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**WHO Meeting on
Strengthening measles and
rubella laboratory network in
the Russian Federation and
Newly Independent States**

**8–10 September 2014
Hammamet, Tunisia**

MEETING REPORT

**WHO MEETING ON STRENGTHENING MEASLES AND RUBELLA LABORATORY
NETWORK IN THE RUSSIAN FEDERATION AND NEWLY INDEPENDENT STATES**

8-10 SEPTEMBER 2014, HAMMAMET, TUNISIA

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1. Introduction

This WHO meeting on strengthening the measles and rubella laboratory network in the Russian Federation and newly independent states was attended by the heads of national and subnational measles and rubella laboratories from nine countries (Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Republic of Moldova, Russian Federation, Turkmenistan, Ukraine), employees of the Regional Measles/Rubella Reference Laboratory in Moscow, specialists of the Federal Centre for Hygiene and Epidemiology of Rospotrebnadzor” of the Russian Federation, head of the Regional Measles/Rubella Reference Laboratory in Tunisia and representatives of the WHO Regional Office for Europe and WHO headquarters.

2. Sessions of the meeting

Session 1 – Opening

During the first session Dr N. Tikhonova greeted the participants on behalf of the Regional Reference Laboratory and highlighted the importance of the annual WHO meetings for coordinating laboratory network activities in the pre-elimination period. Dr Myriam Ben Mamou presented a programme and defined the goals and tasks of the meeting. Dr N. Tikhonova was elected the Chair of the meeting.

Session 2. WHO global and regional updates

Dr Mulders presented a report on the current status of the WHO global measles and rubella programme and laboratory network activities on global level. The programme goals and results in each of the WHO regions were presented with noted slow progress in increasing the coverage with the second measles-containing and rubella vaccines, challenges in receiving reports, increased number of territories with reported increase of measles incidence. The setting of a goal to eliminate measles in all WHO regions increased the workload and responsibility of the global laboratory network. Dr Mulders noted the important role played by molecular studies and the small number of countries providing data on measles and rubella genotypes, and informed about diagnostic kits developed by the United States Centers for Disease Control and Prevention and positive samples for quality control of molecular studies. The need for government support for laboratories, increased linkage of epidemiological and laboratory data, more active work on genotyping measles and rubella and global transition towards weekly individual reporting were named among the top current issues.

Dr D. Jankovic presented the data update on the measles and rubella elimination programme in the European Region and stressed that the situation in the Region remained difficult. An increases in measles incidence takes place both in eastern and western Europe. About 40% of patients are un-immunized and 20 years of age and older. Special attention should be paid to the large proportion of health workers among those infected. Rubella incidence is concentrated mainly in Romania and Poland, where most patients are un-immunized. The need for developing a national set of response measures to outbreaks by all countries and the importance of analysing the causes of increased incidence were stressed. This will make it possible to identify gaps in programme implementation and set up adequate response activities.

Dr M. Ben Mamou presented a report on the status of the European measles and rubella laboratory network and noted that most measles cases in the Region had laboratory confirmations, however there were countries with a large number of clinical diagnoses. 38

countries provide data on measles virus sequencing. The main genotypes for 2013 were D8 and D4, for 2014 – B3 and D8. Rubella cases have mainly clinical diagnosis. Virus sequencing data for recent years were provided by only 7 countries with 2B being the dominating genotype. A long time span for specimen delivery to the laboratory, untimely and incomplete reporting, slow introduction of internal quality control into laboratory operations and delays in providing sequencing results to the WHO databases were listed among the main challenges. Dr Ben Mamou stressed the need for wider study of alternative specimens and the use of FTA-cards for sending viral specimens to laboratories via regular mail. She directed participants' attention to information materials on various aspects of lab diagnostics provided on a flash drive.

