interpreted appropriately.

The costs and interpretation issues for serological data mean that in most cases the populations to be targeted for SIAs can be adequately defined without serological data. Each country needs to assess its own situation before deciding if a serosurvey is needed. Countries that are least able to afford serosurveys are those most likely to have measles transmission and can use surveillance data to obtain immunity profiles – if surveillance is of adequate quality.

Improving surveillance data to provide routine data on the age profile of individuals with measles is a priority for all countries at all stages of measles control. Therefore, more resources should be directed at improving routine surveillance than undertaking serosurveys in most countries and areas.

3.4 Using outbreaks as an indicator of overall population immunity

Once countries have achieved good control, there will be little or no disease data to assess the immunity profile. However, importations are likely to continue, and mathematical models based on epidemiological data from several countries demonstrate that the size of measles outbreaks can be used as an indicator of overall population immunity.

The greater the population immunity, the less likely a person infected with measles will infect another person and so the faster the chain of transmission ends, resulting in a smaller outbreak. Outbreaks of less than 100 cases may suggest that the overall population immunity is at the 95% threshold required to achieve elimination (see Section 5.6).

³ Kelly H, Riddell MA, Gidding HF, Nolan T, Gilbert GL. *A random cluster survey and a convenience sample give comparable estimates of immunity to vaccine preventable diseases in children of school age in Victoria, Australia.* *Vaccine.* 2002; 20(25-26): 3130-6.

⁴ Osborne K, Gay N, Hesketh L, Morgan-Capner P, Miller E. *Ten years of serological surveillance in England and Wales: methods, results, implications and action.* *Int J Epidemiol.* 2000; 29(2): 362-8.

4. IMMUNIZATION STRATEGIES TO ACHIEVE AND MAINTAIN 95% POPULATION IMMUNITY

It is extremely challenging to achieve 95% immunity. This is recognized. It means that every newborn needs to be reached – consistently, systematically and indefinitely. In addition, any groups with less than 95% immunity need to be reached with supplemental activities.

4.1 Protecting every newborn child

Every child should receive two doses of measles-containing vaccine, the second dose at least one month after the first, and after the first birthday for optimal response.

4.1.1 Routine measles immunization with the first dose

Measles is given as part of the routine infant immunization schedule in all countries and areas of the Region. Currently, immunization coverage levels are variable in several countries in the Region. Improving routine coverage is the key outcome for all countries and will be the focus for the hepatitis B control initiative – the other half of the RCM resolution to strengthen EPI.

High vaccination coverage (>95%) with the first dose of measles-containing vaccine among children aged one year is most critical for achieving good measles control and eventually maintaining measles elimination.

4.1.2 Provisions for a second dose

Each country needs to consider how to deliver the second measles dose to attain very high coverage (>95%). Options include adding a second dose in the routine immunization schedule or conducting SIAs until a mechanism for delivering sufficient coverage through routine services is in place.

Every child should have the opportunity to receive two doses of measles-containing vaccine – both for individual protection and to achieve measles elimination.

Countries that achieve very high routine coverage with the first dose should add the second dose to the routine schedule only if there is a strategy to assure very high routine coverage with the second dose. This will include countries that are already achieving high coverage for the first dose, as well as those that can schedule a second dose (e.g. at school entry) that will achieve > 95% coverage, even if first dose coverage is less than 95%.

Countries that add a second dose to the routine schedule will *still* need to conduct SIAs unless the coverage can be validated. Unvalidated coverage estimates do not provide any confidence that children are truly being protected.

For some countries, no immediate mechanism may be available to routinely reach more than 95% of children with a second dose. In this case, SIAs may be required. Each country needs to develop ways of reaching every child that are appropriate for its health services; keeping in mind delivering high coverage of the second dose via routine schedule is necessary to ensure maintenance of elimination in the long-term. SIAs are needed before the build-up of susceptibles (through vaccine failure and failure to vaccinate) reaches the threshold that can sustain an epidemic (estimated at around one birth cohort). Follow-up SIAs may be required. The higher the first dose coverage, the longer the interval between SIAs.

4.1.3 Timing of first and second dose

In most countries, measles immunization is scheduled at age nine months, in line with WHO advice for early protection. As measles incidence declines due to high vaccine coverage, and the risk of early infection declines, countries can consider changing the timing of the first dose to age 12 months; at this age, 5% to 10% more children gain immunity from the first dose.

Shifting the timing of the first dose is especially useful if there is a long gap until the second dose. Simple mathematical modelling can provide insight into the impact of the age (see Annex 2).

The second dose is not a booster, but it is given to protect those who fail to be protected by the first dose. Therefore, it can be scheduled at any time from one month after the first dose. To limit the accumulation of susceptibles among school-aged children, the second dose should be scheduled no later than school entry.

4.1.4 Reporting of routine coverage with the first and second doses of measles-containing vaccine (MCV)

MCV1 and MCV2 (if scheduled) coverage reporting and analysis at subnational level need to be regularly undertaken. The reporting period should be specified, and the denominator of each coverage estimate should be carefully matched to the population reflected in the numerator. For example, if a country schedules MCV1 to be received at age 12 months, an annual coverage estimate could be calculated as the number of children aged 12–23 months who received vaccine during the year divided by the number of children in the population aged 12–23 months. If data on the actual number of children aged 12–23 months is not available, use the estimated births during the previous year.

The denominator for MCV2, if a second dose is scheduled, is that of the birth cohort that is eligible for that dose. For example, if MCV2 is scheduled at 15 months, it will be those who reached their second birthday; if scheduled at 5 years, it will be those who reached their sixth birthday during the reporting period. The numerator will be the number of eligible children who receive a second dose during the reporting period.

4.2 Protecting older children through supplemental immunization activities (SIAs)

In the pre-vaccine era, about 99% of children developed immunity from disease by the time they reached young adulthood. With immunization, measles transmission decreases. Thus, many children born during periods of moderate immunization coverage are likely to be susceptible because they were not immunized and they did not develop immunity from disease.

When countries move towards measles elimination, susceptible groups of children should be identified and vaccinated through SIAs as soon as possible, before they reach adulthood and become much harder to reach.

Detailed advice on implementing SIAs is available (see *Measles SIAs - A Field Guide*, WHO, 2004 in press). Additional support is available from the WHO Western Pacific Regional Office for planning and implementing SIAs (see Annexes 3 and 4). The key points are to:

- ensure adequate political commitment at all levels to achieve high coverage in all targeted age groups;
- allow adequate time and resources for planning at national and subnational levels, including detailed microplans;
- closely supervise and monitor implementation; and
- ensure capacity and commitment to follow up in areas that fail to achieve high coverage.

As indicated by the population immunity profile, countries should make every effort to conduct SIAs in all age groups of children, i.e. up to school-leaving age. **Experience in countries in the Western Pacific Region, where initial campaigns have targeted a more limited age group (e.g. through age five or 10 years), is that measles continues to circulate in older age groups, particularly among school-aged children.**

5. SURVEILLANCE AND LABORATORY SUPPORT

Two key areas where progress needs to be assessed because they are essential for measles elimination are surveillance and laboratory confirmation of diagnosis. Surveillance monitors progress towards, and guides actions to achieve, measles elimination.

Core surveillance functions are case detection, reporting, investigation (including confirmation of diagnosis), analysis, interpretation and dissemination. Laboratory testing to confirm a clinical diagnosis of measles is an essential part of the surveillance system. WHO guidelines on measles surveillance, including details on collection and shipment of specimens, are available.⁵

As the Region moves toward elimination, all countries will need to implement comprehensive reporting with case-based measles surveillance and provide access to an accredited laboratory for the confirmatory testing of suspected measles cases. Annex 5 of the Regional Plan outlines the actions needed to establish case-based surveillance or to strengthen it. Additional guidance for countries is likely to be country specific. Each country needs to prepare and disseminate measles case definitions, reporting and investigation forms, and the actions to take in response to suspected measles cases. One action that all countries should undertake is detailed mapping of cases and coverage to focus activities on priority areas.

Countries should establish communication strategies to encourage prompt reporting and investigation of all suspected cases. Posters and pamphlets can be useful supplements to the surveillance manual for prompting health workers to report (and in some cases start to investigate) measles cases, and reminding them exactly what needs to be done.

Ongoing analysis and interpretation of the surveillance data is the ultimate purpose of the data collection, reporting and investigation of cases. Regular feedback and dissemination of the status of measles epidemiology is needed, and should guide all control strategies. Countries should consider establishing a regular measles elimination bulletin as a mechanism for providing updated feedback.

A sensitive surveillance system is essential for monitoring progress toward measles elimination. Initially, the primary purpose of measles surveillance is to detect, in a timely manner, all areas in which measles virus is circulating, but not necessarily to detect every case. This requires the notification and timely case investigation of all suspected measles infections. Laboratory investigation for anti-measles IgM antibodies of suspected measles cases is important to permit health authorities to confirm or exclude measles virus infection. To be discarded, a suspected measles case must have a thorough epidemiologic investigation, including a negative laboratory result for measles antibodies. Even after indigenous transmission has been interrupted, the maintenance of a surveillance system is important so that any imported measles cases can be detected early. Weekly measles surveillance bulletins — summarizing reporting, current outbreaks, cases under investigation, and confirmed measles cases by geographic area—should be distributed.

5.1 Case classifications

The following are the case classifications recommended by WHO. Each country should either use these definitions or modify them based on local conditions. The case definitions and related actions need to be widely disseminated.

⁵ Guris D. *Module on best practices for measles surveillance* (WHO/V&B/01.43). Geneva: World Health Organization, 2001.

A **suspected measles case** is any illness that meets all the following clinical criteria (case definition): (1) fever; (2) maculopapular rash (i.e. non-vesicular); and (3) cough, coryza (i.e. runny nose) or conjunctivitis (i.e. red eyes). It can also be any person in whom a clinician suspects measles infection.

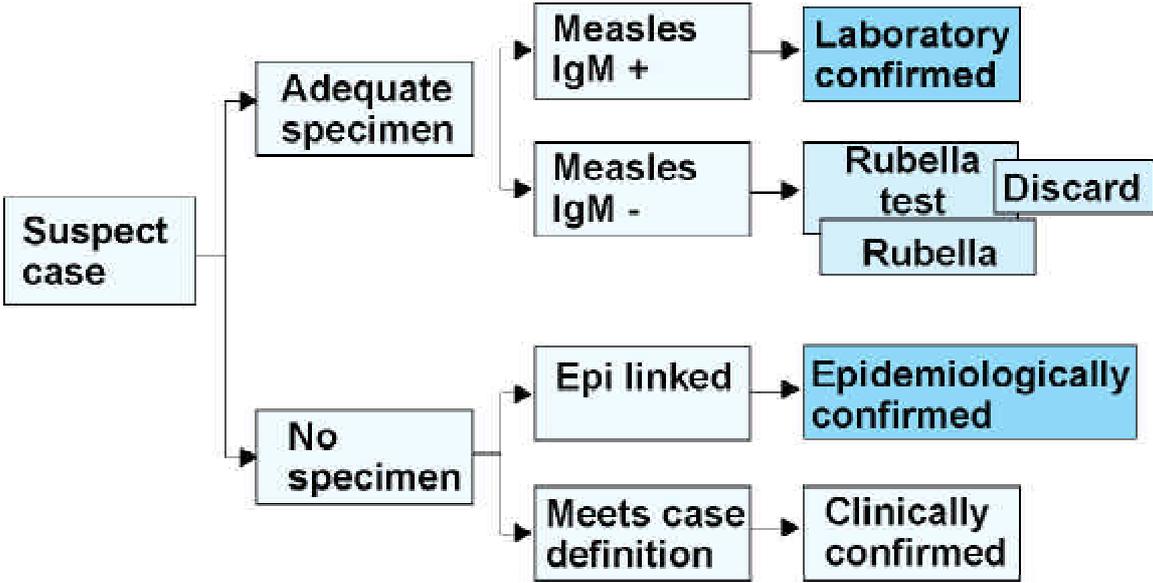
A **laboratory-confirmed case** is a suspected case with a positive laboratory test result for measles-specific IgM antibodies.

