Meeting Report

Second Meeting on Vaccine Preventable Diseases Laboratory Networks in the Western Pacific Region

Manila, Philippines
22–26 February 2010

World Health Organization
Western Pacific Region

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REPORT

SECOND MEETING ON VACCINE PREVENTABLE DISEASES LABORATORY NETWORKS IN THE WESTERN PACIFIC REGION

Manila, Philippines
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NOTE

The views expressed in this report are those of the participants of the Second Meeting on Vaccine Preventable Diseases Laboratory Networks in the Western Pacific Region and do not necessarily reflect the policies of the World Health Organization.

This report has been printed by the Regional Office for the Western Pacific of the World Health Organization for the participants of the Second Meeting on Vaccine Preventable Diseases Laboratory Networks in the Western Pacific Region, which was held in Manila, Philippines, 22-26 February 2010.

SUMMARY

The Second Meeting on Vaccine Preventable Diseases Laboratory Networks in the Western Pacific Region was held in Manila, Philippines from 22 to 26 February 2010. Three consecutive sessions of polio on 22-23 February, Japanese Encephalitis (JE) on 24 February and measles/rubella on 25-26 February, reviewed the performances of three laboratory networks to identify challenges of network laboratories and ways to strengthen the quality of the performances to maintain polio-free status, to strengthen JE and measles/rubella laboratory networks and also to monitor the implementation of recommendations from the first laboratory network meeting in July 2008.

Around 90 people of country participants, advisers from the United States Centers for Disease Control and Prevention (US CDC), National Institute of Infectious Diseases, Japan, WHO staff from headquarters and SEARO as well as secretariats from WPRO and country EPI officers attended the meeting. Participants included 25 representatives from 12 polio laboratories in 11 countries, 16 representatives from nine JE network laboratories and 34 representatives from 19 measles/rubella network laboratories.

The meeting provided a forum to discuss updates on the status of the EPI Laboratory Networks and to identify ways to strengthen the quality of the performances of network laboratories to maintain poliomyelitis-free status and to support achieving measles elimination and JE control in the Western Pacific Region.

The objectives of the meeting were:

(1) to review the performances of poliomyelitis and measles/rubella network laboratories in the Region and to assess their implementation of new requirements;

(2) to identify challenges of poliomyelitis and measles/rubella laboratories and ways to strengthen the quality of the performances of network laboratories to maintain poliomyelitis-free status and to support achieving the regional goal of measles elimination; and

(3) to review the progress of the newly established JE laboratory network in the Region and to introduce quality assurance measures, including future accreditation scheme.

Part I Polio Laboratory Network

The meeting reviewed global progress towards polio eradication and the status of the Regional Polio Laboratory Network which consists of 43 laboratories including 31 provincial laboratories in China. The network tested 11 556 stool specimens from 5685 acute flaccid paralysis (AFP) cases in 2009. Only Sabin-related viruses were detected, including one vaccine-derived poliovirus (VDPV). Timeliness of reporting results was 95% for virus isolation and 93% for intratypic differentiation (ITD) testing.

The network maintained a high standard of performance and provided data to confirm the continued polio-free status of the region. All network laboratories participated in WHO accreditation programmes and had on-site reviews of performance or submitted completed standard checklists for review by WHO personnel. WHO introduced a new format for the accreditation checklists for National Polio Laboratories and ITD laboratories in January 2008 and these have been used in the Region. Based on the evaluation of performance,

all network laboratories, except for the provincial laboratory in Tibet, China (pending on-site review), were fully accredited as of 31 December 2009.

As recommended by the 14th and 15th Informal Consultation of the Global Polio Laboratory Network (GPLN) meetings in 2008-2009, the polio laboratory network in Western Pacific Region (WPR) began implementing rRT-PCR in 2009 after National Institute of Infectious Diseases (NIID), Japan and Victorian Infectious Diseases Reference Laboratory (VIDRL), Australia participated in field trials of rRT-PCR methods developed by the US CDC.

Participants commented on the expanding knowledge and experience of the Polio Eradication Initiative with outbreaks due to VDPVs that warrants critical review of the operational definitions used to define circulation, and access to guidelines for the investigation and response to VDPV detections.

The critical role that polio laboratories played in investigations of EV71 outbreaks highlights their valuable contributions to public health within the Western Pacific region. WHO should continue its advocacy with national authorities and partner agencies for continued support to the regional polio laboratory network.

Conclusions of the polio laboratory network

The meeting concluded that the performance of the regional polio laboratory network is sustained at polio-free certification standard and that acute flaccid paralysis (AFP) surveillance activities are efficiently supported. The network provides critical evidence in support of the continued polio-free status of the Region. The network's activities to implement new test algorithms and real time PCR procedures were all on track. Recommendations for the polio laboratory network include: the implementation of the new algorithm for virus isolation and the new real time PCR technique for intratypic differentiation of polioviruses and VDPV screening to reduce the laboratory reporting time, timely sharing of cell sensitivity testing results and data management issues.

Part II**.** Japanese encephalitis

The Western Pacific Region has seven countries either known to be endemic for Japanese encephalitis or suspected to be endemic for JE. These countries include China, Cambodia, the Lao People's Democratic Republic, Malaysia, Papua New Guinea, the Philippines, and Viet Nam. However, the activities of laboratories are limited among those JE-endemic or suspected JE-endemic countries in the Region. Therefore, it was proposed to create a laboratory network for JE to improve the capability of JE case confirmation in the Region.

As recommended by the 17th TAG meeting in 2008, JE laboratory network has been established to improve the capability of JE case confirmation among countries suspected to be endemic for JE in the Western Pacific Region. One global specialized laboratory (GSL), two regional reference laboratories (RRLs) and six national laboratories (Cambodia, the Lao People's Democratic Republic, Viet Nam North and South, the Philippines and Malaysia) were designated during 2008-2009.

In 2009, the first regional hands-on training for the laboratory diagnosis of JE was conducted in Korea CDC from 15 to 19 June 2009 and the first proficiency testing samples prepared by US CDC was arranged for all network laboratories. Technical service agreement support for JE laboratories has been initiated in 2009 for priority countries and essential equipment as well as JE kits for laboratories using Panbio JE/Dengue combo Immunoglobuline

M (IgM) enzyme-linked immunosorbent assay (ELISA) kits was provided to network laboratories to establish the JE laboratory function.

Conclusions of the JE Laboratory Network

A one day meeting of the Regional JE Laboratory Network was held on 24 February as part of the Second Meeting on the Vaccine Preventable Disease Laboratory Networks in the Western Pacific Region, to discuss the progress of implementation of the recommendations from the last meeting held in July 2008. The progress of the JE network laboratories in the Region was presented, challenges of network laboratories were identified and recommendations were made on ways to strengthen the performances of network laboratories. Participants included 23 representatives from network laboratories, WHO Laboratory Coordinators from Headquarters and Southeast Asia Region (SEAR), WHO country Expanded Programme on Immunization (EPI) officers, Advisers from the US CDC and country EPI focal points. The meeting provided a forum to discuss updates on the status of the regional JE network laboratories. Recommendations for the JE laboratories in the Region include implementation of a confirmatory testing mechanism, initiation of accreditation using the WHO JE laboratory checklist and improving data management and reporting.

Part III Measles and Rubella

The WHO measles and rubella laboratory network in the WPR plays an important role in monitoring progress towards achieving regional measles elimination by 2012. The network performs critical functions by confirming or discarding suspected measles, rubella, and congenital rubella syndrome (CRS) cases, identifying measles and rubella virus genotypes, and helping to determine potential routes of transmission. The network has grown since 2001 to 382 laboratories, including one global specialized laboratory in Japan, three RRLs in Australia, China, and Hong Kong, 13 functional national measles-rubella laboratories (NMLs) and, 31 provincial and 331 prefecture laboratories in China. Among 17 functional laboratories (except subnational laboratories in China), all network laboratories except two are accredited as of 31 December 2009. All provincial laboratories in China except one have been reviewed and accredited. Accreditation for prefectural laboratories in China is conducted by provincial laboratories in collaboration with China CDC. A confirmatory testing mechanism has been established and most network laboratories in the Region have sent a proportion of serum samples to RRLs or the GSL.

A two-day meeting of the Regional Measles and Rubella Laboratory Network was held from 25 to 26 February 2010 to review the performance of the measles /rubella network laboratories in the Region, to identify challenges for the laboratories, to identify ways to strengthen the performance of the laboratories in support of measles elimination and to discuss the progress of implementation of the recommendations from the laboratory meeting held in July 2008. Participants included representatives from network laboratories in member countries, the WHO Laboratory Coordinators from Headquarters, WPR and SEAR, WHO country EPI officers, advisers from US CDC and country EPI focal points.

Conclusions of the measles and rubella laboratory network

The meeting concluded that measles and rubella network laboratories provided high quality support to achieve the regional goal of measles elimination by 2012 by confirming suspected cases and identifying measles virus genotypes circulating in the Region. The network should continue to make full efforts to obtain genotype and sequence information on measles and rubella viruses circulating in the Region.

The network implemented most of the recommendations from the last meeting in 2008 including monthly reporting of a case based linelist to WPRO. The laboratories should regularly communicate and collaborate with the national surveillance or epidemiology groups and WPRO to minimize discrepancy of laboratory and surveillance data, and the delay in testing of samples and regular reporting of laboratory data to WPRO.

Recommendations for the measles and rubella laboratory network include implementation of regular confirmatory testing, obtaining more genotyping and molecular epidemiological information by strengthening strain surveillance for measles and rubella viruses, improving data management and reporting using MS Access format, use of alternative sampling and establishing and improving the quality assurance measures of commercial laboratories in countries where measles/rubella testing is performed in commercial laboratories were made.

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ANNEXES:

1. INTRODUCTION

1.1 Background information

1.1.1 Poliomyelitis Laboratory Network

The Global Polio Laboratory Network (GPLN), comprised of national, regional reference, and global specialized laboratories, plays a very crucial role in the global polio eradication initiative. Besides timely identification of wild polioviruses, the rapid detection of vaccine-derived poliovirus (VDPV) that causes acute flaccid paralysis is becoming increasingly important because of polio outbreaks reported due to circulating VDPV.

The regional poliomyelitis laboratory network of 43 laboratories has played an important role to certify poliomyelitis eradication in 2000 and to maintain polio-free status by providing accurate and timely laboratory results of acute flaccid paralysis (AFP) samples in the Region.

The performance of network laboratories is monitored through a laboratory accreditation programme that is administered by the World Health Organization.

Elements of the programme are proficiency testing, onsite performance reviews, monitoring of accuracy, and timeliness of reporting. The formal system for annual accreditation of network laboratories is well established. All laboratories in the Regional Laboratory Network are performing at WHO accreditation standards. Performance levels have been maintained according to the requirements for certification of poliomyelitis eradication.

However, concern has been expressed about the challenges of maintaining certification standards for reporting and investigating AFP cases and collecting adequate stool specimens. Priorities may have been directed to other public health activities after certification and complacency evolved following the interruption of wild poliovirus transmission in the Region.

Rapid confirmation of the transmission of wild polioviruses and VDPVs is an essential first step towards implementing interventions to prevent virus spread. GPLN has formulated a strategic plan to reduce laboratory reporting times without compromising poliovirus detection sensitivity.

Key elements of the plan include introducing a new test algorithm that has been proven through field evaluation in three locations and subsequent implementation in three polio endemic WHO regions (Africa, Eastern Mediterranean, and South-East Asia). It reduced reporting times by 50% without compromising poliovirus detection sensitivity and increased the number of facilities with onsite capacity for virus isolation and intratypic differentiation (ITD). The new plan also reduced the need for the intercountry shipment of virus isolates for analysis and worked out new diagnostic procedures and reagents. The GPLN is also looking into non-AFP based approach such as enterovirus surveillance in polio free areas by assessing its relevance and comparative sensitivity to using AFP.

1.1.2 Japanese Encephalitis Laboratory Network

Seven countries in the Western Pacific Region are either known to be endemic for Japanese Encephalitis (JE) or suspected to be endemic for JE. They are China, Cambodia, the Lao People's Democratic Republic, Malaysia, Papua New Guinea, the Philippines, and Viet Nam.

In Japan and the Republic of Korea, the disease has been controlled largely through universal vaccination programmes for at least four decades.

Laboratory activities are limited in JE-endemic and suspected JE endemic countries in the Region. Furthermore, JE is not perceived to be a priority public health problem in the Lao People's Democratic Republic, the Philippines, and Papua New Guinea. The latter slowed the implementation of these activities with the concurrence of the Ministry of Health.

The South-East Asia Regional Office established a JE Laboratory Network in 2006–2007, before introducing JE surveillance in the Region; it has been fully functional since 2007 . In the Western Pacific Region, there was an urgent need to create the regional JE laboratory network and to improve laboratory capacities for JE confirmation in order to get a better estimate of the JE disease burden and the impact of disease control measures. At a meeting of JE laboratories in July 2008, it was proposed to create a laboratory network in the Western Pacific Region, similar to the one in the South-East Asia Region, to improve the capability of JE case confirmation.

As recommended by the 17th TAG meeting in 2008, a JE laboratory network has been established to improve the capability of JE case confirmation among countries suspected to be endemic for JE in the Western Pacific Region. One global specialized laboratory (GSL), two regional reference laboratories (RRLs) and six national laboratories (Cambodia, the Lao People's Democratic Republic, Viet Nam North and South, the Philippines and Malaysia) were designated during 2008-2009. The first regional training and proficiency testing were arranged and network laboratories initiated reporting of monthly laboratory testing data to the Regional Office in 2009

1.1.3 Measles and Rubella Laboratory Network

The WHO global measles and rubella laboratory network comprised of national, regional reference, and global specialized laboratories has been developed following GPLN model and a formal accreditation system to ensure the quality of the network laboratories has been established.

The strength of the measles and rubella laboratory network is the standardization of all procedures and participation in the WHO accreditation system. Network laboratories use standardized methods of IgM assays, virus isolation and identification, , participate in annual proficiency testing, confirmatory testing and WHO-coordinated meetings workshops and hands-on training courses and report laboratory data to WHO on agreed intervals .

The WHO measles and rubella laboratory network has played a very crucial role in the measles elimination initiative. Provision of timely and highly reliable laboratory confirmation and virus identification results to the programme is essential as we approach the goal of measles elimination. To establish the baseline genetic data on measles viruses which are currently circulating in the Region will allow us to differentiate importation and indigenous circulation of measles virus strains.

The measles and rubella laboratory network in the Western Pacific Region consists of one global specialized laboratory, three RRL, 16 national and 362 subnational laboratories in China. WHO conducts accreditation of 48 network laboratories including 31 provincial laboratories in China. Among four designated laboratories in Pacific Island Countries, only one laboratory is fully functional while two laboratories still participate in the WHO proficiency programme.

The WHO Western Pacific Region established twin goals of the measles elimination and hepatitis B control in 2003 and held the first regional laboratory meeting for the measles/rubella laboratory network in 2004. In 2005, the target year to achieve twin goals was set as 2012. In

July 2008, the Regional Measles and Rubella Laboratory Network Meeting were held as a part of 17th TAG meeting (first vaccine preventable disease [VPD] laboratory network meeting).

An annual proficiency testing programme has been in place in the Western Pacific Region since 2001. In 2009, all network laboratories including 31 provincial laboratories in China participated in the same WHO proficiency testing programme for the first time. As of December 2009, among 48 fully functional network laboratories including 31 provincial laboratories in China, 46 laboratories are fully accredited by WHO. In addition, 331 measles laboratories in prefectural Chinese Center for Disease Control and Prevention are operated under the WHO standards.

1.2 Objectives

The objectives of the meeting were:

(1) to review the performances of poliomyelitis and measles/rubella network laboratories in the Region and to assess their implementation of new requirements;

(2) to identify challenges of poliomyelitis and measles/rubella laboratories and ways to strengthen the quality of the performances of network laboratories to maintain poliomyelitis-free status and to support achieving the regional goal of measles elimination; and

(3) to review the progress of the newly established JE laboratory network in the Region and to introduce quality assurance measures, including future accreditation scheme

1.3 Appointment of workshop officers

Part I. Polio Laboratory Network

Dr Mark Pallansch and Dr Olen Kew were appointed as chairpersons for day 1 and day 2, respectively and Dr Bruce Thorley as rapporteur.

Part II. Japanese Encephalitis Laboratory Network

Dr Ichiro Kurane and Dr Barbara Johnson were appointed as chairperson and rapporteur.

Part III. Measles and Rubella Laboratory Network

Dr Paul Rota and Dr Wilina Lim were appointed as chairpersons for day 4 and day 5, respectively and Dr Joseph Icenogle as rapporteur.

1.4 Organization

The timetable of the meeting is provided in Annex 1. The list of participants is included in Annex 2.

2. PROCEEDINGS

2.1 Day 1 and Day 2: Polio Laboratory Network

A two-day meeting of the Polio Laboratory Network from 22 to 23 February was held to review the performances of the poliomyelitis network, identify challenges of network laboratories and ways to strengthen the quality of the performances and to discuss the progress of implementation of the recommendations from the network's meeting held in July 2008. Participants included 38 representatives from polio laboratories in 11 countries, WHO Laboratory Coordinators from Headquarters and South East Asia Region, Advisers from United States Centers for Disease Control and Prevention (US CDC) and country focal points for the Expanded Programme on Immunization (EPI).

The meeting reviewed global progress towards polio eradication, including detections of wild and vaccine derived polioviruses. In 2009 wild poliovirus (WPV) of serotypes 1 and 3 remained endemic in four countries (Afghanistan, India, Nigeria and Pakistan) and were detected in an additional 18 countries, either due to new importations or continuation of outbreaks due to imported viruses introduced in previous years.

The meeting also discussed the status of the Regional Polio Laboratory Network which consists of 43 laboratories including 31 provincial laboratories in China. The network tested 11 556 stool specimens from 5685 acute flaccid paralysis (AFP) cases in 2009. Only Sabin-related viruses were detected, including one VDPV. Timeliness of reporting results was 95% for virus isolation and 93% for intratypic differentiation (ITD) testing.

The network maintained a high standard of performance and provided data to confirm the continued polio-free status of the Region. All network laboratories participated in WHO accreditation programmes and had on-site reviews of performance or submitted completed standard checklists for review by WHO personnel. WHO introduced a new format for the accreditation checklists for National Polio Laboratories and ITD laboratories in January 2008 and these have been used in the Region. Based on the evaluation of performance, all network laboratories, except for the provincial laboratory in Tibet, China (pending on-site review), were fully accredited as of 31 December 2009.

All 43 laboratories participated in the virus isolation Proficiency Test (PT) during 2008 and 2009. All obtained passing scores of >80% for national laboratories and >90% for regional reference laboratories. Among 43 laboratories, all except four laboratories scored 100%: three laboratories obtained 80% and one laboratory obtained 95%. Four out of six laboratories that perform ITD procedures participated in a separate proficiency test (PT) that evaluated ITD using reverse transcription (RT-PCR). Two remaining ITD laboratories (China and Japan) normally perform simultaneous ITD and sequencing, but are scheduled to participate in real time Polymerase Chain Reaction (rRT-PCR) ITD PT from 2010, after completion of necessary activities to fully implement this procedure on-site.

Implementation of the new test algorithms had been recommended in July 2008 at a regional laboratory network meeting. The new WHO recommended test algorithms to achieve faster reporting of virus isolation (within 14 rather than 28 days) and ITD (within seven rather than 14 days) were implemented in network laboratories except for China, Viet Nam, Mongolia and the Republic of Korea. Among 11 556 specimens analysed in 2009: 1412 specimens were processed by the new algorithm and 10 144 by the old algorithm. Further, the results of identifying a wild type or vaccine strain of poliovirus with the use of an ITD testing procedure should be available within seven days. The proportion of ITD results reported within seven days increased from 62% in 2008 to 93% in 2009.

As recommended by the 14th and 15th Informal Consultation of the GPLN meetings in 2008-2009, the polio laboratory network in Western Pacific Region (WPR) began implementing rRT-PCR in 2009 after National Institute of Infectious Diseases (NIID), Japan and Victorian Infectious Diseases Reference Laboratory (VIDRL), Australia participated in field trials of rRT-PCR methods developed by the US CDC. The methods will update ITD testing technology and improve the sensitivity for screening for VDPVs.

A regional training workshop in rRT-PCR was held in VIDRL, Australia on 25-28 August 2009 and provided a hands-on training opportunity for participants from China, Japan, Singapore, Malaysia and Australia. Malaysia was included in the training as it will be upgraded to an ITD laboratory for the first time once its proficiency is documented. WHO also provided rRT-PCR equipment to three countries (China, Malaysia and Singapore) in 2009. After the training, five laboratories developed plans to implement rRT-PCR and steps to gain proficiency in coordination with US CDC and WHO. VIDRL, Australia completed the four necessary steps including proficiency testing and is fully operational for the new procedure. The other ITD laboratories will also participate in the rRT-PCR ITD PT in 2010.

The GPLN has begun work towards developing a quality assurance (QA) programme for sequencing laboratories. A draft accreditation checklist for sequencing laboratories was distributed in January 2010 to test pilot it and collect baseline information. Comments are being received to provide regional feedback to WHO HQ. Considering that several laboratories in the Region have sequencing capacity, the planned standardized protocol, accreditation system and proficiency test for sequencing will be implemented in the Region as soon as possible, to improve and document QA practices.

The meeting reviewed the Regional Office's experiences with receipt of laboratory reports and challenges in consolidation of reports into a regional polio database. Some weaknesses in reporting of results were highlighted that impact on tracking of all polioviruses and non-polio enteroviruses (NPEVs) and contribute to difficulty in accurately estimating the true workload of network laboratories. The current database and reporting system requires revision to improve data management requirements. The involvement of some network laboratories in activities supplemental to AFP surveillance (e.g. environmental surveillance and enterovirus surveillance) provides valuable public health information.

It was noteworthy that polio network laboratories made valuable contributions to the investigation of outbreaks of Hand Foot and Mouth Disease (HFMD) due to Enterovirus 71 (EV71). Some patients infected with EV71 had clinical presentations compatible with AFP. At least 10 laboratories in nine countries (Australia, China, Hong Kong SAR China, Japan, Malaysia, Mongolia, the Republic of Korea, Singapore and Viet Nam) were involved in the identification of EV71 in 2008-2009. More than 6300 samples from HFMD cases were processed by the network laboratories in this Region (not including China and Japan) during this period and approximately 500 EV71 strains were detected.

In 2008, the China polio laboratory network processed 4769 samples for virus isolation and 18 153 samples for molecular detection from HFMD patients; NPEVs including EV71 and Coxsackievirus A16 were detected from 1079 samples by virus isolation and from 7468 samples by molecular detection. In 2009, polio network laboratories in China detected 8520 enteroviruses including 4518 EV71 strains from 333 154 cases by the molecular detection method.

Opening session

Dr Youngmee Jee, Regional EPI laboratory coordinator, welcomed all participants and advisers. The Regional Director, Dr Shin, Young-Soo opened the meeting and welcomed all

participants from countries and advisers from partner organizations. He acknowledged the continued contribution made by the polio laboratory network to maintain this Region polio-free as this Region will celebrate the 10th anniversary of the Regional Certification of Poliomyelitis Eradication.

