SEVENTH MEETING OF VACCINE-PREVENTABLE DISEASES LABORATORY NETWORKS IN THE WESTERN PACIFIC REGION

26–29 September 2017
Manila, Philippines
MEETING REPORT

SEVENTH MEETING OF VACCINE-PREVENTABLE DISEASES
LABORATORY NETWORKS IN THE WESTERN PACIFIC REGION

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NOTE

The views expressed in this report are those of the participants of the Seventh Meeting of Vaccine-Preventable Diseases Laboratory Networks in the Western Pacific Region and do not necessarily reflect the policies of the conveners.

This report has been prepared by the World Health Organization Regional Office for the Western Pacific for Member States in the Region and for those who participated in the Seventh Meeting of Vaccine-Preventable Diseases Laboratory Networks in the Western Pacific Region in Manila, Philippines from 26 to 29 September 2017.
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Keywords:

Laboratories / Measles / Poliomyelitis / Poliovirus Vaccines / Rubella / Vaccines
ABBREVIATIONS

AFP   acute flaccid paralysis
bOPV   bivalent oral polio vaccine
cVDPV   circulating vaccine-derived poliovirus
CRS   congenital rubella syndrome
DBS   dried blood spot
EV   enterovirus
ELISA   enzyme-linked immunosorbent assay
EPI   Expanded Programme on Immunization
EQA   external quality assessment
ES   environmental surveillance
FTA®   fast technology for analysis of nucleic acids
GAPIII   Global Action Plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of oral polio vaccine use
GMRLN   Global Measles and Rubella Laboratory Network
GPEI   Global Polio Eradication Initiative
GPLN   Global Polio Laboratory Network
GPLNMS   Global Polio Laboratory Network Management System
GSL   global specialized laboratory
HFMD   hand, foot and mouth disease
IgG   immunoglobulin G
IgM   immunoglobulin M
IPV   inactivated poliovirus vaccine
ISO   International Organization for Standardization
ITD   intratypic differentiation
JRF   WHO/UNICEF Joint Reporting Form
LabNet   laboratory network
L20B   a mouse cell line (L-cells), genetically engineered to express the human poliovirus receptor
MCV   measles-containing vaccine
MeaNS   Measles Nucleotide Surveillance
MMR   measles, mumps and rubella
mOPV   monovalent oral polio vaccine
NGS   next-generation sequencing
NIHE   National Institute of Hygiene and Epidemiology
NIID   National Institute of Infectious Diseases
NMRL   national measles and rubella laboratory
NPEV   non-polio enterovirus
NPL   national polio laboratory
OPV   oral polio vaccine
PAEDS   Paediatric Active Enhanced Disease Surveillance
PASRS   Polio AFP Surveillance and Reporting System
PCR   polymerase chain reaction
PEF   poliovirus-essential facility
PIM   potentially infectious material
PRN   plaque reduction neutralization
PT   proficiency test
PV   poliovirus
RCV   rubella-containing vaccine
RD   human rhabdomyosarcoma
RNA   ribonucleic acid
RT-PCR   reverse transcriptase polymerase chain reaction
rRT-PCR   real time reverse transcriptase polymerase chain reaction
RIVM       National Institute for Public Health and the Environment (Netherlands)
RLC       regional laboratory coordinator
RRL       regional reference laboratory
RVC       Regional Verification Commission for Measles Elimination
RubeNS    Rubella Nucleotide Surveillance
SIA       supplementary immunization activity
SL        Sabin-like
tOPV       trivalent oral polio vaccine
UNICEF    United Nations Children’s Fund
US CDC    United States Centers for Disease Control and Prevention
VDPV      vaccine-derived poliovirus
VIDRL     Victorian Infectious Diseases Reference Laboratory
VI        virus isolation
VIIS      virus isolation, identification and sequencing
VP1       viral capsid protein
VPD       vaccine-preventable disease
WHO       World Health Organization
WPV       wild poliovirus
SUMMARY

The Seventh Meeting on Vaccine-Preventable Diseases Laboratory Networks in the Western Pacific Region was held in Manila, Philippines from 26 to 29 September 2017 to review the performance and identify the challenges of the poliovirus and measles and rubella network laboratories in the Region.

The meeting reviewed ways to further strengthen the performance of network laboratories and also monitor the implementation of recommendations from the Sixth Meeting of Vaccine-Preventable Diseases Laboratory Networks in September 2016. The meeting provided an opportunity to discuss strengthening the quality and sensitivity of poliovirus detection, enhancing poliovirus surveillance through the introduction of environmental surveillance in key countries and the application of the WHO Global Action Plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of oral polio vaccine use (GAPIII) for the containment of poliovirus in the laboratory network. Ways to improve the quality and timeliness of laboratory-based surveillance, the challenges of identifying funds for the procurement and delivery of high-quality laboratory supplies, the importance of improving molecular surveillance for support of verification of elimination of measles and rubella, and the strengthening of rubella and congenital rubella syndrome (CRS) surveillance were also discussed.

This meeting was funded by Korea Centers for Disease Control and Prevention.
1. INTRODUCTION

1.1 Meeting organization

Eighty-nine participants from network laboratories (12 poliomyelitis network laboratories and 18 measles and rubella network laboratories), temporary advisers, observers and WHO staff from 21 countries attended the meeting. The list of participants is available in Annex 1.

The meeting was organized in two sessions over four days to cover poliomyelitis (26–27 September) and measles and rubella (28–29 September). The meeting programme is available in Annex 2.

1.2 Meeting objectives

The objectives of the meeting were:

1) to review the progress and identify challenges of the poliomyelitis (polio) network laboratories, to support the polio eradication programme and to ensure the quality of performance of network laboratories;

2) to identify challenges and define the way forward for the expanding roles of the polio network laboratories in the implementation of the WHO Global Action Plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of oral polio vaccine use (GAPIII);

3) to review the progress and identify challenges of measles and rubella network laboratories to support the measles and rubella elimination programme, and to ensure the quality of performance of network laboratories; and

4) to discuss strategies to strengthen the coordination and collaboration between measles laboratory and epidemiology surveillance to ensure quality and timely collection of appropriate samples for measles virus isolation (VI), efforts to improve obtaining of continuous genotype data of measles virus in some countries, and further improve the molecular detection capacity and data reporting.

