

Eliminating measles and rubella



Framework for the
verification process in the
WHO European Region





**World Health
Organization**

REGIONAL OFFICE FOR **Europe**

Eliminating measles and rubella

**Framework for the verification process in the
WHO European Region
2014**

ABSTRACT

This document describes the steps to be taken to document and verify that elimination of measles and rubella has been achieved in the WHO European Region. The process has been informed by mechanisms put in place for the certification of the global eradication of smallpox and poliomyelitis.

Detailed information about measles and rubella epidemiology, virologic surveillance supported by molecular epidemiology, analyses of vaccinated population cohorts, quality surveillance and the sustainability of the national immunization programme comprise the key components of a standardized assessment to verify the interruption of endemic measles and rubella virus transmission in a country. The different parts of the assessment are interrelated; the verification of one component depends on the status of the others. It is necessary to integrate and link the evidence on the components and to verify their validity, completeness, representativeness and consistency among the different sources of information. National verification committees for measles and rubella elimination should be created in all Member States to compile and submit the data annually.

Review and evaluation of annual national reports will continue in each Member State for at least three years after the Regional Verification Commission for Measles and Rubella Elimination confirms that endemic measles and rubella transmission has been interrupted in all Member States of the Region.

Keywords

EPIDEMIOLOGICAL SURVEILLANCE
MEASLES – prevention and control
RUBELLA – prevention and control
RUBELLA SYNDROME, CONGENITAL – prevention and control
PROGRAM EVALUATION
GUIDELINES
EUROPE

Address requests about publications of the WHO Regional Office for Europe to:

Publications
WHO Regional Office for Europe
UN City, Marmorvej 51
DK-2100 Copenhagen Ø, Denmark

Alternatively, complete an online request form for documentation, health information, or for permission to quote or translate, on the Regional Office web site (<http://www.euro.who.int/pubrequest>).

© World Health Organization 2014

All rights reserved. The Regional Office for Europe of the World Health Organization welcomes requests for permission to reproduce or translate its publications, in part or in full.

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

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either express or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use. The views expressed by authors, editors, or expert groups do not necessarily represent the decisions or the stated policy of the World Health Organization.

CONTENTS

Page

Abbreviations.....	iv
Definitions	1
Introduction.....	1
Rationale for measles and rubella elimination.....	2
Regional elimination goals and objectives	3
Regional strategies	4
Documentation required for regional verification of measles and rubella elimination.....	5
Basic principles	5
Essential criteria and components supporting elimination	6
Indicators for monitoring progress towards elimination	14
Classification of cases.....	15
Structure and function of the RVC and NVCs for verification of measles and rubella elimination.....	16
RVC.....	17
NVC.....	18
Documentation process	19
References	19

Abbreviations

AEFI	adverse events following immunization
CRS	congenital rubella syndrome
ETAGE	European Technical Advisory Group of Experts on Immunization
IgM	immunoglobulin M
MCV	measles-containing vaccine
NIP	national immunization programme
NVC	national verification committee for measles and rubella elimination
RCV	rubella-containing vaccine
RVC	Regional Verification Commission for Measles and Rubella Elimination
SIA	supplementary immunization activity
UNICEF	United Nations Children's Fund

Definitions¹

Disease elimination: the absence of endemic measles or rubella cases in a defined geographical area for a period of at least 12 months, in the presence of a well-performing surveillance system. Regional elimination can be declared after 36 or more months of the absence of endemic measles or rubella in all Member States.

Disease eradication: worldwide interruption of measles or rubella transmission in the presence of a verified, well-performing surveillance system.

Endemic case: a laboratory-confirmed or epidemiologically linked case of measles or rubella resulting from endemic transmission of measles or rubella virus.

Endemic transmission: continuous transmission of indigenous or imported measles or rubella virus that persists for a period of 12 months or more in a defined geographical area.

Re-establishment of endemic transmission: re-establishment of endemic measles or rubella transmission is a situation in which epidemiological and laboratory evidence indicate the presence of a chain of transmission of a virus variant that continues uninterrupted for a period of 12 months or more in a defined geographical area where disease was previously eliminated.

Introduction

The purpose of this document is to describe in detail the steps to be taken to document and verify that the elimination of measles and rubella have been achieved in the WHO European Region. This regional verification process has been informed by the mechanisms that were put in place earlier for the certification of global smallpox (2) and poliomyelitis (3) eradication.

The documents –*Eliminating measles and rubella and preventing congenital rubella infection: WHO European Region strategic plan 2005–2010*(4); *Surveillance guidelines for measles, rubella and congenital rubella syndrome in the WHO European Region, update December 2012*(5); and *Manual for the laboratory diagnosis of measles and rubella virus infection, second edition*(6)– provide the technical foundation upon which the verification process has been built.

HEALTH 21: the health for all policy framework for the WHO European Region(7), approved by the WHO Regional Committee for Europe in 1998, identified targets for nine vaccine-preventable diseases, including measles elimination by 2007 and a congenital rubella syndrome (CRS) incidence of < 1 case per 100 000 live births by 2010. Owing to the widespread use of measles- and rubella-containing vaccines in the Region, the *Strategic plan for measles and congenital rubella infection in the European Region of WHO*(8) targeted both the interruption of indigenous transmission of measles (measles elimination) and the prevention of congenital rubella infection (< 1 case of CRS per 100 000 live births) by 2010.

In 2004, the national immunization programme (NIP) managers in the Region and the WHO European Technical Advisory Group of Experts on Immunization (ETAGE) reviewed the objectives of the measles elimination plan (8) and recommended the inclusion of rubella elimination in the strategy. This was approved at the 55th session of the WHO Regional

¹Source: Adapted from the World Health Organization (1).

Committee for Europe held in Bucharest, Romania on 12–15 September 2005, as part of the *WHO Regional Committee for Europe resolution EUR/RC55/R7 on strengthening national immunization systems through measles and rubella elimination and prevention of congenital rubella infection in WHO's European Region*(9).

Although Member States did make progress towards the European regional goals of eliminating measles and rubella by 2010 through the implementation of the strategic plan, the goal was not achieved because of multiple factors leading to suboptimal population immunity, particularly in the central and western parts of the Region. Acknowledging that the European regional goals of eliminating measles and rubella are achievable, the current status of measles and rubella elimination in the Region was reviewed in depth at the 60th session of the Regional Committee in 2010, and the target for the elimination date was modified to 2015 (10). Progress on measles and rubella elimination was presented at the 63rd session of the Regional Committee in 2013 (11).