2.1.1 Overview of the Global Polio Eradication Initiative (GPEI) and Regional Update to maintain polio-free status

Dr Sigrun Roesel presented an overview of the current status of the GPEI. In 1988, when the World Health Assembly (WHA) adopted resolution WHA 41.28 on global eradication of poliomyelitis by the year 2000, over 125 countries were considered to be endemic for the disease. By 2008, all but four countries (Afghanistan, India, Nigeria and Pakistan) had interrupted indigenous transmission and with a 99% drop in the annual incidence of the disease globally. While the number of indigenous cases of polio has been reduced, an increase in the number of imported was seen. In 2009, over 20 countries were reinfected due to imported poliovirus originating from northern Nigeria and northern India. Many of the re-infected countries, particularly in sub-Saharan Africa, suffered substantial and recurrent polio outbreaks due to low immunization coverage (<80%). A so called "importation belt" stretch from West Africa, into central Africa and to the Horn of Africa. Countries like Angola and Chad, where WPV after importation has circulated for > 12 months, have been designated as having "re-established" transmission.

A special one-year GPEI Programme of Work in 2009 was developed and implemented to examine new vaccine formulations (e.g., high-titre monovalent oral poliovirus vaccine [mOPV1], bivalent oral poliovirus vaccine [bOPV], ID-IPV) and delivery routes, to test new operational approaches in endemic countries and to undertake an "Independent evaluation of major barriers to interrupting poliovirus transmission". The independent evaluation confirmed that polio eradication is technically feasible, however, operational barriers need to be overcome through a very systematic and targeted way. New tactics implemented in the endemic countries were discussed. In Nigeria, the approach was to engage subnational and local leaders, particularly religious leaders, in eradication activities to increase community participation. Such, coupled with the influence of natural immunity, have led to the reduction in the number of infected districts during the fourth quarter 2009 when compared to the third quarter of 2008. In India, more polio/EPI satellite offices were established in the Kosi river areas of Central Bihar to ensure good planning and monitoring of eradication activities. As a result, many new homes (and children) were reached by vaccinators. All, except one, genetic lineages of WPV type 1 have been eradicated. In Pakistan, accountability and heightened political commitment and oversight were enhanced. For example, Polio Action Plan for 2009 was announced by Prime Minister Yousaf Raza Gilani and President Asif Ali Zardari opened the national immunization days (NIDs) in October 2009 with great media coverage. In Afghanistan (and similarly in Pakistan), the key tactic was to continue negotiations for " Days of Tranquillity" with different fighting groups (Taliban and International Security Assistance Force) to allow vaccinators to safely go to security-compromised polio areas.

Since the introduction of mOPV in 2005, alternating outbreaks of WPV types 1 and 3 were reported. A new vaccine: bOPV, found to provide protection that is superior to the trivalent oral poliovirus vaccine (OPV) and "non-inferior" to the respective mOPVs, will be introduced to increase the impact and simplify logistics of OPV campaigns against these two remaining serotypes. Social mobilization, heightened political commitment and fundraising activities have become more prominent in 2009. Robust, innovative and area-specific social mobilization initiatives involved local networks (e.g. National Polio Control Cell in Pakistan) to increase community engagement and local leadership in eradication activities (e.g. religious leaders in Nigeria and women courtyard discussions in Afghanistan). The GPEI also received more

international senior level support from world leaders (e.g. United States of America President Barack Obama, United Nations Secretary-General and Mr Bill Gates).

Dr Roesel ended her presentation by stating the major milestones and impact of the 2010-2012 Programme of Work, incorporating the myriad of lessons learnt since the GPEI began: By mid-2010: all new importations (2009) are interrupted. By the end-2010: all re-established viruses are interrupted. By end-2011: WPV transmission in two of four endemic countries are interrupted, and by end-2012: all endemic viruses are interrupted.

2.1.2 Maintaining Polio-free Status in the Region

Dr Roesel presented the main achievements after certification in 2000 and approaches to maintaining polio-free status amidst the challenges faced in the Region. Keeping the momentum, loss of institutional memory among public health leaders and service implementers due to the delay in achieving global eradication, and decrease in financial support are challenges that the Region has to deal with. Despite all of these, the Region has remained free of poliovirus and VDPV circulation. All countries in the Region, especially China and Japan, have completed Phase 1 wild poliovirus laboratory containment activities. The Regional Certification Commission (RCC) is considered instrumental in maintaining countries adherence to certification level-quality standards. The commission meets annually and requests very detailed annual progress reports for each country. The RCC also visits countries that have technical challenges, observe polio eradication activities (e.g., supplementary immunization activities [SIA] in the Lao People's Democratic Republic in 2008, surveillance activities in Cambodia in 2009) and advocacy with senior political leaders.

The majority of countries in the Western Pacific Region were able to maintain AFP/ poliomyelitis surveillance quality at certification standards during 2009. However, some countries have AFP surveillance quality gaps, particularly subnationally, or deterioration in AFP surveillance sensitivity that needs to be addressed to ensure timely and reliable identification of circulating polioviruses. VDPV were reported in China, one each in 2008 and 2009. The RCC concluded that such occurrences seem to be sporadic, without evidence for sustained circulation. The issues about virological case classification/ definitions of VDPVs, absence of a global investigation and response guideline, and adherence to reporting requirements need to be resolved.

Dr Roesel reported that the RCC was satisfied about the central role that the regional polio laboratory network plays to provide valuable high-quality laboratory support to Member States, noting in particular the contributions of the RRLs and GSL and the progress in the introduction real-time PCR. The RCC reiterated, however, the recommendation to report all wild polioviruses and viruses with discordant ITD results (i.e. potential VDPVs) to national authorities and WHO within 24 hours of detection, and requested that all polio laboratories in the Region to adhere to this recommendation.

Data on immunization activities in 2008 indicate that, overall, countries are maintaining high levels of immunity but with notable exceptions (e.g. in the Lao People's Democratic Republic, Papua New Guinea and a few places in the Pacific Island Countries). While the RCC was impressed with this overall achievement, it noted the lack of uniformity of reported coverage at the district level and recommended continued efforts to boost immunity against polio in areas with relative low performance of routine immunization including specific activities to strengthen routine systems or targeted supplementary immunization activities.

2.1.3 Status of Global Polio Laboratory Network

Dr Esther de Gourville, Global Polio Laboratory Coordinator, provided an update on the workload and performance of the GPLN, quality assurance activities, development of new products, and the detection of wild polio viruses and their transmission links. There are 145 laboratories in the GPLN that continues to support AFP surveillance, and two new laboratories in Cuba and Canada. In 2009, 171 470 faecal samples for 87 014 AFP cases were tested. Workload increases were mainly seen in the remaining endemic regions of Africa, Eastern Mediterranean and South East Asia. Similar trend was seen for non-AFP cases for specimens obtained from various sources. The Western Pacific Region handled 6% of the global workload. Over 10% of samples yielded non-polio enteroviruses (NPEV), > 80% of virus isolation results were reported on time (with decrease by >50% in the time of virus isolation results being reported from 28 days to within 14 days), and > 80% of ITD results provided within seven days of receipt of isolates in laboratories. Overall, high quality performance is maintained in the GPLN despite the ever increasing workload over the past 20 years.

Ninety-four percent of all laboratories were fully accredited, 1.4% provisionally accredited, 2% were non-accredited and 2.8% had pending accreditation. The reasons for not meeting full accreditation were linked to stock out of supplies resulting in delay of reporting ITD results, problems with cell culture, staff changes, and failure in the proficiency test for virus isolation. Upcoming changes to the laboratory quality assurance programme include developing an accreditation programme for sequencing laboratories which will be implemented in 2011. Bio safety training materials have been developed and include a collection of six modules containing and training guidelines for launching in 2010. The aim of this project is to improve implementation of bio safety practices and bio risk management in the laboratory.

The main activities in the GPLN in 2009 included the detection of wild polioviruses and vaccine derived polioviruses (VDPV), implementation of real-time polymerase chain reaction (rRT-PCR) in 39 laboratories, establishing environmental surveillance for polioviruses in Pakistan, revitalization of the polio laboratory in Delhi, India, and involvement of some network laboratories in polio research and development in aid of polio vaccine introduction. Wild polioviruses were detected in 22 countries in 2009 including four endemic countries with both WPV types 1 and 3, 4 countries with only WPV type 3, and 14 countries with only WPV type 1. There are four remaining poliovirus genotypes (WEAF-B PV1, WEAF-B PV3, SOAS PV1 and SOAS –PV3) that continue to circulate since 2005. The environmental surveillance in Pakistan detected a WPV type 1 orphan virus in a sewage sample in Punjab which was only distantly related to viruses circulating among AFP cases in Pakistan and Afghanistan. It also provided evidence of multi-month detection of WPV type 3 in Sindh indicating persistent transmission of the virus (since July) and not sporadic introductions from other locations.

2.1.4 Regional Update of Polio Laboratory Network

Dr Youngmee Jee, Regional Laboratory Coordinator, presented updates on the activities of the polio laboratory network in the Region since the meeting held in 2008. The recommendations from the 15th Informal Consultation on the Global Polio Laboratory Network: 23-25 June 2009 were presented. The activities of the Polio Laboratory network in the Region are well in line with the current priorities of the GPLN in terms of providing accurate and timely detection of WPVs and VDPVs, , introduction of the new algorithm in some laboratories, and implementation of rRT-PCR for ITD and VDPVD screening. Forty-seven laboratories in the Region continue to provide support to AFP Surveillance including 12 national polio laboratories, three RRL, one GSL, and 31 provincial laboratories in China. All, except Tibet, are fully accredited according to WHO standard criteria. In 2009, a total of 11 226 samples from 5868 cases were tested. Of these, 1402 samples were processed using the new algorithm and 9666 samples by the traditional algorithm. In addition, >3000 stools samples and >900 rectal swabs from non-AFP sources were processed for polio and non-polio virus isolation. China had the

highest (80%) workload. Overall, timeliness of reporting virus isolation results was 98 %. Eighty-three percent were reported within 14 days using the new algorithm and 96% were reported within 28 days using the traditional algorithm. ITD results were reported within the target of seven days. Overall NPEV isolation rate was 10% (range 3-31%) in 2008-2009. Timeliness of shipping samples within seven days was 90% (excluding China). All network laboratories passed the virus isolation PT in 2009 using the old PT panel with scores ranging from > 80% to 100%. Similarly, laboratories performing ITD passed the ITD PT with scores of 95% to 100%. Australia RRL passed the rRT-PCR PT provided for the first time in the Region. In 2010, all laboratories will still receive the old PT panel.

Some network laboratories (Mongolia, Viet Nam, the Republic of Korea and China RRL) are also heavily involved in EV 71 identification during HFMD outbreaks. Polio laboratories in the Philippines, Australia and Japan are participating in iVDPV studies looking at poliovirus excretion among patients with primary immunodeficiencies. Environmental surveillance was initiated in China and is also planned in Australia.

In line with the implementation of rRT-PCR, VIDRL, Australia and NIID, Japan participated in the field evaluation of rRT-PCR method in 2008. WHO provided real-time PCR equipment (ABI 7500) and consumables to China, Malaysia and Singapore in 2009. A regional training for rRT-PCR was held in August 25-28, 2009 in VIDRL, Australia and was attended by participants from China, Singapore, Japan, Australia and Malaysia. New Zealand and Hong Kong, China SAR ITD laboratories could switch from conventional ITD PCR to rRT- PCR by 2010 and expansion of ITD capacity using rRT-PCR in other laboratories is planned.

The status of the implementation of the recommendations made in 2008 was reviewed. Five of 11 recommendations were fully implemented and 6 were partly implemented with on-going efforts to meet full implementation. Barriers to implementation were among the topics to be discussed during the meeting. The remaining challenges faced by the regional network include timely sharing of cell sensitivity testing results, mixed use of the new and traditional algorithms for virus isolation, difficulty in gaining proficiency for rRT-PCR for ITD testing and VDPV screening due to the small number of isolates processed in Singapore, New Zealand, Hong Kong and China, and data management issues to reflect the changes in the new algorithm. The plans for 2010-2011 were discussed.

2.1.5 Laboratory Quality Assurance

(i) Report on proficiency testing

Dr Bruce Thorley from VIDRL Polio Regional Reference Laboratory, Australia, reported on the distribution of the PT panels for virus isolation, results of testing and pitfalls. The 2009 PT panels were received from Rijksinstitut Voor Volksgezondheid En Milieu (RIVM), the Netherlands, in November 2009 and will be distributed to 10 laboratories in the Region (China excluded) in two batches in March 2010. Each panel will consist of five samples and laboratories were to test the panel using the old algorithm irrespective of whether the new algorithm has been implemented and report results within 28 days. Common errors observed in proficiency testing from 2006 to 2008 included missed polioviruses in mixed samples, mistyped NPEV and missed isolation of NPEV. The components, process of testing and reporting of the new algorithm PT were discussed.

Dr Mark Pallansch from the Polio and Picornavirus Laboratory Branch, US CDC, discussed the molecular proficiency testing for ITD. Overall, ITD laboratories in the Region achieved very good scores (95% to 100%). The molecular panel consisted of in-vitro ribonucleic acid (RNA) transcripts containing sequences targeted by probe hybridization and PCR. The

same material used for the conventional ITD PCR will be used but separate sets of panel will be provided for real-time PCR ITD and VDPV screening assays while new material is being constructed for the VDPV assay. Reporting time for the new PT panel is seven days (rather than 14 days) and five points penalty will be implemented for every week of delay in reporting results. Australia was the first laboratory to achieve a success in the rRT-PCR PT in the Region.

(ii) Report on Cell sensitivity Testing

Dr Fem Paladin, Technical Officer (Laboratory) reported on cell sensitivity testing from 2008 to 2009 in the Rregion. During the first VPD Regional Meeting held in July 2008, it was recommended that cell sensitivity testing should be performed regularly and that test results should be shared with the Regional Laboratory Coordinator within 48 hours after test completion. Review of the cell sensitivity data from 2008 to 2009 showed that most laboratories in the Region performed cell sensitivity testing regularly. However, gaps in performance were identified such as failure to report results according to the required target time, continued use of cells with reduced sensitivity for >9 months, acceptance of invalid test results and inadequate follow-up when tests clearly showed problems. The recommendation in the previous meeting on timeliness of reporting remains valid. In addition, laboratories will be required to provide a trend chart to monitor trends of cell sensitivity testing over time, to indicate the absolute cell passage number to ensure that cells are used within recommended limits, to implement corrective actions early (e.g., replacement of cells with reduced sensitivity), and to communicate with the Regional Laboratory Coordinators when problems occur.

(iii) Accreditation status of the Polio Laboratory Network in the Region

Dr Youngmee Jee reported that all 43 polio laboratories in the Region including the provincial laboratories in China, except Tibet, are fully accredited as of December 2009. On-site accreditation reviews are usually conducted annually for national polio laboratories (NPL) without ITD function and every two to three years for those laboratories with ITD function. Because of the large number of provincial laboratories in China, on-site visits are conducted every one to three years by a team of international experts from WHO (HQ and WPRO), US CDC and Japan International Cooperation Agency (JICA) and China CDC. Notable in 2009 was the submission of accreditation checklists from 29 provincial laboratories in China including those that were not visited for on-site review. Checklists from Tibet and Ningxia were not received. The ELISA antigenic method for ITD is not used in the Region. Four ITD laboratories perform PCR and VP1 sequencing for ITD and participated in the PCR PT in 2009. China and Japan are using only VP1 sequencing for ITD testing and do not participate in an ITD PT because of the absence of a PT panel for sequencing. All laboratories will participate in the rRT- PCR ITD PT following completion of steps one to three of the implementation plan for real-time PCR. The draft accreditation checklist was sent to China, Japan, Australia, Hong Kong China, New Zealand and Singapore. It is planned to use the draft checklist in 2010 when finalized.

(iv) Country experiences on cell sensitivity testing and lessons learnt

(a) Mongolia

The laboratory experienced a decline in cell sensitivity of the human rhabdomyosarcoma (RD) and L20B cells from 2007 to 2009. The cell viability on recovery was very low and only 41.4% of those recovered grew successfully. The cells were obtained from NIID, Japan, and the National Institute for Biological Standards and Control (NIBSC) reference standard was obtained from VIDRL, Australia. The possible reasons for the low recovery was linked to direct transfer of frozen cells from -20 C to liquid nitrogen due to the absence of -70 °C freezer and the poor storage of the laboratory quality control standards at -20°C for the past six years. When a new NIBSC standard was received in 2009, the cell sensitivity results were satisfactory.

The performance of the polio laboratory from 2007 to 2009 was also presented. During this period, the laboratory processed a total of 727 stool samples including 21 AFP cases, 12 contacts of AFP case, 420 healthy children and 274 diagnostic samples. Timeliness of reporting virus isolation results was 100%. Only one poliovirus was isolated in 2008 and NPEVs were isolated in 166 (22.8%) samples. In 2008, 245 samples were investigated during an outbreak of HFMD from which 102 (41.6%) EV71 and 6(2.4%) CA16 strains were obtained.

(b) Republic of Korea

Cell sensitivity data from 2006 to 2009 showed satisfactory results for both RD and L20B cell lines. Mycoplasma testing of cells (by PCR) did not show evidence of contamination.

During the last four years, the laboratory processed 170 samples (16 to 64 per year) from AFP cases. Inactivated poliovirus vaccine (IPV) was introduced in 2005. And since 2006, when Sabin polioviruses (type 2 and type 3) were detected, no poliovirus has been found. Over 7300 non-AFP diagnostic samples and 43 environmental samples were also tested. In 2008, an outbreak of aseptic meningitis occurred in the country. NPEV detection by PCR ranged from 13.8% to 25.1% (in 2008) and NPEV isolation rate was 9.5% to 15.7% among non-AFP cases and 15% in AFP cases in 2009. In 2009, the laboratory tested 250 samples collected from an EV71 outbreak and 121 (48.4%) samples were positive for EV71 and Coxsackieviruses. Majority of the EV71 genotypes were genetically related (98%) to Chinese strains.

(c) Viet Nam, Ho Chi Minh City

The laboratory received RD (p229) and L20B (p20) cells lines from VIDRL, Australia in August 2006 and established the cell bank following the procedures described in the WHO Polio Laboratory Manual. Thirty-five vials of RD cells (p 232) and 27 vials of L20B cells (p23) were stored in liquid nitrogen. The NIBSC reference strains were received from NIBSC in March 2007 from which LQC standards for each serotype were prepared. Cells are evaluated for sensitivity to all three poliovirus serotypes midway through their 15 passages and results were reported in a tabulated and graphic format to the Regional Laboratory Coordinator within 48 hours after testing is completed. Cell sensitivity testing usually occurs every three months and no evidence of reduced cell sensitivity was found.

From 2007 to 2009, a total of 1009 samples from AFP cases were processed from which eight polioviruses, 16 (1.6%) EV71 virus and 137 (13.6%) non-polio enteroviruses were detected. During the same period, 1751 samples from children with HFMD or central nervous system (CNS) disease were also tested, 175 (10%) EV71 virus and 191 (11%) non-polio enteroviruses were found.

2.1.6 Implementation of the new algorithms for virus isolation and ITD

(i) South East Asia Region experience

Dr Nalini Ramamurty, Regional Laboratory Coordinator, WHO SEARO, presented the polio situation in SEAR, the workload of the polio laboratory network, and the experiences and impact of implementing the new virus isolation algorithm. India is the only country in Southeast Asia Region endemic for wild polioviruses. In 2007, Nepal had WPV type 3 importation from bordering state of Bihar, India, and Myanmar had WPV type 1 importation from Bangladesh which was linked to a virus from India. In 2008, transmission in Myanmar was stopped, however Nepal continued to have periodic importations from India. In 2009, all countries adjacent to India were polio-free. WPV circulation continues in two northern states of India, Uttar Pradesh (UP) and Bihar. As of February 2010, only WPV type 3 was detected, however two importations of WPV type 1 linked to Bihar viruses, occurred in West Bengal and Maharashtra. In 2009, VDPV type 1 and type 2 were also reported in UP and Bihar. One case of VDPV type 1 was an immuno compromised child from UP. Type 2 VDPVs were isolated from 19 cases in UP and Bihar. Two additional VDPV type 2 cases were reported from the same area in UP in 2010. This situation had great impact on the workload of the network laboratories in India.

There are 11 countries in the Region served by 16 polio laboratories including one GSL in Mumbai, two RRLs in Colombo, Sri Lanka (serving Maldives) and Bangkok, Thailand (serving Nepal and Bhutan), nine national laboratories with ITD functions and four national laboratories performing virus isolation only. Workload increased dramatically from 4550 cases in 1997 to over 54,000 AFP cases in 2009 when the indicator for AFP rate was changed in 2005 from 1 per 100 000 to two per 100 000 AFP cases. In 2009, the Region tested over 108 000 samples for virus isolation, representing 56% workload increase since 2005 and 60% of the global workload. Polio laboratories in India handle about 90% of the regional workload.

In 2007, the Region introduced the new algorithm for virus isolation. Prior to introduction, advocacy meetings were held to develop the timeframe for implementation. Key activities included the development of standard operating procedures (SOP), worksheets and reporting formats and approval by the Regional Laboratory Coordinator, modification of the Polio Laboratory Information Action (PLIFA) database programme, and close follow-up with the laboratories through on-site reviews, and ad hoc training of laboratories experiencing problems with implementation. By October 2007, the new algorithm was fully implemented. Two new algorithm PTs were received in 2008 and 2009. Two laboratories failed (<90% of required score) in each occasion, however, 100% score was achieved on repeat testing.

Until 2007, ITD testing was performed using Probe Hybridization and ELISA. Probe Hybridization was replaced by PCR in a phased manner in 2007. Phase 1 included five laboratories with existing PCR facility and Phase 2 was establishment of PCR capacity in four laboratories. The PLIFA database programme was modified and database management training was provided. The implementation plan included an ITD PCR training workshop held in March 2007 for Phase 1 laboratories, parallel testing using Probe Hybridization and PCR methods for six months, PCR PT in September (all laboratories achieved 100% score), and finally, replacement of Probe Hybridization by PCR in September 2007.

For both old and new algorithms, all laboratories in the Region reported virus isolation results within the required target times. The greatest impact of the new algorithms to the programme was the reduction in reporting time of confirmed final results (including ITD results) from 35 to 42 days to 21 to 22 days from receipt of specimens in the laboratory. The new algorithm was beneficial to the laboratories because the number of culture passages was reduced and the neutralization step for virus identification was eliminated. Key to the successful

implementation of the new algorithm in the Region included advocacy (Polio laboratory Directors and Surveillance staff), discussion and consensus planning of implementation plan, close follow-up by the Regional Laboratory Coordinator and open communication among laboratories, GSL and WHO to resolve problems.