2. PROCEEDINGS

2.1 Polio LabNet

2.1.1 Polio endgame strategy: update on global and regional progress

The World Health Organization (WHO) Western Pacific Region was the second of the six WHO regions to be certified as polio free in October 2000. The last indigenous case was reported from Cambodia in 1997. Since certification, the Western Pacific Region has had several imported cases of both wild poliovirus (WPV) and circulating vaccine-derived poliovirus (cVDPV), but transmission was halted each time and polio-free status was retained. The last imported WPV case was detected in China in 2011, and the last cVDPV was detected in the Lao People’s Democratic Republic in January 2016. An ambiguous vaccine-derived poliovirus (aVDPV) was reported from China in 2017 and isolated from an acute flaccid paralysis (AFP) case.

Overall population immunity to polio in the Region is relatively high. In 2016, the WHO/UNICEF Joint Reporting Form (JRF) identified 20 countries that achieved more than 90% coverage with three doses
of polio vaccine, five countries reported coverage between 80% and 90%, five countries reported less than 80%, and six Pacific island countries did not submit reports. Overall, AFP surveillance performance is at a high level in the Region and well above the regional threshold for the main indicators over the last 3–4 years. After the switch from trivalent oral polio vaccine (tOPV) to bivalent oral polio vaccine (bOPV) in April 2016, Sabin type 1 and 3 viruses are being isolated from both AFP cases and environmental samples. Reassuringly, the last Sabin type 2 isolate was from environmental samples collected in China in August 2016. From September 2016, there were no Sabin type 2 viruses isolated either from AFP cases or environmental samples. The polio risk assessment completed in 2016 classified the majority of the Region at low risk. Cambodia and the Lao People’s Democratic Republic were classified as medium risk, while the Philippines and Papua New Guinea were high risk. AFP surveillance reviews were conducted in or are planned for the following priority countries:

- Philippines as part of a VPD surveillance review in 2015
- Lao People’s Democratic Republic as part of outbreak response assessments in 2016 and March 2017
- Viet Nam as part of VPD surveillance review in November 2017
- Papua New Guinea in December 2017

2.1.2 Update on global WPV transmission and status of GPLN

Globally, good progress has been achieved with polio eradication in 2017. As of September 2017, 11 WPV1 AFP cases were detected in two countries – Pakistan and Afghanistan – the lowest numbers ever. Afghanistan reported 10 cases in the previous 12 months and Pakistan reported 8 cases. However, in July 2016, WPV1 was detected in four cases in Borno State, Nigeria with genetic evidence of 2-5 years undetected transmission. No WPV3 cases have been detected since November 2012. Environmental surveillance (ES) has detected five clusters of PV1 in Pakistan and Afghanistan from 82 positive samples. Pakistan WPV transmission hotspots were detected through ES and include the Quetta block and Karachi. Seroprevalence shows population immunity in Pakistan as very high for types 1 and 3 but low for type 2 as many of the study children were born after the switch from tOPV to bOPV.

Following the switch in 2016, cVDPV2 outbreaks were detected in Pakistan (N=5 cases) and Nigeria (N=3 cases) in 2016, and in the Democratic Republic of the Congo (N=12 cases) and Syria (N=39 cases) in 2017. Supplementary immunization activities (SIAs) of monovalent oral polio vaccine type 2 (mOPV2) vaccines were conducted or are planned for each of the outbreaks.

For the polio eradication endgame, surveillance of poliovirus (PV) needs to be sustained, even after certification of eradication and the structure and functions of the Global Polio Laboratory Network (GPLN) need to be maintained. Options include either: mainstreaming the polio activities in an integrated vaccine-preventable disease (VPD) laboratory network (LabNet); a national public health laboratory network; or under a health emergency/high threat pathogens type framework.

GPLN workload peaked in 2016 with 241 999 samples tested. There is an increase in the number of laboratories performing intratypic differentiation (ITD) with 103 having this capacity in 2016 and 47 laboratories are performing VI only. There has been a continual expansion of ES capacity but there have been challenges, including lengthy processes for the procurement of goods, site selection and training activities.
2.1.3 Update of regional polio LabNet: expansion of ITD laboratories and ES

The Western Pacific Region’s polio LabNet consists of 43 laboratories, 38 of which perform ITD and a further three are pending accreditation to perform ITD functions. Five laboratories are performing ES (Australia, China, Japan, Malaysia and the Philippines) with Viet Nam planned to start in 2018. Cambodia, the Lao People’s Democratic Republic and Papua New Guinea are also being considered for starting ES with the support of the specialized/reference laboratories at National Institute of Infectious Diseases (NIID) in Japan and Victorian Infectious Diseases Reference Laboratory (VIDRL) in Australia. Laboratories in the polio LabNet continue to perform well. All of the laboratories passed the VI proficiency test (PT). Two laboratories experienced challenges with the 2016 VI PT, but passed after a repeat PT with a 100% score. Twelve of 41 laboratories did not pass the 2016 ITD/VDPV PT in January 2017, but subsequently eight passed a retest with a 100% score. The remaining four laboratories are awaiting shipment of the retest panels.

2.1.4 Report for global specialized laboratory and regional reference laboratories

Japan

The laboratory of enteroviruses (EVs) at NIID functions: as the national polio laboratory (NPL) for Cambodia, the Lao People’s Democratic Republic and Japan; as the regional reference laboratory (RRL) for Viet Nam, Mongolia and the Republic of Korea; and as the global specialized laboratory (GSL) for the polio LabNet in the Western Pacific Region. The GSL-NIID has been fully accredited. Japan has developed Sabin-derived inactivated polio vaccine, which will improve the safety of IPV production post eradication. An emerging immunity gap in oral polio vaccine (OPV) coverage in Japan occurred between 2011 and 2012 when public awareness of the risk of vaccine-associated paralytic polio (VAPP) was heightened. ES was introduced after IPV introduction in 2013; in 2016, 18 public health institutions performed ES covering a population of approximately 6 million. Several Sabin-like viruses have been detected. Sabin 3 PV was isolated in only one site in October 2014 after the switch to IPV in September 2012. The Japan International Cooperation Agency (JICA) maintains their support for training for VPD laboratory-based surveillance globally. Poliovirus-essential facilities (PEFs) in Japan include the GSL at NIID and four institutes within three Sabin-derived IPV manufacturers. The establishment of GAPIII-based biorisk management and national PEF certification are ongoing in collaboration with the Ministry of Health, Labour and Welfare and IPV manufacturers in Japan.