Session 3 – Update of the European verification process

Dr D. Jancovic presented a report on the importance of individual surveillance for verification of measles and rubella elimination. The characteristics of main and alternative indicators were provided, which enable the assessment of effectiveness of surveillance in a country, with demonstration of the importance of integrating clinic, epidemiological and laboratory data to establish the source of infection and produce final case classification. Dr Jancovic underlined that countries can, among others steps, introduce additional indicators and determine surveillance efficiency assessment in their territories.

Dr Ben Mamou informed the meeting about reporting systems and data management in the European Region and the current status of laboratory reporting. The sources of information arriving from countries and links to data on WHO web pages were provided, measles and rubella reporting mechanisms and quality were analysed and the role of reporting was noted, including reporting on sequencing data as an important criterion of lab accreditation. Responsibilities of the countries for data quality, integration of laboratory and epidemiology data, reporting software, completeness and reliability of provided information were highlighted as areas for improvement.

Dr S. Deshevoi presented a data update on verification of measles and rubella elimination in the European Region. He demonstrated the algorithm used by the Regional Verification Commission for developing conclusions and assessment results of national reports for 2013, in accordance with which measles transmission was interrupted in 16 countries and rubella transmission in 19 countries. Dr S. Deshevoi underlined that the main elimination criteria include absence of endemic cases, with a quality surveillance system in place and causative agent's genotyping data. However each country has the right to present any additional data it sees fit which confirms the progress in achieving elimination goals.

Session 4 – Regional Reference Laboratory/Update on the Russian Federation

Dr A. Melnikova presented achievements and challenges in implementation of the measles and rubella immunization programme during the elimination verification period in the Russian Federation. Along with achieved progress, there was an increase in incidence in some regions of the country with most patients being above 20 years or under 1 year of age. Successfully implemented anti-epidemic activities enabled a 10 times decrease in incidence. Risk groups include hard-to-reach populations, health workers, education and retail workers and students. Dr Melnikova also informed about the large financial and methodological assistance provided by the Government of the Russian Federation to national laboratories of countries in the Commonwealth of Independent States (CIS) under the measles and rubella elimination programme.

Dr Tikhonova presented a data update from the Regional Measles and Rubella Reference Laboratory (RRL Moscow), and informed that all national and subnational laboratories demonstrated very high results in professional testing in 2013 and confirmation of sample testing. So far, three countries (Armenia, Ukraine and Uzbekistan) have delivered specimens for re-testing as a dry drop of serum. The RRL believes that a protocol of dry serum drop study should be developed using an updated test system for IgM identification, made by Euroimmun. The priority issues noted related to specimen study no later than seven days after delivery at the laboratory, testing the number of specimens required for accreditation (at least 50), delivery to the RRL for re-testing of not only positive, but also negative and all doubtful specimens.

Dr S. Shulga presented a report on genotyping and molecular epidemiology of measles and rubella in the Russian Federation and newly independent states (NIS). The report highlighted the importance of defining not only the genotype, but also genetic lines inside the genotype for more accurate establishment of virus origin. In 2013, D8 (5 genetic lines), D4 and B3 were the dominating circulating genotypes. In 2014, D8 remains dominant. Wide spread of viruses of one genetic line does not always allow for differentiation between continued circulation and multiple importations, which is why the importance of epidemiological data remains unchanged. Identification of viruses of different genotypes in one territory makes it possible to exclude endemic incidence and establish a “pseudo” outbreak, which underlines the importance of viral study of all infection transmission chains. The 2B rubella virus genotype has remained dominant since 2011 and according to molecular data is represented by two independently imported clusters. The identified 1E genotype is vastly different from one that circulated in the Region earlier, which indicates its importation. However, the information on rubella viruses remains limited and requires more active effort.

Session 5 – Status updates from national and subnational laboratories

Measles and rubella surveillance results in the countries of the Region were presented in reports of 20 laboratories: national laboratories of Azerbaijan, Belarus Georgia, Kazakhstan, Kyrgyzstan (including one subnational), the Republic of Moldova, Ukraine (including one subnational), , Turkmenistan and 10 subnational laboratories of the Russian Federation.