(ii) Experience in the Western Pacific Region

Following the first VPD laboratory network meeting in 2008, the new algorithm was implemented in six countries including Australia, Hong Kong China, Malaysia, New Zealand, Singapore, the Philippines(with neutralization test). Japan started implementation of the new algorithm in 2010. China, Viet Nam, Mongolia and the Republic of Korea are still using the traditional algorithm. By second quarter of 2010, it is planned that all laboratories, except China, will use the new algorithm. Worksheets have been revised or are being revised to reflect changes in the new algorithm. The Regional Polio Bulletin was modified in May 2009 to reflect results of both traditional and new algorithm. The average days for reporting virus isolation results were 12.1 (range from 10 to 15.3) days. All except Australia reported results within the required target of 14 days. Two low workload laboratories using the traditional algorithm, Mongolia and Korea, also reported results within 14 days. All ITD laboratories were to report results within seven days as required in the new algorithm regardless of the ITD method in-use. Notable reduction in the number of days to reporting ITD results was seen from 9.4 days in 2008 to 5.8 days in 2009. For non-APF samples, 85% of samples had ITD results reported within seven days. Discrepancy was found in the non-AFP cases reported in the polio bulletin and the annual report submitted by the laboratories. Timely reporting, at least monthly, to WHO of virus isolation and ITD results of samples from non-AFP sources including environmental surveillance, enterovirus surveillance or healthy children survey should be reported in a timely manner was recommended. All ITD laboratories are encouraged to report ITD results within seven days of receipt of L20B positive samples from non-AFP sources. Polio laboratories without ITD function should also refer L20B positive isolates from non-AFP sources to designated ITD laboratories as soon as possible.

(iii) Country experience in implementing the new algorithm

(a) Philippines

The new algorithm was implemented in April 2008 in parallel with the traditional algorithm but the observation time was shortened to 5 days rather than 7 days. In 2008 and 2009, 985 and 1076 samples were processed, respectively. Timeliness of reporting results using the traditional algorithm was 100% from January to March 2008 and 97% from April to December using the new algorithm. In 2009, timeliness was 86%. The decline in timeliness of reporting was attributed to the finding of slow growing NPEVs (usually seen at the late stage of second passage) requiring additional passages and serotyping which resulted in delay in reporting results within 14 days. The involvement of staff in H1N1 activities also contributed to the delay in reporting. Poliovirus serotypes are reported to the EPI unit rather than "L20B positive" result because discussion about the implementation of the new algorithm have not occurred yet. Concerns about incompletely filled case investigation forms and lack of coordination with the surveillance officers with regard to shipment of specimens from AFP and H1N1 cases were raised.

From 2007 to 2009, a total of 3068 samples from 1573 AFP cases were tested, from which 33 Sabin-like poliovirus isolates were obtained in 25 samples. Non-polio enteroviruses were isolated in 185 (6.0%) samples; 40% were successfully serotyped.

In 2008, reduced L20B cell sensitivity was consistently observed for all poliovirus serotypes and similarly for RD cells against Polio 3. Mycoplasma infection was confirmed for those cells sent to VIDRL, Australia. A new batch of cell lines were received in December 2008 but decline in L20B cell sensitivity was still apparent in several test runs in 2009 possibly due the change in operator. The sensitivity of the RD cells appeared acceptable.

(b) Hong Kong, China

The Virology Division of the Public Health Laboratory Centre is the centralized laboratory for the diagnosis of enterovirus infections, AFP surveillance, enterovirus surveillance and serological surveys. It also receives AFP samples from Macau (China). Capacity is well established for virus isolation and ITD testing has been performed using PCR and sequencing since 2002. Identification tests are performed on cytopathic effect (CPE) positive cultures using immunofluorescence, neutralization test (not routine), conventional ITD PCR and VP1 nucleotide sequencing. Since the use of IPV in 2007, the number of isolates tested for ITD was very few. From 2005, no polioviruses were isolated from AFP cases and only very few NPEVs were identified. Obtaining clinical samples from AFP cases and the low ITD workload are challenges to maintain proficiency. Introduction of rRT-PCR could be a better platform for staff to carry out the test more easily.

(c) New Zealand

The workload of the laboratory is very low due to the small number of expected AFP cases (eight to nine cases per year). From 2007 to 2009, 24 stool samples were tested and only 2 Echoviruses were isolated. Among 78 clinical samples received, 10 NPEVs were detected. The laboratory performs conventional ITD PCR and VP1 sequencing. The low workload for AFP samples is a challenge and staff need to spend more time to maintain polio technical capability. The use of the rRT-PCR ITD and VDPV screening assays will be much easier and will provide results faster.

Cell sensitivity testing from 2008-2009 showed satisfactory results for RD and L20B cells, except during the period July to October 2009 when a decline in L20B cell sensitivity was observed for polio type 1. Cells were immediately replaced with low passage stock as a corrective action. One of the probable reasons could be the deterioration of L-glutamine in the old cell culture media. Other causes are also being investigated.

New Zealand conducts Enterovirus Surveillance as supplementary activity to AFP surveillance. Examples of common non-polioviruses serotypes (Echo 30, Cox B5, Cox A16, EV 71) circulating in New Zealand were presented. Two examples of rare enterovirus serotypes, Echo 13 and Echo 33, associated with aseptic meningitis, were also described. Echo 13 viruses detected in 2009 were closely related to viruses from Oman. Echo 33 viruses were not related to historical New Zealand isolates but were closely related to Australian strains.

(iv) Integrating laboratory and surveillance data following introduction of the new algorithm

Dr Jorge Mendoza-Aldana presented the current format of the laboratory and surveillance data received at the Regional Office and provided insights about the challenges and action points towards their integration after the introduction of the new algorithm. Reference was made to the 17th Technical Advisory Group recommendation to introduce the new algorithm for virus isolation (in parallel to polio neutralization test) with the necessary revisions in the database and to add required laboratory indicators in the laboratory database for those laboratories implementing the new algorithm. The first VPD Laboratory Workshop in 2008 also recommended that laboratories are to maintain regular communication and coordination with

national EPI and surveillance units in order to have a common understanding of the implications and features of the new algorithm and to some extent discuss the benefits that it will provide to the programme.

In line with the implementation of the new algorithm, the weekly Polio Bulletin was expanded to reflect new algorithm indicators for those countries (Australia, Brunei Darussalam, Hong Kong SAR, Macau SAR, Malaysia, New Zealand, Pacific Island Countries, Papua New Guinea, the Philippines and Singapore). However, the laboratories and EPI surveillance units in these countries have not completed aligning their data and reporting format to WHO. Examples were presented of reports from laboratory and surveillance units that are received at the Regional Office. The examples highlighted gaps in data quality (e.g. discrepancies in case information, missing case identification no.) that will pose difficulty in aligning and reconciling information. Many of the laboratory reports received at the Regional Office lack the variables described as "needed" in the accreditation checklist. Dr Mendoza emphasized that improvements in laboratory skills should go along with quality data that will allow the programme to make timely decisions. Several action points from previous recommendations were re-stated: (a) maintain regular communication between the laboratories and nation EPI and jointly analyze data as needed, (b) report standardized and quality laboratory data, (c) use of EPID No. as unique identification to link surveillance and laboratory data, and (d) use of EPID No. in laboratories at all times to facilitate tracking of AFP test results.

2.1.7 Implementation of Real-time PCR

(1) Introduction of Real-time PCR for ITD and VDPV screening

Dr Esther de Gourville discussed the objectives of introducing real-time PCR technology for ITD and VDPV screening and the mechanisms of implementation.

When the GPLN recommended the adoption of the new ITD algorithm in 2006, the main emphasis was to prioritize the reporting of wild polioviruses and to do simultaneous serotyping and intratyping using conventional PCR, and to flag suspected VDPVs by the ELISA method. The new improved ITD algorithm uses real-time procedures for both ITD and VDPV screening. The main difference in these two approaches was the elimination of one component of analysis targeted at dealing with mixtures but also the replacement of ELISA by real-time assay. The preparatory steps for the implementation of this new method included evaluation of test performance under field conditions, assessment of the availability and gaps in logistics among laboratories, securing funding and procurement of equipment and supplies, training of laboratories using training materials developed by CDC, production of test kits and preparation of rRT-PCR proficiency panels at CDC and the preparation of a supplement to the Polio Laboratory Manual (to be finalized).

In 2009 to 2010, participants from 34 laboratories in six regions were trained. During the workshops, regional and laboratory-specific post-workshop implementation plans were developed, changes in the database were mapped and the mechanism for reporting, coordination and monitoring performance were defined. The elements of the laboratory-specific post-training implementation plan included development, of SOPs and worksheets, changes to data management and reporting, supplies estimation, equipment maintenance, and implementation of testing in phases: a) Phase 1: to attain proficiency and reproducibility of results; b) Phase 2: retrospective VDPV screening of previously reported SL viruses; c) Phase 3: prospective testing (up to 100 isolates) in parallel with conventional ITD algorithm; and d) Phase 4: proficiency testing and attainment of >90% score. Currently, 12 laboratories in five regions are fully operational and have passed the proficiency tests. The main impact of real-time PCR introduction was the detection of new VDPVs, some having been missed by

traditional testing. In some settings, both outbreak strains as well as sporadic emergences have been found.

(2) SEAR Experience

Dr Nalini Ramamurty discussed the experiences in the roll-out of real-time PCR in SEAR. The regional implementation plan included assessment of laboratories, implementation by laboratories in phases, and procurement of real time PCR equipment and supplies before the training. The training was held in March 2009 at the GSL in Mumbai for six ITD laboratories. The agenda allowed participants to gain theoretical knowledge and practical experience. During the training, an outline for the SOPs were developed, changes to the data management programme (PLIFA) were discussed and agreed, additional equipment and supplies needs were assessed, and a Plan of Action was developed.

During the transition period from April to September 2009, four phases of testing as described in Dr de Gourville's presentation were conducted according to the Plan of Action. The laboratories shared the summary results, screen shots and worksheets with WHO (HQ and Southeast Asia Regional Office) and CDC for review and feedback. Each step followed successful completion of the previous step. In July 2009, a workshop was held to review and finalize the changes to the database and reporting formats. The updated database programme was installed in laboratories in September 2009. In October 2009, all laboratories passed the proficiency test with scores > 95%. By October 2009, seven out of the nine ITD laboratories have implemented the real-time PCR. In November 2009, a VDPV was detected. There are plans to introduce rRT-PCR in three ITD laboratories in 2010, strengthen three additional national laboratories for ITD, and by 2011, test > 90% of stool samples in ITD laboratories to save time and cost of shipment for ITD and to further improve reporting time.

(3) WPR Experience

Dr Fem Paladin reported on the real-time PCR training workshop and current status of implementation in the Western Pacific Region. A hands-on training workshop was held in VIDRL, Australia from 25 to 28 August 2009 following the agenda developed in EMR and SEAR workshops with some modifications. Eight participants from five countries (2 Australia, 2 China, 1 Japan, 1 Singapore, 1 Malaysia) attended. Trainers and facilitators were from US CDC, VIDRL and WPRO. The agenda was a combination of didactic lecture sessions, "hands-on" laboratory experiments, interactive sessions (equipment programming and data analysis) and discussions. The proposed changes in reporting format and the need to standardize the database were also discussed. The generic regional and laboratory-specific plans of action were discussed and each laboratory presented their proposed implementation plan. Because all poliovirus isolates in the Region have been sequenced, it was agreed that Phase 2 retrospective testing will be conducted on stored isolates to determine how these isolates will perform in the real time PCR assays. It was also agreed that Phase 3 prospective parallel testing will be done simultaneously with Phase 2 because only very few isolates are received for ITD testing in each laboratory. All other elements of the generic plan will be followed including the development of SOPs, test worksheets and training of back-up staff. The status of real-time PCR implementation is shown in Table 1. There is plan to expand real time PCR assays to other ITD laboratories (New Zealand and Hong Kong) and to establish ITD testing using real-time PCR in other national laboratories where equipment and experience in PCR exist.

Table 1. Status of Real-Time PCR Implementation in the Western Pacific Region (as of February 2010)

Country	Australia	China	Japan	Singapore	Malaysia
Step 1. Reproducibility testing	Yes	Yes	Yes	Yes	Yes
Updated SOPs and worksheets	Yes	Yes	Yes	Yes	Yes
			48 isolates,		

(4) Australia VIDRL experience

The laboratory participated in the field evaluation of the real-time PCR assays in 2008 and tested 97 poliovirus isolates (various strains) from 53 cases from 1975 to 2009. The correlation between results of rRT-PCR and endpoint PCR and VP1 sequencing for the samples tested ranged from 62.5% to 100%. Two known VDPV isolates were identified Sabin-like polio viruses with the old version of rRT-PCR kit. These isolates have some mutations that were not flagged by the VDPV assay. Based on these results, CDC made adjustments to the probe reagents. A new version of the kit was received and all VDPVs were correctly identified on repeat testing. Some testing pitfalls and practical trouble shooting tips were shared.

(5) Japan NIID experience

The laboratory participated in the field evaluation of the rRT-PCR in 2008. Virus stocks consisting of VDPVs, wild and Sabin-like strains were used. Following the training at VIDRL, activities completed include the development of SOPs and worksheets and Step 1, reproducibility testing (Nov. 2009). High background was observed for the negative control and serotype 2 samples. Working closely with CDC, the reason for the high background was linked to the use of an old serotype 2 kit lot and was resolved when a new batch was received. Delay in implementation included problems with the real-time PCR equipment and the computer attached to the machine. The ABI 7500 Fast real-time PCR system had to be recalibrated and the software had to be upgraded to the new version 2.0.3. In December 2009, the computer crashed and was replaced in Feb 2010. The laboratory identified the need for a back-up real-time PCR machine and routine equipment maintenance, and to maintain a back-up file of the results in case of computer breakdown. The laboratory will use both real-time PCR assays and VP1 sequencing for ITD testing. The addition of real-time PCR ITD and VDPV assays into the annual JICA training course conducted at NIID may be considered.

(6) China CDC experience

The laboratory has developed standard operating procedures and the first three steps of the implementation plan, i.e., Step 1: reproducibility testing, Step 2: retrospective testing of SL viruses, and Step 3: prospective testing have been completed. Step 1 consisted of 10 known isolates, seven had 5-7 nucleotide (nt) substitutions, two had 3 nt substitutions in the VP1

Region, and one aVDPV had 9 nt substitutions. Three PV2 isolates (with 3, 5, and 7 nt changes) had discordant ITD and VDPV screening assay results requiring further sequencing. The aVDPV type 1 was not flagged by the rRT-PCR screening assay because the nucleotide substitutions occurred outside the area of the probe targets (VP1 amino acids 98-103 for S1) of the assay. The analysis of isolates from 1996-2006 with nucleotide substitutions in amino acids considered as "hot spots" showed that 84.8% of type 2 polioviruses would require further sequencing. In Step 2: retrospective testing, 110 isolates of known sequences were tested. Of these, 76 isolates had ≥5 and <9 nt substitutions in VP1 region, and 34 were VDPVs. The findings of inconsistent results for the various primers were presented. Results of VDPV screening for 76 isolates showed that 81.8% of type 2 isolates require further sequencing, a finding similar to those observed in Step 1. Of the 34 VDPV isolates, all but 4 isolates (three type 1 and one type 3) were detected. All undetected isolates were "young" VDPVs.

(7) Malaysia IMR experience

Standard operating procedures have been developed, the first two steps (Step 1: reproducibility testing and Step 2: retrospective testing) have been completed, and the third step (Step 3: Prospective testing) is on-going. For Step 1, 10 known samples consisting of NIBSC poliovirus strains, EV71 and HSV were used. Problems with the use of old stocks of enzymes were encountered during the initial stage of testing but was immediately resolved with the use of new ones following advice from CDC. For Step 2, ten samples of known sequences were tested retrospectively and gave similar results. Six new isolates have been tested, four had results concordant with those of VIDRL, Australia, and two isolates are yet to be shipped. This laboratory had run out of rRT-PCR kits. Two staff members have been trained and new staff needs to be trained.

From 2007 to 2009, 662 stool samples and 89 "other specimens" (e.g. throat swab, rectal swab and CSF) were tested from 349 AFP cases. The laboratory is also heavily involved in the investigation of cases of HFMD, meningo-encephalitis and other infections due to enteroviruses. Fifty-five poliovirus isolates were obtained, three isolates were from AFP cases and 52 were from non-AFP cases. All isolates were confirmed as Sabin-like viruses by VIDRL, Australia. NPEV isolation rate is very low (eight isolates in 3 years), perhaps due to cell sensitivity. Vero cells were added to improve detection.

(8) Singapore SGH experience

The laboratory was accredited in 2003 to perform ITD testing using PCR and ELISA and had tested 15 poliovirus strains since. All were Sabin-like strains except for one wild poliovirus type 1 isolated in 2006. The new algorithms for virus isolation and ITD were implemented since April 2008. The laboratory received a real-time PCR equipment (ABI 7500) from WHO and one staff participated in the real-time PCR training workshop held at VIDRL Australia in August 2008. Revisions of the SOPs and worksheets have been completed and additional two staff members have been trained. Step 1: reproducibility testing has been completed using 10 samples tested four times. False signals for negative test controls (NTCs) were initially experienced and were resolved, per advice of CDC, by adjusting the baseline cycles from default (3-15) to 5-25 and by using a new batch of PanPV buffer. The laboratory tested 30 isolates for retrospective testing, 27 of these were Sabin strains received from Malaysia. The laboratory has not isolated any polio for prospective testing. The laboratory is ready to receive the rRT-PCR proficiency panel from CDC. The laboratory has established capacity for sequencing and requested for standardized SOPs for polio VP1 sequencing.

The laboratory conducts an "enhanced" AFP surveillance by investigating all patients with diseases that could lead to acute flaccid paralysis. In addition, raw water samples are also tested.

From 2007 to 2009, 1870 samples were processed for enterovirus culture consisting of 71 stool samples from AFP cases, 1671 samples of various types from non-AFP cases, and 128 raw water samples. Six polioviruses were isolated in 2007 and 2008. NPEV isolation rate from stool samples was > 22%, and between 7% to 17% from other sources. Cell sensitivity testing is performed regularly and no evidence of reduced sensitivity was observed.

2.1.8 Report of Group Discussions

Group 1: Barriers to implementation of new algorithm: how to overcome them

Country	Issues	Ways to overcome
Philippines	New algorithm done in parallel with traditional algorithm. All isolates are serotyped. Cell passage is done 2-3x per week, consumes lots of resources and staff time (week-end duty). Observation of late appearance of CPE in RD cells required additional passages and identification by neutralization test resulting in delayed reporting of results. Report serotype rather than "L20B" positive	Implement only new algorithm according to recommended procedures. Continue serotyping but report NPEV and L20B positives after 10 days of observation. Adjust cell maintenance schedule as appropriate. Orient EPI colleagues on the new algorithm.
Japan	Started implementation in January 2010, receives specimens from Cambodia and Laos usually middle of week. No technical issues yet. Anticipates more work, more passages and use of more cell culture tubes.	Perform cell passage more frequently (2x per week) to cater for timely passages.
China	Staff in provincial laboratories may need to work on weekends because of more frequent passages. More frequent shipments of "L20B+" cultures to China CDC. Staff are quite resistant to change and will be a problem with training. Frequency of mixtures is about 5% requiring separation of individual virus components. Should provincial laboratories perform ITD testing to cope with timeliness? Support for reagents and equipment for polio is not as strong as for Influenza.	Look at data to assist in making decision about establishing ITD capacity in provincial laboratories and provision of equipment. Low workload laboratories to share facilities with Influenza laboratory may be considered.
Mongolia	Introduced new algorithm in March 2009. Problems with cell viability and sensitivity need to be resolved first.	Obtain new batch of cells.
Korea	New algorithm not yet introduced	Agreed to introduce new algorithm
Viet Nam, South	New algorithm not yet introduced. Allay fears of losing some NPEVs, need to	Parallel testing with new algorithm until comfortable. Conduct workshop to

	evaluate in local setting.	improve quality of cell cultures
Viet Nam, North	New algorithm not yet introduced	Agreed to introduce new algorithm

Group 2: Maintaining proficiency for real-time PCR testing with low workload

Countries	Issues with establishing the assay	Ways to overcome
Australia	Participated in the field evaluation of real-time PCR and has passed PT	
Hong Kong SAR, China	Real-time PCR machine (Roche Light Cycler) available but not compatible with the rRT-PCR platform developed at CDC. Stored isolates (including VDPVs) are available for establishing proficiency.	Look at newer software versions for real-time PCR machine and coordinate with CDC in optimizing the assay
New Zealand	Real-time PCR equipment (BioRad) can be optimized to CDC real-time PCR platform Can use stored isolates from routine and previous studies. Isolates from other countries may be received but containment may be an issue.	Refer to CD material from rRT-PCR workshop and coordinate with WHO and CDC in optimizing the assay.
ALL	Buffer B and enzyme storage. Once enzymes are reconstituted and made-up with Buffer B, if not stored correctly and not used within 6 months, problems with non-specific and aberrant results can be encountered	Obtain instructions from CDC about creating aliquots and period of storage. Avoid freezing and thawing. Use freezing blocks to keep reagents cold during testing. Store in freezers that are not subject to frequent temperature changes.
	Issues on maintaining expertise with low workload	
Australia , Malaysia	Receives more than 20 samples each year, enough to maintain expertise	
Hong Kong, New Zealand, Singapore	Less than 20 isolates per year	Prepare interim PT panels, construct challenging PTs using NIBSC or LQCs , re-test annual PT
ALL	Kits usually expire due to low number of samples to test; kits are not available when PT samples come	Have regular control of stocks making sure that kits and reagents are available at all times. CDC could extend kit expiration date?

2.1.9 Detection of Vaccine-derived Polioviruses (VDPV)

(1) Global Update on VDPV detection

Dr Esther de Gourville discussed the definition of VDPVs, their emergence, associated risks, and current status of detection. VDPVs emerge from oral polio vaccines containing live attenuated (from wild polioviruses) Sabin strains of known sequences. During replication of the virus within the gut, various mutations can occur with the potential for reversion of the attenuating mutations (due to errors in replication) and recombination with other polioviruses and co-infecting enteroviruses resulting in genetic changes in nucleotide sequences different from the parent Sabin strains. Following vaccination, regardless of immunological or clinical outcome, vaccine viruses (including mutated ones) are excreted by vaccine recipients. Secondary transmission can occur within and outside households (community contacts) in each of whom virus replication occurs. Therefore, there is potential for mutations, reversion of attenuation mutations and risk of enhanced capacity for person to person spread. VDPVs are Sabin-like (SL) viruses that show > 1% VP1 nt sequence divergence from parental strain. The 1% demarcation between OPV-like isolates and VDPVs is based on the average rate of poliovirus capsid evolution (~1% per year), implying that VDPVs have been replicating (or circulating) for at least one year since administration of the initial OPV dose. The three categories of VDPVs (iVDPVs, cVDPVs and aVDPVs) were defined and their programmatic implications discussed. The categorization of VDPVs depends on follow-up clinical and epidemiologic investigations.