Australia

Australia introduced IPV exclusively from 2015 in the format of a paediatric combination vaccine given at 2, 4 and 6 months and 4 years of age. Three forms of surveillance occur for polio: (i) AFP and Paediatric Active Enhanced Disease Surveillance, (ii) EV, and (iii) environmental. ES started but stopped after an accident in the laboratory occurred, but reintroduction is planned in the near future. AFP detection rates have exceeded 1/100 000 since 2011, but stool collection rates have never reached the 80% minimum for two samples, or even one sample. Brunei Darussalam, Papua New Guinea and Pacific island countries and areas (PICs) are supported for AFP surveillance by VIDRL for the 12 months from September 2016 to September 2017. Non-polio enterovirus (NPEV) rates exceeded 10% except for Brunei Darussalam, which did not ship any samples in the 12-month period. VIDRL is fully accredited and achieved the following 2016 PV PT results: VI PT: 100%; ITD & VDPV reverse transcriptase polymerase chain reaction (RT-PCR) PT: 95%; and sequencing PT: 100%.
China

The Chinese Center for Disease Control and Prevention (China CDC) received 172 polio isolates and 80 polio isolates from polio provincial laboratories in 2016 and 2017 respectively. No PV2 has been found since the switch to bOPV. NPEV rates have dropped since 2012 and in 2017 (September) a 6% NPEV rate (annualized) was reported. A polio type 3 ambiguous VDPV was isolated in Inner Mongolia Autonomous Region in 2016 and in Henan Province in 2017. The viruses were not genetically linked and both were considered “young” VDPVs with 10 and 11 nucleotide differences to Sabin 3 detected, respectively. China CDC and all 31 provincial polio laboratories passed the WHO VI PT for 2016. In February 2017, the NPL in China CDC and 30 trained provincial polio laboratories conducted the ITD PT provided by the United States Centers for Disease Control and Prevention (US CDC)/WHO and all except eight laboratories passed (Qinghai, Guangxi, Guangdong, Chongqing, Inner Mongolia, Fujian, Hubei and Guizhou). A repeat ITD PT panels were provided by US CDC to these eight laboratories and all passed with a 100% score. China CDC conducted the viral capsid protein (VP1) sequencing PT provided by US CDC/WHO and passed with a 100% score. Thirty provincial laboratories are reporting cell sensitivity test results to the NPL regularly and all of their results are in the acceptable range. The Tibet polio laboratory is re-establishing their lot quality control standard and cell bank.

Under the national unified plan of National Authority for Containment (NAC), all WPV and potentially infectious materials (PIM) were destroyed before 31 June 2017 with the exception of the materials contained in Hebei Province and China CDC. The WPV materials from Hebei Provincial Laboratory were transferred to China CDC for further containment in December 2016. After the revival of the materials from Hebei Province, a total of 15 WPV strains were identified and contained. A national OPV2/Sabin 2 PV inventory is being conducted in all biomedical facilities to identify those with infectious and/or potentially infectious OPV2/Sabin 2 PV materials since October 2016 in China. The inventory is planned to be completed by 31 December 2017.

2.1.5 Report from the national polio laboratories

Hong Kong SAR (China)

The NPL in Hong Kong SAR (China) is the centralized virology laboratory for the diagnosis of EV infections and performs AFP, EV and serological surveillance. Performance of AFP surveillance in Hong Kong SAR (China) has been satisfactory and all indicators above the target value have been achieved in 2016. For 2017 (up to August), only seven out of nine cases (78%) had adequate stool specimen for laboratory testing. In 2016 and 2017, 10 cases with 29 stool samples and 9 cases with 27 stool samples were investigated, respectively, and there were no PV or other EVs isolated. EV PCR positive stool/rectal swab samples from non-AFP samples received were inoculated into L20B cell lines and one Sabin-like PV3 was isolated in 2016. Cell sensitivity testing and mycoplasma detection have been carried out in L20B and human rhabdomyosarcoma (RD) cells with satisfactory results. Polio serosurvey was conducted every 5 years and the results showed that over 82% of the subjects had antibody to PV1 and PV3 among four age groups (1–10 years old, 11–20 years old, 21–30 years old and 31 years old or older), although type 2 was not done due to containment issues. Two university laboratories in addition to the public health laboratory (PHL) were identified as having Sabin PV material during a 2015 containment survey. All PV material was destroyed in 2016 and no PEF will be established in Hong Kong SAR (China). The major challenge is to establish an alternative method to replace the microneutralization test for detecting PV antibodies.
Malaysia

Malaysia performs AFP surveillance in addition to surveillance for hand, foot and mouth disease (HFMD), EV and mouse embryonic fibroblasts. A minimum detection of 95 AFP cases per year is required to meet the indicator. A total of 172 cases were detected in 2016 and 96 cases in 2017 (up to September), with adequacy of stool collection exceeding 80% for both years. IPV has been used nationwide since 2010 and OPV was withdrawn in 2015, with all stocks destroyed in 2016. Malaysia has not retained any WPV or PIMs, and there are no plans to establish a national repository for PV. The country has developed a National Contingency Plan for Detection and Response to Importation of Wild Poliovirus. ES started in January 2012. All viruses detected have been NPEVs with no PVs detected. The NPL scored 80% for the VI PT, 85% for the 2016 ITD PT and 100% for the sequencing, but achieved 100% after repeating the VI and ITD PTs. It was reported to be a challenge for specimens from AFP cases to be sent to the laboratory immediately after collection. The issue was addressed by informing hospital wards of the importance of sending the stool specimens immediately to the NPL.

Mongolia

Mongolia has a population of 3,119,935 with 983,075 (31.5%) under 15 years of age; hence, the estimate for AFP cases is nine cases per year. Nationwide coverage on full doses of bOPV vaccination is 98.1% as of August 2017. The AFP surveillance rate is 0.78 and 0.8 for 2016 and 2017 (September) with adequate stool collection rates of 71% and 80%, respectively. In 2016 and 2017, NPEV rates were 7% and 0%, respectively. In response to the low AFP surveillance rate, a preparedness plan, the National Response Plan for Wild Polio Importation, was developed. A Strengthen Surveillance System for Measles/Rubella and AFP training was organized between August and September 2017 and included 21 provinces. Another training will be organized in November 2017 including districts of Ulaanbaatar City. Non-AFP surveillance includes AFP contacts, healthy children and children with differential diagnosis. An NPEV rate of 18.9% (N=60) was found in these non-AFP individuals. Plans are being developed to conduct a serosurvey for poliovirus antibodies to assess immunity levels. It is anticipated that ITD will be fully implemented and then subsequently accredited by the WHO Regional Office for the Western Pacific.

