

Third WHO Global Measles and Rubella Laboratory Network Meeting

Geneva, August 25-26, 2005

Dr Maureen Birmingham (WHO/VAM) welcomed 35 participants, including WHO regional co-ordinators and representatives of the global measles/rubella lab network. The aim of the meeting was to make key technical recommendations for 2005/6.

Peter Strebel (EPI/WHO) gave an historical review of global measles control. He stated that the overall global goal is measles mortality reduction following the objectives set by the 2000 Millennium Development Goals, 2002 United Nations General Assembly Special Session declaration, 2003 World Health Assembly resolution and most recently the 2005 Global Initiative GIVS goals (90% mortality reduction by 2010 compared with 2000). He outlined the progress made by the Region of the Americas which has successfully eliminated circulation of indigenous measles but still has small outbreaks due to imported virus. Other regions have also established regional measles elimination goals. EURO and EMRO have established an elimination target date of 2010 and the Western Pacific Region has recently developed a measles elimination goal with the target date yet to be confirmed by their regional committee.

He outlined the strategy for sustainable measles mortality reduction He concluded by noting that progress by the laboratory network was currently in advance of that achieved by field surveillance. However, the development of surveillance activities will lead to an

increase in laboratory workload and participants were reminded to include the funding needs of laboratories in proposals for immunization and surveillance programmes.

Susan Robertson (IVB/WHO) presented a global update on rubella. She emphasised the important role of serological surveillance in identifying populations at risk and informing vaccination strategies. This was subsequently illustrated in a later presentation by Annedore Tischer (National MMR Reference Lab, Germany), who presented the results of informative serological studies performed by the European Seroepidemiological Network, "ESEN". Dr Robertson also highlighted the current weakness of CRS surveillance and recommended its strengthening. She called for a greater awareness of virus shedding by CRS babies as a potential source of nosocomial transmission.

In the final presentation of the opening session, David Featherstone (WHO measles/rubella lab network) summarised achievements of the lab network. Training had been given in serology, cell culture/virus isolation, molecular techniques, alternative sampling methods and data management. Ana Maria Bispo, the AMRO lab co-ordinator, reported later that in her region GLP training will be provided prior to laboratory accreditation. Workshops are preferred to individual secondment for training as they are financially more viable. A number of specific recommendations were made:

Cell culture should be standardised on Vero/hSLAM because of the following:

- The substitution of B95a by Vero/hSLAM overcomes biosafety risks posed by this EBV-expressing cell line.

- Vero/hSLAM are as sensitive as B95a for primary isolation of measles virus strains (data presented by Masato Tashiro, NIID, Tokyo).
- Techniques have been developed to maintain Vero/hSLAM in the absence of Geneticin without affecting their sensitivity for 10 to 50 passages (Paul Rota, CDC, Atlanta; Masato Tashiro, NIID, Tokyo)
- As Vero/hSLAM may also be used for rubella virus isolation, Joe Icenogle (CDC, Atlanta) proposed a unified approach for measles and rubella cell culture. The team at CDC has developed a colorimetric immunoassay to detect rubella virus in cell cultures, which addresses the need for confirmation in the absence of characteristic cytopathic effect. (Some participants reported that mumps virus also grew in Vero/hSLAM).

WHO lab manual: The first edition of the WHO Measles lab manual was first distributed in 2000 and a revision is in the process of being completed.

A commercially available virus collection and transport device (Virocult™) has been used for collecting throat/pharyngeal swabs in field studies and have been found to facilitate the collection of samples for measles and rubella virus detection.

The second session heard reports from WHO regions. Several common themes emerged.

Communications. It was noted that communications between laboratory and epidemiologists/surveillance teams was not always optimal in some regions.

Lab network structure.

- NIID in Tokyo has been named as the third Global Specialized Laboratory (GSL).

- Some countries had decided to set up a sub-national network of laboratories because of logistical difficulties in shipping samples to a central lab.

Lab staff. Retaining trained lab staff was a problem reported by some regions. Training of lab staff has been undertaken by several methods including regional workshops (cheapest option but often only one staff member may be trained who does not transfer the training opportunities to others in the lab), onsite training through sending lab specialists (which enables several staff to be trained at once) and sending individual lab staff to regional reference or specialized labs for specific training (highly specific training opportunities but expensive and has some of the same limitations as workshops).

