

Final Recommendations
6th Global Measles and Rubella Laboratory Network Meeting
23-25 Sept 2008

1. Concerns were raised about the potential funding shortfall and its impact on maintaining the quality of the LabNet. Suggestions were made for making savings or advocating for additional support ,including:
 - a. Laboratories should consider partnering with labs with limited resources to support laboratory components of surveillance, training and research projects.
 - b. Countries could support LabNet by assisting with the cost of meetings and workshops and with the purchase of assay kits and other reagents.
 - c. LabNet should explore the possibility of developing synergies, where possible, within existing VPD Laboratory networks and consider integrated laboratory approaches as a means to improve the cost-efficiency of measles and rubella surveillance.
 - d. LabNet should provide global genotype data on a regular basic as a helpful advocacy tool.
 - e. Laboratories are encouraged to ensure their needs are incorporated into national disease programme budgets
 - f. LabNet laboratories should consider submitting research proposals for development of new and improved laboratory tools to various funding agencies such as PATH.
 - g. The requirement of the Global LabNet meeting to be held every 12 months will be reviewed and smaller, more focused meetings will be considered as an alternative, when needed.

Action: WHO, LabNet, GSLs, RRLs. **Timeline:** Ongoing

2. The validation process for OF and DBS sampling techniques has been well documented. Countries with logistically challenging surveillance districts are encouraged to consider the advantages of OF and DBS sampling techniques when initiating laboratory-based surveillance strategies. **Action:** WHO Regional Offices. **Timeline:** Ongoing
3. The WHO measles and rubella genotype database is functioning well, is used by the majority of sequencing laboratories in WHO LabNet and is a valuable tool for molecular surveillance. However, some laboratories have yet to contribute genotype data on a regular basis. Laboratories are reminded of their requirement to submit representative genotype information on circulating measles and rubella strains to the WHO genotype database, preferably on a real-time basis, but at least by the end of month the genotyping was completed. The data reporting should be either; directly to the WHO genotype SharePoint database, by email to global and regional laboratory Coordinators, or through one of the other interlinked databases (CDC or HPA, see below). **Action:** LabNet. **Timeline:** Ongoing
4. The HPA MeaNS measles sequence database shows promising development and could be used by a wider number of laboratories than those which have participated in the evaluation phase. It is recommended that:
 - a. Submission of sequence information to the MeaNS database automatically transfers the core epidemiological and genotype data to the WHO database.
 - b. Countries depositing sequence information to MeaNS are strongly encouraged to use the automated function to submit data directly to GenBank.

- c. EURO countries are encouraged to submit measles sequence data following the WHO recommended timeliness indicators (see above). Until a similar database is set up for rubella, these countries should submit rubella genotype data to the WHO database following the same timeliness indicators.
- d. Countries outside EUR may use the MeaNS database, after consultation with HPA and their Regional Laboratory coordinator. However rubella strains should continue to be submitted to the WHO database.

Action: WHO LabNet. **Timeline:** Ongoing

5. Any use of sequence data by a third party is expected to follow the protocol of consulting the contributing and/or sequencing laboratory before any publication occurs. All members of the WHO LabNet will be required to accept agreement with this protocol before gaining access to the genotype database. Access to WHO sequence and genotype databases will also be available to all LabNet Laboratories that perform sequencing or contribute samples to sequencing labs and who agree to the above protocol. All laboratories should be aware that submission of genotype information and sequence data to WHO does not constitute prior publication and that laboratories will be able to publish their sequence data if they wish. **Action:** WHO HQ, LabNet. **Timeline:** Ongoing.
6. Sequencing laboratories should report data from their national measles and rubella surveillance programmes, but should strongly encourage countries for which they provide sequence support to report their own data or obtain written permission from them to submit the data on their behalf. Sequencing laboratories can encourage countries to report their own data by providing sequence data in a format compatible with the LabNet database needs and by assisting with preparation of GenBank entries. **Action:** All LabNet sequencing laboratories. **Timeline:** Ongoing.
7. Sequencing measles and rubella RNA from acute serum samples has proven to be helpful for detecting genotype circulation in countries and regions, especially where routine virological surveillance has yet to be fully established. However, due to the high risk of contamination, laboratories performing RT-PCR should focus on single step standard RT-PCR or real-time RT-PCR procedures. Nested PCR techniques should be performed only in laboratories with extensive experience in these techniques and with appropriate QA/QC protocols in place. **Action:** All LabNet sequencing laboratories. **Timeline:** Ongoing.
8. The LabNet will display tables and maps of the latest genotype information on the public access WHO website and the SharePoint database following the format agreed upon during the meeting. However, this data will only be helpful if genotype and outbreak data are provided to WHO on a timely basis. **Action:** WHO/HQ. **Timeline:** Quarterly update.
9. Serum dried onto filter paper shows considerable promise for facilitating the inter-country transportation of serum for validation purposes. Validation data from EUR and EMR laboratories shows the stability of dried serum over at least one week at 37°C. It is recommended that regions consider introducing these techniques in a phased manner, after the standard protocols are provided to their laboratories. To ensure that a gold standard reference is always available, the corresponding liquid sera should be stored at the submitting lab until confirmatory testing has been completed. **Action:** WHO LabNet. **Timeline:** Ongoing.