An **epidemiologically-confirmed case** is a suspected case with documented exposure (that is, epidemiologically linked) to a confirmed measles case within the incubation period.

A **clinically-confirmed case** is a suspected case with no blood test taken or exposure history, but that meets the clinical case definition.

A suspected case with a negative laboratory test is **discarded** as non-measles, but should be tested for rubella in countries and areas approaching measles elimination.

Figure 2. Case classification scheme



5.2 Surveillance actions

The actions in response to cases will depend on the level of measles control and local resources. As countries move towards elimination, it becomes important to track every chain of transmission and to confirm every suspected case. At all stages, surveillance data should provide overall and age-specific estimates of the incidence of measles, as well as other subnational analysis. Minimum data to be collected are the date of rash onset, age, immunization status, location and outcome (i.e. if the patient died or not). The immunization status data are useful for identifying potential issues with vaccine efficacy.

Figure 3. Suspected measles case investigation form

Suspected measles case definition: [Fill in your country's definition]

Complete this form for: **All cases for which a health worker suspects measles.**

Identification		Case # <input type="checkbox"/>		<input type="checkbox"/> A-Urban <input type="checkbox"/> B-Rural <input type="checkbox"/> Z-Unknown	
State or province: _____		Date of notification: <u>dd/mm/ year /</u>		Source of notification: <input type="checkbox"/>	
Country: _____		Sex <input type="checkbox"/>		<input type="checkbox"/> A-Male <input type="checkbox"/> B-Female <input type="checkbox"/> Z-Unknown	
City: _____		Age <u> </u> <u> </u> <u> </u> <u> </u>		<input type="checkbox"/> A-Public <input type="checkbox"/> B-Private <input type="checkbox"/> C-Laboratory <input type="checkbox"/> D-Community <input type="checkbox"/> E-Active search <input type="checkbox"/> Y-Other <input type="checkbox"/> Z-Unknown	
Name: _____		Years Months		# of documented doses: _____	
Name of mother or father: _____				Date of last dose: <u> </u> <u> </u> <u> </u> <u> </u>	
Address: _____				of measles vaccine. ZZ=Unknown	
<hr/>					
Clinical data					
Date of examination: <u>dd/mm/ year /</u>		Conjunctivitis <input type="checkbox"/>		Coryza <input type="checkbox"/> A-Yes	
Fever: <input type="checkbox"/>		Date of onset of fever <u>dd/mm/ year /</u>		Cough <input type="checkbox"/> B-No	
<input type="checkbox"/> A-Yes <input type="checkbox"/> B-No <input type="checkbox"/> Z-Unknown				Lymph nodes <input type="checkbox"/> Z-Unknown	
Date of rash onset <u> </u> <u> </u> <u> </u> <u> </u>		Type of rash <input type="checkbox"/>		Hospitalized <input type="checkbox"/> Name of hospital _____	
		<input type="checkbox"/> A-Maculopapular <input type="checkbox"/> B-Vesicular <input type="checkbox"/> C-Other <input type="checkbox"/> Z-Unknown		Death <input type="checkbox"/> Date of birth <u>dd/mm/ year /</u>	
<hr/>					
Laboratory data					
Date sample taken <u> </u> <u> </u> <u> </u> <u> </u>	Laboratory _____	Received in laboratory <u>dd/mm/ year /</u>	Type of test <input type="checkbox"/>	Antibody result <input type="checkbox"/>	Date of result <u>dd/mm/ year /</u>
		<u>dd/mm/ year /</u>	<input type="checkbox"/> A-HI	<input type="checkbox"/> A-Measles	<u>dd/mm/ year /</u>
		<u>dd/mm/ year /</u>	<input type="checkbox"/> B-IgM capture	<input type="checkbox"/> B-Rubella	<u>dd/mm/ year /</u>
		<u>dd/mm/ year /</u>	<input type="checkbox"/> C-NT	<input type="checkbox"/> C-Dengue	<u>dd/mm/ year /</u>
		<u>dd/mm/ year /</u>	<input type="checkbox"/> D-CF	<input type="checkbox"/> Y-Other	<u>dd/mm/ year /</u>
			<input type="checkbox"/> E-Indirect IgM	<input type="checkbox"/> Z-Unknown	
			F-IgG-EIA		
			Y-Other		
			Z-Unknown		
<hr/>					
Classification					
A-Suspected <input type="checkbox"/>		B-Discarded <input type="checkbox"/>		C-Confirmed <input type="checkbox"/>	
		F-Rubella I-Dengue Y-Other Z-Unknown		A-Laboratory B-Epidemiologic link Z-Clinical diagnosis	
Date of diagnosis or final classification: <u>dd/mm/ year /</u>					
<hr/>					
Possible source of infection					
Travel during 7-18 days prior to rash onset? <input type="checkbox"/>		Was there contact with another confirmed measles case 7-18 days prior to rash onset? <input type="checkbox"/>		Was there a confirmed case of measles in this area prior to this case? <input type="checkbox"/>	
<input type="checkbox"/> A-Yes <input type="checkbox"/> B-No <input type="checkbox"/> Z-Unknown		<input type="checkbox"/> A-Yes <input type="checkbox"/> B-No <input type="checkbox"/> Z-Unknown		<input type="checkbox"/> A-Yes <input type="checkbox"/> B-No <input type="checkbox"/> Z-Unknown	
Location: _____					
<hr/>					
Investigator					
Name: _____		Position: _____			
Signature: _____		Date of investigation: <u>dd/mm/ year /</u>			
Comments: _____					

5.2.1 Case detection

Widespread dissemination of the national case definition to all health workers, together with encouragement to report cases, is needed. In addition, it may be useful to have public information campaigns to encourage people with fever and rash to present to health workers so that they can be detected and reported.

5.3 Identification and notification of suspected measles cases

Routine reporting is the backbone of a surveillance system. Monitoring of suspected cases should be carried out by an established network, including health facilities, private practitioners, hospitals and laboratories. Investigation of notified suspected measles cases should take place rapidly (i.e. within 24 to 48 hours). The monitoring system should include at least one reporting source identified in each municipality. It may be necessary to convince public and private health personnel of the importance of measles reporting since many consider the disease an unavoidable fact of childhood. Additionally, many private practitioners may not have seen a measles case or remember what one looks like, and therefore may be reluctant to report. To increase physician and nurse participation, visits should be made to association meetings and, if necessary, directly to clinics. It is advisable to provide a specific form indicating key information to report (Figure 3). It is crucial that when zero cases are reported, such reports actually reflect the absence of suspected cases in the community.

5.3.1 Health facilities

Every health facility should designate one individual and one or two alternates to be responsible for keeping track of suspected measles cases and immediately reporting all new suspected measles cases. Reports should be submitted to local and/or state surveillance coordinators. A special 'hot line' should be established to convey this information by the fastest means possible (aerogram, telegram, telephone, facsimile, e-mail, etc.). State, regional, and provincial officials should, in turn, transmit weekly to the national level the reports they receive from the health facilities in their jurisdiction, and national authorities should report weekly to coordinating agencies (see Box 1).

Box 1. Sample health centre measles surveillance procedure

(1) Ensure that all patients with fever and rash illnesses have the **Case Investigation Form attached to the medical chart** when seeing the doctor/nurse.

(2) Nurses and/or doctors should ask parents whether there are any fever and rash illnesses occurring in their villages/towns.

(3) When a health care provider suspects measles virus infection, the **district health officer should be notified immediately**. The surveillance case definition for a 'suspected measles case' is any patient meeting the following criteria: (1) fever; (2) maculopapular rash (i.e. non-vesicular); and (3) cough, coryza (i.e. runny nose) or conjunctivitis (i.e. red eyes). It can also be any person in whom a clinician suspects a measles infection.

(4) For all suspected measles cases, a blood specimen should be sent to the epidemiologist. A copy of the measles case investigation form should be included with the blood specimen.

(5). Plans should be made to visit the home of the patient and the surrounding area to find additional cases.

(6) Whenever suspected measles cases are identified, the doctor or nursing director should call the epidemiologist in charge of measles surveillance.

(7) Each Tuesday, the **weekly surveillance report**, which summarizes the number of suspected cases seen or reporting ZERO cases seen in the previous week, should be sent to the epidemiologist by telephone, facsimile or messenger. A copy of the measles case investigation form should be included.

All health professionals who are likely to be in contact with suspected measles cases should be provided written material that describes their responsibilities and duties. Training and close ongoing supervision are important, as staff turnover may be frequent in many areas. National and provincial/state surveillance personnel should visit all clinic staff to train them. Presentations on surveillance should be made to doctors, nurses, allied health personnel and record clerks. The design and use of posters and other visual materials illustrating responsibilities should be encouraged. Key points to consider are the following:

- Repeated visits by programme surveillance officers will be required to establish and monitor all levels of the reporting system.
- All suspected cases should be investigated by epidemiologists or other specially trained staff (in non-outbreak settings), and an appropriate laboratory specimen should be obtained from each case and tested promptly.
- Each suspected case should be given a unique identification number, which should be used whenever the case is cited. The case numbers should begin with one or more three-letter combinations to designate the geographic location, followed by the year and the case number (for example, PHL-MIN-97-001 indicates case number 1 of 1997 for the state of Mindanao in the Philippines).
- Regular reports should be made each week, even when no suspected cases of measles have been identified. Consideration should be given to developing a special report form for measles that would include other vaccine-preventable diseases.

5.3.2 Private practitioners

It is important that private medical practitioners be included in the surveillance system as they likely will be the first to see suspected measles cases. Communicating by letter is recommended (see Box 2). In some areas, sentinel reporting systems can be set up among a community's key paediatricians. A successful system requires good coordination, training, frequent contact and feedback.

5.3.3 Hospitals

Case finding through the emergency department and paediatrics ward is critical to the success of a measles surveillance system. A doctor or nurse should be assigned at each hospital to check paediatric and infectious disease wards visually and to review admission records for suspected measles cases. Reports may be submitted by telephone, e-mail, facsimile, courier service, etc.

5.3.4 Community sources

In addition to all health facilities, a network of community reporters needs to be organized to report suspected measles cases. These reporters may include pharmacists, private practitioners, health workers at private clinics, village leaders, school personnel, and anyone else likely to learn of or have contact with sick children.

5.3.5 Laboratory reporting

Every effort must be made to ensure that laboratory, epidemiologic, and operational personnel work closely together. It is important to establish routine communications with all local laboratories that may receive serum specimens for diagnosis of suspected measles cases. Laboratory personnel should be instructed to notify the surveillance coordinator immediately when specimens are labelled 'measles', or any other rash illness with fever. In any local laboratory, the logbook should be checked once each week to ensure that all suspected cases are being reported promptly (see Annex 5, for example).