Rationale for measles and rubella elimination

Available evidence indicates that both measles and rubella are diseases that can be eradicated.

- There is no animal or environmental reservoir and humans are critical to maintaining transmission.
- Accurate diagnostic tests are available.
- Vaccines and existing vaccination strategies for both diseases are effective and safe.
- Transmission has been interrupted in a large geographic area (e.g. nationwide) for a prolonged period of time (12).

In 2010, the WHO Strategic Advisory Group of Experts on Immunization conducted a comprehensive review of the evidence to establish the biological and technical feasibility of measles eradication and concluded that measles can and should be eradicated. They also concluded that using the combined measles–rubella vaccine and integrated surveillance for fever and rash provides an opportunity to accelerate the control of rubella and the prevention of congenital rubella syndrome (13).

Before the widespread use of measles vaccination, almost everybody was infected in early childhood and acquired life-long immunity. In the 1980s, measles killed an estimated 2.6 million children globally each year (14). The widespread adoption of the measles vaccine in NIPs since the establishment of the Expanded Programme on Immunization in 1974 has marked a decrease in the number of reported cases. With increasing immunization coverage, the global number of measles deaths was estimated to have been reduced to about 548 300 in 2000 (immunization coverage of 72%), and to an estimated 157 700 deaths, mostly children, in 2011 (immunization coverage of 84%) (15). In the Region, more than 312 000 measles cases were reported in 1991 (16).

Using the experience gained in measles elimination in the WHO Region of the Americas, the other WHO regions² assessed progress made towards regional measles elimination, as well as the

²The six WHO regions are: the African Region, the Region of the Americas, the South-East Asia Region, the European Region, the Eastern Mediterranean Region and the Western Pacific Region.

challenges to meet the goal of achieving measles elimination by 2020 or earlier, which was set by all WHO regions except for the South-East Asia Region. Global measles eradication is considered biologically feasible and cost-effective (17).

The attenuated live measles vaccine is highly effective, yielding seroconversion rates of 95% or more in persons over 12 months old. Almost all children who fail to respond to the first dose will respond to the second dose, thus ensuring seroconversion rates after two doses of 95% or more if the first dose is given at nine months, or 99% or more if the first dose is given at 12 months or older. As a result of the high transmissibility of the measles virus, the herd immunity threshold is very high, and very high coverage ($\geq 95\%$) is necessary to interrupt virus transmission.

Providing all children with two doses of measles-containing vaccine (MCV) is now the standard for all NIPs with the second dose delivered either through campaigns or through routine health services, depending on which approach attains the highest coverage.

Rubella is generally considered to be a mild rash illness; however, it is more severe in infants and adults. If infection occurs during the early stages of pregnancy, the rubella virus can cause multiple birth defects, including CRS, and may result in fetal loss or still births (18,19). Congenital malformations have been reported in up to 85% of children born to women with confirmed diagnoses of rubella during the first trimester of pregnancy (20).

Before widespread rubella vaccination in the Region of the Americas, it is estimated that approximately 20 000 CRS-affected children were born there each year. In 1996, it was estimated that, in developing countries, approximately 110 000 children were born annually with CRS (21).

Rubella vaccine has been available since the 1970s and is highly effective. More than 95% of persons vaccinated with a single dose have protection against both clinical rubella and viremia for at least 15 years. Follow-up studies indicate that one dose of vaccine confers long-term, probably lifelong, protection (18,20). In countries with high coverage, the incidence of rubella has declined remarkably, suggesting the feasibility of elimination. Given that most Member States have already incorporated combined measles-rubella-containing vaccines into their vaccination schedules, and that rubella is less contagious than measles, rubella elimination is feasible within the frameworks of the regional measles elimination strategies. Two WHO regions established rubella elimination goals: the Region of the Americas and the European Region. In September 2010, the Pan American Health Organization announced that the Region of the Americas had achieved its rubella and CRS elimination goals (22,23).

Regional elimination goals and objectives

Measles elimination is defined as the absence of endemic measles transmission in a defined geographic area (e.g. region) for a period of at least 12 months in the presence of a well-performing surveillance system (17). A similar definition is applied for rubella elimination.

WHO Regional Committee for Europe resolution EUR/RC55/R7 on strengthening national immunization systems through measles and rubella elimination and prevention of congenital rubella infection in WHO's European Region acknowledged that measles and rubella can be eliminated in the Region and that congenital rubella infections can be prevented by using

combined measles and rubella vaccines in a routine two-dose vaccination schedule within childhood immunization programmes, by achieving and maintaining high coverage and by targeting susceptible populations, including women of childbearing age (4). In 2010, the Regional Committee recommitted to these goals and the target for elimination was modified to 2015 (10).

In the Region, the objectives are:

- to eliminate endemic measles
- to eliminate endemic rubella, which will lead to elimination of CRS as well.

Regional strategies

To achieve the regional elimination objectives, four key strategies have been defined.

1. Achieve and sustain very high coverage ($\geq 95\%$) with two doses of measles and at least one dose of rubella vaccine through high-quality routine immunization services.

Coverage of $\geq 95\%$ of the general population with first and second doses of measles- and rubella-containing vaccines at subnational administrative level has still not been achieved nor is sustainable in many countries. Strategies need to be developed to increase vaccine coverage to $\geq 95\%$, especially among hard-to-reach populations, including cultural or ethnic minority groups, nomadic groups, populations in areas of civil unrest/political instability, geographically isolated populations and populations refusing vaccination due to religious or philosophical beliefs.

2. Provide measles and rubella vaccination opportunities, including supplementary immunization activities (SIAs), to all population groups at risk for and susceptible to measles and/or rubella.

SIAs should be focused on population groups that have inadequate levels of immunity for interrupting endemic measles or rubella transmission. Such groups include inadequately vaccinated birth cohorts, people attending schools or universities, those working in the military and health care personnel. Susceptible population groups should be defined by evaluating existing epidemiological data on measles and rubella cases, assessing historical vaccine-coverage data or, in some circumstances, conducting serosurveys. Consideration needs to be given to appropriate immunization strategies to reach susceptible populations with a view not only to interrupt endemic transmission but also to ensure that women of childbearing age are protected in case of exposure to the rubella virus.

3. Strengthen surveillance systems by rigorous case investigation and laboratory confirmation of suspected sporadic cases and outbreaks.