New Zealand

New Zealand has an AFP detection target of nine per year; in 2016, 10 cases were detected. AFP cases had a 0% NPEV rate for 2016; however, a 41% NPEV rate was detected for 43 non-AFP stools detected through the national EV surveillance system. The national response plan for WPV and VDPV importation has been established since 2009 and is constantly being reviewed by the National Certification Committee for the Eradication of Poliomyelitis (NCCEP). OPV was replaced by IPV in 2002 and since 2003, three non-AFP cases have been reported with Sabin-like strains – two in 2003 and one in 2005. A proposal for ES after the declaration of the eradication of PV2 will be submitted for grant funding at key border sites. The Institute of Environmental Science and Research (ESR) quality assurance system is doing well, with new polio cell lines received from the WHO RRL in Melbourne in January 2017 and all PV PT panels have passing scores of 95–100%.

In May 2016, all PV2 reference strains and all samples (about 5000 samples) that could contain PV2 were destroyed by double autoclaving at the NPL prior to disposal at a certified biological waste disposal facility. Polio serology testing was also moved to the Physical Containment Level 3 (PC3) facility at the NPL post switch. A follow-up stocktake of all New Zealand laboratories, and research
and academic facilities, identified four other laboratories that have stored PVs who have subsequently confirmed destroying these samples. Challenges identified by the NPL include low volumes of AFP samples and maintaining polio technical back-up capability due to staff turnover.

**Philippines**

The Philippines NPL is responsible for the AFP, HFMD and ES programmes of the Department of Health and also serves as the secretariat of the National Task Force for the Laboratory Containment of Polio.

In 2017, the Philippines attained only 74% of OPV3 coverage while IPV was only at 34%. National AFP detection rates were 1.05 (per 100 000) for 2016 and 0.86 for 2017 (September) with an 80% stool collection rate. An NPEV rate of 7.6% was reported for 2016. As the Philippines is assessed as high risk for PV transmission, ES has been performed since 2017 using a double phase separation method, after training was received in 2015. A total of 25 isolates have been detected from three ES sites surveyed, with 10 NPEV, one Sabin-like PV1 and 14 Sabin-like PV3. Other activities of the NPL include the HFMD testing that started back in 2012, resulting in isolation of 2.1% EV71, 2.2% Coxsackie-A16 (CA16), 22.5% Coxsackie-A6 (CA6) and 42% other EVs from 2868 samples with a widespread infection in the country. In 2016, 441 HFMD cases were identified with 311 yielding EVs, 85% of which were typed as CA6. In 2016, the NPL scored 100% for the VI PT and 90% for the ITD PT. For containment, the Philippines will be considered a non-PEF and has destroyed all stocks of PV2, and OPV2 was withdrawn in April 2016. The national inventory of facilities with PIM and PVs is ongoing. Challenges facing the laboratory include identifying the reason for the low NPEV rate. The NPL has strengthened quality assurance measures and investigated improvement of the reverse cold chain.

**Republic of Korea**

Since 2005, only the IPV schedule was introduced into the Republic of Korea. An AFP surveillance system has been established in 50 paediatric neurology hospitals and in conjunction with an AFP enhancement research project by the Catholic University of Korea. National AFP detection rates are 1.01 for 2016 (per 100 000) and 0.6 for 2017 (September) with an 85.7% stool collection rate in 2016 and 95.1% in 2017. The NPL achieved scores of 100% for both the WHO VI and ITD PTs in 2016.

**Singapore**

The NPL is situated in the Virology Laboratory, Department of Microbiology, Singapore General Hospital (SGH). In 1996, Ministry of Health enhanced AFP surveillance to include all patients with “at risk” diseases that could lead to AFP, whether or not AFP is present. In 2014, the National Committee for the Certification of Poliomyelitis Eradication (NCC) reviewed a list of “at risk” diseases. An AFP rate of 1.17 was reported in 2016. In the period September 2016 –July 2017, samples tested in the NPL included: 10 AFP and 304 samples from non-AFP, non-stool specimens and ES samples. Two EVs, Coxsackie A (CA2 and CA6) and no PVs were detected. In 2016 the NPL achieved scores of 100% for both the WHO VI and sequencing PTs and 90% for the ITD PT. For containment, all PV2 materials were destroyed by autoclaving on 22 July 2016. The NPL reports that clinicians are ordering PCR tests instead of virus culture and the laboratory is receiving only few specimens for EV culture and NPEV rates are becoming very low.
Viet Nam

Hanoi
The EV laboratory, the National Institute of Hygiene and Epidemiology (NIHE), Hanoi plays the role as a NPL responsible for detecting PVs and NPEVs from specimens collected under AFP and HFMD surveillance programmes in the northern part of Viet Nam. The AFP rate is greater than 10% in Hanoi but below 10% in most of the other provinces served by NIHE. The NPL at NIHE in northern Viet Nam serves 28 provinces in the north and 6 provinces in the centre of Viet Nam. Between 2016 and August 2017, 334 AFP cases were enrolled in the AFP surveillance, of which 333 (99.7%) cases have two adequate stool specimens. Out of 667 specimens cultured on both L20B and RD-A, 19 samples were L20B-positive. However, only seven samples from five cases were confirmed as Sabin PVs and 12 were either NPEV or non-enterovirus by ITD. In 2016, NIHE achieved scored 100% for the WHO VI PT and 75% for the ITD PT. A second ITD panel will be tested shortly. All PV2 samples were destroyed in October 2016. The low specificity of L20B for PVs is now a challenge for the laboratory and needs to be resolved including cell cross-contamination. ES is planned to be implemented in NIHE in 2018, for which the provision of equipment, supplies, human resources and training are essential.

Ho Chi Minh City
The Laboratory of Enteroviruses, Pasteur Institute (PI), Ho Chi Minh City, has been a member of the regional polio LabNet in the Western Pacific Region since 1992. The laboratory is ISO 15189 compliant and has been accredited since 2011. The laboratory is responsible for detecting EVs from AFP and HFMD surveillance in the southern half of Viet Nam. No PV was isolated in 2015 and 2017, although there were five polio cases identified in 2016: one case with PV1 SL+PV3 SL, one case with PV2 SL+ PV3 SL, and three cases with PV3 SL. From 2015 to 2017, the NPEV isolation rates were 10%, 9% and 16.5%, respectively.