Box 2. Sample letter to private physicians

26 September 2005

Dear Doctor,

The Ministry of Health has joined with other World Health Organization member countries in a Measles Elimination Campaign. You probably remember the successful immunization campaign, that was conducted in May of 2004.

A national measles surveillance system has been developed to keep track of all suspected cases of measles. As the incidence of measles falls, the need to monitor other infectious diseases with exanthemas becomes more important; these include dengue, scarlet fever, rubella, coxsackie, chickenpox, roseola, etc.

Measles is a highly transmissible acute infectious viral disease. You should suspect measles in patients presenting with the following signs and symptoms:

- high fever, and
- generalized maculo-papular rash, and
- cough, or coryza, or conjunctivitis.

We are requesting your participation in our Measles Surveillance System. Please report any patient of any age in whom you suspect measles infection. Enclosed is the surveillance form that we are asking you to complete on each patient with suspected measles. May we suggest that your receptionist/nurse be provided with these forms and instructed to include this form whenever a patient has suspected measles.

In addition, if you see a patient with a suspected measles infection, please contact your local health officer, Dr Eric Smith, at (555) 674-2432 as soon as possible. To confirm measles infection in the laboratory, a blood specimen should be collected immediately from ill patients. If needed, we can assist with either the collection or pick-up of the specimen.

I am personally looking forward to working with you on this programme. Thank you for your cooperation.

Yours faithfully,

Dr Samuel Jones
Senior Medical Officer of Health

5.4 Case investigation

Suspected measles cases should receive a case identification number, as described in Section 5.3.1, to aid in case tracking. All communications and forms related to the case should cite the identification number. A visit should be made to the home of the initial suspected cases of an outbreak to obtain basic demographic and clinical information. The steps to be followed are explained in Box 3. It is important to remember to obtain blood specimens from initial suspected measles cases. It is recommended that sample be taken at first contact unless it can be assured that the patient is available for a sample to be taken on day 3 or 4 of rash, the optimal time to measure IgM responds in the laboratory. Once the laboratory has confirmed the outbreak, it is not necessary to take blood from every suspected measles case. In addition, surveillance sites and surveillance coordinators in nearby areas should be informed that a suspected case has been identified. If the case is located close to a national border, the neighbouring country should be informed.

Establish the time as soon as possible for a follow-up visit at the patient's home to evaluate the family/friends for evidence of illness and to provide immunizations as needed. Also, conduct contact tracing to identify the source of infection and determine whether other areas have been exposed or are also experiencing outbreaks.

Box 3. Investigation procedures

NOTE: During the first contact, the health care provider must make every effort to obtain the basic information, clinical data and a blood sample, as it may be the only contact with the patient.

(1) As soon as a health care provider suspects measles infection, the patient or parent of the patient should be informed that a public health nurse will be visiting their home. Explain the measles elimination programme and why a visit is necessary.

(2) Arrange for a time to visit the family when all family members are expected to be at home; this may mean an evening visit.

(3) On the field visit, take measles case investigation forms and measles vaccine. Only suspected measles cases should have blood drawn.

(4) Ask about additional cases in the home, adjacent homes or in the neighbourhood. Remember that some cases may be in either the incubation period or at the early stages of the illness, with only a fever and cold symptoms. It is important that the families know whom to contact if a rash should occur. In addition, a visit/call should be made every two days for a period of two weeks to ask if any new cases have occurred in the household.

(5) All families should be advised to keep the patient at home and to keep the number of visitors to a minimum until the rash disappears.

(6) Ask the family if they know where the patient got the illness. It will be necessary to explain the incubation period to them, and that after exposure occurs it takes about 10 days for symptoms to start. Remember that the case may have been exposed to someone who did not have a rash. This is important, as measles is highly contagious even before the rash appears.

(7) Visit adjacent homes (for example, within a radius of 100 to 1000 yards around the case or in the same block or neighbourhood) and ask in person whether any cases of fever and rash have occurred during the previous month. Also check the immunization status of all children under 15 years of age living in the households.

(8) Investigate any reports of either rash illnesses or general fever/colds. It may be necessary to request that other clinics go to the homes of possible sources to see if there has been a rash illness and to fully investigate the case.

(9) In addition, preschools, nurseries, schools, church groups, etc. in the area should be visited to find out if any fever and rash illnesses have been occurring.

(10) Vaccinate or revaccinate immediate household members and any neighbours, playmates or schoolmates who have been exposed directly to the case during the illness. This usually includes children 9 months to 14 years of age. Remember to take vaccination consent forms so that, if necessary, teachers can pass them on to the parents for permission to vaccinate.

(11) Send out pamphlets or notify the neighbourhood and other preschools and schools by word of mouth that there is a suspected measles case in the area, and that anyone between 9 months and 14 years of age who has not been vaccinated needs to be vaccinated as soon as possible.

(12) Call local private medical doctors to inform them about the suspected measles outbreak and to ask if they have seen any cases of fever and rash illness.

Transmission is likely to have occurred from a person who had a rash illness or prodromal symptoms and later developed a rash. Inquiries should be made to determine whether cases are occurring in places visited by the 'case under investigation' between seven and 18 days prior to the onset of the rash, such as a preschool centre, school, or another town or village. If there are more than 10 suspected cases in a single outbreak area, household visits should be reduced or eliminated, depending upon the availability of investigators. However, the Suspected Case Line Listing should be filled out for each suspected case and particular attention paid to obtaining basic demographic data, including the age and vaccine history of the patient.

5.4.1 Case finding

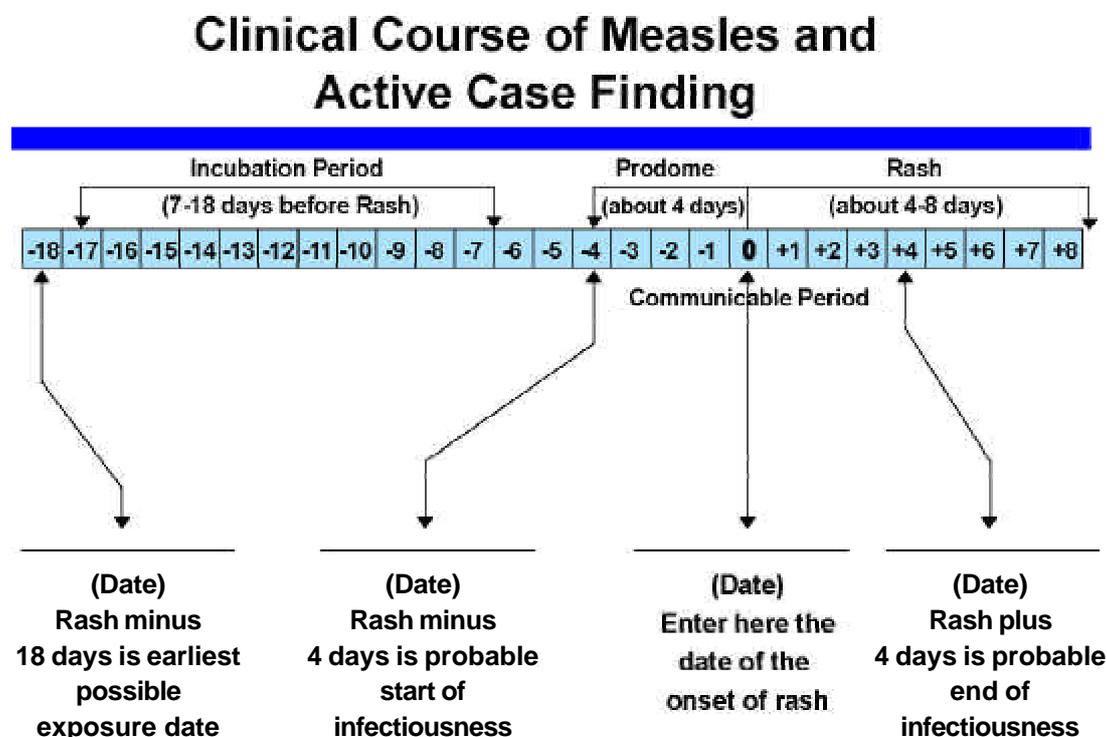
To find additional suspected measles cases in the community, the public should be kept well informed and community leaders should be asked to assist in case finding. Health staff in the affected and nearby areas should use every contact with patients as an opportunity to inquire about rash and fever illnesses in the neighbourhood. Efforts to identify additional cases should also extend well beyond the neighbourhood community in which the suspected case lives. Case-finding activities may include visiting blocks adjacent to the affected household, sending notices to health care providers asking if they have seen or heard of persons with fever and rash illnesses, and/or reviewing records at the local health centres, hospitals and clinics.

The aim of the investigation is to track and describe measles transmission and to identify any failures of the immunization programme that need to be addressed, such as failure to reach certain communities with immunization or potential cold chain problems leading to vaccine failure. The investigator needs to:

- confirm the diagnosis (laboratory test - in five to 10 cases for an outbreak);
- inform neighbouring areas/countries of confirmed measles transmission so that they can be on heightened alert;
- identify the potential source of infection(s) from the travel and exposure history (seven to 18 days before rash onset) and advise the source country/area;
- find other cases, including those exposed to the index case during the communicable period (four days before to four days after rash onset);
- assess immunization status in the community and surrounding areas; and
- make sure that all cases are reported and that the outbreak is documented.

When measles is common, only a sample of cases can be investigated, and less effort needs to be spent on identifying the source of infection if there is endemic transmission. Of course, the age and vaccination status of the cases must be recorded as a minimum. And even at this stage, it is important to develop investigation capacity, as well as to ensure laboratory confirmation of cases.

Figure 4. Clinical course of measles



5.5 Monitoring and feedback

The number of units reporting and the timeliness of the reports should be monitored weekly. To evaluate the weekly reporting system (particularly in areas with all negative reports), interviews should be conducted with personnel involved in surveillance at the regional level and in selected districts, and with individuals from reporting units within a state or area.

Feedback includes providing surveillance participants with the following: (1) the number and location of reported cases, (2) an assessment of the level of promptness and accuracy of their surveillance reports, (3) information on the effectiveness of vaccination and control activities, (4) specific recommendations on how to solve common problems, and (5) commendations of personnel doing excellent work. Regular measles surveillance bulletins, which are sent to the reporting sites and to interested parties, are an excellent way of providing such feedback.

5.6 Outbreak response

Identifying and immunizing susceptible groups can prevent measles outbreaks, and should of course be the primary focus. It is much harder to control an outbreak once started. Because measles virus continues to circulate in many parts of the world and international travel is readily available, importations of measles virus into measles free areas can be expected to occur. Therefore, it is necessary to maintain high levels of population immunity among persons living in these areas. Maintaining high levels of measles immunity will reduce the possibility that measles will spread following an importation. Experience has shown that, because of the very

high communicability of measles, many susceptible persons will already have been infected with measles virus before an outbreak is recognized and control activities can be implemented. The outbreak response, and the definition of how many cases constitute an outbreak will depend on the level of control. As countries approach very near elimination status, a single case of measles would constitute an outbreak and should be investigated immediately and comprehensively.

The reporting, investigation, and response to an outbreak is the same as that for a single case (see Surveillance): (1) confirm diagnosis with laboratory test (five to 10 samples are recommended); (2) alert neighbouring areas/countries; (3) identify source of virus; (4) identify potential spread; (5) assess immunization status of community/surrounding areas; and (6) analyze data and plan response.