The quality of measles, rubella and CRS surveillance activities needs to be sufficient to ensure the detection of sporadic cases and provide adequate information on both the epidemiology and the virus genotype to allow case classification (endemic or imported/import-related). This information needs to be collected, analysed and communicated effectively and in a timely manner to enable prompt and appropriate public health action. Surveillance systems for adverse events following immunization (AEFI) also need to be capable of detecting, monitoring and

responding to suspected AEFI cases in a timely manner. Regular training and the availability of adequate information systems are critical components of this key strategy.

4. Improve the availability and use of high-quality, evidence-based information for health professionals and the public on the benefits and risks associated with immunization against measles and rubella.

In order to increase and maintain the very high levels of vaccination coverage required to meet the objectives of measles and rubella elimination, the knowledge of health professionals and the public about these diseases, and the way in which they perceive them, are extremely important. This strategy should focus on clearly communicating the benefits and risks associated with preventing these diseases through vaccination. A growing number of people in the Member States obtain most of their health-related information from news media and the Internet. While many Member States provide information on immunization to the public, more attention should be paid to how the material is perceived and used by the target audiences.

Documentation required for regional verification of measles and rubella elimination

As part of the verification process, each country will be expected to prepare adequate documentation based on the standardized collection and analysis of essential data. This documentation will be submitted to the respective national verification committee (NVC) and the Regional Verification Commission for Measles and Rubella Elimination (RVC) for review and evaluation with a view to regional verification. It may be necessary for the RVC and NVCs to undertake field visits in connection with the triangulation of the presented documentation. The RVC will consider the regional verification on the basis of the national documentation and the status of measles and rubella elimination in Member States.

The elimination of measles and rubella may occur at different times, which is likely. As such, the two events will be verified separately and with different time frames.

Basic principles

Ongoing process

To attain verification of measles and rubella elimination at regional level, all Member States must have achieved elimination of the diseases at national level. For a period of at least three years, through the submission of annual reports for review and evaluation by RVC, Member States must be able to demonstrate, according to the established criteria, a continuous status of elimination. Then and only then will it be possible for regional elimination to be declared. In addition, it is expected that Member States will continue to submit annual reports for a further period of at least three years after regional elimination has been declared.

Evidence-based

The verification process will be based on evidence documented by each Member State to show that interruption of endemic transmission of measles and/or rubella at national level has been achieved and, if not, that a national plan for the interruption of endemic measles and rubella virus transmission has been developed. A uniform documentation format will be used to

facilitate the collection, interpretation and analysis of relevant data and the identification of missing information. Detailed information on population immunity to and the epidemiology of measles and rubella, supported by information related to molecular epidemiology, quality of surveillance and NIP sustainability comprise the key components for standardized verification of the interruption of endemic measles and rubella virus transmission. The key components are interrelated; therefore, it is necessary to provide evidence that the data are valid, complete, representative and consistent among the different information sources.

Measurable

A set of surveillance performance indicators and two markers (vaccination coverage and disease incidence) will be used to make a reliable conclusion regarding achievement of the objectives. Once a country nears the targets suggestive of elimination, an in-depth review will be recommended to investigate whether it has indeed achieved elimination.

Independent

Independent external panels of leading public health experts will be engaged in the formal verification process at regional and national levels (see the chapter entitled “Structure and function of the RVC and NVCs for verification of measles and rubella elimination”). Participation in the panels will be voluntary and no salary or consultant fees of any kind will be paid.

Essential criteria and components supporting elimination

In accordance with the definition of elimination (1), the following essential criteria are proposed for verification of the elimination of measles and rubella in the Region:

- the absence of endemic measles and rubella cases in all Member States for a period of at least 36 months from the last known case, due to complete interruption of endemic virus transmission;
- the presence of high-quality surveillance system that is sensitive and specific enough to detect, confirm and classify all suspected cases; and
- genotyping evidence that supports the interruption of endemic transmission.

The essential criteria are to be supported by evidence-based information that allows the RVC to determine whether the country or the Region as a whole has achieved elimination. This information presented in five lines of evidence (also referred to as components) should be compiled, analysed and validated by NVCs and submitted to the RVC on an annual basis. Table 1 lists the components essential for the documentation of national status and regional verification.

Table 1. Components for regional verification

Components	Data sources
Epidemiology of measles, rubella and CRS during the previous 36 months	Routine surveillance, sentinel sites (CRS)
Molecular epidemiology of measles and rubella viruses	Routine surveillance, laboratory reports
Performance of measles, rubella and CRS surveillance	Routine surveillance, laboratory reports
Population immunity against measles and rubella	Administrative reports, immunization registry, coverage surveys, seroprevalence studies
Sustainability of the NIP	NIP management

Epidemiology of measles, rubella and CRS

The implementation of elimination strategies in Member States will lead to a rapid decline in measles, rubella and CRS incidence, which in turn will cause changes in the demographic characteristics of cases and outbreak patterns. Exhaustive epidemiological analysis should be carried out by each country to determine whether measles and rubella virus circulation has been interrupted. For this purpose, it is essential that all countries carry out, complete and timely monthly reporting of case-based measles and rubella epidemiological surveillance data (shared with the Regional Office). Countries with adequate capacity should also establish or strengthen existing sentinel-site surveillance of CRS (and share the resulting data with the Regional Office).

The standard analysis of measles and rubella surveillance data should be conducted routinely to determine:

- final classification of cases (laboratory-confirmed, epidemiologically linked, clinically compatible, imported, import-related, discarded);
- age and vaccination status of laboratory-confirmed, epidemiologically linked and clinically compatible cases;
- distribution of cases in time and space (to identify whether confirmed cases occur separately, without temporal association among them);
- cyclical and/or seasonal patterns (to ascertain the loss of endemic-transmission characteristics);
- demographic characteristics and social context, with a focus on cases in populations with low vaccination coverage, mainly in urban and tourist areas; and
- number and location of clinical cases.

Trend analyses should be conducted periodically to determine:

- incidence of measles and rubella during the previous five years;
- size and duration of outbreaks;
- areas free from disease transmission;
- the number and location of suspected cases without final classification;
- special cases (for example, false positives, false negatives, indeterminate cases, vaccine-associated cases, pregnant women exposed to rubella, etc.); and

- viral genotype.