Since the first outbreak in Hispaniola in 2000, the GPLN has documented the occurrence of VDPVs in < 1% of 22,500 potentially problematic Sabin-related strains screened from 1999 to 2007. The trend towards a low proportion of VDPVs continued from 2008 to June 2009. Of approximately 10000 isolates screened during this period, 438 (4.6%) were cVDPVs (mainly due to the large outbreak of cVDPV type 2 in Nigeria), one (0.01%) was an iVDPV and 18 (0.2%) were aVDPVs. Within the period 2000 to 2009, 14 countries had outbreaks due to VDPVs, the biggest outbreak is on-going in Nigeria since 2005. The situation in Nigeria is of particular concern because of continued WPV1, WPV3 and VDPV2 transmission. In particular, the long gap with no use of OPV, conduct of SIAs with mOPVs only to interrupt wild poliovirus transmission, and weaknesses in the routine coverage of OPV in Nigeria was highlighted. Examples of dendograms that illustrate independent or multiple emergences and transmission links of VDPV occurrences in several countries were also presented. Issues related to VDPV definition and circulation was also discussed. The current definition of cVDPV is based on the detection of more than one AFP case with genetically related viruses showing > 1% VP1 nucleotide sequence divergence from Sabin virus of the same serotype. This definition appears inadequate in the light of laboratory data collected in the past five years, and may hinder, delay the characterization, or underestimate the scope of some cVDPV outbreaks. The probable need to revise the definition of both circulation and VDPV was suggested. There are 43 reports of iVDPVs in various locations available in the WHO iVDPV registry. These viruses can be potentially excreted by the immunodeficient person and can spread to the community. The participants also learned about the detection of highly divergent (>15% VP1 nucleotide divergence) aVDPVs (all serotypes) from sewage samples in Tampere, Finland, Estonia, Israel, and India. The increased detection of VDPVs in the last three years is likely to be attributed to increased awareness, improved methodologies of detection, and increased gaps in immunity in some countries. Adequate response to cVDPV confirmation is important for effective control.

(2) VDPV Surveillance in China

Intensified VDPV surveillance with characterization of VDPVs is one of the strategies for maintaining "polio-free status" in China. VDPVs have been detected in various provinces. In 2004, two cases of cVDPV type 1 were detected in Guizhou province and in 2005, one each of iVDPV type 2 and type 3 were detected in Anhui province. In Guanxi province, one VDPV type 1 was identified from an AFP case and 7 contacts. In Shandong province, three VDPV type 1 and one VDPV type 2 were detected in 2007 and 2009, respectively. The type 2 VDPV was isolated from an AFP case that was subsequently enrolled in the WHO coordinated Primary Immunodeficiency Disorders (PID) project. From 1996 to 2009, aVDPVs were identified in Guanzhou, Shanxi, Sichuan, Yunnan, Gansu, Shanghai and Guizhou. Annual NPEV isolation rate from AFP cases is > 10%, however, from 2002 to 2009 poliovirus isolation rates (especially type 2) showed a decreasing trend from 8.35 % to 3.2 %. The number of AFP cases is approximately 5000 cases per year.

It appears that the VDPVs detected in China are relatively "young" (recent), e.g., type 2 VDPVs had 1% to 1.33% nt divergence in the VP1 region, indicating circulation of less than one year. The finding of "young" VDPVs is also an indication of the ability for early detection, limited virus replication after administration of first OPV dose, and limited spread of vaccine virus to close contacts of OPV recipients. Overall implication is the effectiveness of current polio immunization strategies in China in preventing sustained transmission of VDPVs.

(3) iVDPV studies

Dr Sigrun Roesel presented the on-going studies on the prevalence of prolonged and chronic poliovirus excretion among persons with PID in middle and low-income countries. Persons with primary B-cell immunodeficiencies, but not persons with T-cell immunodeficiencies (e.g., from human immunodeficiency virus infection), are at risk for iVDPV infections and the duration of virus excretion varies widely. The first reports of iVDPVs came from high-income countries but cases from middle-income countries have been reported recently. In line with the Advisory Committee on Polio Eradication (ACPE) recommendation in 2005, the objectives of the study were to increase the understanding of the incidence and behaviour of iVDPVs and to increase local capacity to monitor them. Two countries in the WPR, China and Philippines, participate in the study. The study design requires completion of a survey questionnaire, collection of blood samples for quantitative immunoglobulins, and collection of stool specimens for poliovirus isolation. Poliovirus excretors are to be followed-up until virus is no longer detected. The study population includes persons, less than 35 years of age, currently living with PID, and identified through referral health centres, immunologic clinics and PID registries. The recruitment duration is one year for a minimum of 200 persons in China and 45-60 persons in the Philippines. One-hundred and fifty patients have been recruited in four provinces in China. The study in the Philippines is ready to start following approval from the Ethical Review Board. The outcomes of the studies are important to identify future risks to polio-free status in China, the Philippines, and globally. The outcomes are also important to support the development of antiviral compounds for treatment, development of affordable IPV for widespread use in low-income countries, and to form a template for an iVDPV surveillance system. The study further provides opportunity for collaborative project between clinicians, public health professionals and international organizations for future research endeavours.

2.1.10 Data management and communication

(1) Application and challenges of Data Management in the WPR Polio Laboratory Network

Dr Fem Paladin presented the applications and challenges in polio data management, proposed recommendations moving forward, and data reporting formats from network laboratories. The Regional Office collects routine surveillance and laboratory data to generate

feedback reports to the regional and global polio eradication programme, to partners/donors, scientific community and public health implementers. An example of a regular output is the regional Polio Bulletin that is produced and circulated weekly. Datasets from polio laboratories are received weekly or monthly in different file formats (e.g., EPI Info REC file, MS Access MDB file and MS Excel) and these are uploaded into the regional polio AFP database by using conversion software customized for each format and by manual "copy and paste" approach for reports in excel format. There is also extensive variability in the excel format between laboratories and within the same laboratory depending on the person who is providing the report. This practice is tedious, time-consuming and error-prone. Laboratories that have implemented the new algorithm have not revised their reporting format to WHO. The current dataset does not allow for regular collection of information about non-AFP cases or other sources of specimens where polioviruses may be identified. Examples of datasets showing gaps in completeness and consistency were presented. The need to standardize the laboratory datasets and reporting practices in network laboratories to improve efficiency in the management of data in network laboratories and in the WHO regional office was emphasized. The development of a standard database management program for data entry, analysis, feed forward and feed back mechanism, and training of data managers was proposed.

(2) Proposed changes and way forward

Mr Benjamin Bayutas, EPI Informatics Assistant, discussed the proposed changes to polio laboratory data management in the Region and how these changes will be implemented. A generic laboratory database program using Microsoft Access will be developed and installed in each polio laboratory. As a preparatory step, laboratories were assessed through an informal survey to obtain information about storage of data, core variables in the database, method of data conversion for reporting to EPI and WHO, and operator's (e.g., data manager) background in data management. Feedback from five laboratories (Australia, Japan, Mongolia, Singapore and Viet Nam) was received. The format for data storage varied from paper forms to in-house centralized server systems. Laboratory staff usually serve as data managers. The standard variable definitions and reporting codes, additional core variables for case information, laboratory testing for the traditional and new algorithms, and reporting of results were discussed. The draft version of the program will be available by July for field testing and implementation after the training of data managers. A customized approach for data conversion and reporting will be developed, if necessary, for laboratories with in-house centralized database system. The Measles/Rubella laboratory database program was presented as an example. The submission of laboratory datasets to the regional office at least every 10th of the month was suggested.

(3) Discussion on data management

Participants were provided with a spreadsheet containing the proposed WPRO Polio AFP Database variables for review and for feedback to WPRO.

2.1.11 Updates on laboratory containment of wild polioviruses

Dr Sigrun Roesel presented the work done over the years that finally led to the completion of the regional activities for wild poliovirus containment. Phase I of WPV laboratory containment activities began in 1997 with the development of a regional plan of action. In 1999, the RCC required the completion of Phase I for certification of the Region as being polio-free. In October 2000, when the Western Pacific Region was certified as polio-free, all Member States had initiated phase I but only four areas had completed it. Global guidelines were developed on the best practices model with certain key elements to document quality of Phase 1 containment activities and the model format was received in 2004. The RCC also recommended establishing a standard process for expert review and feedback mechanisms. Validation exercise was conducted

in three groups of countries in response to this recommendation. By 2006, Phase I had been completed in all countries except China and Japan. By 2008, based b on the final reports (including those from China and Japan) and findings from the external technical review panel, the RCC declared Phase I wild poliovirus containment laboratory surveys and national inventories to be accurate and complete for the whole Western Pacific Region in December 2008. A total of 77 260 laboratories were surveyed including 55 688 facilities in China and 14069 facilities in Japan. The number of laboratories storing relevant materials has been reduced from 107 in 2007 to 47 in 2009. These laboratories are located in Australia, China, Japan and the Republic of Korea.

2.1.12 Laboratory Management and biosafety

(1) China CDC: Management of China Network Laboratories

Dr Wenbo Xu presented on the management of the China Polio laboratory network. The China CDC Polio RRL coordinates 31 provincial laboratories comprising the polio laboratory network and provides reference services for the confirmation and ITD of all polioviruses isolated from these laboratories. VP1 sequencing is performed on all polioviruses for ITD testing and very recently, additional capacity for ITD using real-time PCR ITD and VDPV screening assays has been established. Approximately, 10 000 stool samples are processed each year for virus isolation using the traditional algorithm. Since 2003, poliovirus isolation rate started to decline, from 835 positive cases in 2002 to 74 in 2003 and 33 in 2009. Similarly, the number of isolates received at the RRL also decreased from 513 isolates in 2005 to 194 in 2009. The RRL also receives isolates from other sources (e.g. non-AFP, contacts and healthy children). In 2009, 65 type 1, 106 type 2 and 103 type 3 polioviruses were sequenced. The RRL provides quality assurance by coordinating the proficiency testing, annual on-site accreditation reviews (usually 12 provincial laboratories each year) and implementation of cell sensitivity testing including the distribution of cell lines and in-house prepared NIBSC standard reference strains. A subset of stool samples is also retested from laboratories experiencing technical problems. All laboratories, including the RRL, passed the proficiency testing for virus isolation. All laboratories, except one provincial laboratory, are fully accredited by WHO. The RRL also provides annual hands-on training courses for new staff members in provincial laboratories. A Workshop for National Polio Network is held annually to update and exchange information about the progress of polio laboratory activities in China, in the Region and globally. Regular meetings with national EPI occur monthly and as soon as possible when high risk AFP cases or pre-VDPVs/VDPVs are identified. The current laboratory surveillance is sensitive to detect pre-VDPVs and VDPVs allowing EPI staff to respond early. The introduction of the new algorithm in China will be a challenge but may be done by phases. There is also high staff turnover requiring continuous training of new ones. Equipment in provincial laboratories is old, and in some laboratories replacement is needed. Some laboratories experience low cell sensitivity requiring follow-up from the RRL. Overall, high laboratory performance is maintained in the China polio laboratory network.

(2) Hong Kong: Coping with surveillance, diagnostic and reference laboratory services

Dr Janice Lo described the experiences and approaches to cope with demands of surveillance, diagnostic and reference laboratory services. The laboratory serves private and public hospitals and clinics in the territory (except for one Region). Specimens from these locations are mostly collected twice daily by courier services. Specimens received from diagnostic services constitute the bulk of the workload and also provide source for surveillance and outbreak investigations. Testing capacity is well established for direct detection, culture, molecular testing, and serology. A strong quality assurance program (availability of SOPs, staff training, participation in proficiency testing schemes) is in place. When challenged with large

increase of specimens over a short period of time (e.g. outbreaks), previously trained staff in Virology are deployed back to the unit. The laboratory also ensures that equipment are adequate (and not stressed), reagents are on stock, results are reported on time by interfacing laboratory data systems with those of hospitals and epidemiologists, and specimens are properly managed (e.g., up-to-date inventory, storage of aliquots). The laboratory maintains a close liaison with public health and clinical units. Surveillance data are available to interested parties on the laboratory's website. The laboratory is also involved in HFMD Surveillance for EV71 and genotype C4 has been the predominant circulating serotype for a number of years. Serosurveys are conducted every five years to monitor herd immunity to all poliovirus serotypes in all age groups. Results of the study done in 2008 showed that high antibody levels are maintained even after the switch to IPV in 2007. Reference services include confirmatory testing of samples from laboratories without specialized testing capacity. Communication and dialogue with laboratories, keeping up with advances in the scientific community, surge capacity preparedness planning, continuing personnel training, maintaining quality assurance, vigilance on laboratory safety and security, enhancing information system for timely results, and maintaining close collaboration with local partners were examples of approaches in the laboratory to cope with their responsibilities.

(3) Viet Nam North: Challenges of shipping isolates for referral and impact on timeline for reporting ITD results

Ms Trieu Thi Thanh, from the National Institute of Hygiene and Epidemiology, presented a summary of the laboratory's work and the challenges encountered in shipping poliovirus isolates to NIID, Japan. The laboratory serves the northern part of Viet Nam supporting AFP and HFMD surveillance activities. From 2007 to 2009, 622 samples from AFP cases were processed, from which eight polioviruses and 64 (10.3%) non-polio enteroviruses were detected. In 2007, 250 samples from children with HFMD and acute encephalitis syndrome (AES) were also tested from which 51 enteroviruses, including two polioviruses were isolated. The majority (43.1%) were Echoviruses of various serotypes. From 2008 to 2009, 115 specimens were processed for HFMD; 8 (7%) EV71 and 191(11%) non-polio enteroviruses were found.

The laboratory still uses the traditional algorithm for virus isolation. Poliovirus neutralization test is performed on both RD and L20B isolates. When some neutralization appears after 1-2 days, the laboratory submits an official letter to the Ministry of Health requesting for "export permission". At the same time, an order for shipment is made to Express Mail Service (EMS) and NIID, Japan is informed of the available date of shipment. Stool extract and poliovirus isolates are frozen and packaged in a cold box. All shipment procedures are completed within 7 days and it takes 2 days to reach Japan. The cost of shipment is approximately $100.

(4) Regional Implementation Plan of Biosafety requirements

Dr Chris Oxenford from Communicable Diseases Surveillance and Response Unit, WPRO, provided an overview of the activities related to biosafety as they occur in the Region. One of the requirements of International Health Regulations (IHR) is for countries to have the capacity to detect and to report events of international concern, and to have the capacity for laboratory analysis of samples, either domestically or through international reference laboratories. There has been increased interest for countries wanting to strengthen laboratory capacity to deal with high-risk pathogens, however, there is lack of biosafety policy, regulation and awareness of the importance of biosafety, standards of construction vary and staff training is limited in clinical and public health laboratories. On this perspective, the Asia Pacific Strategy for Emerging Diseases (APSED) 2005 was jointly developed by Western Pacific Regional Office and Southeast Asia Regional Office to confront emerging disease threats. The strategy was

endorsed in September 2005. The goals were to assist member states to meet IHR obligations, to plan for responses for emerging diseases and to assist in responding to pandemic diseases. Laboratory is one of the areas of work in the strategy. Biosafety is addressed in the laboratory component on 'safe diagnosis'. The areas where activities are targeted were discussed and these include raising awareness of biosafety particularly among laboratories in the sub-national level, design and construction of facilities based on needs assessment and expert advice, and maintenance of equipment, mainly biosafety cabinets. A biosafety consortium of experts has been formed to evaluate and to help laboratories design their facilities. Mention was made of a workshop in 2008 that was attended by laboratory directors and key people from the ministry of health to discuss the importance of biosafety and to encourage laboratories to be role models for other laboratories within their own country. A follow-up "train the trainers" workshop for Biosafety Engineers is planned in 2010.

Two biosafety documents for reference were shared. They can be accessed for free through this links:

(1) WHO Laboratory Biosafety Manual - Third Edition: http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_CSR_LYO_2004_11/en/

(2) Laboratory Biorisk Management Standards (http://www.biorisk.eu/documents/draft_document.PDF)

2.1.13 Expanding the scope of polio laboratory network

(1) Global Plan for integrated laboratory services for VPD surveillance

Dr Olen Kew from the US CDC discussed the global plan for laboratory support for VPD surveillance. The objective of the plan is to provide essential laboratory support for broader Regional and global initiatives to control vaccine-preventable diseases (VPDs). The high performance of the VPD Laboratory Networks has underscored the critical value of the laboratory arm of surveillance and provides a golden opportunity for integration. The postponed eradication of polio has obscured the very real achievements in global immunization, surveillance, and Laboratory Network development. However, WPR has been polio-free for many years and it is poised to show the way on how to build on the existing polio/measles/rubella/JE Laboratory Networks. Successful efforts at integration incorporate integration between and across laboratories, surveillance systems, and programs. Two divergent philosophies on integration were discussed. The "Top-down" approach where integration is a primary goal before building strong individual networks. This approach carries the risk of "strategic overstretch" and loss of functionality. The second approach builds strong individual networks first and then, integration of activities, wherever appropriate. Dr Kew mentioned that the polio/measles/rubella Laboratory Networks took the "Bottom-up" approach and should be the way to go because of its solid foundation; however, full integration of all these Laboratory Networks is a long-term process. The participants also learned that Laboratory Networks built upon National Institutions rather by external donors are more sustainable. Whenever feasible, VPD laboratories should be housed in institutions with strong commitment to public health (e.g. disease control and surveillance) rather than in institutions with primary focus on research. The tiered structure of the VPD Laboratory Networks has worked well and is a successful model of true networks of mutually supportive laboratories because the basic framework of an interlocking alliance of a global VPD Laboratory Network already exists. Expanding Laboratory Networks must include additional support for Laboratory Network Coordinators. Polio eradication will decrease polio surveillance demands and some field and laboratory surveillance will be needed for other VPDs. Most of the polio expertise is transferable to surveillance for other VPDs (already happening). The global plan is built on the recognition of the differing roles of surveillance, goals (e.g. global, regional, new vaccines, new immunization programme), regional experience (e.g., WPR) and the critical role of laboratories within the broader effort to control VPDs.

(2) Enterovirus surveillance in WPR

Dr Youngmee Jee presented the current situation of Enterovirus surveillance in the Region. Since the Region was certified as polio-free many polio laboratories tested more non-AFP samples for polio and enteroviruses. During recent HFMD outbreaks, some NPLs were heavily involved in EV71 identification. Some patients infected with EV71 presented symptoms compatible with AFP. The Enterovirus investigations among the network laboratories in the Region were described. Japan has a well-established enterovirus surveillance system with participation of prefectural laboratories. The Republic of Korea, Malaysia and New Zealand have established enterovirus surveillance with participation of sentinel hospitals. In Singapore and Hong Kong, China, surveillance is based on routine diagnostic testing. Viet Nam, Mongolia and China laboratories receive samples from HFMD AES cases. In addition, the China laboratory also conducts environmental surveillance where enteroviruses are also detected. The laboratory in Australia receives a small number of isolates from diagnostic laboratories for enterovirus typing. The laboratory in the Philippines performs enterovirus testing on a small number of diagnostic samples from aseptic meningitis or HFMD. In 2008 to 2009, more than 6300 samples from HFMD cases were processed by the network laboratories (excluding China and Japan) and approximately 500 EV71 strains were detected.

(3) Detection of EV71 in China HFMD surveillance

China CDC coordinates the HFMD laboratory surveillance network in China following the structure of the Polio/Measles/Rubella Laboratory Networks. Prefectural laboratories perform molecular detection (e.g., real-time PCR or conventional PCR) and provincial laboratories, in addition to molecular detection, also perform virus isolation. China CDC performs genotyping by sequencing, provides quality assurance and training, and conducts research on molecular epidemiology and pathogenesis of EV71.

In 2008, the China polio laboratory network processed 4769 samples for virus isolation and 18153 samples for molecular detection of enteroviruses among HFMD patients. EV71 and Coxsackievirus A16 were isolated from 1079 samples and were identified by molecular detection. In 2009, the network also detected 8520 enteroviruses including 4518 EV71 strains from 33 3154 cases using molecular methods.

(4) Environmental surveillance in China

Dr Yong Zhang described the development of methods to establish the environmental surveillance in China, the pilot studies conducted and the proposed plan for expansion to additional provinces. Environmental surveillance was established to supplement AFP surveillance activities in China. Two sampling methods are used, the grab sampling for wastewater (WW) samples and trap sampling for river samples. Two training workshops have been conducted in 2007 and 2009. Pilot studies were set-up in Beijing in 2005, Shandong province in 2007, and Guandong province in 2008. In Shandong province, one poliovirus type 2 and several NPEVs were isolated in 2008 and 2009. In Guandong province, multi-month detection of any virus was observed in WW samples from April 2008 to Nov 2009; 48 out of 80 samples were positive for polioviruses, 61 single serotypes were identified, 33 of them were type 2 Sabin-like viruses. Several NPEVs were also identified. The plan to expand environmental surveillance was presented. The plan aims to monitor for wild poliovirus introduction in border provinces, to supplement VDPV surveillance in high risk areas, and to assess the effect of SIAs before and after OPV campaigns in some provinces in Eastern China.

(5) Proposed plan of expanding polio laboratory network

Dr Mark Pallansch from US CDC described recent developments in diagnostic methods for poliovirus detection and the role of the poliovirus laboratory in surveillance for other VPDs as a means to sustain interest in poliovirus detection in the future. The participants learned about the key properties of polioviruses that relate to the construction of diagnostic algorithms for poliovirus and enterovirus detections and examples to illustrate the technologies that can be considered by polio laboratories in the future. Generic technology platforms are more useful and flexible assets than an analytic-specific assay. In most regions that are now polio-free, and countries that use IPV, without continued support (e.g., declining resources), the only justification for testing fecal materials in the case of CNS disease on a routine basis is to look for enteroviruses. In the future, the poliovirus laboratory will be a Picornavirus laboratory in order to maintain the ability to find poliovirus globally. Considering this expansion and in the absence of a comprehensive public health laboratory system, Dr Pallansch mentioned that the survival of the expertise and resources of the polio laboratory network requires that changes undertaken today are compatible with future realities and the development of new approaches, assays and algorithms should start now.

2.1.14 Other issues/topic group discussion:

(i) Timeliness of VDPV reporting (China, Malaysia, Japan, Viet Nam North)

The group reviewed the mechanism of reporting VDPV in their laboratories. They reported that sequencing can be done within 7 days after receipt of isolates and results can be reported within 24 hrs to responsible authorities. For Japan, the responsible authority is the country's Ministry of Health; parallel report will be submitted to the laboratory and WHO. For China, the responsible authorities are those in the Ministry of Health and the national and provincial immunization programs. The Ministry of Health reports any VDPV case to WHO. Malaysia and Viet Nam do not perform sequencing and will rely on the sequencing results from RRL or GSL.

(ii) Accreditation of sequencing laboratories (Australia, Hong Kong, New Zealand and Singapore)

All laboratories have received the sequencing checklist and provided the following comments:

(a) Requirement of 25 sequenced isolates before analysing PT will be a problem with low workload laboratories. Suggest sequencing of other RNA viruses to meet the target.

