Framework for Verifying Elimination of Measles and Rubella

SAGE Working Group on Measles and Rubella

Presentation to SAGE

7 November 2012

What is the deliverable?

- Final product:
  - a framework comprising a standard set of definitions, basic principles, essential criteria, and lines of evidence (or components) for verification of measles and rubella elimination
  - global standards for monitoring progress towards elimination
  - To be published as WER article or SAGE report
- This framework is developed for settings where the aim is to interrupt transmission of both measles and rubella, and the revisions to all the elements are tailored for that context
  - modified definitions and indicators may be appropriate in settings where measles and/or rubella are still endemic

Approach

- Five teleconferences of Sub-working group June 14th, 20th, July 17th, August 30th, September 13th , latter four included Regional representatives from EMRO, EURO, PAHO, WPRO
- Face to face meeting of sub-working group on September 19th followed by face to face discussion at Working Group meeting on 20th September
- Spreadsheet developed, approaches taken in each region reviewed against WER, and an approach agreed
- Framework drafted, circulated and revised since September 20th
- Rapid pace in order to meet deadlines of regions to finalize their guidelines

Other consideration

- We have focused on ***monitoring progress towards elimination*** of measles and rubella/CRS (***not*** global 2015 measles targets for immunization coverage, measles incidence or methods for estimating measles mortality)
- The framework does **not** cover definitions and surveillance indicators for determining the elimination of congenital rubella syndrome (CRS). An approach to verifying the elimination of CRS in the Region of the Americas has been published (Castillo et al JID 2011;204:S683-S689) and fieldwork is ongoing to evaluate approaches to CRS surveillance in other regions

DEFINITIONS

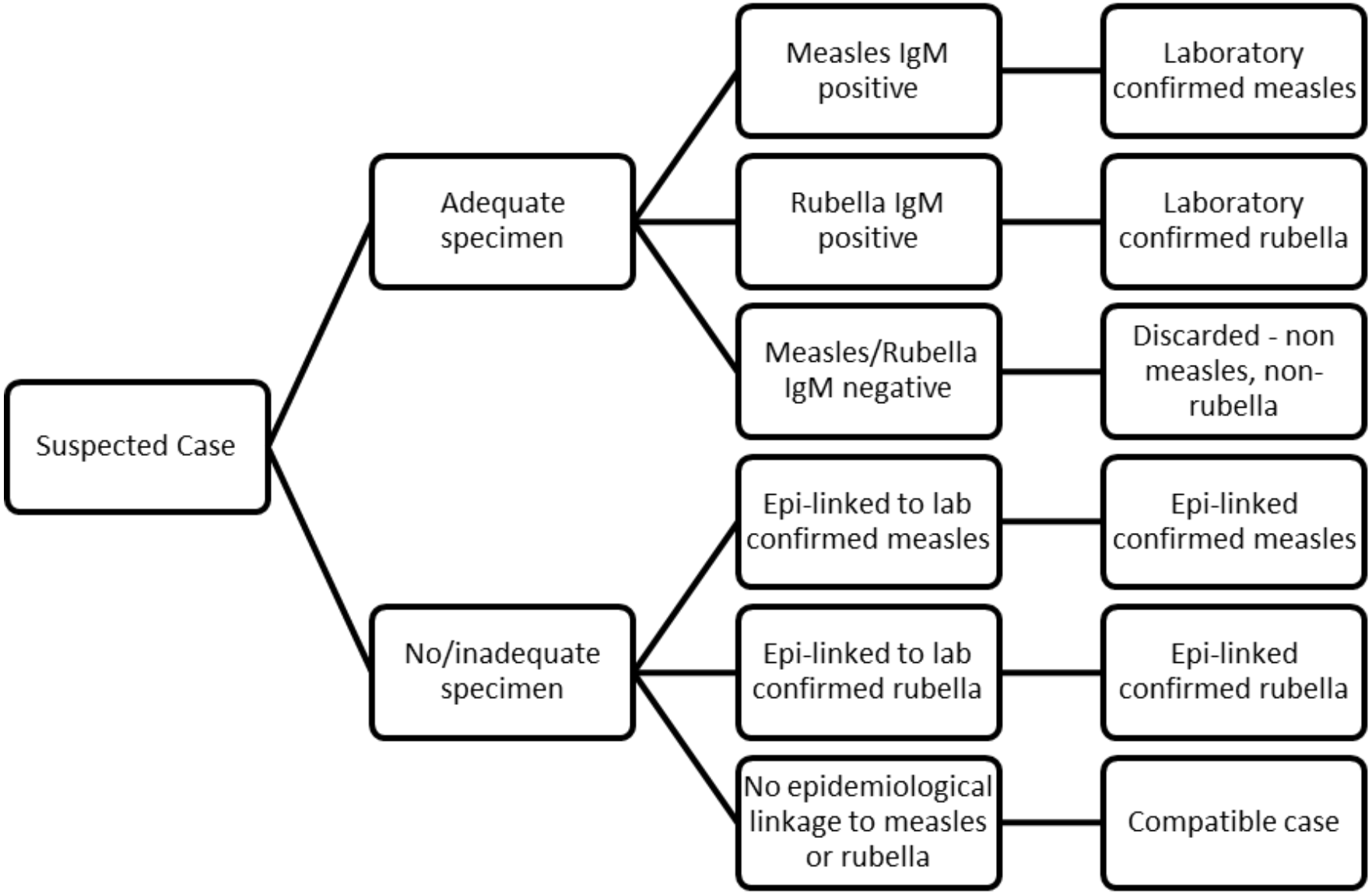
Word or Phrase	Definition
Measles or rubella eradication	worldwide interruption of measles or rubella virus transmission in the presence of a surveillance system that has been verified to be performing well
Measles elimination	the absence of endemic measles transmission in a defined geographical area (e.g., region or country) for ≥12 months in the presence of a well performing surveillance system **Note: verification of measles elimination takes place after 36 months of interrupted measles virus transmission**
Rubella elimination	the absence of endemic rubella virus transmission in a defined geographical area (e.g., region or country) for ≥12 months and the absence of CRS cases associated with endemic transmission in the presence of a well performing surveillance system Note: There may be a lag (up to 9 months) in occurrence of CRS cases after interruption of rubella virus transmission has occurred. Evidence of the absence of rubella transmission from CRS cases is needed because CRS cases excrete rubella virus for up to 12 months after birth. **Note: verification of rubella elimination takes place after 36 months of interrupted rubella virus transmission.**