Analyses of data on imported cases and investigations of outbreaks, clusters or chains of transmission should be carried out to determine:

- size, location and duration of outbreaks;
- procedures used for the investigation, follow-up and confirmation of outbreaks;
- sources of infection (index case) and chains of transmission for each outbreak;
- case contacts (household and non-household);
- additional cases in health facilities and communities (through active search);
- risk factors and groups primarily affected;
- patterns of transmission;
- vaccine effectiveness (field efficacy);
- outbreak response or strategy used to limit and control each outbreak;
- virus detection and isolation;
- final classification of all cases; and
- follow-up of pregnant women (and their newborns) exposed to rubella.

Molecular epidemiology of measles and rubella viruses

The routine laboratory confirmation of suspected cases and molecular epidemiological data are essential components of laboratory-based surveillance for measles and rubella, especially in an elimination setting. Genetic information provides a tool for documenting the transmission patterns of circulating strains of measles and rubella. This information is used to identify endemic viruses and the potential sources of imported viruses. The molecular data can help to ascertain whether elimination has been achieved by documenting the interruption of transmission of endemic viruses, provided that they are fully integrated with epidemiological case-based data.

The success of the molecular epidemiological investigations depends on the collection of appropriate samples, shipment of the samples to network laboratories that can perform virus detection and genetic characterization, the use of unique identification numbers for each suspected case shared by both the epidemiological and laboratory investigators, and the timely and accurate reporting of results. Since viruses can travel great distances in a short time, the application of molecular epidemiological techniques depends on the timely availability of sequence information in a global sequence database. National reference laboratories are encouraged to report genotype information to the WHO Measles Nucleotide Surveillance database (24), the Rubella Nucleotide Surveillance database (25) and to the GenBank database (26).

National reference laboratories should provide high-quality information that will contribute to documenting the achievement of measles and rubella elimination in accordance with the *Manual for the laboratory diagnosis of measles and rubella virus infection, second edition* (6). To be considered adequate, laboratories should be able to demonstrate the following characteristics:

- fully accredited national laboratory according to current WHO laboratory network standards (27);

- a highly collaborative relationship with the national surveillance and immunization systems and the medical community;
- the ability to report case-based laboratory information through the online measles and rubella laboratory data management system (28), including the use of unique identification numbers linking laboratory data to clinical and epidemiological data to facilitate both laboratory reporting and the epidemiological classification of measles and rubella cases;
- a genetic baseline established by the national laboratory to develop and maintain a baseline genotype map of the viruses found in each state/province in the country through characterization of endemic cases or archival samples (serum, oral fluid, nasopharyngeal swab, urine, etc.); and
- the means to support CRS identification and monitoring of virus shedding by CRS cases established by the national laboratory (where resources permit).

Performance of measles, rubella and CRS surveillance

In order to verify measles and rubella elimination, it will be necessary to determine whether the national surveillance system provides timely and sufficient information based on pre-established quality criteria (Table 2). Again, it is essential that all countries carry out complete and timely monthly reporting and share case-based measles and rubella epidemiological surveillance data with the Regional Office.

Table 2. Standard indicators and targets for measuring performance of measles and rubella surveillance

Indicator	Description	Target
Timeliness of reporting (<i>T</i>)	Percentage of measles or rubella routine reports ^a submitted to national level by the deadline ^b A: number of reports submitted by the deadline B: number of expected reports $T = (A * 100) / B$ (%)	≥80%
Completeness of reporting (<i>C</i>)	Percentage of measles or rubella routine reports ^a submitted to national level E: number of submitted reports B: number of expected reports $C = (E * 100) / B$ (%)	–
Rate of laboratory investigations (<i>L</i>)	Percentage of cases suspected for measles or rubella with adequate specimens ^c collected and tested in a proficient laboratory ^d Note: Exclude from the denominator any suspected cases not tested by a laboratory and (a) confirmed by epidemiological linkage, or (b) discarded as non-measles/non-rubella by epidemiological linkage to a laboratory-confirmed case of another communicable disease or epidemiological linkage to a measles or rubella immunoglobulin M- (IgM) negative case. F: number of suspected measles or rubella cases with adequate specimens collected and tested in a proficient laboratory G: number of suspected cases $L = (F * 100) / G$ (%)	≥80%
Rate of discarded cases (<i>D</i>)	The rate of suspected measles or rubella cases investigated and discarded as non-measles or non-rubella cases using laboratory testing in a proficient laboratory ^d and/or epidemiological linkage to another confirmed disease H: number of suspected measles or rubella cases investigated and discarded as non-measles or non-rubella cases J: population $D = (H * 100\ 000) / J$	At least 2 discarded measles or rubella cases per 100 000
Representativeness of reporting discarded cases (<i>R</i>)	Percentage of subnational administrative territories (e.g. at province level or its administrative equivalent) reporting the rate of discarded cases (<i>R</i>) at least 2 per 100 000 population per year K: number of subnational administrative territories reporting the rate of discarded cases (<i>R</i>) at least 2 per 100 000 population per year M: number of subnational administrative territories $R = (K * 100) / M$ (%)	≥80%
Viral detection (<i>V</i>)	Percentage of laboratory-confirmed chains of transmission of measles or rubella with samples adequate for viral detection collected and tested in an accredited laboratory ^e P: number of chains of transmission of measles or rubella for which adequate samples have been submitted for viral detection/genotyping Q: number of chains of transmission identified $V = (P * 100) / Q$ (%)	≥ 80%
Origin of infection identified (<i>O</i>)	Percentage of measles or rubella cases for which the origin of infection (e.g. imported, import-related or endemic) has been identified W: number of measles or rubella cases for which the origin of infection (e.g. imported, import-related or endemic) has been identified X: total number of measles or rubella cases $O = (W * 100) / X$ (%)	≥ 80%
Timeliness of investigation (<i>I</i>)	Percentage of suspected measles or rubella cases with an adequate investigation ^f initiated within 48 hours of notification Y: number of measles or rubella cases with an adequate investigation Z: number of suspected measles or rubella cases, respectively $I = (Y * 100) / Z$ (%)	≥ 80%

^aEach surveillance reporting unit is to submit regular monthly or weekly reports, including “zero” reports.

^b The deadline to submit data on the previous month or week is to be defined by the Member State.

^c A single clinical sample obtained at the first contact with the health care system at any time within 28 days after rash onset is considered adequate for surveillance purposes (5).

^dA proficient laboratory is WHO accredited and/or has an established quality assurance programme with oversight by a WHO accredited laboratory(6).