(b) Laboratories already doing sequencing can systematically summarize the sequencing results on non-polioviruses on a regular, systematic manner for easy tracking. Request WHO to provide format for compilation.

(c) Clarified the calculation of timeliness of reporting sequencing results (at least 80% cases within 14 days) will be after ITD detection. Change of target time to 7 days is possible.

(d) Include more generic methods to prevent cross-contamination in the checklist (not only UV light).

Other issues raised:

(e) Provision of serotype specific primers for mixed cultures in order to report results within 7 days.

(f) Provision of reference sequences, in particular for VDPVs, to allow on-site analysis (e.g. generate phylogenetic trees)

(g) Provision of training before implementation of the sequencing protocol.

(iii) Maintaining biosafety cabinets (Mongolia, the Republic of Korea, the Philippines, South Viet Nam)

The group mentioned about similar concerns and practices (e.g. cleaning). They noted that written SOP for maintenance and cleaning were not available. There is also lack of the basic knowledge about biosafety cabinets (e.g. different types). There are no local companies in Mongolia and Viet Nam who can certify/validate BSCs; there are also no funds to support the service. They can only assume that the BSCs are working because there is no contamination.

The need for BSCs to be maintained and to function properly was emphasized. Training of in-house staff (e.g., engineers) to have local capacity was suggested.

2.2 Day 3: Japanese Encephalitis Laboratory Network

As recommended by the 17th TAG meeting in 2008, the JE laboratory network has been established to improve the capability of JE case confirmation among countries suspected to be endemic for JE in the Western Pacific Region. One GSL, two RRLs and six national laboratories (Cambodia, Laos, North and South Viet Nam, the Philippines and Malaysia) were designated from 2008 to 2009.

The first regional hands-on training for the laboratory diagnosis of JE was conducted in Korea CDC from 15 to 19 June 2009. Technical service agreement support for JE laboratories was initiated in 2009 for priority countries and essential equipment as well as JE kits for laboratories using Panbio JE/Dengue IgM combo ELISA kits was provided to network laboratories to establish the JE laboratory function. The first JE proficiency samples prepared by US CDC were distributed during this training and results were received from laboratories within 2 weeks and are finalized. All participating laboratories obtained passing scores of >80%.

A monthly reporting form of case-based and aggregate data were distributed during the training and reports are being received from 7 out of 9 designated laboratories in the Region. However, the timeliness of laboratory data reporting still needs to be improved.

An informal consultation meeting of three WHO JE laboratories in China, Japan and the Republic of Korea was held in Beijing, China on 18 September 2009 to discuss the progress in establishing the JE laboratory network since the first VPD laboratory network meeting in 2008, the current status of the WPR JE laboratory network and the roles and responsibilities of the three reference laboratories.

A draft of the WHO JE laboratory checklist was evaluated for two Viet Nam JE laboratories in early 2010. Based on discussions and findings from this evaluation, some revision of accreditation criteria was proposed. Accreditation of designated JE laboratories in the Region will be initiated from July 2010.

Laboratory capacity to detect bacterial meningitis pathogens in order to support acute meningitis and encephalitis syndrome surveillance could be integrated where feasible. In 2010-2011, further integration of JE testing with bacterial meningitis testing will be pursued

Opening session

Dr Youngmee Jee, Regional EPI laboratory coordinator welcomed all participants and advisers. The Director of Programme Management, Dr Hans Troedsson opened the meeting and welcomed all participants from countries and advisers from partner organizations. He emphasized the importance of strengthening laboratory capacities of the Japanese encephalitis laboratory network to control Japanese encephalitis in the region.

2.2.1 Overview of JE control in the Western Pacific and Southeast Asian regions

(1) Surveillance for acute encephalitis syndrome (AES) and Japanese encephalitis (JE) in the Western Pacific Region

Dr Kimberly Fox, EPI Technical Officer, presented JE and AES surveillance in the Region. JE is the most common type of encephalitis in Asia. It is primarily a disease of children

<15 years old in endemic regions, but in countries with JE vaccination implemented for many years, JE can occur in any age. In the Western Pacific Region, 11 countries are known to be endemic or suspected to be endemic for JE or controlled JE by vaccination in this Region. Surveillance for AES only detects the tip of the JE iceberg despite the broad definition of AES (suspected JE). JE cases in this Region are reported from China and Vietnam and there are estimated 20 000-40 000 JE cases annually. Reported JE related deaths in 2008 were around 200 cases but estimated actual number of deaths would be 3000-12 000 annually in the Region. Objectives of JE surveillance during pre-vaccine introduction and post-vaccine introduction as well as integrated JE and bacterial meningitis surveillance and purpose and recommended types of JE surveillance depending on country situations were presented. In countries in which JE vaccination is used nationwide, sentinel surveillance will be less useful, as these countries will need to detect all cases. Technical support will be provided to countries to initiate, strengthen or expand JE surveillance through direct support for surveillance design, considering integration with meningitis surveillance, provision of tools for data collection and management including database development and capacity building for data management and analysis.

(2) Progress of Western Pacific Region JE laboratory network

Dr Youngmee Jee presented the progress of JE laboratory network since the laboratories were designated in 2008. The Region has one GSL in Japan, two RRLs in China and the Republic of Korea, and six national laboratories in Cambodia, the Lao People's Democratic Republic, Malaysia, the Philippines, Viet Nam (North and South). In 2009, the first regional hands-on training course was conducted in the Korea CDC RRL. The first proficiency testing was arranged and all laboratories passed the PT (>80% score).The Panbio assay was used in the seven in- house assays, if no commercial assay was used. To establish JE laboratory function, equipment, kits and financial support for operational costs were provided to priority countries in the Region. Monthly reporting of case based linelist and summary of JE laboratory data was initiated in July 2009 and all laboratories except China and Laos are reporting laboratory data. For quality assurance of JE samples, confirmatory testing at the GSL and RRLs will be arranged twice a year.

(3) Achievement of JE/AES surveillance in South-East Asia Region

Dr Nalini Ramamurty presented the achievement of JE/AES surveillance in the South East Asia Region which was initiated in 2006. The designation process of JE laboratories, which was based on polio laboratory model, was described. Eleven National JE laboratories were designated, six in India, and one each in Bangladesh, Indonesia, Myanmar, Nepal and Sri Lanka. Other designations included one GSL at US CDC, two RRLs in Sri Lanka and two RRLs in India for training, confirmatory testing, validation of kits and proficiency testing. The first regional training workshop was held in 2006 with 22 participants and Panbio and XCyton kits were used for serum and CSF samples respectively. Laboratories were fully functional by January 2007. Since 2006, laboratories have participated in a regional proficiency testing. All laboratories gained proficiency by 2007. All samples from 2007 from Bangladesh and representative samples from Nepal were confirmed by the GSL (US CDC for Bangladesh or the RRL in India confirmatory testing was done by Bangladesh) RRL (NIMHANS Bangalore) for all other countries which was then followed by testing at confirmation by the GSL. Concordance of results were >80% for all laboratories. From 2007-2009, 1193, 3074, and 1732 serum samples and 943, 2311 and 2348 CSF samples were tested by network laboratories, respectively. The results showed that only 10-15% of those cases were due to JE. All laboratories gained proficiency and a referral procedure from hospital laboratories has been established. Testing of bacterial pathogens, Hib, streptococcus pneumoniae and N meningitides was added to AES surveillance after the training in May 2007. Real time PCR for

bacterial meningitis was established in a RRL in India. Accreditation of JE laboratories using developed WHO JE laboratory checklist has been conducted.

(4) Report of JE laboratory working group

Mr David Featherstone reported activities of the JE laboratory working group. The JE core working group was established to develop JE surveillance standards in 2002 and a finalized version was developed in 2008. The JE laboratory network was developed gradually based on the polio and measles/rubella model. A quality assurance system was established and various assays were evaluated. Evaluations of XCyton and Panbio kits showed some batch to batch variability and some sensitivity issues were raised for those kits when compared with US CDC assays. Currently, only a small number of commercial and in-house JE assays are available, but there is no commercial kit with good sensitivity and specificity. US CDC is preparing the validation panel samples for in house assays used in JE network laboratories.

2.2.2 Use of in-house and commercial assays

(1) Results of evaluations of in-house and commercial assays

Dr. Barbara W. Johnson from US CDC presented the results of evaluations of three commercial kits and one in-house kit used by Southeast Asia Region and Western Pacific Region JE laboratory networks. A panel of 438 acute phase serum and cerebrospinal fluid (CSF) samples from India and Bangladesh were tested using the CDC JEV IgM ELISA and neutralization test as the reference standard. Among the three commercial kits, Inbios, XCyton and Panbio, the agreement with CDC results showed 88%, 86% and 81%t, respectively. Another evaluation of the Panbio kit was done with 1195 samples from Cambodia. Compared to the CDC reference standard results, the Panbio kit had 70% sensitivity, 97% specificity and 84% agreement. The JE IgM ELISA kits had decreased sensitivity in settings with collection of single acute specimen and low sensitivity was observed with very acute specimens collected within 7 days after onset, when IgM or neutralizing antibodies may not have yet reached levels detectable by the assays (negative MAC ELISA or Plaque Reduction Neutralization Testing [PRNT]). JE IgM ELISA kits may need to be modified to increase sensitivity or specificity and acceptable levels of sensitivity and specificity need to be determined. Development of a JE reference serological panel, which will be distributed for validation and evaluation of in-house and commercial assays, will allow assessment of the numerous assays in use in the laboratory network. JE laboratory network laboratories will receive proficiency panel samples from the reference serological panel which will allow standardization and comparison across the regions. Confirmatory testing by PRNT, used in the US CDC testing algorithm, was explained. PRNT titre >10 is considered to be positive for JE. The need for improved diagnostic assays for flavivirus detection was also presented.

(2) Approaches for improving the accuracy of JE Immunoglobulin M assays

Dr Tomohiko Takasaki presented an approach to improve JE IgM assays by using Vero cell derived inactivated JE antigen to replace dengue antigen in the commercial Focus Diagnostic Dengue kits.

2.2.3 Quality assurance for JE laboratory network

(1) Results of the first JE proficiency test

Results of 2009 WPR JE laboratory network proficiency testing was presented by Dr Barbara W. Johnson. Seven laboratories, including non-network laboratories in the Lao People's Democratic Republic (Mahosot hospital) and Cambodia (Namru-2), used Panbio kits. Three laboratories used in-house assays: NIID Japan, and NIHE and PI. The Viet Nam used in house assays and China CDC laboratory used Beixi kits produced in China. All laboratories obtained passing proficiency scores of >80% and 5 out of the 7 laboratories that used Panbio kits obtained 100% proficiency.

(2) WHO JE laboratory checklist and accreditation

Dr Nalini Ramamurty presented the experience using the WHO JE checklist for the accreditation of JE laboratories in SEAR. Six major criteria to evaluate the laboratory performance were used for accreditation. While WPR used the criteria of <180 days for referral of samples to the RRL, SEAR proposed 90 days for sample referral to RRLs. Among nine network laboratories, seven laboratories were accredited.

2.2.4 Country reports

(i) Cambodia

In May 2006, the Cambodian CDC, National Institute of Public Health (NIPH), National Immunization Programme (NIP)/Ministry of Health (MOH), PATH and WHO started the JE Surveillance Project, which is hospital-based sentinel site surveillance for JE among children less than 15 years of age with suspected meningo-encephalitis. NIPH received samples from six hospitals and tested samples using the Panbio JE-Dengue IgM COMBO ELISA.

From 2006 to 2009, 2733 samples from 1,023 patients were received from 6 sentinel sites (Phnom Penh, Kampong Cham, Siam Reap, Svay Rieng, Takeo and Battambang). Among 1023 cases, 138 cases were positive for JE IgM and 198 cases were positive for Dengue IgM. JE positive rates were highest among 6-10 years old (56%) followed by 1-5 years (41%). Samples with sufficient amount of CSF or serum remaining from patients (from May 2006 to December 2007) were sent to the WHO JE Global Specialized laboratory at US CDC. A total of 1195 samples from 451 cases were sent to US CDC and confirmed. Of samples tested to date, 61 were JE (17%), 205 were negative (59%) and 82 were dengue (23%). It was noted that Dengue IgM was detected in serum in most cases, so may not have been the cause of the ME). In addition, CSF samples from children 5 years of age and under that were JE and dengue IgM negative were tested by real time PCR at US CDC Meningitis and Vaccine Preventable Diseases Branch, Atlanta. Among 183 CSF samples tested, 6 (3.3%) were positive for Hib, 2 (1.1%) were positive for N. meningitides, 1(0.5%) was positive for Strep. Pneumoniae.

(ii) Lao People's Democratic Republic

A total of 17 samples were received in 2009 at NCLE from five surveillance sites (Bokeo, Oudomsay, Luang Prabang, Sayaboury and Vientiane), of which three were JE IgM positive and three were equivocal. Diagnostic methods available are PanBio JE-Dengue IgM Combo ELISA, XCyton JEV CheX, Protein saver filter paper-Whatman and Hapalyse Dengue JE PA kit-Pentax. WPRO, the Wellcome Trust and University of Oxford Infectious Disease Centre, Mahosot Hospital collaborated in (1) determining the incidence of JEV infection in patients with AES at Mahosot Hospital, (Vientiane) and provincial hospitals, (2) determining the diagnostic accuracy of PanBio JE-Dengue IgM Combo ELISA versus reference assays, (3) developing and validating filter paper diagnostic techniques, using elutes of ‘Proteinsaver’ filter paper (Whatman) for JEV

serology and PCR on 'FTA' filter-paper (Whatman) for detection of JEV in serum + CSF and (4) determining the frequency of JEV infection among patients admitted with AES at diverse sites in the Lao People's Democratic Republic. 302 CSF, 216 acute sera and 140 convalescent sera were collected from 335 AES cases in Vientiane from January 2003 to April 2007. Of the 335 AES patients tested, 18% had acute JEV in sera and CSF samples and 13% had anti-JEV IgM in CSF samples. Even though the Lao People's Democratic Republic NCLE could not participate in the first regional training in Hong Kong, NCLE participated in the first proficiency testing programme in 2009 and obtained passing score. WHO JE PT samples were also sent to the Mahosot Hospital and 91% score was obtained.

The Mahosot hospital has ongoing collaboration with Luang Namtha, Saravane and Attapeu provincial hospitals.

(iii) Malaysia

The Virology Unit at the Institute for Medical Research is the main laboratory that receives JE samples, but other laboratories can also perform JE diagnostic testing (National Public Health Laboratory, University Malaya Medical Centre and University Malaysia Sarawak). Viral encephalitis in Malaysia is a notifiable disease (no specific aetiological agent recorded), thus, cases of JE cannot be quantified accurately. The JE vaccination programme in Sarawak started in 2002 (9 months, 10 months and boosters 18 months and every 3 years until 15 years of age). In Peninsular Malaysia and Sabah, vaccination is given within a 2 km radius when there is a case of JE. JE immunization coverage rates in Sarawak state were 85% and 99.1% in 2008 and 2009, respectively. Age distribution of JE cases shows that most cases occurred among 5-15 years in 2007-2008 but in 2009, more cases were detected among those over 25 years. Sarawak and Perak states had high incidence of JE in 2008 but in 2009, Terengganu, Kuala Lumpur and Penang had higher incidence than other states in Malaysia.

While IMR and NPHL will be involved in testing samples from outbreaks or surveillance, IMR will be also involved in testing clinical samples along with university hospital laboratories in Malaysia. Diagnostic methods available are haemagglutination inhibition test, JE IgM Capture ELISA (1991), virus isolation in suckling mice (till 1993) and C6/36 cells and rRT-PCR. As an external quality assurance, Institute of Medical Research (IMR) implements the ISO 15189 and participates in the external quality assurance programme. Of the 322 samples tested in 2009, 18 CSF and serum, 1 CSF and 17 serum samples were positive for JE IgM. 11 cases came from 5 to 15 years of age bracket and six cases from the 25-59 years old age bracket. In addition to laboratory-based JE surveillance (85% in children ages 5 to 15 and the overall incidence is 5.2%), hospital-based surveillance was performed in Sarawak from 1997 to 2006 (92% in children 12 years old or younger and the mean age is 6.3 years).

(iv) Philippines

The surveillance of AES, Meningitis and Meningococcal Disease (AESMMD) has been integrated into the Philippine Integrated Disease Surveillance and Response (PIDSR) System in 2008. While meningococcal disease is an immediately notifiable disease, AES and bacterial meningitis are weekly notifiable diseases. Sample collection for AESMMD started in March 2009 from three sentinel sites (Bulacan, Tarlac and Iloilo) out of five sentinel sites and testing began in June 2009 using JE/Dengue IgM Combo ELISA kits provided by WPRO. Among 71 samples, 10 samples were confirmed as JE positive. Out of six CSF samples, four were positive for JE and two positive for dengue. Out of six serum samples tested, one was positive for JE and five positive for dengue. Among six cases with both six CSF and serum samples collected, five cases were positive for JE and one positive for dengue. Quality assurance measures were implemented through staff training, temperature monitoring of equipment, regular

maintenance of equipment, validation of test run and participation in the external quality assessment programme. This laboratory participated in the first WHO proficiency testing and obtained 100% score. It is planned to conduct quarterly on site monitoring and assessment of surveillance sites.

(v) Viet Nam

Three sentinel sites (one in the north, one in the central region and one in the south) were selected for the hospital-based research on acute CNS infections in Viet Nam. From 2004 to 2009, 4651 AES cases were reported, 2248 specimens were collected and 180 (8%) were positive for JE. While around 28% were positive for JE among samples collected form 2004 to 2005, around 8% were JE positive among samples collected from 2006 to 2009.

The National Institute of Hygiene and Epidemiology (NIHE) perform JE testing for the northern part of Viet Nam. JE vaccination covers 25 Northern provinces and 260 districts. In 2009, 1863 cases/100 000 morbidity and 0.008/100 000 mortality was reported from AES cases in Northern Viet Nam. June and July were peak months during the year. JE vaccine coverage rates were 95.1% for the second dose and 90.4% for booster dose in 2009 in Northern Viet Nam. NIHE produces an in-house MAC ELISA and also distributes the kits to Northern provinces. From 2007-9 the NIHE laboratory received 977 samples, 223 (22.8%) of which were positive for JE. JE positive rates decreased from 38.1% in 2007 and 24.6% in 2008 to 11.1% in 2009. Age distribution of JE cases showed 35% of JE cases in an age group of 1-4 years, 33% among 5-10 years and 28% among >10 years.

Molecular epidemiological analysis of JEV grouped viruses detected in humans into genotype 3, and those from pigs and mosquitoes into genotype 1.

However, recent genotype data on JE viruses is not available from human, mosquito and pig samples.

The Arbovirus Laboratory at the Pasteur Institute, HCMC, performs JE testing for the southern part of Viet Nam. JE vaccination in 2009 covered 20 Southern provinces and 152 districts where 448,114 children under 5 years old were vaccinated. This laboratory uses their in-house MAC ELISA JE kit for diagnosing JE along with haemagglutination inhibition (HI), PRNT, virus isolation and RT-PCR for CSF samples. In 2009, 182 CSF samples and 250 acute and 112 convalescent serum samples were collected from 288 cases. Among 182 CSF samples, 11 were positive for JE IgM and 6 were positive for dengue IgM. Out of 250 acute serum samples, 12 were positive for JE IgM and nine were positive for dengue IgM. Out of 112 convalescent serum samples, seven were positive for JE IgM and six were positive for dengue IgM.

Country	**Challenges**
Cambodia	▪ Qualities of some samples are not good (Haemolysis etc.) ▪ Inadequate sample volume ▪ Difficulties in second serum collection ▪ JE surveillance will shift to ME surveillance which NIP will be responsible for. More responsibility is expected under the surveillance system. ▪ The CSF will be tested by PCR and bacterial culture for other pathogens such as Hib, pneumo and N-*meningitidis* ▪ NIPH Laboratory needs more technical and financial support from WHO laboratory network.

	▪ Sentinel site laboratories need to be strengthened for basic bacteriology including culture.
Laos	▪ Laboratory supplies do not arrive on time. ▪ Inadequate number of skilled staff to fulfil all laboratory demands ▪ Staff needs more technical and data management training ▪ Provincial and District staff require more training on field collection of blood specimens ▪ Insufficient amount of freezers and refrigerators ▪ Additional air conditioner is required to maintain temperature outside the freezer area ▪ It would be good to have some long term technical and data management assistance
Malaysia	▪ JE is not a specific notifiable disease ▪ Problem in getting a CSF sample ▪ Problem in getting a 2nd sample ▪ Shortage of manpower ▪ Expensive
Philippines	Low recruitment of cases, funding provided by the project per patient does not cover the cost of tests for clinical management. ▪ delay in the approval of the project two hospitals stopped sending specimens (no endorsement to newly responsible person)

2.2.5 Data Management: Laboratory data reporting

Mr Benjamin Bayutas presented a new monthly laboratory reporting format for the JE laboratories in MS Access. Laboratories should submit both aggregate and case line list by 10th of every month.

2.2.6 Future plans for the Western Pacific Region JE laboratory network

Dr Youngmee Jee presented the future plan of JE laboratory network in WPR and reviewed the implementation status of recommendations from the Labnet meeting in 2008. Most recommendations have been implemented or initiated including training, proficiency testing, laboratory data reporting and on-site review for laboratory accreditation. Confirmatory testing for national laboratories will be initiated and completeness and timeliness of JE laboratory data reporting will be monitored beginning in 2010. Hands-on training followed by the second proficiency testing is planned in 2010-2011.

2.2.7 Reports from GSL and RRLs

Dr Tomohiko Takasaki presented JE surveillance in Japan and development and use of new Vero cell derived JE vaccines and JE laboratory testing at NIID. The genotype of JE virus circulating in Japan shifted from 3 to 1 since 1994 but recently genotype III virus has been detected in Okinawa. In Japan, most JE testing is performed in commercial laboratories by HI on paired sera and samples are not kept after the testing.

Dr Wang Huanyu presented the activities of JE laboratories in China CDC. China CDC organized national workshops of JE surveillance and laboratory from 2004 and hands on training courses for JE virus isolation and identification were held from 2006. JE surveillance based on clinical JE case reporting started in 1951 and covers 13 provinces and 26 counties. Detection of IgM and IgG and JE virus as well as vector surveillance are conducted in China. This laboratory uses the Chinese Commercial Beixi kit, which is locally produced for IgM detection. IFA and

PRNT are also performed. Molecular diagnosis using conventional and real time RT-PCR is also conducted. Among AES patients, JE positive rate among flaviviruses is the highest with the exception of Xinjiang province and the positive rate was >50% in Yunnan province. Proficiency testing (PT) was implemented from 2006 and the number of participating laboratories increased from 8 in 2006 to 19 in 2009. Designation of subnational JE laboratories is being approved by Ministry of Health. JE vaccination is conducted in all provinces except Tibet, Xinjiang and Qinghai. Both live attenuated (two doses: 8 months and 2 year) and inactivated cell derived JE vaccines [4 doses: 8 months (two doses with 7-10 days interval), 2 year and 6 years] are used in China. Laboratory data reporting to WPRO has not been initiated yet.