Testing of specimens from severe and fatal HFMD cases from 2015 to 2017 showed the presence of EV71 in 55% of specimens in 2015, 20% of specimens in 2016 and 17% of specimens in 2017. In 2015, CA6 made up 45% of the other EVs. In 2016, however, CA10 made up 50% of other EVs. Sequencing the VP1 region of EV71 strains showed sub-genotypes B5 (75%) and C4 (25%). In 2016, PI achieved scores of 100% for the WHO VI PT, and 50% for the ITD PT. A second ITD panel will be tested shortly.

2.1.6 Progress on direct detection of PV in stool samples/laboratory detection without VI

In order to speed up detection of PV and to reduce the amount of infectious PV that must be contained, the GPLN has been developing methods for direct detection of PV in stool specimens, environmental samples or environmental concentrates. Various approaches have been explored in the past, such as enrichment of PV by binding virus particles to magnetic beads bound to the poliovirus receptor (PVR), a method pioneered by the GSL NIID in Japan. The GSL US CDC has done exploratory work with various methods and has developed two direct detection procedures/workflows that are being piloted at US CDC using about 180 stool specimens in parallel with the standard WHO VI algorithm. One procedure uses Zymo ZR Viral RNA Kit (Zymogen columns) to concentrate PV into a smaller volume prior to ribonucleic acid (RNA) extraction, which increases the amount of viral RNA that can be added to an rRT-PCR reaction. The other procedure uses His-tagged PV receptor. The commercially available His-tagged receptor binds to PV particles, and nickel beads pull down the virus–receptor complex, resulting in enrichment of PV particles. RNA can be extracted from the enriched PV material. Partial direct detection pilot results will be presented at the Small Working Group (SWG) meeting on 9–11 October 2017. It is expected to make recommendations to proceed with additional pilot
experiments in GPLN laboratories, if warranted. WHO headquarters and the Small Working Group have started planning for logistics of implementation of direct detection methods, including cost, training, phasing and referral of samples.

2.1.7 Progress on Rotor Gene/Bio Rad/Stratagene ITD 5.0 validation

The ABI7500 real-time PCR instrument is widely used in the GPLN. In order to provide additional instrumentation options, alternate platforms have been validated for use with ITD 5.0: Stratagene MX3000/3005, BioRad CFX and Rotor Gene Q. Appropriate conditions for each instrument have been added to the ITD5.0 insert. The Light Cycler has not been validated for ITD5.0. Additional instrumentation is under evaluation. Advantages of the BioRad CFX are LED technology, relative low cost and low maintenance. BioRad CFX can be run from a touchscreen; a separate computer is not required. Rotor Gene has LED technology, has no need for calibration and is a good option from a manufacturer outside the United States of America.

2.1.8 Alternative method for microneutralization test (Luminex)

A Luminex assay for EV microneutralization was compared with conventional cell culture microneutralization at the NPL in Hong Kong SAR (China). For the Luminex, PVs (Triton X-100 inactivated) were covalently conjugated to three different color-coded microspheres for direct detection of the three types of PV immunoglobulin G (IgG) antibodies. Luminex IgG detection versus microneutralization (PV1 & PV3) showed 45 discordant results from 355 samples. A total of 40 samples were positive by Luminex and negative by microneutralization, and five were positive by microneutralization and negative by Luminex. Discrepancies between Luminex and microneutralization results occurred in up to 11.3% (45 out of 400 test samples). The Luminex method evaluated was not recommended for further development for detecting PV IgG antibodies.

2.1.9 Next-generation sequencing

A small working group has been formed to examine the utility of next-generation sequencing (NGS) for future use in the polio eradication initiative. The group consists of representatives from the Pasteur Institute (France), National Institute for Biological Standards and Control (United Kingdom of Great Britain and Northern Ireland), NIID (Japan), National Institute for Public Health and the Environment (RIVM) (Netherlands) and US CDC. A pilot proficiency panel for NGS testing of stools, culture material and sewage samples was created and disseminated to participating laboratories.

The National Enterovirus Reference Laboratory, Australia developed a new algorithm for the detection and characterization of EVs in 2016, which incorporates NGS methods. The laboratory received the NGS pilot study panel, which was investigated using the new EV typing algorithm. Full-capsid PCR amplification of NPEVs and PVs followed by sequencing using NGS methods was found to be sensitive and cost-effective for the examination of samples known to contain multiple EV serotypes.

2.1.10 Report on 2016 VI PT from RIVM

A panel of 10 VI samples was distributed to 130 of 146 laboratories in the GPLN as the VI PT for 2016. The results are summarized in Table 1.
Table 1: VI PT 2016 results

<table>
<thead>
<tr>
<th></th>
<th>Global</th>
<th>Western Pacific Region</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labs that passed VI PT-2016-I</td>
<td>81.5%</td>
<td>91%</td>
</tr>
<tr>
<td>Labs with 100% score</td>
<td>93/130</td>
<td>40/42</td>
</tr>
<tr>
<td>Retests/VI PT-2016-II:</td>
<td>13 laboratories</td>
<td>1 lab</td>
</tr>
</tbody>
</table>

The Western Pacific Region laboratory that received the retest subsequently achieved a 100% score. Samples 2 and 10 were challenging and contained PV1 in low concentration. Sample 5 contained EV18 and was missed by 22 laboratories, which may reflect a lack in sensitivity of RD cells. The 2017 VI PT will be shipped to laboratories of the Western Pacific Region directly by RIVM sometime between September and November 2017.

2.1.11 Report on 2016 ITD PT and report on 2015/2016 sequencing PT

The 2016 ITD PT tested the ability of a laboratory to follow the ITD5.0 algorithm and was designed to be challenging, in anticipation of the possible need to work at the limit of detection in future direct detection methods. Frequent laboratory errors included lack of detection of WPV1 in a homotypic mixture and incorrect reporting of type 2 results. Administration of the ITD PT highlighted a change, which is the discontinuation of a threshold cycle (Ct) cut-off in determining positive signals. All amplification signals must be compared to the negative control during data analysis. There are plans to distribute the 2017 ITD PT in the coming months.