^eMeasles and rubella viruses can be detected in nasal secretions, urine, serum and whole blood, and dry blood spots up to seven days after onset of rash and in oral fluid for even longer (5).

^f An adequate investigation includes the collection of at least the following essential data elements from each suspected measles/rubella case: case identifier, age (or date of birth), date of rash onset, date of specimen collection and vaccination status. Countries may wish to collect other data that may be important for epidemiologic investigation (1).

Alternative indicators

The two indicators in Table 3 should be used by countries that are unable to report standard indicators on timeliness of reporting and/or rate of discarded cases as described above.

Table 3. Alternative indicators and targets for measuring performance of measles and rubella surveillance

Indicator	Description	Target
Timeliness of notification (T_n)	Alternative to timeliness and completeness of reporting Percentage of measles or rubella case-based reports to surveillance system submitted within 48 hours of rash onset A: number of reports submitted within 48 hours of rash onset B: number of suspected cases $T_n = (A * 100) / B$ (%)	≥ 80%
Rate of cases tested negative for measles or rubella IgM (N)	Alternative to rate of discarded cases The rate of cases of measles or rubella-like illnesses (MLI/RLI) whose specimens tested IgM negative in a proficient laboratory ^a E: number of suspected measles or rubella cases investigated and discarded as non-measles or non-rubella cases F: Population $N = (E * 100) / F$ (%)	At least 2 MLI/RLI cases tested negative per 100 000 population (nationwide)

^aA proficient laboratory is WHO accredited and/or has an established quality assurance programme with oversight by a WHO accredited laboratory(6).

Surveillance indicators should be monitored in each country to provide evidence about the overall quality of measles and rubella surveillance. Additional information, such as results of active case searches or epidemiological studies, if appropriately documented, may facilitate the verification process and provide further evidence to support the essential elimination criteria or ensure proper interpretation of specific indicators.

Population immunity against measles and rubella

To achieve and maintain the elimination of measles and rubella, it is necessary to achieve a level of population immunity sufficient enough to interrupt endemic transmission and prevent the re-establishment of transmission if importation occurs. The strategies implemented and vaccination coverage should indicate that all population cohorts are protected against measles and rubella.

Data obtained through administrative immunization reports, such as the annual WHO–United Nations Children’s Fund (UNICEF) Joint Report Form, and results from rapid coverage monitoring and coverage surveys (when applicable) should be analysed. This would determine whether vaccination coverage levels of ≥ 95% have been reached and sustained over time at municipal, district and national levels, as well as among population cohorts and age groups targeted in routine and supplementary vaccination strategies. In analysing the data, special attention should be paid to the following aspects:

- first-dose measles-containing vaccine (MCV1) and first-dose rubella-containing vaccine (RCV1) coverage among infants by 24 months of age provided through the routine programme;
- second-dose measles-containing vaccine (MCV2) and second-dose rubella-containing vaccine (RCV2) coverage in respective age groups provided through the routine programme according to the national immunization schedule (varies across Member States);

- vaccination coverage for measles and/or rubella SIAs (“catch-up” and “follow-up” campaigns), by cohort, years of campaign implementation, target population and type of vaccine used (measles, measles-rubella, or measles-mumps-rubella), as appropriate; and
- additional information requested from a country to support administratively reported coverage estimates.

To permit an estimation of the immunity profile of population cohorts, the analysis should begin with the data (both overall and age-specific) resulting from interventions implemented since the introduction of the measles and rubella vaccines in the country, taking into account the different vaccination strategies used over time.

An examination of additional information sources may be helpful in verifying or triangulating reported vaccination data relating, for example, to:

- annual doses of vaccine administered since the introduction of MRV and RCV;
- coverage (%) achieved through vaccination campaigns, by age group (stratified by appropriate administrative level to ensure that there are no gaps in coverage);
- results of coverage surveys, and evaluation of MCV and RCV coverage by geographical region;
- vaccination dropout rates;
- coverage of specific population groups (migrants, nomadic populations, etc.);
- modelling of the accumulation of measles- and rubella-susceptible persons;
- ranges and levels of coverage in the municipalities of different regions, provinces or zones in the countries (e.g. < 50%, < 80%, 80–94%, ≥ 95%), resulting in identification of poorly performing municipalities and/or areas at risk of transmission;
- RCV vaccination in the post-partum and/or post-abortion period, if available;
- seroprevalence studies, if reliable and accurate; and
- correlation of the above information with the impact of measures taken on the epidemiology of measles, rubella and CRS.

Sustainability of NIPs

In analysing NIP sustainability, all management levels should be included and any existing decentralization processes taken into account. The analysis is not an external evaluation of NIPs; most of the data would be available in the annual reports submitted by all Member States through completion of the WHO–UNICEF Joint Report Form. The objective of this analysis is to highlight that the NIP will contribute to the essential elements of the documentation and verification of measles and rubella elimination, as well as to maintaining elimination.

It is important to investigate NIP capacity for maintaining achievements made through the measles and rubella initiative. To this end, a description of the development, structure and organization by management level of the NIP, and of its function within the public and private health care systems should be provided. Special attention should be paid to measles and rubella vaccination services (strategies and outreach tactics), as well as to their surveillance capacity (reporting, investigation, outbreak response and case classification) and laboratory capacity for serological diagnosis and virus detection/isolation.

In addition, an analysis should be made of the legal foundations, financing issues and flow of information between the institutions participating in the programme, as well as the ability of the NIP to make timely decisions. Its involvement in the work of interagency coordinating committees, advisory committees on immunizations or operative technical committees may also be of interest. An organigram demonstrating the organization of the NIP and related networks should be included.

The availability of updated information on vaccination coverage for all antigens and population strata, as well as timely epidemiological information, is essential. For this reason, it is crucial to determine if the programme's information system is efficient, integrates all management levels and includes both the public and private sectors. Furthermore, NIPs should have an effective system for monitoring and supervising surveillance activities and response measures, and health personnel at all levels should be trained in the application of strategies for measles and rubella elimination, and for maintaining elimination.

To achieve and sustain measles and rubella elimination, it is essential to achieve a very high level of public acceptance of the value of vaccination in protecting health. Currently, public acceptance of vaccination is not routinely monitored in most countries, but a range of monitoring strategies could be tested in specific countries to determine whether they produce reliable results under local conditions. The strategies include ad hoc surveys, periodic operational research activities and, where feasible and appropriate, the inclusion of questions related to the public acceptance of vaccination in polls and surveys commissioned for other purposes. In communities where public acceptance of the value of vaccination is found to have declined below acceptable levels, strategies and activities to restore public confidence are indicated and the impact of these activities may constitute useful evidence for the sustainability of the NIP.