Mr Young-Eui Jeong presented diagnostic methods used for JE testing, vector and host surveillance and flavivirus surveillance in the Republic of Korea. This laboratory tested about 200-300 samples each year from 2004-2009 but only a few JE cases (less than 10) have been detected every year mostly among >50 years old. Both vector and animal host surveillance is conducted from July to October every year. Laboratory diagnosis of other flaviviruses such as Dengue and West Nile viruses are presented. In 2009, 269 and 84 samples were tested for Dengue and West Nile viruses, respectively, by ELISA and RT-PCR and 88 Dengue positive cases were detected in 2009. Vector surveillance for Dengue is also conducted in the main harbours and at the international airports in Korea. The nested RT-PCR kit for JE, which can detect all genotype 1 and 3 strains targeting 226 bp of the C protein gene Region (~400$ for 96 tests), and an immunochromatographic test, which detects whole antibody in pigs, were developed and patented by this laboratory. These kits could be used in JE endemic countries.

2.3 Day 4 and Day 5: Measles and Rubella Laboratory Network

The WHO measles and rubella laboratory network in the Western Pacific Region consisting of 382 laboratories including 362 subnational laboratories plays an important role in progress towards achieving regional measles elimination by 2012. The network performs critical functions by confirming or discarding suspected measles, rubella, and CRS cases, identifying measles and rubella virus genotypes, and helping to determine potential routes of transmission.

The network consists of one global specialized laboratory in Japan, three RRLs in Australia, China, and Hong Kong China, 13 functional NMLs and, 31 provincial and 331 prefecture laboratories in China. All provincial laboratories in China except one have been reviewed and accredited. Accreditation for prefectural laboratories in China is conducted by provincial laboratories in collaboration with China CDC.

Among 17 functional national, regional reference or global specialized laboratories, 14 laboratories are fully functional and three laboratories still need to improve laboratory performances to be fully accredited. The national measles and rubella laboratory in Fiji has been accredited for the first time in 2009. Laboratories in the Lao People's Democratic Republic and Papua New Guinea are not yet fully functional.

In 2008, Western Pacific Region network laboratories tested around 115 973 and 32 311 serum samples for IgM for measles and rubella, respectively (The number of 2009 samples tested was not available yet).

Measles outbreaks in Viet Nam and the Philippines in 2009-2010 were confirmed by the designated measles laboratories at the National Institute for Hygiene and Epidemiology (NIHE) in Hanoi and Pasteur Institute (PI) in Ho Chi Minh City and in Research Institute for Tropical Medicine (RITM). Molecular analysis of measles viruses which caused the measles outbreak in Viet Nam was provided by Hong Kong RRL and H1 strains were detected from samples from both NIHE and PI laboratories.

Laboratory confirmation of measles cases in China and Japan was strengthened during 2008-2009. China measles and rubella labnet produced substantial amount of genotyping data for measles and rubella. Most provincial laboratories in China can perform virus isolation and identification by molecular detection for measles, rubella and mumps. Japan established 10 measles reference centres for serological confirmation among prefectural laboratories and proficiency testing samples for 10 measles reference centres were arranged by NIID.

All Western Pacific Region national laboratories passed the proficiency test in 2009 and confirmatory testing has been implemented by all national laboratories. Results of confirmatory testing showed good concordance rates between National laboratories and RRLs.

The third regional hands on training course was organized at the RRL in HK in October 2009 to provide updates on measles /rubella ELISA using serum and DBS samples, cell culture/virus isolation and identification by IFA and RT-PCR for measles and rubella viruses. In addition to the regional hands on training course, China CDC also has organized the workshops and hands-on training courses for 31 provincial laboratories every year since 2005. In 2009, the molecular analysis of measles and rubella virus strains was strengthened and some genotype and sequence information was obtained from most countries in the Region. Hong Kong RRL provided genotype and sequence information using confirmatory serum samples from countries.

Opening session

Dr Youngmee Jee, Regional EPI laboratory coordinator, welcomed all participants and advisers. The Director of Programme Management, Dr. Hans Troedsson, opened the meeting and welcomed all participants from countries and advisers from partner organizations. He acknowledged the contribution of the laboratory made during last few years and emphasized the critical role of measles/rubella laboratory network to achieve the regional measles elimination goal by 2012.

2.3.1 Overview of Global and regional measles elimination initiative

(1) Global and regional measles elimination initiative: Progress, Challenges and Plans

Dr David Sniadack made a presentation on "Progress, Challenges and Plans on Measles elimination and rubella control". Measles incidence in this Region dropped 58% in 2009 compared to 2008. Two countries with biggest populations, China and Japan have made a good progress in reducing measles incidence in the past two years. The Region already achieved 92% reduction of measles mortality by 2008 compared to the 2000 level. Countries are reporting monthly linelists of measles cases starting from 2008 except China and completeness and timeliness of reporting to WPRO improved from 51% and 19% in 2007 to 85.3% and 60.8% in 2009, respectively. The Region also began to look into accelerating rubella control and CRS prevention. In 2008, 126 534 rubella cases were reported in the Region. Recently, unexpected outbreaks occurred in Viet Nam and the Philippines and affected age group shifted from children to younger infants and adults. Despite remaining challenges for the Region's measles elimination initiative, 25 countries and areas including Australia, the Republic of Korea, Brunei, Macao and 21 Pacific Island Countries may already have eliminated measles. Regional plans for eliminating measles by 2012 including supplementary immunization activities in countries, strengthening epidemiologic and laboratory surveillance and communication as well as establishing regional and national verification committee for measles elimination were presented.

(2) Progress of global measles and rubella laboratory network

Mr David Featherstone presented the updates of global measles and rubella laboratory network. The network processed ~430 000 samples for measles and rubella IgM detection in 2008. From 2009, all 31 provincial laboratories in China also participated in the global WHO PT programme. Use of alternative sampling methods such as dried blood spot or oral fluid and strengthening of molecular surveillance capacities across the regions through training were emphasized. Numbers of reported laboratory confirmed measles cases from WPRO surveillance and laboratory reports in 2009 show huge discrepancy : 20 116 cases from surveillance report and 4192 cases in laboratory report and this needs to be resolved as the Region moves closer towards elimination. Timely data sharing of ELISA testing and genotyping results with WHO are critical to monitoring progress towards countries achieving the indicators for elimination and to determine whether measles cases are due to importation or from endemic circulation. Challenges and implications for measles and rubella laboratory network as regions move towards enhanced molecular surveillance were discussed.

(3) Updates of regional measles and rubella laboratory network

Dr Youngmee Jee provided the regional updates of measles and rubella laboratory network in the Western Pacific Region. Region's achievements since 2008 were presented. All national laboratories established confirmatory testing mechanism with the RRL and case-based laboratory reporting has been implemented in most countries. China and Japan measles laboratories made a good progress to ensure the quality of ELISA testing for measles and rubella.

WHO hands on training was organized in Hong Kong RRL for priority countries to provide updates on ELISA/ dried blood spots (DBS), cell culture and RT-PCR of measles and rubella.

Workload and testing results, key performance indicators of network laboratories, monitoring of completeness and timeliness of monthly laboratory reporting were presented. Confirmatory testing results of each laboratory as well as genotyping results from RRLs using serum samples were discussed as this would be an alternative source to obtain genotype information when virus isolation samples are not readily available. Distribution of measles virus genotypes in 2008-2009 in the Region was presented. H1 strains were endemic strains in China and Viet Nam but also often detected in other countries and D9 strains were increasingly detected from many countries in the region. D4, D5, D8 and G3 were also detected. While H1 strains were predominantly detected in China, D4, D7 and possible new d11 stains were also detected in one county in China which appeared to have been imported from neighboring Myanmar. Implementation of recommendations from the last labnet meeting in 2008 was reviewed and plans for 2010-2011 were also presented.

2.3.2 Quality assurance

(1) Measles proficiency test updates

Ms Vicki Stambos from VIDRL, Australia provided the purpose, preparation of WHO measles and rubella IgM proficiency testing samples and presented the results and the analysis of 00805 PT samples which were used for 168 network laboratories. In addition, results of 00905 PT samples which were only distributed in WPR laboratories in 2009 were presented. Laboratories with enough positive samples were requested to contribute positive samples for preparing PT.

(2) Confirmatory testing

Dr Wilina Lim from Hong Kong RRL presented objectives and principles of quality control including the use of in-house control samples and summary of confirmatory testing results from participating laboratories during 2007-2009.

(3) Internal quality assurance measures

Mr Mao Naiying from China CDC, WHO RRL presented the quality assurance measures used in China measles and rubella laboratory network including confirmatory testing, proficiency test, use of in-house control samples, SOP, documentation and calibration.

(4) Developing quality assurance programme for molecular techniques

Dr Paul Rota from US CDC presented the need for quality control measures for molecular tests as most regions are expanding virological surveillance for measles and rubella. WHO and GSL's plan to develop QC standards for sequence chromatograms and sequence data were also presented.

2.3.3 Country reports

(i) Cambodia

The immunology unit at the National Institute of Public Health (NIPH) was designated as a NML. The laboratory receives samples from all provincial referral hospitals and health centre sites. The ELISA method is used for detecting Measles and Rubella antibody IgM (by Dade Behring/Siemens Enzygnost). Dried blood spot samples are collected for children less than 1 year of age and serum samples for children above 1 year of age. For the 2009 PT, NIPH scored 100% in the measles test and 97.1% in the rubella test. From 2007 to 2009, 8054 cases were tested and 1008 were positive for rubella and 104 for measles. This laboratory started plotting optical density readings of positive kit control samples but has not implemented the use of an in-house control yet. This laboratory is planning to perform virus isolation and molecular detection of measles and rubella viruses in the future.

(ii) Fiji

The laboratory in the Mataika House is designated as the NML and on site reviews were conducted in 2008 and 2009. Based on the findings of 2009 visit, this laboratory was fully accredited. Ms Mere Cama presented outcomes of 2008 review and various activities conducted towards the accreditation in 2009. One laboratory staff was invited to the laboratory hands on training in 2009 in Hong Kong and national training to implement DBS was also conducted in Nov 2009. After the WHO accreditation in Nov 2009, this laboratory is very keen on receiving samples from other Pacific Island Countries.

(iii) Pacific Island Countries

VIDRL, Australia received acute fever and rash samples from Pacific Island Countries and Ms Vicki Stambos presented the testing results of those samples. In 2008, 24 samples were received from 6 countries including Fiji (13), Kirabati (2), Niue (5), Solomon Islands (4) and Tuvalu (1). In 2009, 74 samples were received from 6 countries including Fiji (69), Guam (1), New Caledonia (1), Solomon Islands (2) and Vanuatu (1). Three Pacific Island Countries (Fiji, Guam and New Caledonia) participated in WHO measles and rubella IgM ELISA proficiency test and all obtained 100% score.

(iv) The Lao People's Democratic Republic

The Virology section at the National Center for Laboratory and Epidemiology (NCLE) serves as the NML in the Lao People's Democratic Republic.

Though equipment for influenza molecular work is available in NCLE, NML does not conduct molecular testing/ genotyping, virus isolation and IFA. All virus isolation samples are sent to Hong Kong RRL. Since 2007, all measles IgM negative samples are also tested for rubella using Dade Behring/Siemens Enzygnost. Samples tested for measles and rubella increased to 223 and 196, respectively in 2009 compared to 129 in 2008. In 2008, no measles positive sample was detected and 45 rubella positives samples were detected. In 2009, 27 samples were positive for measles and 42 were positive for rubella. This laboratory obtained 95% for measles testing and 100% for rubella testing for 2009 PT. During the measles outbreak in Champasack in 2009, some swab samples were collected and sent to Hong Kong RRL. D9 strains from this outbreak with 100% homology to D9 strains from Thailand were detected. From samples collected in 2007, H1 strains were detected.

(v) Macao China

The Public Health Laboratory was designated as the National Measles Laboratory in Macao China in 2001 and the first review of this laboratory was conducted in December 2009. Serology, molecular and viral culture units are conducting the activities of virology laboratory. In 2008 and 2009, 130 and 59 samples were tested for measles IgM, respectively. The measles survey programme in Macao was initiated in 2002 and about 500 samples randomly selected from routine diagnostic specimens have been tested for both measles IgM and IgG in NML every year. Only a few measles positive samples (less than 10) were detected from clinical and survey samples each year. A proportion of samples were retested in Hong Kong RRL and 100% concordance rate was observed. This laboratory participates in various external quality assessment programmes and results of WHO 2004-2009 measles/rubella proficiency testing results were 100%. Additional genotyping was conducted in Hong Kong RRL and H1 strains were detected from 2008 serum samples. The routine immunization programme provides two doses of measles–mumps–rubella (MMR) vaccines, at 12 and 18 months, and the coverage rates were 84.4% for MMR1 and 87.2% for MMR2 in 2007. Macao is considered to have almost achieved measles elimination.

(vi) Malaysia

Two doses of MMR vaccines are given at 12 months and 7 years in Peninsular Malaysia and Sarawak but in Saba, the first dose of single measles vaccine is given at 6 months followed by two doses of MMR vaccines given at 12 months and 7 years. The National Public Health Laboratory (NPH) is designated as WHO national measles laboratory for Malaysia. The Serology laboratory, cell culture laboratory and molecular laboratory in the Virology Division of NPHL are involved in NML activities. Siemens IgM and IgG kits are used. Different algorithms are used for outbreak and sporadic cases in Malaysia based on previous experience. For outbreak cases, rubella IgM is performed first followed by measles IgM. For sporadic cases, measles IgM is performed first followed by rubella IgM. For sporadic rubella cases, measles IgM testing is not performed. In house control samples have been well implemented and proficiency test results of 100% were obtained for 2007-2009. Confirmatory testing samples were sent to VIDRL Australia and concordance rates were >95% during 2007-2009. Additional measles virus isolates were sent to VIDRL RRL for genotyping and 6 D9 and one G3 strain were detected in 2008-2009.

(vii) Mongolia

The National Center for Communicable Diseases serves as NML Mongolia and cell culture laboratory and serology laboratory. In 2007, 2030 samples were received and 13 and 964 samples were positive for measles and rubella IgM, respectively. In 2008, 301 samples were tested for measles and 279 samples were tested for rubella. 30 samples were positive for measles and 67 samples were positive for rubella. In 2009, 177 samples were tested for measles and rubella and three samples were positive for measles and another three samples were positive for rubella. From 2007 to 2009, 36 virus isolation samples were received but no virus was detected from those samples. From 2007 to 2009, this laboratory obtained 100% for WHO measles and rubella IgM proficiency test. Confirmatory testing samples for 2008 and 2009 were sent to NIID Japan and 100% (n=100) and 90% (n=10) concordance rates were observed.

(vii) New Zealand

The Canterbury Health Laboratory serves as NML for New Zealand. The serology laboratory conducts IgM and Immunoglobuline G (IgG) serological detection and molecular laboratory can perform molecular diagnostic detection of viruses. Siemens kit is used for measles IgM and Biomerieux MiniVidas kits are used for measles IgG, rubella IgM and IgG. In addition to measles and rubella IgM, Parvovirus IgM and HHV-6 IgM tests are conducted to help confirm that measles IgM positive samples are not due to other exanthemas. In 2009, two measles outbreaks were detected in Dunedin and Christchurch, respectively. H1 and D4 strains were detected from Dunedin and Christchurch outbreaks, respectively. The H1 outbreak (n=31) was thought be imported from Viet Nam and there were a few other occasions which might be related to importation in New Zealand. This laboratory participated in various external quality assurance programmes and implemented in house controls for serological testing. Molecular diagnostics for measles including nested PCR and real time PCR was established in August 2009.

(ix) Papua New Guinea

The Central Public Health Laboratory at Port Moresby was designated as NML for Papua New Guinea. In August 2007, nine laboratory members were trained for DBS ELISA and three members were re-trained in Nov 2009. Suspected cases received from Central and provincial hospitals are tested for both measles and rubella IgM. In 2008, 50 samples were tested for measles and 45 samples were tested for rubella and no measles positive and six rubella positive samples were detected. In 2009, 79 samples were tested for measles and 50 samples were tested for rubella and 20 samples were positive for rubella. Major challenges of this laboratory are

delayed shipping and testing of samples. Despite the training for DBS as an alternative sampling method, only a few DBS samples were collected.

(x) Philippines

The Virology Division of the Research Institute of Tropical Medicine is designated as NML in the Philippines and measles surveillance has been integrated into the Philippine Integrated Disease Surveillance Response (PIDSR) system as one of 26 syndromic diseases surveillance. This laboratory initiated virus isolation and identification in addition to serology after the hands-on training in Hong Kong in 2009. Good quality assurance measures including the use of in-house control samples have been taken in the laboratory. In 2010, increased measles activity was noted and 1077 samples have been tested and 618 samples (57.4%) were positive for measles as of mid February.

(xi) Republic of Korea

The measles laboratory has been separated from the influenza laboratory and is responsible for testing of all respiratory viruses except influenza viruses. NML performs virus isolation and serology for measles and rubella identification and also test suspected cases for also parvovirus B19 using Biotrin IgM EIA and Human Herpes Virus 6 using Panbio IgM EIA kits. This laboratory conducts conventional and real time PCR for respiratory viruses including measles, rubella, Parvovirus B19 and HHV-6. In 2007-2009, 999 cases were reported and tested for measles and 338 cases were laboratory confirmed. In 2007, among 284 positive cases, 217 cases were IgM positive and 8 and 67 cases were confirmed by virus isolation and RT-PCR, respectively. In 2008-2009, 22 and 32 cases were laboratory confirmed as measles IgM positive and 2 samples in 2009 were positive for measles RT-PCR. HHV-6 IgM was detected among 20-41% of samples tested and parvovirus B19 IgM was detected among 4-15% of samples tested from 2007-2009. H1 genotype strains were continuously detected in the Republic of Korea from 2006-2009 and one imported case of B3 strain from Libya was also detected in 2009. NML also coordinated the quality assurance of eight provincial health and environmental research institutes (PHERI) and five private diagnostic centres in 2007-2009. While all PHERI use Siemens measles and rubella IgM kit, five private laboratories used different kits such as Radim (two laboratories), Euroimmune (two laboratories) and DSL (one laboratory) for testing PT samples and routine diagnostic samples.

(xii) Singapore

The Virology Laboratory, Pathology Department Singapore General Hospital serves as the NML Singapore and can perform virus isolation and identification as well as serology and virus genotyping. Measles activities remained low since the measles catch up immunization in 1997 and introduction of two dose MMR vaccination in 1998. Siemens kits are used for measles and rubella IgM but testing algorithm is based on clinician's request. Good quality assurance measures have been taken and results of PT and confirmatory testing showed 100% in 2009. This laboratory also conducted measles virus genotyping of 11 measles isolates from 2007 to 2009 by sequencing. D5 (n=1) and D9 (n=2) strains were detected in 2007 and D9 (n=1) and D4(n=4) in 2008 and H1(n=1), D8(n=1) and D9 (n=1) in 2009. WHO testing algorithm is not followed in this laboratory because there is no additional funding for other testing.

(xiii) Viet Nam

The NIHE (National Institute of Hygiene and Epidemiology) and PI (Pasteur Institute) serve as the National Measles and Rubella Laboratory for North and South Viet Nam,

respectively. Both laboratories use WHO provided Siemens kits and government provided Biorad kits.

NIHE: Due to the huge outbreaks of measles in 2009, NIHE tested 3890 samples for measles and 2208 samples for rubella in 2009 and 2187 (56%) and 545 samples (25%) were positive for measles and rubella IgM, respectively. Virus isolation and molecular detection of measles and rubella have been initiated in 2008. Quality assurance measures including the use of in house control samples were well implemented. This laboratory obtained 100% for 2007 to 2009 proficiency testing and confirmatory testing results of 2007-2008 also showed good concordance rates: 100% for measles and 90% for rubella.

PI : PI also detected 2727 measles IgM positive and 1028 rubella positive cases in 2009. Compared to four measles positive and 360 rubella positive cases in 2008, this laboratory also experienced huge increase of measles positive cases in 2009. This laboratory also initiated virus isolation and molecular detection for measles and rubella.

Nha Trang PI also attended this meeting and presented measles and rubella laboratory testing results. In 2009, this laboratory tested 447 samples received from 11 central provinces using Biorad kits and 42.28% and 17.67% were positive for measles and rubella IgM, respectively. It also plans to conduct molecular detection of measles viruses in 2010 and to be certified for ISO 15189.

Country	Challenges
Cambodia	▪ Quality of some samples is not good (Haemolysis etc.) ▪ Inadequate volume ▪ Take time for reagent supply
Fiji	▪ Human resource ▪ Transport ▪ Local Networking ▪ Laboratory reports not reaching clinicians ▪ Insufficient sample volumes and sample load ▪ Equipments – old & worn out ▪ Meeting requirements for accreditation
Lao PDR	· Staff needs more technical and data management training Provincial and District staff require more training on field collection of blood specimens It would be good to have some short term data management assistance · Additional computer and printer for data management
Malaysia	• Improvement in getting second sample from equivocal cases • Lack of commitment from private practitioner • Failure of clinician/field investigator to collect appropriate clinical samples for virus isolation • Coordinating and interacting with other laboratories (Private

	sectors, universities)
Mongolia	o Strengthening of molecular epidemiological surveillance for measles and rubella. o Provision with required equipments and diagnostic reagents.
New Zealand	• Comprehensive and complete data set collection • Centralising the national data set • Funding • Setting up virus culture • Case definition
Papua New Guinea	• Late reporting & investigation of suspected cases. • Delay in sample collection and transport; haemolysed or infected or lost (7% in 2008, 1% in 2009) • Education on more use of DBS • Reagent outdates and stock outs • Computer programme in 2009 • Staff issues
Philippines	• Manpower • Reagent supply No Case Investigation Form, incomplete entries, illegible entries, abbreviated addresses
Republic of Korea	Need to secure enough amount of measles and rubella IgM positive sera for panels • Need to obtain second samples • Need to train staffs in PHERIs for laboratory diagnosis of measles and rubella Fund
Singapore	• Test is performed based on clinician's request, paid by patients. • WHO algorithm for measles and rubella testing is not followed because no funding to support additional testing. • Funding of samples sent to RRL. • Little clinical and epidemiological information is available. So it is difficult to supply this information to WHO.
Viet Nam (north)	• Update training for 02 staff of Measles laboratory. • Siemens kits should be delivered in December annually.

2.3.4 Use of alternative sampling:

(1) Use of dried blood spots and oral fluid

Mr David Featherstone presented usefulness and stability of dried blood spots and oral fluid samples as alternative to serum. Oral fluid samples could be advantageous for virus detection using RT-PCR and virus detection was possible from samples collected up to 15-19 days after rash onset. While oral fluid sampling method is not used in WPR countries, DBS sampling method has been used in Cambodia and Papua New Guinea and will be implemented in Fiji and Philippines. DBS collection could provide an opportunity to enhance case confirmation in areas where sample transport to the laboratory under cold chain is challenging. Oral fluid sampling method has been successfully used in United Kingdom for measles (and rubella and mumps) surveillance for more than 12 years and has the potential to enhance molecular

surveillance to help monitoring virus transmission patterns and fill in the gaps of molecular surveillance.