10. National laboratories should keep measles and rubella samples for global PT and for future virus identification. Regional laboratory coordinator should be contacted before disposing any positive samples. Those laboratories with plenty of positive samples are encouraged to contribute to WHO proficiency testing panels. **Action:** WHO LabNet. **Timeline:** Ongoing.

11. Filter paper transport techniques should be evaluated for other reagents including monoclonal antibodies for rubella ICA, PCR primers and PCR products. **Action:** WHO, LabNet. **Timeline:** End of 2009

12. A regular communication link between working sub-groups of LabNet members should be established to facilitate development of protocols and procedures for the LabNet. The key issues requiring more efficient or frequent communication include;
 - a. Review of current laboratory protocols for rubella and CRI/CRS surveillance
 - b. Coordination of the development of laboratory tools in GSLs and RRLs
 - c. Sub-classifying genotypes of rubella (specifically genotypes 2B, 1G and 1E) for the specific purpose of molecular epidemiology
 - d. Sequencing laboratories should explore methods to increase the sensitivity of molecular epidemiologic data for measles and rubella
 - e. Development of QA/QC procedures for virus isolation and molecular techniques.**Action:** WHO, LabNet. **Timeline:** Regular meetings established and key issues identified by end of 2008. Ongoing

13. Serosurveys have been demonstrated by some countries to be a useful tool for determining population immunity, especially where other data, such as laboratory based surveillance and vaccine coverage, may be limited or suspect. Serosurveys can be used, when appropriate, to contribute evidence of progress towards achieving measles elimination. Countries considering carrying out serosurveys may consider using "convenience" samples such as those from blood banks, pre-natal screening etc, where possible. **Action:** WHO, LabNet. **Timeline:** Ongoing.

14. Several WHO regions are developing protocols to document elimination of measles and/or rubella. Regional Laboratory focal points should share laboratory-specific components of these protocols with other LabNet members to ensure consistency within the LabNet. **Action:** WHO, LabNet. **Timeline:** Ongoing.

15. It is essential that laboratories performing RT-PCR use standardized assays with appropriate controls. GSLs and RRLs should evaluate appropriate measles and rubella RT-PCR protocols using a well-characterized validation panel. A protocol for distributing proficiency panels for sequencing and diagnostic RT-PCR assays will be established, and QC protocol for sequence analysis will be developed. **Action:** WHO, GSLs. **Timeline:** 2nd quarter 2009.

16. Several Laboratories in the LabNet reported experiencing mumps outbreaks in their countries and shared the diagnostic challenges with confirming cases in vaccinated individuals. It was agreed that:

- a. When possible, LabNet laboratories should endeavor to obtain representative samples from mumps outbreaks for genetic analysis and share data with the LabNet
- b. The current mumps nomenclature should be reviewed and a standard nomenclature and analysis protocol formally adopted as it was for measles and rubella
- c. The detection of IgM for the diagnosis of mumps in vaccinated cases is unreliable and though not supported by the LabNet, RT-PCR on mouth or throat swabs should be considered as a back-up diagnostic tool.

Action: WHO, LabNet. **Timeline:** Nomenclature review 2nd quarter 2009, remainder Ongoing.