If the investigation estimates population immunity at 95%, no additional response is needed. High population immunity is sufficient to prevent ongoing transmission. Thus, a benefit of achieving and maintaining high levels of measles immunity is that outbreak response (other than investigation) is no longer needed following an importation. If population immunity is much lower than 95%, the priority is to improve population immunity via any immediate response to the outbreak.

Although effective control of an outbreak may be very difficult, and resources are best expended on outbreak prevention, an appropriate public health response must be made (see Box 4).

Box 4. Steps in outbreak response

- (1) Isolate in household and investigate suspected measles case(s).
- (2) Obtain appropriate blood specimens for laboratory confirmation.
- (3) Inform other health authorities.
- (4) Assess coverage in affected and surrounding areas.
- (5) Provide measles vaccine to unvaccinated persons.
- (6) Ensure appropriate case management, including vitamin A administration in an age-appropriate dose.
- (7) Enhance surveillance.
- (8) Analyze/summarize outbreak.

5.6.1 Isolation instructions

At home, a suspected measles case should only be permitted contact with immediate family members until five days after the rash appears. Communicability greatly decreases after the second day of rash. In hospitals, patients with suspected measles should be isolated from the onset of symptoms through the fifth day of rash. However, suspected measles cases should not be hospitalized unless absolutely necessary because of the high risk of transmission in the hospital.

5.6.2 Close contacts

- Contacts are defined as all persons living in a household or other close quarters with the case during the infectious period (five days before to five days after the onset of the rash).
- Contacts without evidence of measles immunity should immediately be vaccinated. They should also be instructed about the symptoms of measles prodrome and told to avoid contact with other persons for two full weeks after exposure.

- If less than 14 days have elapsed since the case's rash began, all contacts should receive the isolation instructions whether or not they have been immunized.
- During the second week after exposure, at the first sign of possible measles (fever, runny nose, cough, or eyes bothered by light), the contact should be instructed to stay at home. The contact should not attend school, preschool, work, church, clubs, meetings, parties, babysitting groups, etc. If the illness is measles, it will become apparent in one or two days by the severity of the illness and the presence of a rash. Parents should be advised to notify the health care provider immediately upon rash onset.

5.6.3 Investigation

A suspected measles outbreak may be defined as a greater number of cases than expected in a defined geographic area within a one-month period. General guidelines for outbreak investigation are given in Box 5. When a measles outbreak occurs in a defined geographic area and includes more than 20 cases, data gathering efforts should be limited to obtaining basic information from each case, such as name, address, age, immunization history, date of rash onset, and outcome (see Annex 6). Visits to affected households should be greatly reduced as they are time-consuming and may divert attention from the more important control measures such as vaccinating previously unvaccinated children. Once the presence of measles virus circulation has been confirmed in the laboratory and appropriate specimens have been collected for viral isolation, blood does not need to be collected from every suspected measles case. During an outbreak, patients in whom a health care provider strongly suspects measles infection may be considered confirmed via epidemiologic linkage if contact is documented, or clinically confirmed otherwise. When the number of reported suspected cases has decreased to low levels, the collection of blood specimens may be useful in order to document the end of the outbreak. Limiting the number of blood specimens collected will save valuable staff time and prevent overloading of the laboratories.



Box 5. General guidelines for investigation of measles outbreaks

(1) Confirm the diagnosis.

- (a) Serologic testing of suspected measles cases
 - collect one blood specimen
- (b) Appropriate specimens for viral isolation
 - collect midstream urine specimen in sterile container

(2) Identify and investigate suspected measles cases.

- (a) Basic surveillance variables
 - age, sex, residence
 - date of rash onset
 - date of last measles vaccination/number of doses received
 - date of collection of blood specimen
 - date of collection of urine specimen
 - possible source of exposure 12–17 days prior to rash onset
 - exposure to another laboratory-confirmed measles case?
 - travel to foreign country with known measles virus circulation?
 - possible transmission to others three days prior to rash onset to three days after rash onset?
- (b) Questions to be asked
 - Where was patient born?
 - When did patient move to current residence?
 - Have there been other cases within the household?
 - Have there been other cases in the neighbourhood?
 - Where does patient work/study?
 - How does the patient travel to work/school?
 - Are there other cases in the workplace/school?
 - Where does the patient socialize (e.g. market, church, club, school)?
 - Are there other cases in these social groups?

(3) Describe the outbreak (descriptive epidemiology).

- (a) What was the total number of confirmed cases?
- (b) What were the age distribution and vaccination status of confirmed measles cases?
- (c) Which municipalities have measles circulation occurring? (maps)
- (d) In each affected municipality, what was the age and vaccination status of the first case?
- (e) In each affected household, what was the age and vaccination status of the first case?
- (f) How long did the epidemic last? (epi-curve)

(4) Determine source of outbreak.

- (a) Classical epidemiology (who acquired infection from whom)
- (b) Molecular epidemiology via genotypic analysis of measles virus isolates

(5) Determine risk factor for measles infection (analytical epidemiology).

- (a) Age and vaccination status of cases
- (b) Place of exposure (school, office, church, etc.)
- (c) Attack rates
- (d) Possible risk factors
 - age group and vaccination status
 - travel to areas where measles is endemic
 - occupation (e.g. health care, tourism industry)
 - school/church attendance
 - visit to health facility

5.6.4 Evaluation of vaccination coverage

Vaccination coverage data should be reviewed as soon as a measles outbreak is suspected (see Box 6). Persons and areas potentially at risk for measles transmission should be identified.

The priority of the vaccination activity is to provide measles vaccination to previously unvaccinated infants and children (see 'Measles Vaccination' below).

Box 6. Points to consider at the start of an outbreak

Population data – Obtain most recent population size and age distribution.

What's been done – List any actions already taken.

Case review – List reports of cases in area during previous six months.

Vaccination coverage rates – Obtain existing coverage data and include unofficial estimates.

Spot map – Use pins or a pen to mark the location(s) of case(s) and areas targeted for immunization on a map.

Resources – Determine what resources are available at all levels for outbreak control (transportation, vaccine, cold chain materials, promotional materials, etc.). Human resources should include field staff to assist in the outbreak, including staff from other programmes, district staff, medical and nursing students, interpreters and drivers. Arrange for transport and for travel advances.

Arrivals – Inform appropriate health/community authorities when and where any special teams will be arriving, and ensure that specific health staff/community representatives will be present.

Supplies - Organize necessary supplies. This includes:

- (1) adequate vaccine based on estimated target population;
- (2) cold chain materials (ice packs, cold boxes, vaccine carriers, thermometers, refrigeration capacity (locally available or must be brought in);
- (3) adequate supply of forms, such as:
 - Line Listings of Suspected Cases (Annex 6)
 - Case Investigation Forms (such as Figure 3)
 - Outbreak Control Summary (Annex 8)
 - Mop-up Work Sheets;
- (4) promotional materials (pamphlets, posters, etc.); and
- (5) adequate case management
 - vitamin A
 - antibiotics
 - staff training, if necessary.

5.6.5 Cross-notification

Health authorities at all levels should be informed of and involved in all aspects of surveillance and outbreak response. Health officials in nearby jurisdictions also should be notified and updated as frequently as possible, so that they may begin appropriate preventive actions as needed. If an importation may have occurred, the local health officials in the country from which it was imported should be provided with full details of the case. If a suspected case has travelled or had close contact with individuals from other areas of the country 7–18 days before the onset of the illness, the surveillance coordinator in those areas should be notified immediately. Neighbouring countries should be notified as well. The public should be informed through the media about the outbreak and any control efforts (see Annex 7).

5.6.6 Measles vaccination

There are virtually no contraindications to receiving measles vaccine. The following recommendations serve as a general guide. Specific measures must be based on the prevailing epidemiologic situation in the outbreak area.

5.6.7 Who to vaccinate

Generally, when a measles outbreak is suspected, all children 9 months to 15 years of age without history of measles vaccination should be vaccinated. In addition, consideration should be given to providing measles vaccination to adolescents and young adults residing or working in certain institutions where they may be at risk for measles virus transmission, including military bases, university dormitories, hospitals and factories. Finally, children hospitalized or attending outpatient clinics for any reason who cannot provide written proof of measles vaccination should be vaccinated with measles vaccine, if not contraindicated.

5.6.8 When to vaccinate

Vaccination of previously unvaccinated persons should start immediately when a measles outbreak is suspected, without waiting for laboratory confirmation of the suspected measles cases. Soon thereafter the suspected cases should be evaluated by laboratory testing. Though unlikely to stop the outbreak, the vaccination intervention should help to decrease the number of susceptible children and perhaps result in the interruption of measles virus circulation. If the initial suspected cases do not turn out to be measles, then the vaccination activity has helped to raise the level of measles immunity in the community and prevent measles outbreaks in the future.

5.6.9 Where to vaccinate

In both urban and rural areas, the focus of vaccination efforts should be any potential pockets of susceptible (i.e. unvaccinated) infants and children. The largest possible area should be covered. Gathering points such as schools, churches, health posts, etc. may also be chosen as mass vaccination sites.

5.6.10 Enhancement of surveillance

Measles surveillance should be intensified to search for additional suspected cases. All reporting units should be notified of the suspected measles outbreak and be alerted to be “on the look-out” for additional cases. Daily calls or visits to schools, hospital emergency rooms and selected paediatricians may prove useful, especially in urban areas.

5.6.11 Outbreak monitoring

The most recent information on suspected and confirmed measles cases, vaccination activities, and areas visited should be monitored and updated continuously during an outbreak. This information should be recorded in such a way that it can be summarized quickly on the Measles Outbreak Response Summary form (Annex 8). When no new cases are reported during a three-week period, despite the presence of enhanced surveillance, the outbreak may be considered to be over.

5.6.12 Outbreak summary

Careful investigation of measles outbreaks can provide useful information regarding factors that may have facilitated measles virus circulation. The investigation may help to identify risk factors for measles infection and provide information that can be used to refine and improve the measles eradication strategy. To benefit from the investigation and outbreak control activities, it is necessary to organize and report on data related to the outbreak. The report should include at least the following sections:

- (1) introduction
- (2) surveillance methods
- (3) description of the outbreak
- (4) analysis of the outbreak
- (5) control measures
- (6) problems
- (7) conclusions and recommendations.

5.7 Information systems and analysis

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

5.7.1 Data collection

Whether or not the information system is computer-based, it should cover two basic areas: case tracking and site reporting.

Case tracking. At the state and district levels there should be a system that is capable of tracking all reported suspected measles cases until they are either confirmed or discarded. Such a system is characterized by several important elements:

- uniform case identification numbering;
- a standardized case investigation form;
- basic demographic data on each case;
- basic clinical data on each case; and
- the recording and monitoring of laboratory specimens from collection to final laboratory results.

At the central level, essential information, as presented in the Suspected Case Line Listing (Annex 6), should be available for monitoring the basic surveillance indicators of the programme.

Site reporting. At the country level and the subregional level, a system capable of keeping track of reporting units is needed (Annexes 9 and 10). Such units may be a geopolitical jurisdiction such as a county, district or municipality, or a service unit such as a hospital, private clinic or private practitioner. The critical data to maintain on such sites are:

- submission of weekly reports, including negative reporting; and
- timeliness of reporting (on time or late).