Word or Phrase	Definition
Endemic measles or rubella virus transmission	the existence of continuous transmission of indigenous or imported measles virus or rubella virus that persists for ≥12 months in any defined geographical area
Endemic measles or rubella case	laboratory or epidemiologically-linked confirmed cases of measles or rubella resulting from endemic transmission of measles or rubella virus.
Re-establishment of endemic transmission	occurs when epidemiological and laboratory evidence indicates the presence of a chain of transmission of a virus strain that continues uninterrupted for ≥12 months in a defined geographical area (region or country) where measles or rubella had been previously eliminated Note: a measles or rubella virus strain is determined by sequencing the WHO standard 450nt region of the N gene for measles and the 739nt of the E1 gene for rubella.
Measles or rubella outbreak in an elimination setting	**a single laboratory confirmed case**

Word or Phrase	Definition
Suspected case of measles or rubella	**a patient in whom a health-care worker suspects measles or rubella infection or a patient with fever and maculopapular (non-vesicular) rash**
Laboratory confirmed measles case or rubella case	a clinically-compatible case of measles or rubella that has been confirmed by a proficient laboratory Note: a proficient laboratory is one that is WHO accredited and/or has an established quality assurance programme
Epidemiologically-linked confirmed measles case	a clinically-compatible case of measles that has not been confirmed by a laboratory but that was geographically and temporally related (with dates of rash onset occurring **between 7 and 21 days apart**) to a laboratory-confirmed case or (in the event of a chain of transmission) to another epidemiologically confirmed measles case
Clinically-compatible measles case	a case with fever and maculopapular (non-vesicular) rash and one of cough, coryza, or conjunctivitis but for which no adequate clinical specimen was taken and which has not been linked epidemiologically to a laboratory confirmed case of measles or another laboratory-confirmed communicable disease
Clinically-compatible rubella case	a case with maculopapular (non-vesicular) rash and fever (if measured) and one of arthritis/arthralgia or lymphadenopathy but for which no adequate clinical specimen was taken and which has not been linked epidemiologically to a laboratory confirmed case of rubella or another laboratory-confirmed communicable disease