In analysing NIP sustainability, special attention should be paid to the following components: NIP development; priority at political level and legal basis; human, material, financial and operational resources; and vaccination, monitoring and evaluation strategies. In countries that have implemented health-system reforms, the impact of operational decentralization should be monitored and analysed. In some countries, health reforms and decentralization have had the effect of fragmenting health-service delivery and, despite the promise of greater management efficiency, there is evidence that the quality of immunization-service delivery has declined. Decentralization has, in some instances, also had a negative impact on the national capacity to conduct epidemiological surveillance and outbreak investigation, and to provide complete and timely surveillance data.

Table 4 describes the indicators of and targets for NIP sustainability.

Table 4. NIP sustainability – indicators and targets

Indicator	Description	Target
Adequate planning	NIP strategic plan written and disseminated	Yes
Adequate technical preparation	Standard operating plans written and disseminated	Yes
Adequate funding and demand forecasting for vaccine supply	Stockouts of MCV or RCV at peripheral level	Zero
Secured funding for vaccine supply	Funding for MCV and RCV secured by government	100%
Public acceptance	Monitoring system in place and active for measuring public acceptance of vaccination	Yes

Indicators for monitoring progress towards elimination

Vaccination coverage and incidence of measles/rubella cases (per million people) are indirect measures of population immunity, suggested to monitor progress towards elimination. However, incidence monitoring is reliable only when the quality of surveillance is high and outbreaks are thoroughly investigated.

These measures are useful for providing general guidance and may not apply to small populations (particularly those isolated, for example, on small islands). As countries approach elimination status, the size and duration of outbreaks will diminish and the majority of outbreaks should be import-related in origin.

Vaccination coverage and disease incidence will be monitored at regional level and accompanied by markers suggesting achievement of elimination. Verification of elimination could entail further analyses of the measures (for example, to assess the reliability of the coverage data of a country) and the use of additional elements (such as an analysis of the origins and genotypes of all confirmed cases in the country in question).

Vaccination coverage

Data on vaccination coverage should be collected for all birth cohorts since the introduction of measles/rubella vaccine to permit assessment of the population immunity profile.

The *measure* of population immunity is vaccination coverage with both first and second doses of routine measles and/or rubella vaccines, whether delivered through routine or SIA strategies, among appropriate age groups.

The *target* for population immunity is the achievement and maintenance of at least 95% coverage annually with both first and second doses of measles and/or rubella vaccines in all districts (or their administrative equivalents) and at national level.

Incidence

The incidence of measles (or rubella) is a basic measure of progress in measles (or rubella) control.

To enable meaningful comparisons across countries and regions, the *measure* proposed is incidence per million total population of all cases of measles or rubella (laboratory-confirmed, epidemiologically linked and clinically compatible) to describe the overall level of disease control.

The *target* for incidence is < 1 measles or rubella case per million total population. The numerator is the total number of measles cases, including laboratory-confirmed, epidemiologically linked and clinically compatible cases but excluding imported cases.

Achieving this target is consistent with progress towards measles elimination but does not define measles elimination or confirm that it has been achieved.

As countries approach measles or rubella elimination, cases should be classified according to method of case confirmation (i.e. laboratory-confirmed, epidemiologically linked or clinically compatible) and origin of infection (i.e. endemic, imported, import-related or of unknown origin). Table 5 illustrates the 12 possible categories for every measles (or rubella) case in low-incidence settings.

Table 5. Classification of measles or rubella cases, by method of case confirmation and origin of infection

Origin of infection	Method of case confirmation		
	Laboratory-confirmed	Epidemiologically linked	Clinically compatible
Endemic	A	B	C
Imported	D	E	F
Import-related	G	H	I
Unknown	J	K	L

Classification of cases³

Cases of measles and rubella are classified as follows.

Suspected measles case: a case with signs and symptoms consistent with measles clinical criteria:

- fever and
- maculopapular rash and
- cough or coryza (runny nose) or conjunctivitis (red eyes).

Suspected rubella case: a case with signs and symptoms consistent with rubella clinical criteria:

- maculopapular rash and
- cervical, suboccipital or post-auricular adenopathy, or arthralgia/arthritis.

³Adapted from the World Health Organization (1).

Laboratory-confirmed measles case: a suspected case that meets the laboratory criteria for measles case confirmation.

Laboratory-confirmed rubella case: a suspected case that meets the laboratory criteria for rubella surveillance case confirmation.

Epidemiologically linked measles case: a suspected case that has not been adequately tested by laboratory and that was in contact with a laboratory-confirmed measles case 7–18 days before the onset of rash.

Epidemiologically linked rubella case: a suspected case that has not been adequately tested by laboratory and that was in contact with a laboratory-confirmed rubella case 12–23 days prior to onset of the disease.

Clinically compatible measles case: a suspected case that has not been adequately tested by laboratory and has not been epidemiologically linked to a confirmed measles case.

Clinically compatible rubella case: a suspected case that has not been adequately tested by laboratory and has not been epidemiologically linked to a confirmed rubella case.

Discarded case: a suspected case that was investigated and discarded, either through negative results of adequate laboratory testing for measles and rubella or by an epidemiological link to a laboratory-confirmed case of another disease; in addition, IgM-positive cases in recent vaccine recipients can be discarded if they meet all of the following criteria:

- history of vaccination with relevant vaccine seven days to six weeks prior to specimen collection;
- onset of rash 7–14 days after vaccination;
- no evidence of virus transmission revealed by active search in community; and
- no history of travel to areas in which the virus is known to be circulating.

Imported case: a case exposed outside the country during the 7–18 days (measles) or 12–23 days (rubella) prior to rash onset as supported by epidemiological and/or virological evidence.

Import-related case: a locally-acquired measles or rubella infection occurring as part of a chain of transmission originating in an imported case, as supported by epidemiological and/or virological evidence. (Note: if transmission of import-related cases persists for 12 months or more, cases are no longer considered as import-related but as endemic).

Structure and function of the RVC and NVCs for verification of measles and rubella elimination

The RVC will work in close collaboration with the Regional Office and report to the WHO Regional Director for Europe. It will provide periodic updates to, and coordinate technical and policy issues with ETAGE.