5.7.2 Data Analysis

Each geopolitical subdivision within a country should be part of the weekly reporting system and should summarize its experience with measles and other rash-like illnesses on a regular basis. Data from a region should be presented in a standardized format and should include, at a minimum:

- monthly numbers of reported cases and case rates;
- laboratory results;
- final diagnoses of discarded cases;
- age distribution of confirmed cases;
- vaccination status of confirmed cases;
- geographic distribution (urban versus rural); and
- number of cases with case investigation form.

Data from case investigation forms and line listings should be analyzed to provide a descriptive picture of the cases and determine whether standards for case reporting and investigation are being met, including: age distribution, geographic location, source of infection, source of notification and vaccination history of cases.

Age distribution. It is useful to know the age distribution of cases to detect any changes in the epidemiology of the disease and to establish which age groups to target for vaccination.

Geographic location. Cases should be plotted on a map according to their place of residence, and the map compared with vaccination coverage data and surveillance reporting sites. These maps can be useful for coordinating activities (such as setting up vaccination points, etc.).

Source of infection. This information will help to identify areas where the measles virus is still circulating.

Source of notification. This knowledge will help to determine whether improvements are needed regarding notification sources. For example, if cases are being reported only from public health facilities, then additional contacts with private medical doctors and private clinics are required.

Vaccination history of cases. Accurate information on the vaccination history of persons with measles is essential for evaluating vaccine effectiveness and detecting potential problems with the cold chain.

Information dissemination. At the country level, a bulletin, preferably updated on a weekly basis, should be issued with results on reported and confirmed cases. In addition, this newsletter should indicate the number of units reporting each week (including negative reporting). Information about the current epidemiology of acute flaccid paralysis, neonatal tetanus, and other EPI target diseases should also be included. Bulletins should be distributed to all health care providers and other interested health care personnel on a weekly or monthly basis. Regionally, sending regular reports to WPR office will assist regional efforts in measles elimination and provide data for monitoring progress, directing assistance, and providing feedback.

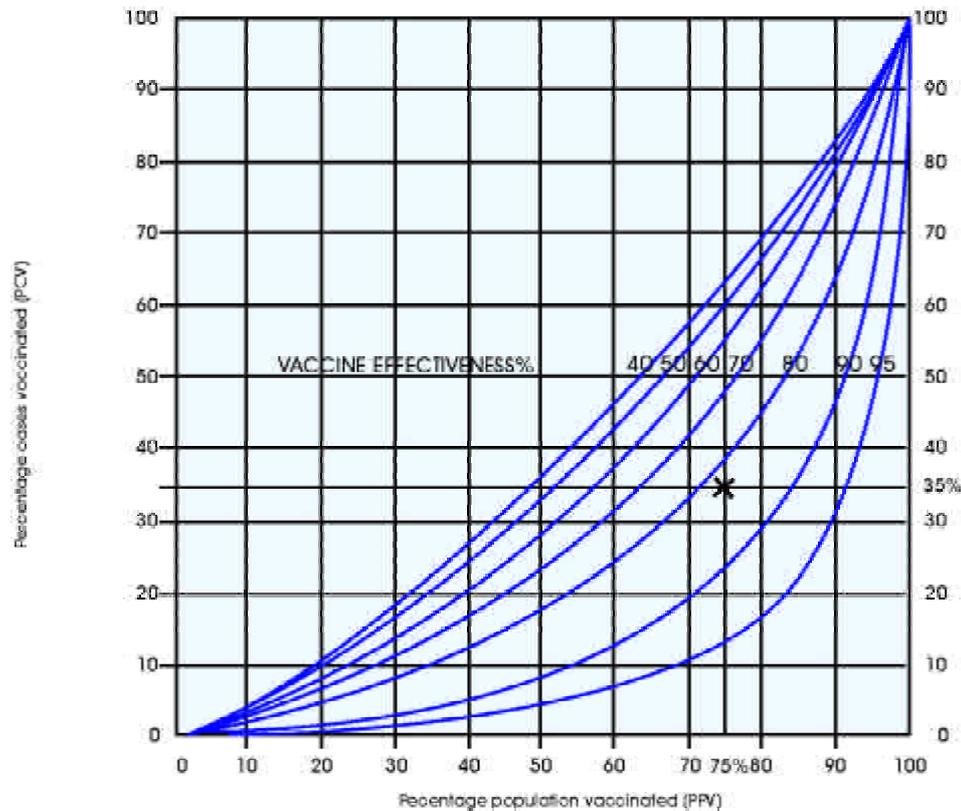
5.7.3 Vaccine efficacy

One aspect of analysis is the estimation of vaccine efficacy (VE) from the immunization status of reported cases. The coverage must be known or estimated for the age group in which cases are occurring. This method is based on the difference between the attack rates among vaccinated persons (ARV) and the attack rates among the unvaccinated (ARU) expressed as a fraction of the attack rate among unvaccinated persons (ARU):

$$VE = (ARU - ARV) / ARU \times 100$$

Vaccine efficacy can also be estimated by using the monogram, as in the example in Figure 5 where the intersection of the lines for 35% of cases are vaccinated and 75% of the population vaccinated at the curve of 80% vaccine efficacy.

Figure 5. Vaccine efficacy monogram



While there are important biases in using this method for estimating vaccine efficacy, it does provide some useful information, including highlighting potential problems with vaccines.

5.8 Case reporting

Routine reporting is the backbone of a surveillance system. All health workers and facilities including private practitioners, hospitals and laboratories should be part of the reporting network.

To encourage reporting, it is important to respond to all reports with at least acknowledgement for the report. In most cases, a more active response in the form of a rapid investigation should be undertaken. A system of local and national feedback on current measles epidemiology based on reporting provides further reinforcement for reporting.

Countries need to establish to whom and how health workers should report suspected cases, and to widely disseminate this information. Only the minimum data required should be requested in the report to minimize the burden of reporting. In most countries, the report will just be the initiating event for an investigation, which allows the collection of more data. Therefore, the report could be limited to notification of a suspected case of measles. To encourage ease and speed of reporting, methods such as telephone reporting or “texting” should be used, where appropriate. The report should lead to an investigation of the suspected measles case(s) within 48 hours to encourage reporting. In some countries, the initial investigation may be undertaken by the reporting health worker.

5.9 Surveillance system indicators

The key indicators and operational definitions were described in Section 3.1. Additional indicators and targets used to monitor, on an ongoing basis, the quality of measles surveillance, include:

- *Proportion of reporting sites that report each week:* At least 80% of surveillance sites should report each week on the presence or absence of suspected measles cases.
- *Interval between rash onset and notification:* At least 80% of the reported suspected cases should be reported within 48 hours of rash onset.
- *Interval between notification and investigation:* At least 80% of the reported suspected cases should be investigated within 48 hours of report.
- *Percentage of laboratory tests undertaken in cases with adequate specimen:* At least 80% of specimens should be taken from initial contact until 28 days post rash onset and reach the laboratory in a suitable state for testing.
- *Percentage of laboratory test results received within 7 days of receipt in laboratory:* At least 80% of specimens must be tested and the results reported back to the surveillance unit within 7 days of receipt of the specimen in the laboratory.

5.10 Laboratory test for classification

Classification of cases is based on the results of laboratory testing for measles-specific IgM (see Section 5.1). A single serum specimen when collected within 28 days of rash onset is used to diagnose most measles cases with antibody-capture measles IgM enzyme-linked immunoassay (ELISA) kits. An antibody-capture enzyme immunoassay (EIA) configuration for the detection of measles-specific IgM is highly sensitive and specific. In previously vaccinated persons, there may be a small increased risk of not detecting an IgM response to measles when specimens are collected more than two weeks after rash onset due to increased rate of decay of IgM. There is some increased sensitivity if the sample is taken on or after day 3 of rash onset (though taking the sample at first contact is recommended, see page 21).

5.10.1 Virus isolation

Where possible—for example to monitor transmission pathways of measles virus—urine (within five days of rash onset), nasopharyngeal (within seven days of rash onset) or lymphocyte (within four days of rash onset) specimens from suspected cases are collected. These specimens from the measles IgM-positive cases are sent to a regional measles reference laboratory for measles virus isolation.

Genomic sequencing of wild-type measles virus isolates from laboratory-confirmed cases will distinguish the origin of measles viruses as indigenous or imported and thus will corroborate whether the transmission of indigenous measles strains have been fully eliminated or not.

5.11 Assessing the existing surveillance system

Although measles surveillance is well established throughout the Region, not all countries have yet established case-based surveillance, or else have not yet fully implemented it to ensure that any areas of measles transmission are identified.

Each country should assess its current surveillance system to identify areas that need improvement for measles elimination. The indicators above will provide a framework for current status as compared to goals, as well as possible surveillance milestones that the country decides to achieve.

Assessing the degree to which the AFP surveillance has been used for measles surveillance, and for countries that have not yet done so working towards adding measles in the AFP surveillance system should be considered. However, measles surveillance will eventually need to be community based, as most cases will not come to hospital.

In some cases, a more formal assessment of surveillance may be needed and the WHO Western Pacific Regional Office can assist in providing an external assessment team.

6. USING IMMUNIZATION AND DISEASE DATA TO IMPROVE PROGRAMME MANAGEMENT

National and subnational analysis of data can provide valuable information to improve programme management.

Each country should decide on the lowest level that it is appropriate to undertake subnational analysis. The performance of each unit at that level should be compared. The comparison between disease incidence and coverage data can be plotted on a chart to identify outliers for both coverage and disease incidence, and to identify areas reporting discordant data, e.g. high coverage and high disease incidence.

In this way, immunization coverage, disease reporting performance as well as data quality may be improved through systematic identification of problem areas. Comparison of coverage data and vaccine utilization data can also provide additional insights.

These analyses can be done for the other vaccines as well, and should be undertaken as part of the comprehensive strengthening for EPI. The focus on measles for disease surveillance makes sense because it is the EPI disease that is most sensitive to coverage.

7. ACKNOWLEDGEMENTS

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ANNEX 1: SYNOPSIS OF MEASLES DISEASE AND VACCINE

The disease

Measles is diagnosed clinically on rash and fever (>38.5°C) illness. The three other symptoms for diagnosis of measles are cough, conjunctivitis, and coryza (runny nose). Koplik spots on the buccal mucosa are found early in the illness. A characteristic red, spotty rash appears on the third to seventh day, beginning on the face, becoming generalized, lasting four to seven days and sometimes ending in branny desquamation.

The disease is more severe in infants and adults than in children. Poor nutritional status (especially vitamin A deficiency) and human immunodeficiency virus (HIV) infection increase the risk of severe disease, complications, and death.

The virus and its transmission

Measles is a Paramyxovirus of the genus *Morbillivirus*; a single-stranded RNA virus with six structural proteins and no known antigenic variation. Small differences in gene sequences enable mapping of a measles family tree, and molecular epidemiology can help identify the source of the virus.

Measles is transmitted through respiratory droplets and through microdroplets (airborne). The primary site of infection is the upper airway (respiratory epithelium of the nasopharynx). Two to three days after invasion and replication in the respiratory epithelium and regional lymph nodes, a primary viraemia occurs with subsequent infection of the reticuloendothelial system. Following further viral replication in regional and distal reticuloendothelial sites, there is a second viraemia, which occurs five to seven days later, which is the best time to collect samples for culture.

The incubation period, from fever to rash onset, varies from seven to 18 days and usually is 10 to 14 days. Measles virus is shed from the nasopharynx beginning from the time of fever onset until four days after rash onset. An infected person is infectious from four days before until four days after the appearance of the rash.