Word or Phrase	Definition
Non-measles non-rubella discarded case	a suspected case that has been investigated and discarded as **a non-measles and non-rubella case** using (a) laboratory testing in a proficient laboratory or (b) epidemiological linkage to a laboratory-confirmed outbreak of another communicable disease that is neither measles nor rubella
Measles vaccine-associated illness	a suspected case that meets all 5 of the following criteria: (i) the patient had a rash illness, with or without fever, but did not have cough or other respiratory symptoms related to the rash; (ii) the rash began 7–14 days after vaccination with a measles-containing vaccine; (iii) the blood specimen, which was positive for measles IgM, was collected 8–56 days after vaccination; (iv) thorough field investigation did not identify any secondary cases; and (v) field and laboratory investigations failed to identify other causes. Alternatively, a suspected case from whom virus was isolated and found on genotyping to be a vaccine strain.
Imported measles or rubella case	a case exposed outside the region or country during **the 7–21 days for measles and 12-23 days for rubella** prior to rash onset and supported by epidemiological or virological evidence, or both. Note: for cases that were outside the region or country for only a part of the 7-21 day interval (12-23 day interval for rubella) prior to rash onset, additional evidence, including a thorough investigation of contacts of the case, is needed to exclude a local source of infection.
Importation-related measles or rubella case	a locally acquired infection occurring as part of a chain of transmission originating from an imported case as supported by epidemiological or virological evidence, or both. Note: if transmission of measles or rubella cases related to importation persists for ≥12 months, cases are no longer considered to be import-related, they are endemic.

Figure 1. Flow chart for classification of suspected cases



Conceptual framework: Hierarchy of evidence for verification of elimination

Definition

- Absence of endemic transmission in a defined geographical area (e.g., region or country) for a period ≥12 months in the presence of a well-performing surveillance system

Criteria and principles

- Verification of interruption of transmission for at least 3 years in the presence of high quality surveillance
- Maintenance of high quality surveillance systems
- Verification of absence of endemic transmission through viral surveillance

Component or lines of evidence

- Epidemiology of measles, rubella and CRS
- Immunity levels of multiple population cohorts
- Quality of surveillance systems
- Sustainability of the national immunization program
- Molecular epidemiology

Surveillance Quality Indicators

- Examples:
- Rate of reporting discarded non-measles non-rubella cases at the national level (Target: ≥2 cases per 100 000 population per year)
- Proportion of suspected cases with adequate specimens for detecting acute measles or rubella infection collected and tested in a proficient laboratory (Target: ≥80%)

ESSENTIAL CRITERIA, PRINCIPLES AND LINES OF EVIDENCE

Essential criteria and principles

- Essential criteria
  - Absence of endemic transmission of measles for a period of 36 months
  - High quality surveillance
  - Genotype evidence supporting interruption of endemic transmission

Basic principles and process of verification

- Annual review - national verification commission pulls countries towards verification, gathers and validates data
- Regional review after 3 years
- Independent verification process: People who are involved with program delivery are not involved with commission, Declare conflict of interest
- Multi-disciplinary commissions– lab, epi,ph
- Disaggregated data should be available at lowest administrative level – 100,000/500,000
- Need to consider marginalized/(indigenous)/migrant and remote communities and border areas that may have poor access to health care

Lines of evidence

- Detailed epidemiology of measles, rubella, CRS over the past 36-60 months and description of the epidemiology including programmatic changes
- Population immunity presented as a birth cohort analysis with the addition of evidence related to any marginalized and migrant groups per birth cohort
- Quality of laboratory and epidemiological surveillance systems for measles, rubella, CRS (see indicators)
- Sustainability of the National Immunization Program and resources for mass campaigns in order to sustain elimination
- Evidence from circulating genotypes that measles and rubella virus transmission is interrupted