Both the RVC and NVCs will be external, independent entities whose members should not be involved in the managerial or operational aspects of immunization programmes in their

respective countries. In addition, the individuals should not be involved in the surveillance or laboratory-related components of elimination activities, nor have any direct responsibility in connection with achieving the goal at regional or national levels.

It is expected that the RVC and NVC members will be leading scientists, senior physicians or university staff committed to the verification process. They will apply a rigorous and scientific approach to assessing the evidence and will present their judgments frankly and objectively.

RVC

Mission

The RVC will evaluate the documentation submitted by NVCs with a view to verifying the elimination of measles and rubella at regional level, i.e. that all Member States have been free from transmission of endemic measles and rubella virus for at least 36 consecutive months. Individual RVC members will be assigned to groups of Member States to conduct field visits, monitor progress and verify data analyses, in close consultation with the Regional Office, which will act as the Secretariat.

Membership

The RVC will comprise experts, including epidemiologists, clinicians, virologists and molecular biologists. It will include a chairperson, a vice-chairperson and a maximum of eight additional members, all of whom will be independent of the managerial and operational aspects of elimination activities.

Functions

The RVC will:

- conduct at least one meeting annually;
- define internal procedures and the responsibilities of its members in supervising the documentation and verification process;
- advise NVCs on the process for collecting and analysing data to verify elimination in the countries;
- analyse annual reports submitted by NVCs;
- review and apply the criteria, parameters and procedures for documenting and verifying the achievement of elimination in the Region, in consultation with Member States and ETAGE;
- prepare and submit annual reports to the Regional Director, with feedback to Member States;
- conduct field visits in the countries, if necessary, to monitor progress and verify data analyses, in close consultation with the Secretariat (Regional Office); and
- when appropriate, declare the regional interruption of measles and rubella transmission.

NVC

Mission

NVCs will develop and monitor the documentation and verification process in their respective countries. They will be responsible for establishing, reviewing and monitoring verification activities at national level, following standardized operational procedures and preparing national reports for the Regional Office.

NVCs will advocate for strengthening measles and rubella elimination programmes by promoting the documentation and verification process, encouraging their authorities to implement appropriate strategies and monitoring progress towards elimination goals.

Membership

Members of NVCs will be external, independent individuals who are not involved in the managerial or operational aspects of their NIPs. In addition, they may not be involved in surveillance- or laboratory-related components or have any direct responsibility in connection with achievement of the elimination goals at national level.

NVCs will comprise a maximum of five members: a chairperson, a secretary, and 2–3 additional members. They include recognized specialists from various fields (clinicians, laboratory experts, epidemiologists, etc.), who will participate on a voluntary basis. Members of NVCs will be designated by ministers of health in their countries in accordance with official national procedures. Where appropriate, and if approved by the respective ministers of health, NVCs may include members from other countries, for example, members of NVCs in neighbouring countries or officials from international public health agencies.

Functions

The functions of NVCs are to:

- conduct and preside over at least two meetings annually, as required by elimination activities;
- prepare plans of action for the documentation and verification of measles and rubella elimination in the countries, defining responsibilities, products, resources and timelines for the activities, in collaboration with national immunization and surveillance programmes and (on technical matters) the Regional Office and the RVC;
- present the national plans of action to the respective health authorities and RVC;
- compile and analyse the information received from national immunization and surveillance programmes for verification of measles and rubella elimination and CRS prevention in the countries, in accordance with the established criteria and procedures;
- propose alternative solutions if the available country data are insufficient or inconsistent;
- advise national surveillance, laboratory and immunization teams on activities related to the process of documenting and verifying the interruption of endemic measles and rubella virus transmission in the countries;
- conduct field visits in selected areas of the countries, if necessary, to monitor progress and verify data analyses;
- participate in RVC work sessions and visits to the countries at different stages of the documentation process; and

- prepare and submit annual country reports to national health authorities, which will officially present the documentation to a WHO country office or directly to the Secretariat if there is no WHO country office in the Member State.

Documentation process

Once NVCs have been established, the Regional Office will provide all information related to the concepts and methods of developing each component of the documentation process for measles and rubella elimination, as well as the relevant criteria and practical guidelines. The documentation process includes the identification of data sources, both official and unofficial, which provide information to determine the consistency of data documented with those reported by the national surveillance system.

Each country will prepare a plan of action for implementation of the documentation process to be endorsed by its national health authorities. The plan should include the activities necessary for collecting and integrating the required data, and define the responsible parties, as well as products, resources and timelines. The epidemiological surveillance and immunization teams should collect and submit all the required data to the NVC, in accordance with WHO European Region guidance.

When NVCs have been established, countries will be requested to provide annual national reports on progress towards measles and rubella elimination. NVCs will prepare the reports based on information received from immunization and surveillance systems and submit them to the Regional Office through the national health authorities.

At annual meetings, the RVC will review and validate national reports and updates. Based on the evidence provided and in line with definitions as described in the chapter entitled “Documentation required for regional verification of measles and rubella elimination”, the RVC will determine the status of each Member State as

- interrupted endemic transmission (absence of endemic cases for at least 12 months);
- endemic transmission (documentation of endemic transmission or lack of evidence showing interruption);
- re-established endemic transmission; or
- inconclusive (lack of or conflicting evidence to determine status of disease elimination).

The review and evaluation of annual national reports will continue for each Member State until the RVC has confirmed that, according to the established criteria, endemic measles and/or rubella transmission have been interrupted in all Member States in the Region for at least 36 months. Then the RVC can declare regional elimination.

References⁴

1. Framework for verifying elimination of measles and rubella. *Wkly Epidemiol Rec.* 2013;88(9):89–98 (<http://www.who.int/wer/2013/wer8809.pdf>).

⁴All references accessed 3 March 2014.

