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# WHO meeting on strengthening the Measles and Rubella Laboratory Network in the Russian Federation and newly independent states (NIS)

Tashkent, Uzbekistan
5–7 November 2013

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## Acknowledgement

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## Introduction

The meeting was attended by the heads of national and subnational measles and rubella diagnostics laboratories from 11 countries (Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Republic of Moldova, Russia, Tajikistan, Turkmenistan, Ukraine and Uzbekistan), employees of the measles/rubella Regional Reference Laboratory (RRL) in Moscow, Russian Federation, and representatives of the WHO Regional Office for Europe and WHO headquarters.

## Session 1: Opening

Dr Myriam Ben Mamou presented the programme and defined the goals and tasks of the meeting during the first session. Dr Tihonova, Dr Mamaeva and Dr Shulga were chosen to be chairpersons for each of the three days of the meeting.

## Session 2: Global and regional updates

The second session of the meeting was devoted to global and regional programme data updates on measles and rubella. Dr Mulders (WHO headquarters) informed on the implementation of the elimination programme and the global activities of the laboratory network. He presented the WHO global strategic plan on measles and rubella for 2012–2020 and reported that measles incidence has decreased by 77% since 2000, and immunization coverage has reached 84%. The increase of rubella immunization coverage was achieved by transferring to the use of measles-rubella combination vaccine. Introduction of external quality control of molecular studies and implementation of appropriate training, development of unified internal quality control sampling, publishing of WHO recommendations on implementing serological studies, and revision of laboratory accreditation procedures are planned for the improvement of laboratory network performance.

Key issues addressed during this session included the increased workload of the laboratories at the stage of nearing elimination, provision of timely and complete reporting, introduction of individual case reporting and adequate diagnostics using supplementary study methods.

Dr Huseynov presented a data update on measles and rubella elimination in the European Region. In 2013, measles incidence rose to 25 per 1 000 000 population, and outbreaks were reported both in western and eastern Europe, with the largest numbers of cases in Georgia and Turkey. A large rubella outbreak was observed in Poland. In 2013, the number of countries with incidence below 1 per 1 000 000 decreased. In response, a *Package of accelerated action for measles and rubella elimination* was adopted in the Region, a manual on immunization programme adaptation was tested and a manual on response measures to outbreaks was published. Dr Huseynov stressed the need to maintain a priority status for measles and rubella elimination in each country.

The activities of the European Laboratory Network on measles and rubella (MR Labnet) were covered by Dr M. Ben Mamou. In 2012, more than 50 000 samples were studied by laboratories, the majority of which was blood serum – oral fluid is under-utilized. 66 of 67 national and subnational laboratories were accredited by WHO, and one is in the process of assessment. Dr Ben Mamou stressed the importance of strengthening the role of laboratories as we approach infection elimination, and noted the importance of strengthening the interaction of laboratory and epidemiological services, introduction of unified case numbers, provision of timely reporting, and obtaining of information from all countries on genotypes of circulating measles and rubella viruses.

## Session 3: Update from the Regional Reference Laboratory (RRL), Moscow

Data provided by the measles and rubella RRL in Moscow were presented during the third session. Dr T. Mamaeva informed that 23 of 24 laboratories of the Region (excluding Turkmenistan) participated in quality control activities in 2012. All of them successfully passed professional testing and demonstrated good results in sample re-testing. Good match of results was demonstrated when studying blood serums in Siemens and Vector-Best test systems for measles and Ecolab for rubella. The complexity of measles diagnosis verification in immunized persons was among the key issues and required the use of highly sensitive IgM test systems, both for avidity studies and IgM antibody growth dynamics. When discussing the number of samples for proof-testing it was confirmed that even at the lowest incidence levels, laboratories should

send at least 50 samples to the RRL, including of all positive and doubtful samples, with inclusion of some negative samples.

Dr Shulga provided a detailed characteristic of measles virus genotypes identified in the Region. He stressed the importance of molecular studies, which enable the confirmation of numerous agent importation cases, co-circulation of its genetic variations and demonstration that incidence has “pseudo-outbreak” features. Surveillance results confirmed the interruption of D4/Bandar Abbas strain variation circulation in the Region and dominating spread of D8 genotype in 2013. Rubella was featured by importation and limited circulation of 2B genotype of Asian origin and possible disappearance of 1H genotype. However, molecular-epidemiological data on rubella are limited and require more active effort on timely case identification and study.

## Session 4: Situational updates from national and subnational laboratories

The fourth session covered measles and rubella surveillance results in the countries of the Region, which were presented in the reports of 23 laboratories (the Armenian representative was not present): national laboratories of Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan (including subnational), Republic of Moldova, 10 subnational laboratories of the Russian Federation, national laboratories of Tajikistan, Ukraine (including 2 subnational) and Uzbekistan.

The following topics were raised in the reports and actively discussed by participants:

- laboratory study significance in establishing the spread of infections;
- diagnosis verification in immunized persons;
- the need for unification of requirements for serological studies;
- timely collection and delivery of samples for serological and viral studies;
- insufficient identification of measles- and rubella-suspected patients;
- decreased interest of national health care authorities in elimination programme implementation;
- the need for financial support for laboratories.

The reports from the regions of the Russian Federation included results of types of surveillance implemented: measles, rubella and other exanthematic diseases. It was noted that measles and rubella cases are identified during all types of surveillance, and the issue of their unification should be discussed.