SURVEILLANCE INDICATORS

Indicator	Description
Timeliness of reporting	Proportion of surveillance units reporting to the national level on time (Target: ≥80%) Proportion of countries reporting to their WHO Regional Office on time (Target: 100%) Proportion of Regions reporting to WHO Headquarters on time (Target:100%) Note: At each level reports should be received on or before the requested date
Reporting rate of discarded non-measles non-rubella cases	Reporting rate of discarded non-measles non-rubella cases at the national level (Target: ≥2 cases per 100 000 population per year)
Representativeness of reporting	Proportion of subnational administrative units (e.g., at the province level or its administrative equivalent) reporting at least **2 discarded non-measles non-rubella cases per 100,000 population** (Target: ≥80%) **Note: if the administrative unit has a population <100 000, then the rate should be calculated by combining administrative units to achieve a population of ≥100 000**

Indicator	Description
Laboratory confirmation	Proportion of suspected cases with adequate specimens for detecting acute measles or rubella infection collected and tested in a proficient laboratory (Target: ≥80%). Any suspected cases of measles that are not tested by a laboratory and are (a) confirmed as measles by epidemiological linkage or (b) discarded as non-measles by epidemiological linkage to another laboratory-confirmed communicable disease case should be excluded from the denominator of suspected cases. Note: Adequate specimens are: blood sample, minimum of 0.5 ml; dried blood sample, at least 3 fully filled circles on filter paper collection device; oral fluid, sponge collection device should be rubbed along the gum until the device is thoroughly wet (this usually takes one minute). Adequate samples for serology are those collected within 28 days after rash onset. Note: a proficient laboratory is one that is WHO accredited and/or has an established quality assurance programme

Indicator	Description
Viral detection	Proportion of **laboratory-confirmed chains** of transmission with samples adequate for detecting measles or rubella virus collected and tested in an accredited laboratory (Target:≥80%). The numerator is the number of chains of transmission for which adequate samples have been submitted for viral detection and the denominator is the number of chains of transmission identified. Note: Where possible, samples should be collected from 5–10 cases early in a chain of transmission and every 2-3 months thereafter if transmission continues. For virus isolation, adequate throat or urine samples are those collected within 5 days after rash onset. For virus detection using molecular techniques, adequate throat samples are those collected up to 14 days after rash onset, and adequate oral fluid samples are those collected up to 21 days after rash onset.

Indicator	Description
Adequacy of investigation	Proportion of all suspected measles and rubella cases that have had an adequate investigation initiated within 48 hours of notification (Target: aim for 80%). The numerator is the number of suspected cases of measles or rubella for which an adequate investigation was initiated within 48 hours of notification and the denominator is the total number of suspected measles and rubella cases. Note: An adequate investigation includes collection of all the following data elements from each suspected measles and rubella case; name or identifiers, place of residence, place of infection (at least to district level), age (or date of birth), sex, date of rash onset, date of specimen collection, measles-rubella vaccination status, date of last MR vaccination, date of notification and date of investigation and travel history. Note: Some variables may not be required for cases that are either confirmed as measles by epidemiologic linkage (e.g., date of specimen collection)

Indicator	Description
Timeliness of specimen transport	Proportion of specimens received at the laboratory within 5 days (Target: ≥80%)
Timeliness of reporting laboratory results	Proportion of results reported by the laboratory within 4 days of receiving the specimen (Target: ≥80%)

Next steps

- Finalize framework with SAGE
- Circulate to Regions
- Publish framework
- Develop CRS indicators

Acknowledgments

- Members of the monitoring sub-group (Narendra Arora, Natasha Crowcroft (chair), Dave Durrheim, Pier-Luigi Lopalco, Makoto Takeda). Additional members of the SAGE working group on measles and rubella (Peter Figueroa, Helen Rees, Susan Reef, William Moss, Hyam Bashour, and Heidi Larson).
- WHO Regional Advisors (Xiaojun Wang, Eltayeb Elfakki, Balcha Masresha, Arun Thapa, Sergei Deshevoi, Katri Kontio, Carlos Castillo) and to Mark Papania for constructive and essential contributions.
- WHO secretariat (Peter Strebel, Alya Dabbagh, Robert Perry)