The important issues covered in the reports were administrative challenges and delays in receiving test-kits and resulting delays in studies; the need for standard IgM antibodies for registration and procurement of test-kits by the country; challenges with transporting specimens from remote regions; the large proportion of immunized among measles patients and challenges with laboratory diagnostics in this group of patients; the need for closer cooperation of lab workers with epidemiologists and clinicians; high workload, staff turnover and the need for additional staff training. Many laboratories plan to introduce viral and molecular methods of studying measles and rubella, but are experiencing problems with procuring costly reagents and shortages of trained personnel. Also, countries consider the participation of WHO experts in national seminars and trainings to be very important.

Group work

The following activities were implemented in two parallel groups (subnational laboratories of the Russian Federation in one group and national and subnational laboratories of newly independent states in another) and were devoted to establishing priority needs and operative activities directed at increasing individual surveillance and reporting. Group work results were presented during the sixth session.

Session 6 – Best practices, lessons learnt and meeting recommendations

Dr H. Triki presented a report on the performance of the measles and rubella laboratory network in the Eastern Mediterranean Region and noted that measles incidence indicators became worse due to the worsened political situation in a number of countries of the Region. At the same time, the laboratory network successfully handles an increased workload. About 100% of serological studies are implemented within 4 days after delivery. Thanks to implemented trainings, the volume of genetic information increased drastically and all countries have data on measles virus genotyping. In 2013 the B3 genotype was the most widespread. Shrinking routine immunization, vaccine shortages, distraction of attention from the measles programme towards polio outbreaks were among the main challenges.

The parallel group work results were also presented in this session. Both groups expressed interest in discussing ways to improve individual surveillance and reporting, but each of them concentrated their attention on a single problem. The laboratories of the Russian Federation noted the large workload of entering information into the existing database and the impossibility of developing reports, and challenges with case identification when patients with exanthematic diseases have no epidemic numbers. The NIS laboratories concentrated on reviewing complications in achieving compliance with lab accreditation criteria and measles and rubella surveillance quality indicators. Both groups paid attention to the issue of conformity of epidemiological and laboratory data. During the discussion, participants stressed the importance of unified understanding of terms by all elements of surveillance and more active involvement of clinicians in surveillance. Group work results were recognized as a good foundation for the countries' work to improve surveillance and reporting.

3. Recommendations

Based on the provided data, the meeting highly valued the effective performance of the subregional measles/rubella laboratory network in 2013-2014 (8 months) and made the following conclusions and recommendations.

Political commitment, responsibility and partnership

1. There is a need to increase the countries' contributions to support national reference laboratories to ensure their ongoing and sustained performance in conditions of increased pressure at the stage of infection elimination.
2. Government support is also needed to resolve issues which laboratories face in the process of obtaining reagents and when sending specimens to the RRL for confirmation testing. Countries are encouraged to simplify customs clearance in that regard. In large countries, attention should also be paid to in-country transport of samples from the field to reference laboratories.
3. The contribution of the Russian Federation to support measles and rubella elimination in the WHO European Region deserves the highest appreciation. The supply of equipment by Rospotrebnadzor to NIS laboratories scheduled for 2014-2015 has great significance for the process of verifying elimination. The WHO Regional Office for Europe welcomes the cooperation and coordination of activities with the RRL in Moscow targeted at joint laboratory network activities.

Individual surveillance and linkage of epidemiological and laboratory data

Improving integration of laboratory and epidemiological data and upgrading individual case registration are the key factors for infection elimination verification.

Individual surveillance with laboratory confirmation of diagnoses is critical for monitoring the progress achieved in measles and rubella elimination programme implementation. Clear linkage of epidemiological and laboratory data plays a crucial role in timely case classification, identification of outbreaks, developing response measures, a country's elimination status assessment and in general, to make informed decisions.