Confirmatory testing. The referral of samples to the RRLs for confirmatory testing was working well in some regions, e.g. AFRO ,China and the parts of Eastern EURO, but needs to be encouraged in other regions. In China, ‘problem’ samples are referred to the Regional Reference Lab with corresponding worksheets. Meeting participants concluded that submission of OD values for kit controls and test samples was useful for resolving discordant samples or problems with assays quickly.

Virus isolation specimens. The collection of specimens for virus isolation/molecular characterization has shown some improvement but there are large areas of the world where measles and rubella virus surveillance is sub-optimal. Providing collection devices which are easy to use and transport, such as the Virocult™ or Oracol™ tubes can encourage virus sampling.

Alternative sampling methods. Most regions have performed evaluations, especially of dried blood samples (DBS). David Featherstone dealt with practical issues such as costs of sample collection and shipping. Further recommendations on implementing alternative

sampling methods will depend on the outcome of studies on the stability of samples and their transportation from the field.

The discussion of alternative sampling methods continued with two presentations on rubella. David Brown (HPA, London) described a new rubella IgM ELISA developed in collaboration with the company Microimmune. The assay has been optimized for oral fluid testing and a proposal was made to evaluate the assay in an endemic country. Rita Helfand (CDC) presented encouraging DBS results for a rubella outbreak investigation in Peru. Annick Dosseh (AFRO) reported that DBS had been trialed in six African countries. Several countries reported difficulty in collecting sufficient quantities of blood and lab staff reported extra workload with processing and testing the dried blood samples. It was reported that holding the hand of the patient being sampled below the waist encouraged blood flow from finger pricks. The DBS method may have applications in countries where the elimination phase has not yet been introduced and where there are populations which are logistically difficult to access.

Standardization

Attempts to standardize a laboratory protocol for measles plaque reduction neutralization (PRN) assay were described by Bernard Cohen (HPA, London). The method is required for WHO studies of aerosol vaccination for measles. Henda Triki (Institut Pasteur de Tunis) described the role of measles PCR for *serum* samples. It is valuable for case confirmation in early samples where IgM may be negative or indeterminate. Although viral load in serum is much lower than in respiratory or urinary samples, the detection of measles RNA in serum is a worthwhile option when these other samples are not

available. Dr Triki reported that measles genome has been identified and genotyped in serum samples from a nosocomial outbreak in Tunisia in 2002 (genotype B3) and from outbreaks in Libya (B3), Syria (D4) and Iran (D4). These findings were later corroborated by Sheilagh Smit (NICD, Johannesburg) who had found 78 (53%) of 146 measles IgM positive sera referred for confirmatory testing to be PCR positive.

Measles IgM proficiency testing was addressed by two members of the lab network. Jennie Leydon (VIDRL, Melbourne) showed that 90% or more of the expected results were obtained by 90% of participating labs of the global network. The most commonly used measles IgM assay was Dade Behring ELISA (in 71 of 99 labs). In the most recently distributed panel, one serum (from a vaccinee) with low IgM was found to be equivocal by some labs. Misinterpretation and clerical mistakes were other sources of error. Labs were reminded that as proficiency-testing sera were distributed in small volumes (50 µl), the containers should be centrifuged on arrival to ensure that the entire sample was available for testing. David Featherstone praised VIDRL for their excellent work and called on the lab network to supply further samples of IgM positive sera to support this activity. Proficiency testing by Provincial level, sub-national labs in China was described by Wenbo Xu (China CDC, Beijing). Following these presentations, David Featherstone reported that the process of laboratory accreditation was gaining momentum and that proficiency testing was an essential part of the process. Accreditation on-site visits were discussed and it was suggested that annual on-site visits for every network lab are logistically and financially challenging to conduct and that a lab being visited once every 2-3 years would be more manageable. However the accreditation process still needs to

be completed for each national and regional lab every year, whether or not an on-site visit occurs. There is a shortage of consultants for accreditation visits and in some regions, eg EURO, there are too many labs to be visited annually by the regional network coordinator and accreditation is being completed by questionnaire and on-site visits when possible. Comments were made about the lack of clarity of the kit instructions for Dade Behring ELISAs and it was not certain that all labs were applying appropriate correction factors. Guidelines for carrying out quality assurance activities will be issued to assist labs in correctly implementing this component of the accreditation process.