2. Fenner F, Henderson DA, Arita I, Ježek Z, Ladnyi ID. Smallpox and its eradication. Geneva: World Health Organization; 1988 (<http://whqlibdoc.who.int/smallpox/9241561106.pdf>).
3. Smith J, Leke R, Adams A, Tangermann RH.. Certification of polio eradication: process and lessons learned. *Bull World Health Organ.* 2004;82:24–29 (<http://www.who.int/bulletin/volumes/82/1/en/24-30.pdf>).
4. Eliminating measles and rubella and preventing congenital rubella infection. WHO European Region strategic plan 2005–2010. Copenhagen: WHO Regional Office for Europe; 2005 (<http://www.euro.who.int/document/E87772.pdf>).
5. Surveillance guidelines for measles, rubella and congenital rubella syndrome in the WHO European Region, update December 2012. Copenhagen: WHO Regional Office for Europe; 2012 (http://www.euro.who.int/__data/assets/pdf_file/0018/79020/e93035-2013.pdf).
6. Manual for the laboratory diagnosis of measles and rubella virus infection, second edition. Geneva: World Health Organization; 2007 (WHO/IVB/07.01; http://www.who.int/ihr/elibrary/manual_diagn_lab_mea_rub_en.pdf).
7. HEALTH 21: the health for all policy framework for the WHO European Region. Copenhagen: WHO Regional Office for Europe; 1999 (European Health for All Series, No. 6; http://www.euro.who.int/__data/assets/pdf_file/0010/98398/wa540ga199heeng.pdf).
8. Strategic plan for measles and congenital rubella infection in the European Region of WHO. Copenhagen: WHO Regional Office for Europe; 2003 (http://www.euro.who.int/__data/assets/pdf_file/0020/79022/E81567.pdf).
9. WHO Regional Committee for Europe resolution EUR/RC55/R7 on strengthening national immunization systems through measles and rubella elimination and prevention of congenital rubella infection in WHO's European Region. Copenhagen: WHO Regional Office for Europe; 2005 (http://www.euro.who.int/__data/assets/pdf_file/0003/88086/RC55_eres07.pdf).
10. WHO Regional Committee for Europe resolution EUR/RC60/R12 on renewed commitment to elimination of measles and rubella and prevention of congenital rubella syndrome by 2015 and sustained support for polio-free status in the WHO European Region. Copenhagen: WHO Regional Office for Europe; 2010 (http://www.euro.who.int/__data/assets/pdf_file/0016/122236/RC60_eRes12.pdf).
11. Report of the sixty-third session of the WHO Regional Committee for Europe. Çeşme Izmir, Turkey, 16–19 September 2013. Copenhagen: WHO Regional Office for Europe; 2013 (http://www.euro.who.int/__data/assets/pdf_file/0005/234734/Report-of-the-sixty-third-session-of-the-WHO-Regional-Committee-for-Europe-Eng.pdf).
12. Orenstein WA, Strebel PM, Papania M, Sutter RW, Bellini WJ, Cochi SL. Measles eradication: is it in our future? *Am J Public Health.* 2000;90(10):1521–5 (<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1446359/>).
13. Meeting of the Strategic Advisory Group of Experts on immunization, April 2011 – conclusions and recommendations. *Wkly Epidemiol Rec.* 2011;86(21):205–20 (<http://www.who.int/wer/2011/wer8621.pdf>).
14. Measles initiative partners gear up to tackle challenges ahead. In: *Global Immunization News.* Geneva: World Health Organization; 2011;9:4 (http://www.who.int/immunization/GIN_September_2011.pdf).

15. Progress in global control and regional elimination of measles, 2000–2011. *Wkly Epidemiol Rec.* 2013;88(3):29–36. (<http://www.who.int/wer/2013/wer8803.pdf>).
16. Spika JS, Wassilak S, Pebody R, Lipskaya G, Deshevoi S, Guris D et al. Measles and rubella in the World Health Organization European Region: diversity creates challenges. *J Infect Dis.* 2003;187(Suppl 1):S191–7.
17. Global eradication of measles. Report by the Secretariat. Sixty-third World Health Assembly. Geneva: World Health Organization; 2010 (http://apps.who.int/gb/ebwha/pdf_files/WHA63/A63_18-en.pdf).
18. Cooper LZ, Ziring PR, Ockerse AB, Fedun BA, Kiely B, Krugman S. Rubella. Clinical manifestations and management. *Am J Dis Child.* 1969;118(1):18-29. doi:10.1001/archpedi.1969.02100040020004.
19. Plotkin SA, Reef SE. Rubella Vaccine. In: Plotkin SA, Orenstein WA, Offit PA, editors. *Vaccines*, fifth edition. Philadelphia (PA), Saunders-Elsevier, 2008, 735–71.
20. Miller E, Cradock-Watson JE, Pollock TM. Consequences of confirmed maternal rubella at successive stages of pregnancy. *Lancet.* 1982;2(8302):781–4.
21. Centers for Disease Control and Prevention. *Epidemiology and prevention of vaccine-preventable diseases. The pink book: course textbook.* Atkinson W, Wolfe S, Hamborsky J, editors. 12th edition, second printing. Washington (DC), Public Health Foundation, 2012.
22. Reef SE, Strebel P, Dabbagh A, Gacic-Dobo M, Cochi S. Progress toward control of rubella and prevention of congenital rubella syndrome—worldwide, 2009. *J Infect Dis.* 2011 Jul;204 Suppl 1:S24–7. doi:10.1093/infdis/jir155 (http://jid.oxfordjournals.org/content/204/suppl_1/S24.full.pdf+html?sid=3b30d10e-0c5d-4136-b33d-e8fa7d392d13).
23. Progress reports on technical matters: elimination of rubella and congenital rubella syndrome. 50th Directing Council, 62nd session of the Regional Committee; 27 September–1 October 1 2010. Washington DC: Pan American Health Organization, WHO Regional Office for the Americas; 2010 (<http://www2.paho.org/hq/dmdocuments/2010/CD50-INF-6-G-e.pdf>).
24. GenBank [online database]. Bethesda (MD): National Center for Biotechnology Information, United States National Library of Medicine; 2014 (<http://www.ncbi.nlm.nih.gov/genbank/>).
25. Measles Nucleotide Surveillance (MeaNS) [online database]. London: Health Protection Agency, World Health Organization; 2014 (<http://www.who-measles.org/>).
26. Rubella Nucleotide Surveillance (RubeNS) [online database]. London: Public Health England, World Health Organization; 2014 (<http://www.hpa-bioinformatics.org.uk/rubella>).
27. Measles and Rubella Laboratory Network. In: WHO Regional Office for Europe. Copenhagen: WHO Regional Office for Europe; 2014 (<http://www.euro.who.int/en/health-topics/communicable-diseases/measles-and-rubella/activities/measles-and-rubella-laboratory-network>).
28. Online measles and rubella laboratory data management system (MRLDMS) [online database]. Copenhagen: WHO Regional Office for Europe; 2014. (<http://mrldms.euro.who.int>).