## Session 5: Improving the performance of MR Labnet

The fifth session covered the performance improvement of MR Labnet. Participants were provided with a new interactive laboratory data management system (LDMS), which should replace the current monthly summary reporting from the beginning of 2014. The new system will make it possible to introduce individual measles and rubella reporting and connect this data with the information provided in the Centralized Information System for Infectious Diseases (CISID) database.

## Working group session

Three working groups performed a strengths, weaknesses, opportunities, and threats (SWOT) analysis of the Russian Federation and NIS MR Labnet, in its contribution to verifying the elimination of measles and rubella in WHO European Region.

All groups actively discussed achievements of the laboratory network, current issues and ways to address them using internal and external capacities. In presenting their conclusions, all of the working groups agreed that the 2014–2015 priority issues and their related actions included ongoing supply of test systems, availability of trained personnel, legal and financial support for sample delivery, coordination of activities of laboratory and epidemiology segments, the need for more active commitments in supporting the elimination programme from the Ministry of Health, provision of modern laboratory equipment, and confirmation of the status of national and subnational laboratories as reference centers.

## Recommendations

Based on the provided data, the Meeting concluded that the subregional laboratory network's performance on measles and rubella was high in 2012 and the first nine months of 2013, but special attention should be paid to the following issues.

1. The number of countries which started the verification of measles and rubella elimination in their territories has increased. At the same time, a large outbreak in Georgia and maintained high incidence in Ukraine point to gaps in measles immunization coverage in these countries and the threat of spreading disease in the Region. In many countries, health care authorities' interest in implementing the measles and rubella elimination programme has diminished. Taking into account the importance of political commitment

and more active efforts at the elimination stage, the meeting recommended that the heads of health care agencies of all countries in the Region demonstrate their commitment to the programme and support laboratory and surveillance segments.

2. To implement measles and rubella laboratory studies (identification of IgM and IgG antibodies) WHO- and RRL-approved test systems were recommended for use in national and subnational laboratories. Intra-laboratory control samples were recommended for use when implementing immune-line essays for additional control and results should be entered into protocol. Development and dissemination of global samples for internal control with WHO assistance will facilitate increased quality and reliability of data provided by the laboratory network.
3. To establish the actual picture of the epidemiological situation on measles and rubella in territories with persistent sporadic incidence, at least two patients with clinical signs similar to measles and rubella per 100 000 population should be observed for one year.
4. Laboratory confirmation should be ensured of at least 80% of measles and rubella cases in territories with persistent low incidence (lower than 1 per 100 000 population) and 5–10 cases from each infection outbreak. Implementation of a serological study of all patients from large outbreaks will require additional funding from country resources.
5. The increased number of patients with two doses of measles vaccine requires expansion of laboratory tests used for diagnosis confirmation. If no IgM-specific antibodies are present in immunized patients with clinic signs of measles, IgG antibody avidities, IgG antibody concentration in paired serums and viral studies can be used to confirm the diagnosis. A coordinated study with involvement of the global laboratory will be needed for deeper understanding of this matter.
6. RRL confirmation test results are the important laboratory performance assessment criteria. According to the requirements of the updated accreditation list in the context of measles and rubella elimination verification, the fulfillment of these criteria is of special importance. At least 50 samples from the country should be sent for confirmation testing, including all positive and doubtful, and some negative samples, uniformly selected throughout the year. Non-matching results during confirmation testing of doubtful samples are not included in the final assessment during accreditation.
7. Completeness and timeliness of reporting is an important component of high-quality laboratory performance. Taking this into account, laboratories should ensure adequate reporting on implemented studies and prevent the decrease of this indicator, which

became a trend in recent years. In order to optimize and simplify the reporting process, the "Measles rubella laboratory data management system" (MRLDSM) – an interactive database with online-access, is being introduced in the Region, the full use of which should start in 2014.

8. The use of the laboratory data management system will enable countries to ensure individual reporting of measles and rubella cases at the infection elimination stage, and will provide the opportunity to integrate epidemiological and laboratory data and document the level of suspected, confirmed and discarded cases.
9. Taking into account special significance of molecular-epidemiological data in measles and rubella surveillance at the state of verification of elimination, national and sub-national laboratories should ensure material collection for viral studies from at least 80% of virus circulation segments. Sending samples to the RRL for genotyping should be implemented on a regular basis. Obtained genetic information is entered into the WHO MeaNS (measles) and RubenNS (rubella) databases.
10. To simplify the process of clinic sample delivery to the RRL, national and subnational laboratories can use alternative sample collection and transportation methods: blood serum dried on a filter paper, dry drop of blood for IgM antibody identification, and nasopharyngeal and urine samples on FTA paper to isolate viral nucleic acid.
11. Taking into account the significance of molecular study results during the closing to the infection elimination stage, countries with at least 2 discarded cases per 100 000 population are prioritized for appropriate training and methodological assistance (protocols). Professional testing for molecular studies in laboratories using these methods is planned as of 2014.
12. Using group immunity is an important tool for monitoring progress in measles and rubella elimination and identification of immunization gaps. To unify and coordinate serological studies in the laboratories of the Region, the Meeting resolved to request WHO to provide a manual on studying population immunity, including recommendations on study, sample collection and test system selection protocols.
13. Meeting participants noted the methodological significance of implemented meetings and their role in improving performance and the professional level of laboratories. They therefore requested the WHO Regional Office to continue implementation of annual meetings on strengthening the WHO Regional Laboratory Network on Measles and Rubella in NIS, also involving epidemiologists.

# Annex 1: List of participants

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