Table A. Comparison of complications of measles infection and AEFI

Complication	Number per 100 000 infections	Number per 100 000 immunizations
Allergic reaction	0	~1
Anaphylaxis	0	0.1
Febrile convulsion	500	~33
Otitis media	7000–9000	0
Pneumonia	1000–6000	0
Blindness	50-200	0
Diarrhoea	6000	0
Encephalitis	100	0.1#
SSPE	1	0
Thrombocytopenia	??	3.0
Death (60% from pneumonia)	10–100 (Industrialized countries) 5000–15 000 (Developing countries)	0

It is not certain that measles vaccine causes encephalitis, figures approx background prevalence.

?? – rate not known, but likely to be much higher than with vaccine

Annex 1

Measles vaccine

Measles vaccine contains a live attenuated virus and is stored as a freeze dried powder (lyophilized) and reconstituted with an accompanying diluent. The recommended storage temperature for lyophilised measles vaccine is 2-8°C at peripheral levels, but can be safely frozen. Exposure to higher temperatures will lead to loss of potency before its expiry date.

Only the diluent produced by the same manufacturer as the vaccine should be used. It must not be frozen as that may crack the vial. The vaccine may contain traces of neomycin with hydrolyzed gelatin and sorbitol added as stabilizers.

After re-constitution, the vaccine becomes very sensitive to light and heat. If kept in a dark place at 2-8°C and used within six hours loss of potency is minimized. The vaccine or diluent does not contain a preservative, so the reconstituted vaccine must be discarded after six hours or at the end of the day, whichever occurs first.

There are several different strains of measles vaccine used globally, all considered equivalent in terms of safety and efficacy in immunization programmes. The vaccine is administered by subcutaneous injection in a dose of 0.5 mL that contains 1000 TCID₅₀ (tissue culture infective doses, median).

There are practically no contraindications for giving measles vaccine, apart from severe immune suppression and severe allergic reaction (anaphylaxis) to a previous dose or constituent (particularly gelatin). Measles vaccine can be safely given to individuals already immune through previous infection or immunization. A mild illness or fever is not a reason to defer immunization, but immunization should be deferred if a child is very unwell or has a high fever.

Measles immunity

Immunity results either from infection or immunization, and is generally life-long. The effectiveness of immunization is age-dependent, in part because of maternal antibodies passed from mother to child in utero, protecting the child for the first few months of life (longer for mothers with immunity from wild measles virus infection rather than vaccine). Maternal antibody interferes with a child's immune response to the vaccine.

Measles vaccine efficacy is ~85% at age 9 months; ~90% at 12 months and ~95% at 15 months. If two doses are given, and the second is given after 12 months of age, about 99% of recipients are protected.

Need for a second dose of measles vaccine

A single dose of measles vaccine gives life-long immunity, and there is no need to have additional doses to 'boost' immunity. As 95% population immunity is needed to eliminate measles, it is not possible to achieve with a single dose – unless coverage is 100% and the first dose is given at age 15 months or later. No country has managed to achieve measles elimination with a single dose schedule; two doses are needed.

If first dose coverage approaches 95% or more, then a second dose (achieving at least 95% coverage) will lead to adequate population immunity to achieve measles elimination. However, even if first dose coverage is lower, measles elimination can still be achieved as long as at least 95% coverage can be achieved by the second dose.

ANNEX 2: MATHEMATICAL MODELLING AND POPULATION IMMUNITY

(supports Section 3.2 on Estimating the population immunity profile)

1. Introduction

Transmission of measles depends on many factors, including the demography of the population, the level of mixing in the community, the level of immunity due to previous exposure and vaccination, and how the immunity is distributed over age and location. All these can be modelled mathematically to provide insights useful for disease control.

2. Three types of transmission pattern

Models indicate three types of possible transmission patterns: ‘sustained endemic transmission’ (pre-vaccine epidemiology), ‘epidemics that fade-out’ (control), and ‘elimination’. Because of a cycle of several years for each of these, observations made in any one year are not typical of what is likely in the next year.

Sustained Endemic Transmission

Transmission of measles can be sustained in a large population where people live in close proximity of each other. The number of new susceptibles (births) are balanced by the number removed (number of cases). However, seasonal and chance factors lead to more-or-less regular epidemic waves with ‘epidemic’ years every two to three years, and continued measles transmission at lower levels in between.

As immunization is added to the population, the size of the epidemics decrease and the length between epidemic years increase.

Epidemics that Fade-Out

Smaller communities cannot sustain endemic transmission. The minimum size depends on the density of the population, the degree of social mixing and the birth rate, but it is typically observed for cities or island communities with less than a few hundred thousand (up to a million) people. In these communities new susceptibles do not arrive fast enough to keep transmission going at all times. Following an epidemic there will be a period of no measles incidence, or an occasional cluster of cases arising from the re-introduction of measles infection. However, without adequate immunization of susceptible individuals the number of susceptible individuals eventually becomes large enough for a re-introduced infection to initiate an epidemic. The pattern is therefore one of epidemics separated by periods of minimal measles incidence. This pattern is also observed with moderate to high coverage with a single dose of measles vaccine.

Elimination

Measles elimination does not mean zero cases. There will continue to be small clusters of cases, as long as there are importations of measles. Introduced cases of measles will sometimes be accompanied by secondary infections, because 100% population immunity is not achievable. But, when all nations reach elimination measles will become eradicated.

Annex 2

3. What population immunity is required to achieve measles elimination?

Models indicate that measles elimination is achieved by maintaining the fraction of fully immunized individuals below a threshold value. It is estimated that this threshold value lies somewhere between 90% and 95%, depending on the community. To achieve elimination the target population immunity should be 95% and this immunity must be uniform over all sectors of the community.

The population immunity is generally unknown, because serological surveys to monitor it are very costly. However, transmission models indicate if an importation leads to an outbreak causing less than 100 cases, then population immunity is likely above the critical threshold for elimination.

4. Timing of doses

Countries should be encouraged to increase the age of administration of MCV1 from nine months to 12 months as soon as disease incidence is reduced to low levels and the risk of infection at very young age is minimal.

A second dose should be given before the child enters school or a childcare centre/pre-school, as most measles transmission occurs in places where many children interact.

5. The impact of immunization

Immunization will reduce measles transmission – the impact more or less proportional to coverage, until the point where there is a temporary interruption of transmission. After that there will be several years of no or limited transmission. Eventually there will be a large outbreak after this “honeymoon period”, unless 95% population immunity is achieved and maintained for elimination.

Pulse immunization (a campaign) for a wide-age range of children will have a greater impact than the same doses given every year to children of a certain age, because of the faster removal of susceptible people.

6. Control eventually leads to a large outbreak

Achieving higher vaccination coverage will protect more individuals against infection and thereby reduce measles incidence. However, a consequence of higher vaccination is that those individuals who remain susceptible will be older. Therefore, with high immunization coverage that is below the level required for elimination, there will eventually be many susceptible individuals. When measles is reintroduced, this will lead to a large outbreak, including affecting many older children and young adults.

7. The effect of imported infection

Importation into a large population with endemic measles transmission has a minimal impact on measles incidence, as it adds little to the amount of circulating virus. As control improves, the importance of importation increases. The extreme example is when transmission has been interrupted but the number of susceptibles has built up to be greater than the epidemic threshold. A single importation can then lead to a large outbreak. However, if population immunity remains above the threshold there will only be a small number of cases.

8. Comparing measles elimination and polio elimination

Polio has been eliminated in many parts of the world. Following interrupted transmission of poliomyelitis, a single new case of poliomyelitis disease creates considerable anxiety and leads to a very extensive and expensive local control program. This is because only about one in 200 poliomyelitis infections leads to a case of poliomyelitis disease, so a new case indicates that a considerable amount of transmission has most likely occurred. In other words, a single new case of poliomyelitis disease is a strong sign that the population immunity is below that required for poliomyelitis elimination.

In contrast, most individuals infected with measles are diagnosed as cases. Therefore a single case, or even a small cluster of cases, is not a strong indicator of a population immunity that is too low for elimination. Consequently, a small cluster of cases does not indicate a need for an extensive and expensive local control program.

9. Estimating population immunity

One way to estimate population immunity is to mathematically model the experience of each birth cohort up to the present. For each birth cohort, there is a progressive accumulation of immunity from immunization and infection. Ignoring the transient immunity from maternal antibodies, each cohort starts as being 100% susceptible to measles. Immunization and infection then progressively increases the proportions who are immune.

For immunization, the estimate of population immunity is dependent on the quality of reported coverage data, including the age at which the immunization was given. In addition, deficiencies in the cold chain as well as programme errors can lead to a reduction in the efficacy of vaccine.

Thus, estimation of immunity is not likely to be very precise, but is likely to be useful in indicating those cohorts with large gaps in population immunity. This is the primary aim of the calculation, and it is possible that useful results can be obtained even with poor quality data.

If there is 80% immunization coverage at age 9 months (assumed vaccine effectiveness of 85% at this time), then an estimate 68% will be immune. The proportion who are immune will then be increased by subsequent infection and/or immunization. To work out the additional proportion who are immune is an arithmetic calculation based on either the age-specific incidence of measles or of immunization coverage (adjusted for vaccine efficacy at the age delivered).

The simplest way to model these cumulative experiences is to have a table with year of birth by row, and measles experience (infection or immunization) by year in each column. In each column the proportion of that cohort that has developed measles immunity is added. A spreadsheet is available from WPRO that can be used to develop these estimates.

10. Limitation of modelling population immunity profile

There are important limitations to the method. For the impact of immunization, data on coverage need to be known, as well as the age that immunization was delivered. In addition to the effect of age on vaccine efficacy, there may be other factors (such as cold chain failure) that need to be incorporated in estimating the impact of immunization on immunity levels.

Annex 2

For the impact of infection, considerable extrapolation from surveillance data are likely to be needed. If a reliable age-specific incidence can be estimated, it is then relatively straightforward to add the immunity from infection for each year of measles experience. The incidence gives precisely the proportion of susceptibles added. However, obtaining age-specific measles incidence from surveillance data is likely to be problematic in many countries because of under-reporting and biases in the reporting systems.

Despite these limitations it is still possible to model the experience of each birth cohort can be modelled, based on available immunization and disease data – suitably adjusted to reflect known biases and limitations. The likely uncertainties in the assumptions, mean that some sensitivity analyses should be undertaken, using different assumptions.

11. Validation of modelled data on population immunity profile

The results of this modelling are likely to be only indicative for identifying birth cohorts (or groups) that are likely to have less than 95% population immunity. The results of the modelling can be validated by analysis of current surveillance data or through a serosurvey.

If there is ongoing measles transmission, the age distribution of cases should be similar to the modelled susceptibility profile – once adjustments for biases in reporting are incorporated. One benefit from improving surveillance quality is to obtain a better age-profile of measles cases so that the population immunity profile can be assessed.

When measles is already well controlled, the only way to validate the estimates of population immunity from the modelling, is through a serosurvey. A sample of about 100 for each age group is needed to provide sufficient statistical confidence (within 5% points) of the estimate.

Given the limitations on data quality of both vaccination coverage and disease surveillance data, another option is for countries to assume that there is less than 95% population immunity in all cohorts born since the introduction of measles immunization. In addition, to immunize all children who are still accessible to an immunization campaign - such as all those under the age of 15 years.