A total of 27 laboratories took the sequencing PT 2015–2016: 22 laboratories passed and five failed. Three of the five failing labs passed upon re-testing. The 2017 sequencing PT is ongoing at this time. A sequencing PT panel has been shipped to one lab in the Western Pacific Region; the remaining sequencing laboratories are waiting to receive the panels, which are at the WHO Regional Office for the Western Pacific. The 2017 sequencing PT panels consist of six samples; three lyophilized non-infectious RNA transcripts and three fast technology for analysis of nucleic acids (FTA) cards containing IPV isolates. Results must be forwarded along with documentation and raw data within the seven-day time limit that is required for routine AFP samples.

2.1.12 Quality assurance and quality control

Regional polio network laboratories continue to report results of cell sensitivity tests and titration experiments to the regional laboratory coordinator for review and for implementation of appropriate corrective actions. All 42 of the 43 laboratories which reported to the Regional Office regularly presented data in a graphic format by serotype for easy monitoring of trends over time. Sabin 2 reference strains have been omitted from cell sensitivity testing (as per GPLN recommendation in June 2015) since April 2016. Cell lines are obtained from authenticated sources such as US CDC, NIID, VIDRL and China CDC, and mycoplasma testing is performed by most laboratories. Some laboratories are using Introne e-MycotM plus Mycoplasma PCR Detection kit. PV antibody testing in GPLN facilities is recommended to document the immune status of polio laboratory staff against all three types of PV, and to determine their potential need for immunization as a requirement for meeting GAPIII conditions. A total of 35 of 43 laboratories in the Region have had 160 staff members tested with 8 laboratories yet to supply information. Of these, 85.6% have protective PV2 titres.
2.1.13 Implementation of GAPIII in the Western Pacific Region

Progress is continuing within the Region for the implementation of GAPIII. Biorisk management training for PEFs and NACs was carried out in 2015 and 2016, and auditors training for the Containment Certification Scheme (CCS) occurred in 2017 with trainings in the local language for China, Japan and Viet Nam. The strong advocacy from the WHO Regional Office for the Western Pacific and the commitment from the Region’s countries has resulted in a reduced number of PEFs than originally proposed by Member States. The Western Pacific Region is working with countries to establish NACs and to include containment in certification reports for the Regional Certification Committee (RCC). NACs have been identified but most are not functional and have not developed an audit team. Phase 1a for the containment of WPV2/VDPV2 has been completed in the Region. The Western Pacific Region will have 16 PEFs: Australia (N=1), China (N=8), Japan (N=5), Republic of Korea (N=1) and Viet Nam (N=1). Every country in the Region has reported challenges in implementing GAPIII in their national legislation. The Philippines has used a presidential decree to implement their legislation. PEFs are reporting they are not ready for GAPIII, especially the requirement for showers and the necessary upgrading of biosecurity procedures.

2.1.14 Regional status of PV containment activities in the European Region

The European Region consists of 53 Member States and a population of 900 million. The Region has 47 polio laboratories in 37 countries with an overall proliferation of laboratory infrastructure in both government and private sectors. Forty countries are non-PEF, and some of the 13 PEF countries are considering the value and scale of work of being a PEF. National PV containment coordinators have been identified in most countries. One of the challenges specific to Europe is the high number of vaccine manufacturing facilities: 13 countries have at least 30 PEFs and 6 countries are hosting 12 vaccine manufacturing sites.

In April 2017, one of the workers in a vaccine manufacturer of IPV was infected with WPV after an incident in the facility, highlighting the hazards of IPV manufacturing in a post-eradication scenario.

2.1.15 Update from Global Certification Commission and Containment Advisory Group meetings

Containment is critical to maintain polio eradication and involves all 194 WHO Member States and 21 non-member countries and territories. It has a long time horizon, for as long as PV is retained, containment will be required. The two phases of containment are: (i) to reduce the number of facilities containing PV2 by destroying unneeded PV2 and designating PEFs for needed PV2; and (ii) to reduce the risk in remaining facilities. The Global Commission for the Certification of Poliomyelitis Eradication (GCC) is a containment oversight body with a meeting planned in October 2017 to determine global readiness criteria to declare polio eradication and to address containment plans for PVs 1, 2 and 3. A Containment Advisory Group (CAG) was established in March 2017 to address issues related to GAPIII, including guidance on handling of identification and categorization of PV PIMs. For the issue of “showering out” in PEFs, the Containment Advisory Group recommended that it is mandatory except for facilities employing closed systems demonstrating validated primary containment. IPV supply needs to increase to meet global demands and of concern is the evidence of recent WPV release from IPV production facilities in 2014 and 2017.
2.1.16 WHO guidance on identification of PIMs – completion of Phase 1

Phase 1a has been completed but several cVDPV2 outbreaks in the period post switch have required a response with mOPV2. Phase 1b requires guidance for the completion of phase 1 of GAPIII by assisting non-PV facilities to assess the risk of PV PIM in their possession and to implement appropriate risk reduction consistent with GAPIII. PIMs are considered as faecal or respiratory secretion samples collected for any purpose in a time and a geographic area where WPVs (including cVDPV) were in circulation, or OPV was in use and products of such materials that were propagated in PV-permissive cells or animals. Examples of non-PV facilities at risk include laboratories responsible for testing samples for measles, rotavirus, EVs, enteric bacteria, hepatitis, influenza and other respiratory illnesses, sewage and water. Strategies consistent with GAPIII include risk elimination and the scientific value of retaining PIM should outweigh the public health value of its destruction. If the decision is for the PIM to be maintained in a facility, then strong risk reduction and oversight requirements are required of the Member State. It was recommended by the Containment Advisory Group that GAPIII be amended so that PV nucleic acid can be handled outside of containment, under certain specified conditions.

2.1.17 Challenges with identification of NACs

China has a State Council-issued policy for the Regulation on the Biosafety Management of Pathogenic Microorganism Laboratory, which encompasses biosafety management of laboratories and laboratory activities. The National Health and Family Planning Commission (NHFPC) defined a policy in December 2016 to establish PV containment offices at national and provincial levels and required the transfer to PEF or destruction of WPV by end of December 2016. Registration and proper containment of all PV2 (seed, bulk, products and testing materials) in polio vaccine manufacturers and quality control laboratories responsible for polio vaccine is required by June 2017. There are currently two proposals for the establishment of NACs in China: (i) one NAC with expertise from NHFPC and the China Food and Drug Administration; or (ii) NHFPC to validate the NPL and the China Food and Drug Administration to validate the National Control Laboratory (NCL) and manufacturers.