4. Countries should maintain well-functioning measles, rubella and congenital rubella surveillance as a key component of their measles and rubella elimination programmes.
5. Lab data should be evaluated in combination with epidemiological data and analysed regularly at national level. Introduction of unique case identification numbers at national level will facilitate improved data collection and analysis.
6. The WHO Regional Office developed an online system for registration of measles and rubella laboratory study data (MRLDMS). This system is currently utilized only by Belarus and Ukraine to provide data to WHO. To expand MRLDMS, reference laboratories were invited to participate in an online survey sent out by the Regional Office. Received feedback enables WHO to improve the system and increase its effectiveness, user-friendliness and demand within the laboratory network.
7. Well-conducted seroprevalence studies are a supplementary tool for the verification of measles and rubella elimination and identification of immunization gaps. In order to obtain comparable and quality results, countries wishing to conduct these studies are requested to implement WHO global and regional guidelines on seroprevalence studies.

Full accreditation of reference-laboratories

Compliance with the WHO Laboratory network standards and achieving performance indicators make it possible to obtain full accreditation and ensure measles and rubella elimination verification.

The full accreditation of the national laboratory in accordance with WHO standards is the most important condition to provide reliable information, which enables documenting the achievement of measles and rubella elimination.

8. All laboratories should participate in the assessment procedure to obtain accreditation and attempt to comply with all required criteria, including timeliness and completeness of reporting to WHO, regular implementation of external quality assessment, introduction of internal control sample. In case of noncompliance with accreditation criteria, the given accreditation may be conditional or revoked.
9. The increased number of patients among people who received two doses of measles vaccine requires expansion of laboratory tests used to confirm diagnosis and deepening studies on this issue with coordination of WHO and the global measles and rubella laboratory.
10. Network laboratories should actively participate in outbreak investigations. If a laboratory does not conduct genotyping, PCR-products or relevant clinic specimens should be sent to the

RRL in a timely manner. FTA cards should be used more often for sending specimens, as this does not require cold chain, maintaining biological safety and large financial expenditure. Only informative specimens should be selected for genotyping, according to earlier provided protocol. Specimens sent should contain information on the patient, immunization status and epidemiological situation.

11. RRL and national laboratories conducting molecular studies on measles and rubella should participate in a new laboratory network programme on external quality assessment of molecular studies.
12. To ensure high quality of studies at the country level, national laboratories should develop control mechanism for subnational laboratories participating in implementing measles and rubella studies that are not part of the WHO network.

Molecular surveillance

Expanding molecular-genetic studies of measles and rubella viruses and providing data to MeaNS and RubeNS databases

Information on virus genotypes, under the elimination verification process, is one of the three main criteria to confirm the interruption of endemic transmission of a causative agent. To expand knowledge on molecular epidemiology of measles and rubella we need to activate specimen collection for viral studies and ensure timely reporting based on molecular data.

13. Laboratories should provide for genotyping of at least 80% of epidemiologically identified chains of virus transmission and immediately provide sequencing data to the national surveillance system and within two months to the WHO MeaNS and RubeNS databases.
14. To improve timeliness and completeness of sequencing data provided to MeaNS and RubeNS and decrease the pressure on the RRL, national laboratories are recommended to place nucleotide sequences of their viruses into database on their own. WHO should implement the training of national laboratory personnel on operating MeaNS and RubeNS databases and provide instruction on registration in the system. Meeting requested the WHO to provide information to heads of laboratories on principles of operating MeaNS and RubeNS databases during next annual meeting.
15. National laboratories with experience in conducting molecular studies can also introduce measles and rubella virus studies. To accomplish this, WHO provides relevant primers and probes. National laboratories can send obtained amplicons to RRL (Moscow) for genotyping, and resending using FTA-cards.
16. We need to concentrate our efforts on identification and laboratory studies of rubella-suspected cases and rubella virus genotyping.

The WHO Regional Office for Europe

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