ANNEX 3: CHECK-LIST FOR PLANNING MEASLES CAMPAIGNS

Micro planning for SIAs

1. Microplanning at any level above health centres should have two phases:
 - a. Phase one: Facilitate next level to develop detailed, comprehensive microplans, roles, responsibilities, agreements, etc.
 - b. Phase two: Based on microplans from the next level below, develop a detailed microplan containing a schedule of supervisory visits, inventory management, etc.
2. Microplans should have input from levels above and below. For example, a regional microplan should have national, provincial and city input. It is preferable this input is given from the beginning and not for comments at the end.
3. Microplans should be developed based on data (situation analysis).
4. Microplanning applies to all levels. However, the objectives, roles, responsibilities and tasks change from one level to the next.
5. A microplan should address the following:
 - a. Goal: Why does this program exist? Examples may include: To interrupt measles transmission. To remain poliomyelitis-free. To eliminate neonatal tetanus. To prevent diphtheria.
 - b. Broad Objectives: All objectives should be SMART (Specific, Measurable, Achievable, Reality-based and Timely). This should specifically define what the overall program wishes to achieve. E.g., to safely and effectively vaccinate all infants with a birth dose of BCG, three doses of OPV, three doses of DPT and three doses of HBV; all 1 year olds and all 4-5 year olds with 1 dose respectively of measles; and all pregnant mothers with 2 doses of tetanus toxoid. It is best if the objectives state increase in coverage. E.g., Increase fully-immunized child coverage from 84% to 95% by December 2005).
 - c. Operational Objectives: They should address each aspect of the program necessary to reach the goals. E.g., standards and guideline development including vertical and horizontal role definition, inventory management, cold chain management, human resource management, other resource management, training, supervision/mentoring/monitoring, reporting/recording/ dissemination of information, surveillance.
 - d. Strategy: What strategies will be employed to achieve each objective? For example, the normative guideline development may be a national coordinating committee who reviews existing guidelines, commissions and reviews a country situation analysis and writes the guidelines.
 - e. Activity: What activities are necessary to achieve the strategy? For example, forming a national coordinating committee is necessary in the above example.
 - f. Steps: What steps are necessary to achieve the activity? For example, defining the purpose of the guidelines, developing Terms of Reference for staff, defining who should be a part of the committee, identifying persons meeting the definition and contacting them are all necessary steps to achieve the above illustrative activity.

Annex 3

- g. Role Definition: Roles for organizations should be defined in relation to other groups/partners, including horizontal relationships, (e.g., what are the national vs. the region, provincial and municipal roles during planning and/or during implementation?) and vertical relationships (e.g., among partners).
 - h. Responsible person per step: Each step should have a person responsible to ensure the step is completed.
 - i. Indicator of success: How do we know we have achieved the step? How do we know how far we have come and how far to go?
 - j. Resources required: What financial, human and other resources do we need to achieve the step?
 - k. Resources available: What of the above resources are readily available?
 - l. Steps to obtain resources: What steps do we need to obtain the resources necessary to achieve the step?
6. Mentoring/supervision should be planned so that
- .. National staff visits every region at least quarterly and has a chance to visit (in situ) and discuss key issues with regional EPI and logistics staff, one city health officer, one provincial health officer, one municipal health officer, and one village health centre . National staff should take this opportunity to observe how policies are put in practice, as well as, elicit feedback about how they can best help improve the program.
 - .. Regional EPI and cold chain staff visit every province and city at least quarterly, and have the chance to visit (in situ) at least one municipal health officer, one village health centre and one municipal and city village.
 - .. Provincial EPI and cold chain staff to visit every municipal health officer monthly and at least one village.
 - .. City health staff to visit every health centre at least monthly and at least one village.
 - .. Municipal and village health staff to visit village at least weekly and monthly with village leaders and other community members.

Primer on Rapid Coverage Assessment

Intra-campaign monitoring of coverage is important for 3 reasons : to provide immediate feedback to the vaccinators of any unvaccinated children, use as a supervisory tool, and as a measure of campaign progress. Rapid Coverage Assessments (RCA) used during the Philippines Follow up Measles Elimination Campaign identified thousands of villages (communities) with many missed children. It transformed the campaign in several ways:

- It focused attention on severe problems with population estimates and staff shortages.
- It identified that door-to-door vaccination is the only way to reach 95% of children in urban environments and provided information for advocacy.
- It converted opinionated discussions to data-driven problem solving.

Key to an effective RCA is joint national/international partner participation. During this campaign, Filipinos validated over 15 000/42 000 villages and requested 8000 to be revaccinated using a door-to-door technique. This compares with WHO consultants who validated 400 and requested 300 to be revaccinated. **Validators became the strongest advocates when they discovered: old strategies (i.e. fixed post) led to missed children; door-to-door led to vastly fewer missed children; and prompt feedback led teams to use the door-to-door strategy.**

Annex 3

The following pages (Figure a) contain the instrument used during the campaign. Briefly, national staff validated all urban and selected rural villages. WHO validated randomly selected villages proportionate to population in large urban centers. Per village, four sites were selected. At least two sites were overcrowded or difficult to access. Per site, validators “grabbed” the five nearest children and selected five nearby houses at least half with difficult entry. After completion and entering data on the Rapid Coverage Assessment form, staff determined “grab” and “door” samples coverage, reported findings to health staff and recommended to revaccinate a village with less than 95% coverage.

The sampling technique was simple enough that anyone could learn to do it. Persons who had never previously participated in a supplemental immunization activity were trained, including a role-play and a community practicum, in a few hours. With supervision and mentoring, national validators became better at identifying children than the international partners.

The technique is not foolproof. It can only work with unbiased selection and data collection. Demanding random selection of village, systematic selection of households/children and unbiased asking of questions were the largest problems encountered. People do not want to show the unfavorable side of their work. Avoiding being led to areas with known good coverage is difficult. Community health workers sometimes nonverbally biased respondent’s answers. Finally, validators sometimes did not discuss with health teams the results or implications.

FIGURE a. Checklist for Measles Campaign

Facilitator's Name: _____ Date: _____ Province/City: _____ Municipality: _____
 Community Name: _____ Population: _____ Region: _____ Reported number vaccinated: _____ Filled: _____ Modified: _____

Grab Sample				Assessing Coverage Through Looking at Doors and Interviews					
Child No	Vaccinated? (Y/N)	Age (Years) **	Gender (M/F)	Q1: Was the house marked? (Y/N)	Q2: Which mark was present? (0, X or O)	Q3: How many 9-35 months stay here? (#)	Q4: Of these (from Q3), how many were vaccinated during this campaign? (#)	Q5: Why were the children not vaccinated (comment)	Q6: Was this house correctly marked? (Y/N)
Site 1									
1.									
2.									
3.									
4.									
5.									
Site 2									
1.									
2.									
3.									
4.									
5.									
Site 3									
1.									
2.									
3.									
4.									
5.									
Site 4									
1.									
2.									
3.									
4.									
5.									
Total	Number vaccinated	(Sum column)	(Number males)	(# marked)	(# 0 or O)	(add up Q3)	(add up Q4)		(# confirmed) / (# interviewed)

* Confirm by looking at fingers and injection site. If subject claims to have been vaccinated, but has no marks, ask the subject, "What was done?" If the subject describes both injection in appropriate site, a popliteal or a vitamin A and/or dates vaccinated, indicate "verbally confirmed". Unless they can provide a reasonably convincing story that they were vaccinated during the campaign, indicate with "N."

** If less than one year, indicate as fraction of one year (e.g., 10/12)

Instructions: for figure a:

After having selected a village for conducting a coverage assessment:

- (1) Use the village map to identify 2 sites remote from general access (e.g., riverside, bordering other village, away from roads) and 2 central sites (a total of 4 sites).
- (2) Go to the first site identified on the map.
- (3) Briefly describe the site on the table (e.g., riverside, bordering other village, along road).
- (4) Identify the nearest children to the site.
- (5) Determine the vaccination status, age and gender of each child and determine their eligibility (i.e., age 9-95 months)
- (6) Complete one line for each eligible child in the section of the table labeled “Grab Sample.”
- (7) Identify 5 doors nearest to the site. If there is a variety, select at least a couple of the hardest to reach doors. E.g., the top floor, or ones with complicated entry.
- (8) Complete one line of the table for each door:
 - Question 1: Was the house marked with chalk?
 - Question 2: Was the house marked with a “O”, “X” or “⊗”?
 - Knock on the door. If there is someone present, ask the following questions.*
 - Question 3: How many children 9-95 months stay here?
 - Question 4: How many of these children were vaccinated during the campaign against measles?
 - Question 5: Why were the children not vaccinated?
 - Question 6: Was this house marked correctly? *NB: Unlabeled houses are not correctly marked.*
- (9) Repeat steps 2-8 until all four sites have been completed.
- (10) After completion of the 4 sites add up the columns as indicated in the bottom row.

If there is one child missed either in the grab sample or on knocking on door, or there is one door that is not completed or missed, indicate to the vaccination team supervisor that the area needs to be redone.

ANNEX 4. ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI) DURING MEASLES CAMPAIGNS

1. Purpose

This annex provides a summary on adverse event following immunization (AEFI) surveillance for mass measles immunization campaigns. More detailed information is in the WHO Western Pacific Regional Publication *Immunization Safety Surveillance*.

2. Adverse events following measles immunization

An adverse event following immunization (AEFI) is any adverse event that follows immunization that is believed to be caused by the immunization. AEFIs are classified into five categories (Table 1). Immunization can cause adverse events from the inherent properties of the vaccine (**vaccine reaction**), or some error in the immunization process (**programme error**). The event may be unrelated to the immunization, but have a temporal association (**coincidental event**). Anxiety-related reactions can arise from the fear or pain of the **injection** rather than the vaccine. In some cases the cause of the AEFI remains **unknown**.

Table 1. Classification of adverse events following immunization (AEFIs)

Vaccine reaction:	event caused or precipitated by the vaccine when given correctly, caused by the inherent properties of the vaccine.
Programme error:	event caused by an error in vaccine preparation, handling, or administration.
Coincidental:	event that happens <i>after</i> immunization but not caused by the vaccine - a chance association.
Injection reaction:	event from anxiety about, or pain from the injection itself rather than the vaccine.
Unknown:	event's cause cannot be determined.

2.1 Vaccine reactions

Measles vaccine, used since 1963, has an excellent safety record. It does commonly cause minor reactions, and rarely more serious reactions (Table 2). Measles is a live virus vaccine, and most reactions result from vaccine virus infection, 6-12 days after immunization. These reactions do not occur if the child is already immune. Therefore, in campaigns, where many vaccinees are already immune, fewer vaccine reactions are to be expected.

Measles vaccine infection causes fever, rash and/or conjunctivitis, and affects 5-15% of non-immune vaccinees. It is very mild compared to 'wild' measles, but for severely immunocompromised individuals, it can be severe, *even fatal* (note the risk of measles vaccine causing severe reactions in immunocompromised is not included in table of vaccine risks, because of rarity of events). The fever can be high enough to trigger a seizure in those predisposed to febrile seizures. Thrombocytopenia (low platelets) is a reaction that can happen with any viral infection. It shows up by bruising, and is usually mild and self-limiting. Although encephalopathy is included as a rare reaction to measles vaccine, it may be a coincidental event rather than a true vaccine reaction. (See Table A in Annex 1 for comparison of disease and vaccine risks)

Measles vaccine can also cause a local reaction at the injection site, and allergic reactions that can rarely be very severe (anaphylaxis). Anaphylaxis, while potentially fatal, is treatable without leaving any long-term effects.