2.1.18 Laboratory performance strategies in the GPLN in the context of PV containment

The global containment programme has reached the stage of certification of WPV2 containment (phase Ila) for PEFs holding WPV and in the early phase of certification of OPV2/Sabin 2 PV containment (phase IIb) for PEFs holding OPV/Sabin only. Non-PEFs require the adoption of measures for the safe handling of new samples potentially containing PV material. A Biorisk Management Programme (BRM) started in 2010 for the inventory and destruction of existing PV2 material and safe handling of new samples potentially containing PV material. Although training sessions on the Biorisk Management Programme and GAPIII were held in all six WHO regions, the level of implementation within laboratories has been variable. Currently, the GPLN is supporting laboratories to identify and correct gaps and weaknesses in their programme. There are challenges in meeting GAPIII requirements while maintaining diagnostic capacity, including PV2 RNA storage and handling, need for a “shower-out” in PEFs, certification of PEFs and the verification of containment. A series of guidance papers has been developed for the GPLN: (i) Safe handling and storage of PV2; (ii) Update on ITD molecular assays and testing algorithm; and (iii) PV antibody testing for GPLN personnel using dried blood spot collection.
2.1.19 Preparing polio laboratory to become a PEF

In December 2015, the Australian Government’s Department of Health nominated the GPLN RRL, VIDRL, as a PEF for Australia. The reasons are its historical, national and regional role in polio surveillance, its ISO and WHO accredited diagnostic and reference facilities, and their experience of rapid laboratory investigation of PV importations in the Western Pacific Region. Some of the reservations raised include uncertainty around the certification process, what resources will be needed and the cost of running a PEF. VIDRL has facilities to meet the containment levels required of a PEF, including: Physical Containment Level 3 (Biosafety Level 3 (BSL-3)) with shower; class 2 biosafety cabinets (BSC) and shower on exit; class 3 biosafety cabinet and shower if the biosafety cabinet fails; and PC-4 (BSL-4), which currently exceeds requirements. VIDRL laboratory staff and the appointed NAC have completed Biorisk Management training. Some of the challenges for establishing a PEF are: providing and documenting evidence; checking for compliance with GAPIII line by line; ensuring all WPV2, VDPV2, Sabin 2 are contained or destroyed; and establishing a single inventory that accounts for every sample tube held by the laboratory.

2.1.20 Preparing polio laboratory to become a non-PEF

The Philippines NPL, the Research Institute for Tropical Medicine (RITM), has elected to become a non-PEF in the Region and destroy their stocks of PVs. The Institute will continue to provide AFP surveillance, HFMD surveillance, ES, laboratory containment of polio, research and training, and routine diagnostics, but it will implement a non-retention policy and will destroy PV materials, starting with PV2.

2.1.21 Global perspective on ES

The focus of ES of PV is the detection of evidence of any infection with PV in a community, including AFP cases (< 1%) and the non-paralytic or asymptomatic individuals (> 99%) infected with PV. ES is a lengthy and tedious process and has challenges in its implementation and sustainability, but it enhances the detection of PV where AFP surveillance may be suboptimal or suspect. ES initiated by the Global Polio Eradication Initiative (GPEI) includes more than 32 countries outside Europe (N=25) and in every WHO region. It is planned for more countries to establish ES in the Western Pacific Region, including; Papua New Guinea, Viet Nam, Cambodia and the Lao People’s Democratic Republic, in addition to China, Malaysia, the Philippines, Singapore and Australia, which have already established ES. ES has a number of limitations, including appropriate selection of sampling sites with geographic and demographic representativeness. It is critical that ES be integrated in the national polio surveillance programme. A proposal for developing ES standards is under way with indicators and targets to monitor performance. A PT will be developed and rolled out in 2018 and an accreditation checklist will be implemented in 2018 after piloting in 2017.

Environmental surveillance of poliovirus and non-polio enteroviruses in China

China conducts AFP surveillance, ES, and EV surveillance (HFMD and acute haemorrhagic conjunctivitis). ES was established in China 2008 for the early detection of WPV or VDPV in high-risk areas in the country and to monitor Sabin virus in sewage after the tOPV switch to bOPV in 2016. A two-phase separation concentration method, based on the National Public Health Institute of Finland (KTL) method, is used. Eight ES workshops and training courses have been held in China since 2008. Since 2011, nine provinces have established routine ES for regular and long-term surveillance and will contribute to maintaining polio laboratory capacity after global polio eradication. Large
numbers of EVs have been detected from ES, including 1396 PVs and 1379 NPEVs from 2008 to June 2017. WPV1 was found in Xinjiang during the outbreak in 2011 and eight VDPV2s were detected in five provinces between 2012 and 2015. The large number of PV and NPEV isolates identified from ES has stretched resources, and the programme requires further funding support.

2.1.22 Data management and reporting

Countries report data to the WHO Regional Office for the Western Pacific in several different databases – Excel, CVS, Access – and different reporting formats – line list (all countries for AFP) and aggregated (China for ES), and either web-based (Polio AFP Surveillance Reporting System, or PASRS) or Access database for reporting. Reporting timelines to the Regional Office are weekly for AFP specimens and environmental samples and at least monthly for aggregated laboratory data for non-AFP specimens. The web-based PASRS is used by some countries and has been enhanced in the past 12 months, including the standardization of variables based on input and review from the Regional Office and headquarters and the addition of “zero reporting” button.

2.1.23 Post-certification strategic plan: impact on the Western Pacific Region

To sustain a polio-free world after eradication, some activities and functions will need to continue: the containment of the virus in PEFs to prevent its accidental or intentional release; disease surveillance to rapidly detect the re-emergence of the virus; outbreak response capabilities, for quick and effective response to any polio events; and continued vaccination so that the population is protected in the event of an outbreak. A governance and management structure is required for these ongoing, essential functions, which are included in a transition plan being developed by the GPEI partners (WHO, UNICEF, US CDC, Rotary International, Bill & Melinda Gates Foundation) for the post-eradication era. GPEI is responsible for defining the essential functions, policy decisions and financial requirements required to maintain a polio-free world. Each partner agency will be responsible for transitioning these essential functions and personnel to the agreed upon future governance and management structure. In addition, the partners will play a facilitating role to provide background and support knowledge transfer of the polio assets and functions that can be transferred or used elsewhere. GPEI will not be responsible for the transition of these functions or personnel to other health programmes – this responsibility lies within the non-polio groups of the partner agencies or other health initiatives. GPEI will support country planning through technical assistance and tools and will track progress.