2.3.5 Mumps virus surveillance: Application of real-time reverse transcription-polymerase chain reaction (rRT-PCR) in China

Dr Aili Cui presented the status of mumps epidemiology and molecular surveillance of mumps virus from 1995 to 2009 in China. Mumps surveillance was incorporated into National Diseases Reporting Information System in 2004 and mumps vaccine was introduced into national immunization programme in 2007. Most mumps cases were detected among 5-15 years and showed May –June peak. SH gene was used for molecular analysis and only genotype F strains were detected in China. Real time PCR method has been introduced in provincial laboratories as well as in China CDC.

2.3.6 Measles outbreak investigation and enhancing molecular surveillance

(1) Viet Nam experience in 2009:

Dr Dang Thi Thanh Huyen, EPI officer in Viet Nam presented the epidemiology of measles outbreak in 2008-9 in Viet Nam. The peak month of outbreak was February 2009 in the northern Viet Nam but the Southern regions continuously detected measles cases in 2009. An age group of 18-27 years was greatly affected together with under 6 years in northern regions but less affected in southern regions. Rubella cases were also detected during similar epidemiologic weeks in 2009 and 58% of cases were 15-39 years.

(2) Use of molecular techniques in Japan

Dr Katsuhiro Komase presented immunization strategies of supplementary immunization campaign targeting 12 and 17 years old students for 5 years and case based reporting which were implemented from 2008 in Japan. In addition, laboratory strategies to detect measles cases in early phase of disease and minimize secondary infections using molecular detection as primary detection method were introduced. Among 77 prefectural laboratories, 10 measles reference centres will conduct IgM ELISA as well as molecular detection of viruses. NIID, Japan will be responsible for quality assurance of 10 centres. Problems of measles confirmation in Japan, such as low laboratory confirmation rate, use of commercial laboratories in most cases and lack of genotype analysis were also discussed.

(3) China experience

Dr Xu Wenbo presented the updates of measles surveillance in China and reported imported measles cases in China in 2009. From 1993 to 2009, 1730 measles virus strains were isolated. In 2009, 272 isolates were detected from 27 provinces and all except three strains were H1 strains. One D9 and one D4 strains were detected from Sichuan in February and Shanxi in May and d11 (new genotype) viruses were detected from Menglian county in Yunnan province which is geographically close to Myanmar.

Dr Jianhui Zhou from Jilin CDC, China presented investigation of five measles outbreaks in Jilin province in 2009. Number of cases from each outbreak ranged from 2 to 81. About 47% of cases occurred among <8 months and >15 years and 34 % of 8 months-14 years old among cases has no vaccination or unknown vaccination history. As responses to those outbreaks, emergency vaccinations were conducted.

(4) Australia experience

VIDRL, Australia is responsible for genotyping of measles viruses in Australia and uses N gene PCR to detect measles viruses. During 2008-2009, 619 samples from 465 patients were received for measles RT-PCR and 142 samples (23%) were positive. Among 110 measles virus strains genotyped in 2009, 83 were from Australia, 20 from New Zealand and seven from Malaysia. Importations of measles viruses from at least 10 countries, namely United Kingdom (D4, D8), Iran (H1), India (D8, D4), Viet Nam (H1), Thailand (D4 , D5), Malaysia (G3, D9), the Philippines (D9), China (H1), Indonesia (D9) and USA (D8) were detected in 2009. H1, D5 and D8 are the most common genotypes detected in Australia in 2008-2009 and six cases of genotype A Edmonston strain were also detected from vaccine related cases.

(5) New Zealand experience

Two measles outbreaks were detected in New Zealand in 2009. Thirty one cases were reported from one outbreak related to an imported H1 case from Viet Nam during January to April 2009. From June to November 2009, 169 cases were reported in Christchurch and D4 strains were detected. Genotyping results, completed by VIDRL, were available from 19 cases among 103 IgM confirmed cases.

(6) Pan American Health Organization experience

Dr Paul Rota from US CDC presented PAHO's experience with molecular epidemiology of measles viruses and utility of molecular analysis for documentation of verification of measles elimination was discussed. It can also be a valuable tool in establishing a genetic baseline as a first step for regional and global molecular epidemiology and elimination activities, to monitor virus transmission during and after outbreaks and to differentiate between ongoing transmission of endemic virus from new imported virus and import related cases. Sharing sequence information as well as genotypes was emphasized since genotype information alone cannot confirm independent sources of infection with the same genotypes. Still sequencing analysis cannot differentiate between continuous circulation of the same virus and multiple introduction of the same virus from the same source. In United States of America, 511 cases from 235 chains and 37 outbreaks were detected from 2002 to 2009. Among 235 chains and 37 outbreaks, genotype information is available from 86 chains (36%) and 26 outbreaks (70%), respectively.

Measles virus genotype information in Latin America and Canada was also presented. Ways to improve viral surveillance for measles and challenges for case classification and diagnosis in countries and regions at or near elimination phase were discussed. Vaccine specific real time RT-PCR can be used to differentiate vaccine reactions with disease caused by wild type virus.

2.3.7 Strengthening rubella virus surveillance

(1) Improving rubella virus surveillance

Dr Joe Icenogle from US CDC presented serological and virological techniques to improve rubella surveillance among network laboratories using blood spots and serum spots. Archival sera have been successfully used to obtain baseline genotype information. An immunocolorimetric (ICA) method developed by US CDC to identify rubella virus from cell culture and real time PCR methods with increased sensitivity were introduced. The need for additional laboratory tools for low incidence areas such as IgG testing, avidity testing and virus detection were presented to resolve false IgM positive results.

(2) Rubella and congenital rubella syndrome (CRS) surveillance in China

Dr Li Chongshan presented rubella virus surveillance in China. In 2009, 69 821 cases were reported with incidence rate of 5.26/100 000. A total of 329 out of 378 and 96 out of 207 outbreaks had serum samples collected in 2008 and 2009 (January to September), respectively. Samples were collected from 23 617 out of 76 203 and 10 108 out of 39 208 suspected rubella cases, respectively and about one half were confirmed as rubella. All provincial laboratories in China perform rubella virus surveillance from clinical samples using virus culture and confirm rubella virus using diagnostic RT-PCR. China CDC performs rubella genotyping PCR to amplify a longer fragment followed by sequencing. From 2008 to 2009, 278 rubella strains were detected from 18 provinces and 104 strains from 15 provinces were confirmed. The predominant genotype was 1E and 2B was detected from only two provinces (Shandong and Hainan). The estimated number of CRS cases in China in 2005 was at least 20 000. A retrospective study of rubella and CRS was conducted in Shandong province and the estimated number of CRS cases annually was 79/100 000. Two provinces in China, Shandong and Heilongjiang have established prospective surveillance for CRS as a three year Ministry of Health-WHO project.

2.3.8 Reports from GSL, RRL

(1) Current status of measles and rubella in Japan

Dr Katsuhiro Komase presented the activities of NIID, Japan as WHO GSL/RRL and a seroepidemiological study of measles and rubella among children aged 6-12 years in Vientiane, Lao People's Democratic Republic. Four hundred samples were collected between December 2007 and March 2008 and Denka Seiken measles IgG and rubella IgG kits were used. It was found that 97.6% were positive for measles IgG while 46.4% were positive for rubella IgG. Since rubella vaccine is not used in Lao People's Democratic Republic, seropositivity for rubella IgG would indicate past rubella virus infection. The status of measles and rubella in Japan was also presented. Compared to 2008, the measles incidence in 2009 was dramatically decreased to 741 cases and laboratory confirmed measles cases among total cases increased to 59% in 2009 from 38% in 2008. In addition to D5 strains which were circulated in Japan for some years, imported D8, D9, D4 and H1 strains were detected in 2008-2009. The number of rubella cases also decreased in 2009 compared to 2008. Coverage rates of third and fourth dose for 12 and 17 years old were 85.1% and 77.3% in 2008. Case-based surveillance for measles was introduced from January 2008.

(2) WHO Measles/rubella RRL, Australia

Ms Vicki Stambos presented VIDRL's activities as WHO measles/rubella RRL. In addition to preparation of PT samples for global network laboratories, confirmatory testing for New Zealand, Malaysia, the Republic of Korea and the Philippines, Fiji and Papua New Guinea

was conducted in 2008-2009. For measles and rubella IgM, Chemicon Light Diagnostics assay for measles and Beckman Access (IgM capture) and Diasorin assay for rubella are also used in addition to Siemens assay. In addition, measles IgG, rubella IgG and parvovirus IgG and IgM assays are conducted. VIDRL serology laboratory ensures quality assurance by using kit control, internal control and validated methods, implementing ISO 15189 (NATA standards for accreditation) and participating in RCPA serology quality assurance programmes. In Australia, Diesse, Vital Diagnostics, Bion and Euroimmune EIA are also used for measles IgM and Abbott Diagnostics for rubella IgM testing in addition to Siemens.

(3) Current status of measles surveillance in China

Mr Mao Naiying presented the measles epidemiology in China, summary of serologic tests for suspected measles cases from outbreak and sporadic cases during 2008-2009 in China. About 95% and 90% of outbreak cases were laboratory confirmed in 2008 and 2009, respectively and ~50% of sporadic cases were laboratory confirmed in 2008-2009. China CDC performed confirmatory testing for 30 provincial laboratories except Tibet and received 2100 measles and rubella sera in 2009. Confirmatory testing results of all referred samples were reported within 14 days. Samples from 21 provinces showed 100% concordance but concordance rates of samples from remaining 9 provinces were also >90%. From 2009, all 31 provincial laboratories received PT samples from WHO and all provincial laboratories obtained 100% score. The use of in-house control samples were implemented in provincial laboratories as well as China CDC. Annual national workshop and hands-on training course for provincial laboratories were organized by China CDC in 2009. On site review of provincial laboratories has been annually conducted for six to 12 provincial laboratories since 2000 by WHO, US CDC and China CDC. China network laboratories introduced RT-PCR, real time RT-PCR, multiplex RT-PCR-RFLP for measles genotyping. A total of 1730 measles virus strains were obtained from 1993 to 2009 and only H1 strains have been detected until 2008. China CDC also conducted genotyping of measles virus isolates received from the Democratic People's Republic of Korea (DPRK) in 2007 and confirmed H1a strains. In 2009, three different genotypes of measles virus, D9, D4 and D7-like (d-11) were detected among 292 strains. As some provincial laboratories can perform virus sequencing, timely sharing of sequencing results with China CDC and shipping of isolates to China CDC were emphasized.

(4) Measles National Laboratory and Regional Reference Laboratory in Hong Kong China

Dr Wilina Lim presented laboratory activities of WHO measles RRL as well as National measles laboratory in Hong Kong. This laboratory uses Microimmune and Siemens kits for measles IgM detection, performs complement fixation, virus isolation and identification using Vero/SLAM cells and IFA as well as RT-PCR and sequencing targeting 545bp of N gene. Measles surveillance data from 2004 to 2009 and measles virus genotyping data were presented, until 2008, H1 strains were detected as the predominant strain but only 5 H1 strains were detected in 2009. For rubella, Siemens and VIDAS kits are used for IgM detection; inhibition assay, virus isolation and identification using Vero/SLAM cells and IFA as well as RT-PCR targeting 103bp of the E1 gene are also performed. Rubella surveillance data and genotyping data were presented. Genotype 1E and 2B strains were detected in 2008-2009. Seroprevalence study for measles and rubella showed very high immunity against measles (>96% for all age groups) and rubella (>90% except in the 30-34 and >39 years age groups) in 2007. As WHO RRL, this laboratory provided confirmatory testing for many countries in the Region including Mongolia, Viet Nam, Cambodia, the Lao People's Democratic Republic, Singapore, and Macau in 2008-2009. Confirmatory testing showed good concordance rates of >90% for all countries. Virus isolation samples were referred from Cambodia, the Lao People's Democratic Republic and Macau in 2008-2009. Genotyping using serum samples positive or equivocal for measles IgM was performed and provided valuable background genotype information on circulating

measles virus strains in Cambodia, the Lao People's Democratic Republic, Viet Nam, Macau and Singapore. H1 from Viet Nam, D4 and D9 from Singapore, H1 from Laos, D9 and H1 from Cambodia, D9 and H1 from Macau were detected in 2008-2009. Confirmatory testing for rubella IgM also showed good concordance rates of >90% for all countries that referred samples in 2009. Rubella genotyping was also conducted for IgM positive or equivocal samples and 1E from Laos and 2B from Viet Nam were detected.

2.3.9 Current issues

(i) Use of real time RT-PCR and RT-PCR –RFLP application for measles virus genotyping in China

As the incidence of measles and rubella decrease to <1/1 000 000, the positive predictive value is low and sensitivity and specificity of the detection methods are critical. Therefore, real time RT-PCR method has been introduced for measles, rubella and mumps surveillance in China. Measles incidence in 2009 has decreased to 39.5/1 000 000 in China is planning to detect all sporadic and outbreak cases using molecular methods for early detection. The real-time RT-PCR method has been introduced in provincial and prefectural laboratories in China. For CRS surveillance, both real time PCR and IgM serology are used. Real time PCR methods to detect measles and rubella are also commercially available in China

Application of RT-PCR-RFLP for screening the H1 genotype of measles viruses during measles epidemic and identifying China measles vaccine strains were presented. Since H1 strains are predominantly detected in China, a simple screening method to differentiate endemic and imported strains at provincial level as early as possible would be useful. RT-PCR-RFLP method is a simple and easy method which can be applied for both measles virus isolates and clinical samples at the provincial level. Twenty five clinical samples in 2009 and 55 measles virus isolates from 2001 to 2009 from Jilin province were all correctly confirmed as H1 genotype using PCR-RFLP.

(ii) Need for cell sensitivity testing

Mr David Featherstone presented the possible options to establish the cell sensitivity testing of Vero/SLAM cells. Current laboratory manual recommends replacing the cells after 15 passages and using Geneticin for developing and freezing cell stocks. Unlike polio, (1) wild measles virus strains only grow when SLAM receptor is present while vaccine strains can grow on Vero cells without SLAM. Therefore, only wild measles virus strains can be used for cell sensitivity testing of Vero/SLAM cells, (2) virus isolation is not critical for laboratory diagnosis. The need and how to develop the cell sensitivity testing for Vero/SLAM cells are still being discussed.

(iii) Standardization of measles serosurvey

Mr David Featherstone presented standardization of measles serosurveys. Performing serosurveys could be one way of monitoring population immunity. Serosurveys may be appropriate when the protocol, assay and expertise are available and adequate number of samples from appropriate age groups can be collected. The gold standard for determining susceptibility of population is PRNT which measures neutralizing antibody. Some previous studies show that Ab titre >120mIU/ml is considered to be protective. Some measles IgG ELISAs (eg. Siemens) have reasonable correlation with PRNT but some ELISA IgG assays have poor correlation with PRNT. With Siemens kits, IgG positives are PRNT >120mIU/ml and some, but not all, equivocals are PRNT positive. Other IgG assays can be used for serosurveys if calibrated with standard sera. Standardization of serosurveys can be done by:

(1) Using PRNT with international standard 3 (IS-3) or a secondary standard as controls for each run. (2) Using an IgG ELISA which has been well calibrated (eg Siemens) and include a panel of validated in house controls. (3) Using a non-validated assay but only after consultation with WHO and with use of comprehensive panel of samples validated by a reference laboratory. Assay selection, QC and the use of international standard serum are key issue for accurate seroepidemiology studies. In countries with effective measles control, where most antibodies are derived from vaccination, some ELISAs may have insufficient sensitivity for these studies.

2.3.10 Data management and reporting measles and rubella laboratory data

(1) Monthly laboratory data reporting

Mr Benjamin Bayutas presented the case based measles and rubella laboratory data reporting format in a new Microsoft Access format with automatic data check to replace an old excel format which is prone to errors.

(2) WHO genotype and Measles nucleotide Surveillance (MEANS) sequence database

Mr David Featherstone presented the details of WHO genotype and MeaNS sequence database. Sequence information in combination with epidemiological data can allow mapping of transmission pathways, identify possible source of virus and determine whether indigenous or imported, provide an indicator of surveillance system quality, determine whether IgM response is due to vaccine or wild virus, assist with confirmation of true positives, and improve diagnostic resolution in first few days after rash onset (especially for rubella) in combination with IgM.

Laboratories with genetic data are not always aware of importance of sharing the data with surveillance programme and data are sometimes released months or years after sample collection or kept until publication. Centralized database will allow ready access to all reported viruses among limited WHO laboratory network members. During the 2006 global meeting, it was agreed to have two databases: (1) WHO genotype database and (2) health protection agency (HPA) MeaNS sequence database. Both are maintained on a real time basis with restricted access to laboratory network members only. Variables for WHO genotype database is ISO country code and country name, date of case (month and year), WHO name of virus, genotype, Epi-link (if known), submission data (who, when), GenBank Accession number –accession number to GenBank. As of Feb 22, 2010, 7186 measles viruses of all 23 genotypes from 117 countries and 581 rubella virus strains of all 11 genotypes from 35 countries are deposited. By depositing sequence data into MeaNS database, the sequence data can be automatically depositived into the WHO genotype database and optionally into GenBank. As of September 2009, 4026 measles virus sequences of N gene 450 bp and full 476 bp of H gene are deposited in MeaNS database. It is recommended to deposit measles viruses in MeaNS database (with sequence) and as there is not an equivalent to MeaNS for rubella virus yet, rubella viruses should be deposited in the WHO database.

2.3.11 Asia Pacific Strategy for strengthening health laboratory services

Dr Gayatri Ghadiok from Division of Health Sector Development presented Asia Pacific Strategy for strengthening health laboratory services from 2010 to 2015 developed by WPRO and SEARO. The goal of this strategy is to provide comprehensive laboratory support to public health and curative services leading to improved health in Asia Pacific Region. Seven strategic elements of this strategy are: (1) establish a coherent national framework; (2) ensure sustainable financing; (3) build capacity; (4) assure quality; (5) promote rational use; (6) strengthen safety; and (7) support research and ethics.

2.3.12 Topic discussions

Dr Wilina Lim presented the experience of using confirmatory serum samples for genotyping. Importance of selecting suitable samples for molecular detection was explained and the optimal dilution for in-house controls should be 10 fold above the limit of detection. Nested RT-PCR is conducted in this laboratory and second PCR can improve detection limit up to 10 . Using serum samples collected between 0-3 days after rash onset, the RT-PCR detection rate was 81% compared 91.2% for IgM detection. Among samples collected between 4-7 days, RT-PCR detection rate was 77.5% compared to 98.5% for IgM detection. For samples collected after 7 days, RT-PCR detection rate was 50% compared to 100% for IgM detection. From throat or nasal swab samples and urine samples, RT-PCR detection rate was much higher for samples collected between 0-3 days, 4-7 days and >7 days after rash onset and RT-PCR detection rate was much higher than virus isolation rates ranging from 40 to 67%. Among serum samples tested for RT-PCR, detection rates varied greatly depending on countries. Among serum samples collected in Hong Kong, 70-80% samples were positive for RT-PCR and most PCR products were genotyped. Among serum samples referred from other countries, 0-80% was positive for RT-PCR. Serum samples can be useful for measles virus genotyping when virus isolation samples are not available and best results can be obtained if the samples are collected within 7 days after symptom onset. Detection of rubella virus genome using serum samples is more difficult due to amplification of longer fragments and the methods need further optimization.

The use of dried serum spots for confirmatory testing was presented by Mr David Featherstone and this option can be considered for countries with shipping cost problem. When dried serum spots are used, an aliquot of the original sample should always be kept by the national laboratories. In case of discordance, the gold standard sample, serum should be re-tested again in RRL.

Participants also discussed the quality assurance for DBS samples and shipping viral isolates on filter paper

3. CONCLUSIONS AND RECOMMENDATIONS

Laboratories from three vaccine preventable disease networks in the Western Pacific Region met held in Manila, Philippines from 22 to 26 February 2010. Three consecutive sessions of polio (22 to 23 February), JE (24 February) and measles/rubella (25-26 February) reviewed the performances of three laboratory networks to identify challenges of network laboratories and ways to strengthen the quality of the performances to maintain polio-free status, to strengthen JE and measles/rubella laboratory networks and also to monitor the implementation of recommendations from the first laboratory network meeting in July 2008.

The meeting provided a forum to discuss updates on the status of the EPI Laboratory Networks and to identify ways to strengthen the quality of the performances of network laboratories to maintain poliomyelitis-free status and to support achieving measles elimination and JE control in the Western Pacific Region.

3.1 Conclusions

3.1.1 Polio Laboratory Network

The meeting concluded that the performance of the regional polio laboratory network is sustained at polio-free certification standard and that AFP surveillance activities are efficiently supported. The network provides critical evidence in support of the continued polio-free status of the Region. The network's activities to implement new test algorithms and real-time PCR procedures were all on track.

Participants commented on the expanding knowledge and experience of the Polio Eradication Initiative with outbreaks due to VDPVs that warrants critical review of the operational definitions used to define circulation, and access to guidelines for the investigation and response to VDPV detections.

The critical role that polio laboratories played in investigations of EV71 outbreaks highlights their valuable contributions to public health within the Western Pacific region. WHO should continue its advocacy with national authorities and partner agencies for continued support to the regional polio laboratory network.

3.1.2 Conclusions for the JE Laboratory Network

A one day meeting of the Regional Japanese encephalitis (JE) Laboratory Network was held on 24 February as a part of the second meeting on the Vaccine Preventable Disease laboratory networks in the Western Pacific Region to discuss the progress of the JE network laboratories in the Region, identify challenges of network laboratories, discuss ways to strengthen the performances of network laboratories and report the progress of implementation of the recommendations from the last meeting held in July 2008. Participants included 23 representatives from network laboratories, WHO Laboratory Coordinators from Headquarters and Southeast Asia Region, WHO country EPI officers, Advisers from the US CDC and country EPI focal points. The meeting provided a forum to discuss updates on the status of the regional JE network laboratories. Recommendations for the JE laboratories in the Region include implementation of confirmatory testing mechanisms, initiation of accreditation using WHO JE laboratory checklist and improvement of data management and reporting.

3.1.3 Measles and Rubella Laboratory Network

A two-day meeting of the Regional Measles and Rubella Laboratory Network was held from 25 to 26 February 2010 to review the performance of the measles /rubella network laboratories in the Region, to identify challenges for the laboratories, to identify ways to strengthen the performance of the laboratories in support of measles elimination and to discuss the progress of implementation of the recommendations from the laboratory meeting held in July 2008. Participants included representatives from network laboratories in member countries, the WHO Laboratory Coordinators from Headquarters, Western Pacific Region and Southeast Asia Region, WHO country EPI officers, Advisers from US CDC and country EPI focal points.