Annex 4**Table 2. Measles vaccine reactions, onset interval, and rates**

Reaction	Onset interval	Number of reactions per dose	Reactions per million doses
Local reaction at injection site	0-2 days	~ 1 in 10	(~10%)
Fever	6-12 days	1 in 6 to 1 in 20	(5-15%)
Rash	6-12 days	~ 1 in 10	(~5%)
Febrile seizures*	6-12 days	1 in 3000	330
Thrombocytopaenia (low platelets)	15-35 days	1 in 30 000	30
Anaphylactoid (severe allergic) reaction	0-2 hours	~ 1 in 100 000	~10
Anaphylaxis	0-1 hour	~ 1 in 1 000 000	~1
Encephalopathy	6-12 days	< 1 in 1 000 000	<1

Reactions (except local reaction, anaphylaxis,) do not occur if already immune (~90% of those receiving a second dose); children over six years unlikely to have febrile seizures.

* Seizure risk is age-dependent, and lower for older children.

2.1.1 Prevention and treatment of vaccine reactions

Parents should be given advice on the chance of 'mild measles' 6-12 days after immunization. Advice should include advice on how to manage the common minor reactions and instructions to return if there are more serious symptoms. This will help to reassure parents about immunization and prepare them for these common reactions.

Paracetamol, at a dose of up to 15mg/kg every four hours with a maximum of four doses in 24 hours, is useful for the common minor reactions. It eases pain and reduces fever. A feverish child can be cooled with a tepid sponge or bath, and by wearing cool clothing. Extra fluids need to be given to feverish children. For a local reaction, a cold cloth applied to the site may ease the pain.

Current WHO advice is to immunize all children with measles vaccine, regardless of HIV status, and there is no need to screen for HIV status. But, children with known immune deficiency from HIV or other condition should not be given measles vaccine.

2.2 Programme errors

Programme errors are the most likely cause of adverse events during a campaign. The errors and accidents in vaccine preparation, handling, or administration (Table 3). They are preventable and detract from the overall benefit of the immunization programme. The identification and correction of these errors are of great importance.

A programme error may lead to a cluster of events associated with immunization. These clusters are usually associated with a particular provider, or health facility, or even a single vial of vaccine that has been inappropriately prepared or contaminated. Programme errors can also affect many vials (eg, by freezing vaccine during transport leading to an increase in local reactions).

Table 3. Programme errors leading to adverse events

Programme errors	Adverse event
Non-sterile injection: <ul style="list-style-type: none"> • reuse of disposable syringe or needle • improperly sterilised syringe or needle • contaminated vaccine or diluent • reuse of <i>reconstituted</i> vaccine at subsequent session.. 	Infection (E.g., local suppuration at injection site, abscess, cellulitis, systemic infection, sepsis, toxic shock syndrome, transmission of blood borne virus (e.g., HIV, hepatitis B or hepatitis C)).
Vaccine prepared incorrectly: <ul style="list-style-type: none"> • vaccine reconstituted with incorrect diluent • drugs substituted for vaccine or diluent. 	Local reaction or abscess from inadequate shaking. Effect of drug (e.g. muscle relaxant, insulin).
Contraindication ignored.	Avoidable severe vaccine reaction.

The most common programme error is an infection (including blood-borne virus) as a result of non-sterile injection. The infection can manifest as a local reaction (e.g., suppuration, abscess), systemic effect (e.g. sepsis or toxic shock syndrome), or blood borne virus infection (e.g., HIV, hepatitis B or hepatitis C).

The symptoms arising from a programme error may help to identify the likely cause. For example, children immunised with contaminated vaccine (usually the bacterium *Staphylococcus aureus*) become sick within a few hours; local tenderness and tissue infiltration, vomiting, diarrhoea, cyanosis and high temperature are the most frequent symptoms. Bacteriological examination of the vial, if still available, can confirm the source of the infection.

To avoid programme errors:

- vaccines must only be reconstituted with the diluent supplied by the manufacturer
- **reconstituted vaccines must be discarded at the end of each immunization session and never retained**
- no other drugs or substances should be stored in the refrigerator of the immunization centre
- immunization workers must be adequately trained and closely supervised to ensure that proper procedures are being followed
- careful epidemiological investigation of an AEFI is needed to pinpoint the cause and to correct immunization practices.

2.3 Coincidental events

An event may occur coincidentally with immunization and at times may be falsely attributed to be a result of the vaccine. In other words, a chance temporal association (i.e., event happens *after* immunization) is falsely considered to be *caused* by immunization. These purely temporal associations are inevitable given the large number of vaccine doses administered, especially in a mass campaign.

Coincidental adverse events are predictable. The number of events to be expected depends upon the size of the population and the incidence of disease or death in the community. Knowledge of these background rates of disease and deaths allows estimation of the expected numbers of coincidental events.

For example, assume that one million children aged 1-15 years are immunised in a mass campaign and the background mortality rate for this population is 3 per 1000 per year. Then, 250 deaths can be expected in the month after immunization and 8 deaths on the day of the immunization, simply by coincidence. These deaths will be temporally associated with, even though entirely unrelated to, immunization.

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2.4 Injection reactions

Anticipation and anxiety about injection, and the pain of the injection, can lead to a reaction. This reaction is unrelated to the content of the vaccine, but is especially likely with campaigns. Fainting is relatively common, but usually only affects children aged over five years. Fainting does not require any management beyond placing the patient in a recumbent position.

Hyperventilation as a result of anxiety about the immunization leads to specific symptoms (light-headedness, dizziness, tingling around the mouth and in the hands). An anxiety reaction to injection can include convulsions in some case.

These reactions are not related to the vaccine, but to the injection. Some individuals may be needle phobic, aggravating such reactions. In a group situation, mass hysteria is possible, especially if a vaccinee is seen to faint or have some other reaction. Clear explanations about the immunization and calm, confident delivery will decrease the level of anxiety about the injections, and thus reduce the likelihood of an occurrence.

Injection reactions are the most common type of adverse event reported in measles campaigns.

3. AEFI surveillance for mass measles campaign

A campaign involves a **large number of doses** given over a **short period of time** leading to more vaccine reactions and coincidental events. The **rate** of events remains **unchanged**, but the **increased number** of events tends to be noticed by both staff and the public, particularly when injectable vaccines are used and at a time of intensive social mobilisation.



Common events in campaigns

- A **real increase in programme errors** is possible with staff who are unfamiliar with a given vaccine or situation and under pressure, from a lot of children needing vaccine quickly; staff may not observe normal safe injection practice.
- A wider age group (usually older) is immunized and staff have less experience in dealing with adverse events in this older group (e.g., fainting).
- Antagonism from some sectors, for a variety of reasons, e.g. adds fuel to any concerns about AEFI during the campaign to justify criticism of the campaign.
- Rumours spread rapidly and damage the campaign before there is a chance to counter them.

Even if a national programme has not yet developed a functioning adverse events surveillance system, some form of adverse event response is essential in mass campaigns. Without this, the public is likely to hear of an adverse event before the programme manager, and the situation becomes very difficult to control. **The surveillance should be simple, flexible and rapid.**

Decide **who** will have overall responsibility and who should be the focal point and the spokesperson (e.g. EPI manager, person in charge of surveillance at national level, National Regulatory Authority (NRA)). This is particularly important if surveillance of adverse events is done by a surveillance structure other than EPI, or if an NRA exists or if there is a common monitoring scheme for drugs and vaccines.

Annex 4

Decide **what** to report, how to report and what to investigate. Decide who should receive reports and who will be involved with an investigation if needed. In general, all cases of AEFI that cause concern need prompt investigation and response. The three most likely events are:

- faints and psychogenic events related to immunization,
- coincidental events, and
- programme errors

A thorough investigation is needed to identify what type of AEFI it is and to make the appropriate response (including communication) to prevent it disrupting the campaign.

In conclusion, the key points are to **plan so that there is a capacity to investigate and respond** to any AEFI or vaccine rumour effectively. A **focal point for media and communication** needs to be established at every appropriate level to ensure that clear and consistent message are relayed. These focal points should **build relations with the local media** ahead of the campaign, both to promote the campaign and to educate them about coincidental events that are likely to be blamed on the vaccine. Always be honest, sincere, caring, and responsive to media enquiries.

**ANNEX 7: MEASLES ALERT NOTICE
(Sample)**

Children with measles have been found in our neighbourhood, and YOUR CHILD MAY BE AT RISK of getting this disease!

This type of measles is also called the 10-day red measles and can cause SEVERE ILLNESS with pneumonia, ear infections, brain disease, and EVEN DEATH.

If your child has a FEVER AND RASH ILLNESS, inform a doctor or health worker of this illness now.

Measles can be PREVENTED BY MEASLES VACCINE. ALL CHILDREN 6 MONTHS OF AGE AND OLDER should NOW receive the vaccine. Even if your child has already had a measles vaccination, an additional dose should be given to be sure that this disease will be prevented.

The measles vaccine is very safe and effective and will help to keep YOUR CHILD HEALTHY. Please contact your doctor or clinic to get your vaccine.

ANNEX 8: MEASLES OUTBREAK RESPONSE SUMMARY FORM

MEASLES OUTBREAK RESPONSE SUMMARY FORM

Name of index case _____ CASE ID _____

PROVINCE/STATE _____ COUNTRY _____

MUNICIPALITY/COUNTRY _____ VILLAGE / CITY _____

List neighboring areas wick also have measles outbreaks: _____

Date of measles rash onset of earliest case ____/____/____ Date of measles rash onset of last case: ____/____/____

NUMBER OF CASES BY AGE (YEARS)

	<1	1	2	3	4	5-9	10-14	>15	TOTALS
Suspected									
Confirmed									

IMMUNIZATION STATUS OF CASES

CONFIRMED MEASLES CASES

AGE	Not Immunized.	Documented Vac History		Unknown	Total No.
		1 DOSE	2 + DOSES		
<1					
1-2					
3-4					
5-9					
10-14					
15+					
TOTALS					

COMMUNITY COVERAGE

AGE	1 + DOSES %
<1	
1-2	
3-4	
5-9	
10-14	
15+	
TOTALS	

IMMUNIZATIONS FOR OUTBREAK CONTROL

	<1	1-4	>5	TOTAL
Date first started ____/____/____				
Date ended ____/____/____				
Number vaccinations given				
Number of households visited				

LIST VILLAGES/CITIES WHICH WERE VISITED IN THE COURSE OF THE INVESTIGATION

Name	Date	# Immunized	Comments (cases found?)
_____	____/____/____	_____	_____
_____	____/____/____	_____	_____
_____	____/____/____	_____	_____
_____	____/____/____	_____	_____

Describe control activities: _____

Describe follow-up activities: _____

Name of investigator: _____ Place: _____ Date: ____/____/____

ANNEX 10: WEEKLY REPORTING SUMMARY

WEEKLY REPORTS SUMMARY							
COUNTRY: _____				YEAR: _____			
WK #	# SITES IN SYSTEM	# SITES NOTIFYING	% REPORTING	WK #	# SITES IN SYSTEM	# SITES NOTIFYING	% REPORTING
1				27			
2				28			
3				29			
4				30			
5				31			
6				32			
7				33			
8				34			
9				35			
10				36			
11				37			
12				38			
13				39			
14				40			
15				41			
16				42			
17				43			
18				44			
19				45			
20				46			
21				47			
22				48			
23				49			
24				50			
25				51			
26				52			
				53			