In the next session, Joe Icenogle reviewed the current status of rubella nomenclature and genotyping. This is an area where great progress has been made since the previous meeting of the lab network in 2003. Marilda Siqueira addressed the issue of CRS surveillance. She recommended that routine ante-natal screening for rubella IgM should *not* be performed because there were many cases of difficulty caused by false positive reactions. Other participants endorsed this recommendation. Dr Shigataka Katow (formerly NIID, Japan) analysed data on spontaneous and therapeutic abortions associated with rubella in Japan and calculated that the ratio of abortions to CRS cases was 60 : 1 during the period 1978-2002, indicating the burden of disease due to this congenital infection.

Limitations of IgM testing were discussed by Graham Tipples (Public Health Agency of Canada). In general, IgM responses in rubella appeared 'a few days' later than corresponding IgM in measles. Dengue positive sera were found to be a source of false

positive reactions with some measles and rubella IgM kits. Dade Behring assays are being used widely by Network labs. They are more specific (no problem with dengue sera) but less sensitive than some other commercially available assays such as Meddens. It is reasonable to consider manufacturers producing similar quality assays when selecting kit suppliers, and any concerns about supply and shipping issues should be discussed with the manufacturer. Annick Dosseh described the management of kit distribution in AFRO. A system has been developed to minimise waste yet insure that kits were available for emergency use by holding stocks in three RRLs in Côte D'Ivoire, Uganda, South Africa and at the Regional Office.

Alya Dabbagh (VAM, WHO/HQ) raised the issue of monthly reporting of lab data including genotypic information for global updates. Most participants felt this was not realistic and a goal of two months was set for reporting genotypes. Brenda Thomas (HPA) subsequently illustrated 'Real-Time' exchange of virus sequence information using a computer system developed for the European Union-funded 'Enhanced Laboratory Surveillance of Measles' (ELSM) project. The system is hosted by HPA and worldwide participation is now encouraged. David Featherstone expressed the view that the level of sophistication of the ELSM system exceeded that required by the lab network and favoured monthly reporting of genotypes. Paul Rota reviewed other options for sequence data reporting and articulated a preference for submission to GenBank. Brief reports of activities at the two global measles virus strain banks (HPA and CDC) were given. It was noted that genotype B2 was once again 'active' and that D10 has been formally recognized (Paul Rota, CDC).

Measles/rubella surveillance updates were received from five countries.

UK: Oral fluid testing is a major component of surveillance in UK. Samples are submitted to the lab via the postal system. Measles and rubella incidence is low (elimination phase). Proposals for mumps genotyping were presented (David Brown and Li Jin, HPA).

USA: Measles and rubella in elimination phase since 2001; <50 measles and <100 rubella cases recorded per year as a result of importations. (Paul Rota and Joe Icenogle, CDC).

South Africa: Recent measles outbreaks due to importation from Angola and Mozambique (genotypes D2, D5). One outbreak affected infants as young as one month. It was suspected that the mothers were HIV positive (Sheilagh Smit, NICD, Johannesburg).

China: Outbreak of 80,000 measles cases in 2005, genotype H1. Four rubella genotypes currently in circulation (Wenbo Xu, China CDC)

Japan: Predominant measles genotypes: A (1960s); C1 (1980s); D3 (1984); D5 (1990s); H1 (2001-2005, imported from Korea); a cluster of D9 (2004, likely imported from an Asian country). Rubella genotype shifted from 1A in the 1960s to 1D from 1975-1998. Outbreaks in 2003/4 were due to a possible novel genotype.

The meeting continued with a presentation on integration with other lab networks by Esther de Gourville (WHO global polio lab network). There are ~700 measles/rubella labs in the WHO network, more than for any other vaccine preventable disease. Overlap

with polio and/or yellow fever work already exists in 136 labs. Other disease networks where potential for integration with measles/rubella network exists (on the basis of clinical features of the disease or commonality of laboratory methods such as serology, cell culture, PCR) are: influenza, JE, Dengue, Rotavirus, HIV and HPV.

The meeting concluded with a discussion of technical recommendations lead by David Featherstone.

Acknowledgements: Thanks to Dr Bernard Cohen for compiling this document and to all who participated in the meeting.