The meeting concluded that measles and rubella network laboratories provided high quality support to achieve the regional goal of measles elimination by 2012 by confirming

suspected cases and identifying measles virus genotypes circulating in the Region. The network should continue to make full efforts to obtain genotype and sequence information on measles and rubella viruses circulating in the Region.

The network implemented most of the recommendations from the last meeting in 2008 including monthly reporting of a case based linelist to WPRO. The laboratories should regularly communicate and collaborate with the national surveillance or epidemiology groups and WPRO to minimize discrepancy of laboratory and surveillance data, and the delay in testing of samples and regular reporting of laboratory data to WPRO.

Discussions focused on how to solve remaining challenges for the Western Pacific Region Laboratory Network including improving sample collection for IgM detection and virus identification, validation of test kits used in subnational Laboratory Networks and timeliness and completeness of laboratory reporting using case-based linelist.

3.2 Recommendations

3.2.1 Polio Recommendations

(1) Implementation of new test algorithms

- All national and ITD network laboratories should fully implement the appropriate new test algorithms by end of the second quarter of 2010. Implementation should be in accordance with Supplement 1 to the Polio Manual, and should include revisions of Standard Operating Procedures (SOPs) and test worksheets. Revised SOPs and test worksheets should be shared with the Regional Laboratory Coordinators for review by the end of April 2010.

- With full implementation of new test algorithms in the Region, network laboratories should closely monitor the timelines of reporting to identify and remove obstacles to reporting of virus isolation results within 14 days and ITD results within 7 days. Network laboratories without ITD capacity should refer L20B positive isolates to designated regional reference laboratories for characterization within 7 days of detection.

- Results of wild poliovirus and VDPV detection should be reported to the national authorities within 24 hours of detection. To reduce the risk of within country and international spread of VDPVs and the risk of outbreaks of poliomyelitis, laboratories should promptly report VDPV detections to national authorities, especially country EPI units, who should promptly share such information with the WHO country and regional offices.

- Network laboratories should review work practices and staff assignments to identify barriers to implementation of the new test algorithms and to timely reporting of results. Resource needs workflow, cell preparation cycles, frequency of testing and staff assignments may require adjustments to meet the new testing algorithm requirements.

- Network laboratories should brief national EPI focal points and data managers on the implementation of the new test algorithms and how the new reporting formats will impact programme needs.

- WHO should continue to support implementation of the new test algorithms in network laboratories through provision of technical assistance (e.g. review of SOPs, test worksheets, reporting) and training in order to meet the set deadline.

(2) Quality Assurance

- As previously recommended during the laboratory network's meeting in July 2008, all network laboratories should report results of cell sensitivity tests to the laboratory coordinators for review within 48 hours of completing each test run. This is to facilitate collaboration in rapidly identifying problems and implementing actions to optimize procedures for accurate detection of polioviruses, including re-testing of specimens, as appropriate. Results should be provided in a trend chart including full details of titration experiments. Where available, the absolute passage number of cell lines should be provided in the format of PX/Y where X is the passage number of the frozen cells stock used and Y is the number of cell passages after retrieval from storage.

- For the 2010 proficiency test panel, to be distributed late 2010 or early 2011, all polio network laboratories except China will use the new test algorithm for virus isolation.

(3) Implementation of Real-time ITD RT-PCR and VDPV Screening

- Laboratories that introduced the real-time RT-PCR assays following the training in August 2009 (China CDC, Singapore SGH, Japan NIID and Malaysia IMR), should complete the implementation plan by end of April 2010 including performance of proficiency tests to be provided by US CDC.

- Once success in the implementation of real-time RT-PCR assays is achieved, discordant ITD-VDPV results in real-time RT-PCR assays should be resolved by VP1 nucleotide sequencing for identification of VDPVs.

- Expansion of the real-time RT-PCR assays to other network laboratories should be considered. Priority should be given to the laboratories with existing real-time PCR equipment, infrastructure and experience with real-time PCR assays.

(4) Data Management

- The WHO regional office, in collaboration with network laboratories, should develop a standardized polio laboratory database programme to improve data management in the region. Network laboratories should review the proposed database variables distributed during the meeting and submit by 15 March 2010 additional variables needed to customize country-specific database programmes.

- The WHO regional office should distribute standardized laboratory variable codes and guidelines on the new laboratory database structure to network laboratories and national EPI focal points to guide revisions in test worksheets and case investigation forms consistent with new test algorithms.

- The proposed database programme should be field tested in the network laboratories including provision of training of data managers by end of the third quarter of 2010. In the meantime, network laboratories should continue to report data to WPRO using the current reporting format at least monthly and no later that the 10th of the following month. WPRO should continue to monitor data quality and communicate findings to network laboratories in a timely manner.

(5) Expanding the scope of the polio laboratory network

- Network laboratories should report to national authorities and WHO regional and country offices results for polioviruses isolated from all sources including those identified through

special surveys such as environmental surveillance and enterovirus surveillance. Reports for non-AFP specimens should be submitted at least on a monthly basis and poliovirus isolated from non-AFP cases should be reported using the standardized database and reporting format of AFP cases.

- Recognizing the importance of maintaining the polio-free status of region, poliovirus isolates from all specimen sources should be rapidly and appropriately characterized to identify isolates that can potentially circulate. Individual countries should establish mechanisms for referral of isolates from AFP and non-AFP sources for appropriate and timely characterization. All poliovirus isolates and L20B positive specimens should be referred for ITD testing using WHO recommended procedures within 7 days of detection, regardless of whether from AFP or non-AFP sources.

- Recognizing the public health importance of EV71 in the region, and evidence of an overlap in its clinical presentation with AFP, network laboratories with the capacity to characterize NPEVs are encouraged to do so for isolates obtained from AFP cases. Regional training opportunities for molecular identification of polioviruses and NPEVs should be considered in 2010-2011.

- Polioviruses isolated from patients >15 years of age who present with clinical symptoms compatible with poliomyelitis or AFP should be reported to the Regional Office in a timely manner. Laboratories can use the same reporting format as for AFP data.

(6) Biosafety Issues

- WHO regional Laboratory Coordinators should develop a regional plan to implement a biosafety campaign using training materials developed for use in the GPLN. Each polio laboratory will also be required to nominate a biosafety focal point who will liaise with WHO.

3.2.2 JE Recommendations

(1) Data management and reporting

- Designated national, regional reference and global specialized laboratories should report their laboratory testing data including zero reporting on a monthly basis using the reporting form (both aggregate and case linelist) to the Regional Office by the 10th of every month. Action: all JE Labnet members Timeline: Ongoing

(2) Confirmatory testing

- National laboratories are recommended to send a proportion of samples to designated regional or global specialized laboratories for confirmatory testing. This should occur at least twice a year and include all positive and equivocal samples and from 10-100% of representative (in time and of geographical areas) negative samples. The number and selection of samples to be sent for confirmatory testing should be discussed in advance with the regional laboratory coordinator.

- The volume of samples should be at least 100µl for CSF and 250µl for serum. Samples should be shipped undiluted in leak-proof, externally threaded, screw cap vials.

- The GSL/RRLs should complete confirmatory testing and provide feedback to national laboratories and WPRO within 45 days of receiving the samples from the national laboratories.

- Samples for the first batch of confirmatory testing should be sent by the end of March 2010.

  Action: all National JE Laboratory Network members Timeline: March 2010.

(3) Proficiency testing

- All WHO JE network laboratories should participate in the JE proficiency testing programme arranged by WHO. Testing of the proficiency panel should be completed and results report within two weeks of receipt of the proficiency panel.
- National JE laboratories are recommended to keep all JE or dengue IgM positive samples for future QA purposes and for consideration for inclusion in the JE proficiency panel. Action: all WPR JE Labnet members, Timeline: Ongoing

(4) Validation of assays

- In-house JE IgM assays should be evaluated using the WHO reference serological panels. In-house assays with adequate sensitivity and specificity (to be decided by the JE Laboratory Working Group) should be used by WHO JE Labnet. Laboratories without in-house kits are recommended to use the Panbio JE/Dengue Combo kit.

  Action: all JE Labnet members Timeline: 2nd quarter 2010

- Laboratories that are considering using the Japanese JE cell derived antigen to enhance their in-house assays should follow the protocol to be developed by NIID on discussion with the other GSL and RRLs and report their data to the JE laboratory Working group for analysis and advice.

  Action: Selected JE Labnet members Timeline: 2nd quarter 2010

(5) On site review and accreditation

- After the field trial of the draft checklist in 2010, a formal accreditation procedure to evaluate laboratory performance of the network laboratories will be initiated by the end of 2010.

  Action: WHO HQ, WPRO, Timeline: end of 2010

(6) Communications with Ministry of Health

- It is recommended that the WHO JE network laboratories establish regular communication with their Ministry of Health and National EPI and surveillance groups for Japanese encephalitis control. Action: All WPR JE Labnet members and WPRO, Timeline: as soon as possible.

(7) Training

- It is recommended that hands-on training courses similar to that held in the Republic of Korea in 2009 be conducted on a regular basis to develop capacity in the JE LabNet. Short-term training on advanced techniques for staff from the RRLs should be held at the GSL.
  Action: WPRO, GSL and RRLs, Timeline: 2010-2011

(8) Coordination

- Considering the common goals and challenges in establishing JE laboratory-based surveillance in the two regions, Western Pacific Regional Office and Southeast Asia Regional Office should consider organizing bi-regional JE laboratory network meetings.
  Action: WPRO, SEARO Timeline: 2011

- Other programmes or initiatives working on emerging infectious diseases including JE are encouraged to share their plans and coordinate with WHO JE Labnets to avoid duplication of activities.
  Action: WHO and other initiatives, Timeline: Ongoing

3.2.3 Measles and Rubella Recommendations

Recommendations for the measles and rubella laboratory network include implementation of regular confirmatory testing, obtaining more genotyping and molecular epidemiological information by strengthening strain surveillance for measles and rubella viruses, improving data management and reporting using MS Access format, use of alternative sampling and establishing and improving the quality assurance measures of commercial laboratories in countries where measles/rubella testing is performed in commercial laboratories were made.

Based on discussions and findings from network laboratories, the following recommendations were made:

For all EPI network laboratories, strengthening communications between network laboratories and EPI/surveillance programmes was emphasized.

Recommendations

(1) Data reporting

Case based measles and rubella laboratory data reporting should be fully implemented in all network laboratories. Data should be reported to the regional office on a monthly basis by the 10th day of the month. The new data reporting format in MS Access discussed at the meeting should be adopted by all network laboratories. . Countries where case based reporting is not feasible should also make every effort to share aggregated data with WPRO in a format and frequency agreed upon with the regional office

(2) Confirmatory testing

The confirmatory testing mechanism of serum samples established in the Region should be maintained and it is recommended that national laboratories send a representative 10% of samples or a minimum of 15 samples to the designated regional reference or global specialized laboratories, at least annually but preferably twice a year. A table including a linelist of the samples and the raw data (OD readings) obtained by the national laboratory should be included with the shipment. Before sending samples, the national laboratories should notify and consult with the regional laboratory coordinator to confirm the number and selection of samples to be sent.

(3) Molecular surveillance

As recommended by the Global Measles Laboratory Network Meetings (Sep 2008 and Oct 2009), laboratories are encouraged to submit representative genotype/sequence information on their measles and rubella viruses to the WHO genotype and MeaNS databases, preferably on a "real-time" basis, but at least by the end of the month in which the genotyping was completed. A copy of the information should be sent also to the regional laboratory coordinator.

(a) Laboratories which participated in the regional hands on laboratory training in 2009 and other sequencing laboratories are encouraged to perform virus isolation and/or molecular detection of measles and rubella viruses to identify the genotype and obtain sequence information on circulating measles and rubella viruses.

(b) Efforts should be made to collect sequence data from all chains of infection, especially in those countries where no baseline sequence data exists.

(c) The Laboratory Network should utilize the well *validated* tools and samples available for enhancing molecular surveillance where appropriate, such as;

(i) Oral fluid, throat swabs, urine and PBMC as samples for virus detection

(ii) Detection of viral RNA in archival sera

(iii) Shipping of samples dried onto filter paper

(iv) Standardized PCR methods including the use of a validated, unique PCR control.

(4) Use of dried blood spots

Dried blood spots are in routine use in some countries. It is recommended that countries consider introducing the dried blood spot specimen collection technique where challenges in collecting samples and/or shipping under cold chain to national or reference laboratories exist.

(5) Measles and rubella positive samples for global PT

As recommended by the Global Measles Laboratory Network Meetings, National laboratories should store measles and rubella positive serum samples at -20°C or lower to use; for internal laboratory controls, for global proficiency test panels and for virus identification. Those laboratories with stocks of positive samples (preferably volumes larger than 0.5ml) are requested to contact the regional laboratory coordinator to facilitate using these samples in the WHO proficiency and QC programme.

(6) Quality assurance of commercial laboratories

As recommended by the Global Measles Laboratory Network Meetings in 2009, in countries where most measles and rubella IgM testing is performed in private/commercial laboratories, it is vital that the performance of private/commercial laboratories be monitored. Performance of these laboratories may be assessed through an external quality assurance programme and pre-existing quality assurance data should be assessed by the national laboratories, where possible.

(7) Communications

Laboratory and immunization/surveillance colleagues are encouraged to have *regular* interactions *and* meetings to ensure classification of suspected cases and to harmonize laboratory and surveillance data.

(8) Trainings

Follow-up hands on training courses focusing on molecular detection of measles and rubella viruses are encouraged in the Region.

THE SECOND MEETING ON VACCINE-PREVENTABLE DISEASES LABORATORY NETWORKS IN THE WESTERN PACIFIC REGION

Manila, Philippines
22-26 February 2010

20 February 2010
ENGLISH ONLY

TENTATIVE TIMETABLE

Time	Monday, 22 February	Time	Tuesday, 23 February	Time	Wednesday, 24 February	Time	Thursday, 25 February	Time	Friday, 26 February
	SESSION I: Poliomyelitis laboratory network				SESSION II: Japanese encephalitis laboratory network		Session III: Measles/Rubella Laboratory Network		
0800-0830	REGISTRATION	0830-1000	8. Detection of vaccine-derived poliomyelitis virus (VDPV) (a) Global update on VDPV detection (b) VDPV surveillance in China (c) iVDPV Study 9. Data management and communication (a) Application and challenges (b) Proposed changes and way forward (c) Discussion and hands-on training on data management	0800-0815	REGISTRATION	0800-0830	REGISTRATION	0800–1000	7. Measles outbreak investigation and enhancing molecular surveillance (a) Viet Nam experience in 2009 : National surveillance officer, Viet Nam (b) Use of molecular techniques in Japan (c) China experience (d) Australia experience (e) New Zealand experience (f) Pan American Health Organization experience
0830-0900	1. Opening session (a) Opening remarks (b) Self introduction (c) Administrative announcements (d) Election of chairperson and rapporteur (e) Group photograph			0815-0830	1. Opening session (a) Opening remarks (b) Self introduction (c) Administrative announcements (d) Election of chairperson and rapporteur (e) Group photograph	0830-0900	1. Opening session (a) Opening remarks (b) Self introduction (c) Administrative announcements (d) Election of chairperson and rapporteur (e) Group photograph		
0900--1000	2. Overview of Global Polio Eradication Initiative and maintenance of poliomyelitis-free status in the Western Pacific Region (a) Global Polio Eradication Initiative and regional updates to maintain poliomyelitis-free status (b) Status of global poliomyelitis laboratory network (c) Regional updates of poliomyelitis laboratory network			0830-1000	2. Overview of Japanese encephalitis (JE) control in the Western Pacific and South-East Asia Regions (a) JE and acute encephalitis syndrome (AES) surveillance in the Western Pacific Region (b) Progress of Western Pacific Region JE laboratory network (c) Achievement of JE/AES surveillance in South-East Asia Region (d) Report of JE laboratory working group	0900-1000	2. Overview of global and regional measles elimination initiatives (a) Global and regional measles strategy updates (b) Progress of global measles and rubella laboratory network (c) Updates regional measles and rubella laboratory network		
1000-1030	*COFFEE BREAK*	1000-1030	*COFFEE BREAK*	1000-1030	*COFFEE BREAK*	1000-1030	*COFFEE BREAK*	1000-1030	*COFFEE BREAK*
1030-1200	3. Laboratory quality assurance (a) Report on proficiency testing: Virus isolation and intratypic differentiation (ITD) testing (b) Report on cell sensitivity testing (c) Accreditation status of the Western Pacific Region network laboratories 4. Country experiences on cell sensitivity testing and lessons learnt (a) Mongolia (b) Republic of Korea (c) Viet Nam	1030-1200	10. Updates on laboratory containment of wild polioviruses 11. Laboratory management and biosafety (a) China CDC: Management of China Network Laboratories (b) Hong Kong (China): Coping with surveillance, diagnostic and reference laboratory services (c) Viet Nam (Ha Noi): Challenges of shipping isolates and impact on timeline for referral and reporting ITD results (d) WHO and laboratory biosafety in the Asia Pacific Region	1030-1200	3. Use of in-house and commercial assays (a) Results of evaluation of in-house and commercial assays (b) Approaches for improving the accuracy of JE IgM assays 4. Quality assurance for JE laboratory network (a) Results of the first JE proficiency test (b) WHO JE laboratory checklist and accreditation 5. Country reports (a) Cambodia (b) Lao People's Democratic Republic	1030-1200	3. Quality assurance (a) Measles proficiency test updates (b) Confirmatory testing (c) Internal quality assurance measures (d) Developing quality assurance programme for molecular techniques 4. Country and area reports (a) Cambodia (b) Fiji	1030-1200	8. Strengthening rubella virus surveillance (a) Improving rubella virus surveillance (b) Rubella and congenital rubella syndrome surveillance in China 9. Reports from GSL and RRL (a) Japan (b) Australia (c) China (d) Hong Kong (China)
1200-1300	*LUNCH BREAK*	1200-1300	*LUNCH BREAK*	1200-1300	*LUNCH BREAK*	1200-1300	*LUNCH BREAK*	1200-1300	*LUNCH BREAK*

1300-1400 1400-1500	5. Implementation of the new algorithms for virus isolation and ITD testing (a) South-East Asia Region experience (b) Western Pacific Region experience: Progress and remaining challenges (c) Country and area experiences: - Philippines (Virus isolation) - Hong Kong (China) (Virus isolation and ITD) - New Zealand (Virus isolation and ITD) (d) Integrating laboratory and surveillance data following implementation of new algorithms 6. Implementation of real-time polymerase chain reaction (PCR) (a) Introduction of real-time PCR for ITD and vaccine-derived poliomyelitis virus screening screening (b) South-East Asia Region experience	1300-1500	12. Expanding the scope of polio laboratory network activities (a) Global plan for integrated laboratory services for vaccine-preventable diseases (VPD) surveillance (b) Enterovirus surveillance in the Western Pacific Region (c) Detection of EV 71 in China: Hand, footh and mouth disease surveillance (d) Environmental surveillance in China (e) Proposed plan of expanding polio laboratory network from US CDC (f) Group discussion on expanding scope of Polio LabNet activities: - Group 1: (China, Hong Kong [China], Japan, Republic of Korea, Viet Nam-north and south) - Group 2: (Australia, Malaysia, Mongolia, New Zealand, Philippines, and Singapore) (g) Report of group discussion	1300-1500	(c) Malaysia (d) Philippines (e) Viet Nam (Ha Noi) (f) Viet Nam (Ho Chi Minh) 6. Data management: lab data reporting 7. Future plans for the Western Pacific Region JE laboratory network	1300-1500	(c) Pacific island countries: Victorian Infectious Diseases Reference Laboratory (d) Lao People's Democratic Republic (e) Macao (China) (f) Malaysia (g) Mongolia (h) New Zealand (i) Papua New Guinea (j) Philippines	1300-1500	10. Current issues (a) Use of real-time PCR techniques in China (b) Need for cell sensitivity testing (c) Standardization of measles serosurvey 11. Data management and Reporting measles and rubella laboratory data (a) Monthly laboratory data reporting (b) WHO and measles nucleotide surveillance (MEANS) genotype and sequence databases (c) Group discussions: practical
1500-1530	*COFFEE BREAK*	1500-1530	*COFFEE BREAK*	1500-1530	*COFFEE BREAK*	1500-1530	*COFFEE BREAK*	1500-1530	*COFFEE BREAK*
1530-1730	(c) Western Pacific Region experience: Field evaluation and implementation of real-time PCR - Report on the real-time reverse transcription (rRT)-PCR training workshop - Victorian Infectious Diseases Reference Laboratory experience - National Institute of Infectious Diseases experience - Chinese Center for Disease Control and Prevention (China CDC) experience - Malaysia - Singapore 7. Group discussion (a) Group 1: Overcoming barriers to implementation of new algorithm: (China, Japan, Mongolia, Philippines, Republic of Korea, Viet Nam – north, south and Ho Chi Minh) (b) Group 2: Maintaining proficiency of real-time PCR testing with low workload (Australia, Hong Kong [China], Japan, Malaysia, New Zealand, Singapore) (c) Report of group discussion	1530-1630 1630-1730	13. Other issues and topic for group discussions (a) Timeliness of VDPV reporting (China, Japan, Malaysia, Viet Nam-North) (b) Accreditation of sequencing laboratories (Australia, Hong Kong [China], New Zealand, Singapore) (c) Maintaining biosafety cabinets (Mongolia, Republic of Korea, Philippines, Viet Nam-South) (d) Report of group discussion 14. Conclusions and recommendations	1530-1630 1630-1730	8. Reports from global specialized laboratory (GSL) and regional reference laboratory (RRL) (a) Japan (b) China (c) Republic of Korea 9. Conclusion and recommendations	1530-1630 1630-1700 1700-1800	(k) Republic of Korea (l) Singapore (m) Viet Nam (Ha Noi) (n) Viet Nam (Ho Chi Minh) (o) Viet Nam (Nha Trang) Discussions on country reports 5. Use of alternative sampling (a) Use of dried blood spots (DBS) and oral fluid (b) Cambodia experience 6. Mumps virus surveillance: Applicationof rRT-PCR in China	1530-1640 1640-1700 1700-1800	12. Topic discussions (a) Use of serum samples for genotyping (b) Use of conventional and real-time PCR for case classification and molecular surveillance (c) Quality assurance for DBS samples (d) Use of dried serum for confirmatory testing (e) Shipping viral isolates on filter paper (EMRO experience, rubella experience) (f) Integration of JE testing with measles/rubella 13. Asia Pacific Strategy for Strengthening Health Laboratory Services 14. Conclusions and recommendations
1800	*INFORMAL GET-TOGETHER*					1830	*INFORMAL GET-TOGETHER*		

W O R L D H E A L T H ORGANIZATION

ORGANISATION MONDIALE DE LA SANTE

REGIONAL OFFICE FOR THE WESTERN PACIFIC
BUREAU REGIONAL DU PACIFIQUE OCCIDENTAL

THE SECOND MEETING ON VACCINE PREVENTABLE DISEASES LABORATORY NETWORKS IN THE WESTERN PACIFIC REGION

WPR/DCC/04/EPI(1)/2010/IB/2
19 February 2010

Manila, Philippines
22 to 26 February 2010

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