Third WHO Global Measles Laboratory Network Meeting 25-26 August 2005

Vaccine Assessment and Monitoring, Immunization, Vaccines and Biologicals WHO HQ

**VENUE: SALLE D WHO, GENEVA
PROVISIONAL AGENDA AS OF 25 JULY 2005**

Thursday 25 August 2005

TIME		PRESENTER
8:45-9:00	<i>REGISTRATION</i>	
9:00	1) <i>WELCOME AND OPENING REMARKS</i>	
	<i>OVERVIEW AND GOALS OF MEETING</i>	
	MEASLES GLOBAL UPDATE	P STREBEL
	RUBELLA GLOBAL UPDATE	S ROBERTSON
	PROGRESS AND CHALLENGES IN THE DEVELOPMENT OF THE MEASLES AND RUBELLA LABNET	
	• GLOBAL LABNET	D FEATHERSTONE
	• AFRO	A DOSSEH
	• EMRO	H AHMED
	• EURO	M MULDER
	• SEARO	A THAPA
	• WPRO	K KOJIMA
	• PAHO	A-M BISPO
	STATUS OF ALTERNATIVE SAMPLING TECHNOLOGIES	
	• REPORT FROM REVIEW MEETING	D FEATHERSTONE

• PROGRESS WITH DETECTION OF RUBELLA IGM AND VIRUS	R HELFAND
• IMPLEMENTATION OF DRIED BLOOD SAMPLING TECHNIQUES IN THE FIELD	A DOSSEH

QUALITY ASSURANCE STATUS

• PROFICIENCY TESTING - GLOBAL <ul style="list-style-type: none"> ○ Progress ○ Future developments 	M CATTON
• PROFICIENCY TESTING - CHINA	XU WENBO
• ACCREDITATION STATUS REVIEW	DF

Friday 26 August 2005

STANDARDIZATION:

• PLAQUE NEUTRALISATION ASSAY	B COHEN
• ROLE OF SEROSURVEILLANCE STUDIES	A TISCHER
• DETECTING MEASLES VIRUS IN SERUM	H TRIKI
• CELL LINES FOR MEASLES AND RUBELLA VIRUS ISOLATION	P ROTA / J ICENOGLE

RUBELLA

• REPORT FROM NOMENCLATURE MEETING	J ICENOGLE
• ROLE OF LABNET IN CRI/CRS SURVEILLANCE	M SIQUEIRA
• LIMITATIONS OF ELISA IGM DETECTION	G TIPPLES

DATA MANAGEMENT

• MEASLES/RUBELLA SURVEILLANCE AND MONITORING UPDATE	A DABBAGH
• KIT AND CONSUMABLES MANAGEMENT IN AFRO	A DOSSEH
• BRIEF VIROLOGICAL SURVEILLANCE UPDATES	HPA/CDC/NICD/ CHINA CDC
• UPDATE OF MEASLES STRAIN NOMENCLATURE	P ROTA
• VIRUS SEQUENCING, REPORTING, STRAIN BANK	P ROTA / B THOMAS

GLOBAL CHALLENGES

• INTEGRATION WITH OTHER DISEASE NETWORKS	E DE GOURVILLE
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RECOMMENDATIONS



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Summary and Recommendations

Advocacy

Development of the measles and rubella laboratory network has expanded in all WHO regions, especially in AFR and WPR. Currently there are more than 700 measles laboratories including sub-national laboratories, an increase of more than 30 since the last Global meeting in October 2003. However the Measles and Rubella Laboratory Network is supported by a very limited number of partners and is facing increasing resource needs as more laboratories become operational and increased measles surveillance activities result in heavier workloads.

Recommendations

1. Laboratories need to develop more proactive strategies for promoting the achievements of the LabNet including distributing regular reports of the LabNet development. Advocacy is needed both within WHO HQ, Regional Offices and countries as well as with partners and other stakeholders. Laboratory testing is an integral component of measles and rubella surveillance and countries are strongly encouraged to incorporate laboratory costs into their surveillance budgets. **Action: WHO HQ and Regional Offices, Laboratory Network. Ongoing**
2. Laboratories should establish a close working relationship with epidemiologic staff to make sure that adequate specimens are collected, that data are recorded and reported in a timely and accurate manner, and to be able to manage increasing workload as case-based surveillance is increased. **Action: WHO Laboratory Network, EPI staff, WHO. Ongoing**

Alternative Sampling Technologies

More than 840 cases with parallel dried blood, oral fluid and serum samples have been assessed for measles IgM in three evaluation sites. Good correlation has been shown between the detection of measles IgM in both oral fluid and dried blood compared with serum collected at the same time. Data for the detection of rubella specific IgM in dried blood is limited to a small number of samples collected after the second week of disease onset. An ongoing study in Peru to explore if dried blood and oral fluid samples are feasible for laboratory confirmation of rubella is under way. A commercially available rubella IgM assay has been designed which is suitable for use with oral fluid. Further evaluations are currently underway.

Roll out of the dried blood sample collection method in a limited number of countries has revealed minor problems with the collection and testing of samples. These include difficulty in collecting adequate volumes of finger prick blood and increased workload for laboratories in following the recommended extraction and testing protocols.

Recommendations

3. Further validation data for the detection of rubella IgM in oral fluid and dried blood samples need to be evaluated before considering a broader use of these alternative sampling techniques in the Laboratory Network. The collection, extraction and testing protocols for testing dried blood samples for both measles and rubella IgM should also be optimized to minimize the increase in workload for labs performing these tests. Optimized protocols should be included in the new version of the WHO Laboratory Manual **Action: WHO HQ and Regional Offices, Global Specialized Labs. By end of 2005**
4. A systematic protocol for the implementation of the alternative sampling techniques should be developed for "field" validation including a systematic approach for collecting parallel samples and sampling areas where measles cases are still prevalent. **Action: WHO HQ, Global Specialized Labs. By end of 2005**
5. The stability of IgM in oral fluid and dried blood samples has been validated at 20°C, but should also be evaluated at the higher temperatures often found in countries where these sampling methods are likely to be used. The long term stability of viral RNA and IgM in oral fluid should also be determined for various storage temperatures. **Action: WHO HQ, GSLs, Laboratory Network. June 06**
6. Before establishing Sub-national lab networks, consideration should be made of the advantages alternative sampling techniques can have in overcoming logistical and economical challenges. **Action: WHO HQ and ROs, Laboratory Network. Ongoing**

Standardization

Findings were presented from a meeting held in April 2005 to standardise a laboratory protocol for a measles plaque reduction neutralization (PRN) assay specifically for WHO studies of aerosol vaccination. Variations in incubation time and temperature for virus and antiserum interaction had the most impact on endpoints. However these variations were minimized when the WHO international standard antiserum was used to calibrate the assay. A standardized protocol was developed following the conclusion of the meeting.

Molecular techniques being used by GSLs and some RRLs are providing valuable information for the measles and rubella control programmes, though large areas of the world still have sub-optimal virus surveillance. The conclusions from a meeting for standardizing rubella nomenclature held in August 2004 were outlined and updated. A proposal for updating the measles genotypic information and an update of the global distribution of measles virus genotypes was also presented.

Recommendations

7. The PRN assay cannot be considered for routine use in the LabNet. However the standard PRN protocol developed following the meeting held in HPA should be shared with those specific labs in the LabNet having a need to use PRN for special studies. **Action: HPA and specialized laboratories. By December 2005**
8. A review of current molecular procedures and practices should be undertaken and shared with Network laboratories designated to perform these procedures. Reference materials and validated protocols will be provided on an ongoing basis to the appropriate laboratories. **Action: GSLs, WHO/HQ. December 2005**
9. An ad hoc rubella nomenclature advisory group should be set up to advise on issues arising from new molecular epidemiological surveillance information and rubella phylogeny developments. **Action: GSLs, WHO/HQ. June 2006 and ongoing.**
10. To prevent the chances of cross contamination and misleading results being provided to measles and rubella control initiatives, laboratories should be encouraged not to perform PCR testing unless they have adequate facilities to perform the testing with minimal risk of cross contamination. All PCR procedures should include adequate controls as described in the standard LabNet protocols (item 8), and follow good laboratory practices guidelines. **Action: All LabNet Laboratories. Ongoing.**

Cell culture detection of measles and rubella virus

Evidence of the stability of the transfected CD150 (hSLAM) receptor in Vero/hSLAM cells was provided by labs at NIID, CDC, and Luxembourg. Sensitivity to measles virus isolation was apparently unaffected by up to 50 passages in the absence of Geneticin, though a maximum of 15 passages is recommended for routine passage of any cells used in the Network. Vero/hSLAM cells have shown similar sensitivity to Vero cells for the culture of rubella virus.

Recommendations

11. Standard protocols for handling Vero-SLAM cells for measles and Rubella including the most economical use of Geneticin to maintain Vero-SLAM cell lines should be developed and included in the new edition of the Laboratory Manual. **Action: WHO HQ and GSLs. December 2005.**
12. Standard protocols further integrating culture of measles and rubella viruses in Vero/hSLAM cells should be developed and evaluated in at least two selected regional reference laboratories. **Action GSLs and RRLs. Dec 2005**
13. Laboratories should encourage surveillance staff to use the Virocult swab as a suitable means of obtaining a throat/oropharyngeal swab for virus detection, either alone or in combination with urine samples. **Action: All labs. Ongoing.**

Quality assurance

The LabNet accreditation process has been implemented in five WHO regions, with 47% of labs having been assessed, though not all have included on-site reviews. The labs that have been assessed have found the process helpful for strengthening their performance. Some of the challenges Lab coordinators have faced include; initiating sample confirmation procedures, lack of guidelines for some QA processes and the large number of labs requiring annual assessment. On-site reviews need only be performed every 2-3 years for high quality labs. GSLs are usually performing functions which do not necessarily match the activities covered in the NL or RRL accreditation checklists but it is considered important to have them included in the accreditation process. WHO has limited resources to provide budgetary and technical support, and to monitor the performance of Sub-national laboratories.

Recommendations

14. The current accreditation checklists should be updated to include recent changes in standard laboratory network procedures. **Action; WHO/HQ by end of 2005.**
15. Laboratory coordinators should endeavour to accelerate the accreditation process for their National labs. Laboratories need only to receive on-site reviews once every 2-3 years and a paper-based assessment is acceptable for the intervening years. WHO HQ will be responsible for the accreditation process of RRLs and GSLs. **Action; WHO Lab Coordinators in measles endemic regions. At least 80% of labs having a minimum of one assessment by end of 2006.**
16. Protocols/guidelines for performing recommended QA procedures for the meeting the accreditation performance indicators will be developed and distributed to all laboratories. **Action; WHO/HQ, GSLs. By end of 2005.**

17. National Labs should be encouraged to report the kit used and optical density (OD) values of all samples sent for IgM validation. To facilitate trouble shooting, Lab worksheets should be sent to the RRL for any discrepant samples found. For proficiency test samples ODs for negative and positive kit controls and other QC information with proficiency panels. A protocol outlining these needs will be included in the new Lab Manual. **Action; WHO Lab Coordinators, LabNet. By end 2005**
18. To facilitate the collection of measles and rubella sera for proficiency and assay validation panels Regional Laboratory Coordinators should contact each of the RRLs and NLs in their region at least annually to enquire about availability of serum samples that could be used for these purposes. HQ and GSLs will facilitate transport of samples, and testing. **Action; All labs and Lab Coordinators. End of 2005 and then ongoing. .**

Sequence Data management

Measles and rubella virus sequence information is providing a valuable adjunct to epidemiological information in determining whether outbreaks are due to imported or indigenous strains and can be helpful in evaluating vaccination campaigns. However genotype information should be shared in a timely manner with programmatic staff for maximum benefit to be gained.

Recommendations

19. It is recommended to continue to investigate mechanisms for developing real time exchange of genotyping data to allow programmatic action to occur in a timely manner. **Action; WHO HQ, ROs and GSLs. Ongoing.**
20. GenBank should continue to be used with linked databases as primary repositories of Measles and Rubella sequence data with the required annotation, however, evaluation of other databases to capture epidemiologic and virological information with links to GenBank accession numbers should be investigated. **Action; WHO HQ, ROs and GSLs. Ongoing**
21. Virological surveillance is still incomplete. It is important to collect specimens for virological surveillance during all phases of measles/rubella control. It is especially important to conduct baseline surveillance in countries that have not previously reported viral genotype information and that are entering an accelerated control phase. Laboratories are reminded to follow the procedures recommended in the WHO Manual and updated in the WER. **Action; WHO HQ, ROs, GSLs. Ongoing from January 2006.**
22. Genotype data should be completed within two months of reception of specimen at the sequencing lab and reported to the appropriate WHO regional office on a monthly basis. This performance indicator can be incorporated into the accreditation assessment of sequencing labs. **Action; WHO HQ, ROs, GSLs. Ongoing from January 2006.**