Countries will be responsible for the development of their own transition plans. The post-certification strategic (PCS) plan has three goals: (i) Contain PV sources to ensure potential sources of PV are properly controlled or removed; (ii) Protect populations by immunizing populations against unanticipated polio events; and (iii) Detect and respond to any PV introduction to prevent transmission. For the Western Pacific Region, the post-certification strategic plan will be used to: (i) maintain polio-free status; (ii) introduce IPV and withdraw OPV; (iii) contain PVs; and (iv) develop the polio legacy. The process will be to present and discuss the regional plan at the 26th meeting of the Western Pacific Region TAG and, after revision and feedback, present to the 68th session of the Regional Committee.

2.2 Measles and rubella LabNet

2.2.1 Global and regional updates on measles and rubella elimination

Three WHO regions (Region of the Americas, Western Pacific Region and European Region) have achieved high overall coverage for measles-containing vaccine (MCV). With the exception of countries of the Pan American Health Organization, however, it is not sufficiently high in all countries to prevent
outbreaks. Based on WHO/UNICEF coverage estimates, 123 (63%) countries have over 90% coverage with the first dose of MCV. The global measles incidence rate is down by 87% to 19 million in 2016 (N=132 129 measles cases reported) but well short of the target of less than 5 cases per million.

Countries in the Western Pacific Region reported 57 879 measles cases in 2016. Measles deaths have decreased by 79%, which has resulted in measles moving from being the 5th to the 15th leading cause of child mortality for those under 5 years of age. Despite this impressive reduction, it is still short of the 2015 target of a 95% reduction. Importantly, for both cases and deaths, progress has levelled off for the past eight years and all three 2015 control targets were not met. The Western Pacific Region was estimated to have had 2100 deaths, 2% of the global estimated total. There has been a steady increase in rubella-containing vaccine (RCV) used globally. A total of 152 countries used RCV1 in 2016 with a reported global coverage of 47% of the infant population. The Western Pacific Region reported a coverage of over 98%. The regional milestone for measles and rubella is measles elimination by 2012 and elimination of rubella and prevention of congenital rubella syndrome (CRS). A new Regional Strategy and Plan of Action for Measles and Rubella elimination, as well as a target year for regional rubella elimination is expected to be endorsed by Member States during the 68th session of the Regional Committee. During 2014–2016, a resurgence of measles was predominantly due to an increase in reported cases in China, as well as large outbreaks in the Philippines, Viet Nam and Mongolia. Following successful control of the outbreak in Mongolia by mid-2016, the Western Pacific Region has enjoyed a period of relatively low incidence in 2017 (to July). In 2016, a total of 5450 cases of rubella were reported in the Region (83% from China), the lowest number since 2003. Of 27 countries reporting CRS information through the 2016 JRF, four have nationwide surveillance (Australia, Hong Kong SAR (China), Japan, the Republic of Korea and the United States of America) and 10 have sentinel site surveillance. No country is sharing case-based CRS data with the WHO Regional Office for the Western Pacific.

Some of the challenges for measles and rubella elimination in the Region include: addressing the gaps in population immunity among persons not ordinarily targeted during routine or supplemental immunization; countries with large population size and density; nosocomial outbreak amplification or propagation in health-care settings; and ongoing endemic transmission among neighbouring countries/areas and nearby regions. At the 6th Regional Verification Commission for Measles Elimination (RVC) meeting in Beijing in September 2017, RVC members discussed further refinement of the measles and rubella elimination process, particularly regarding how to better guide post-elimination countries. A total of 16 national and subregional verification committee (21 PICs) reports were reviewed: New Zealand was verified to have achieved the interruption of endemic measles and rubella, and the Republic of Korea the interruption of endemic rubella virus transmission for over 36 months.

2.2.2 Global Measles and Rubella LabNet

The Global Measles and Rubella Laboratory Network (GMRLN) is the largest globally coordinated laboratory network providing high-quality laboratory support for surveillance to measure progress towards measles and rubella elimination. Serological testing is performed by all network laboratories, with increasing use of molecular methods for case confirmation. However, reporting of monthly measles data is discordant with annual data reported through the JRF, mostly due to some countries not reporting monthly data. Rubella data are more concordant. Molecular surveillance for measles has improved over the years, but gaps still exist and there is a need to communicate across the regions as adjoining countries share viruses and the importance of sharing sequence information is critical. GMRLN has identified that of 11 wild-type measles genotypes detected since 2005, only five or six are
still circulating. For rubella, current genotype data are missing in most countries in the world. As CRS cases usually excrete virus for up to six months after birth, these cases can be utilized to collect virus. Some challenges identified include: the requirement for regular laboratory training activities to maintain technical expertise and for the introduction of new techniques, especially as some countries experience regular staff turnover. New technologies are being developed by GMRLN to support the measles and rubella programme and include: next generation, extended window, and whole genome sequencing (NEW); measles vaccine virus specific PCR; point-of-care testing (POCT); and multi-antigen immunoassays (MIA) using the Luminex platform. Further financial support for the continued expansion of GMRLN is needed to provide laboratory support for surveillance, not only for measles and rubella, but also for other VPDs and emerging pathogens. DiaSorin has recently taken over Siemens and they plan to transition the current immunoglobulin M (IgM) enzyme-linked immunosorbent assay (ELISA) used by most of GMRLN to a new testing platform. Therefore, a well-validated replacement assay is critical due to the large number of laboratories currently using the Siemens system.

2.2.3 Regional measles and rubella LabNet

The regional measles and rubella LabNet in the Western Pacific is composed of 386 laboratories. This includes one change from last year in that the Singapore national measles and rubella laboratory (NMRL) has been moved from the Singapore General Hospital to the National Public Health Laboratory (NPHL) in February 2017. For countries in the Region except China, more than 20 000 samples were tested for measles IgM in 2016, mainly due to large measles outbreaks in Mongolia and Malaysia. More than 15 000 rubella IgM tests were completed in 2016, mainly in Mongolia, Malaysia, the Philippines and Viet Nam. Laboratories in China performed a total of 66 768 measles IgM tests and 59 285 rubella IgM tests in 2016. Most laboratories in the Region met the four-day turnaround target for IgM reporting, though subnational laboratories in Papua New Guinea and the Viet Nam experienced challenges in meeting the target in 2016 due to lack of resources.

The predominant measles genotypes detected in the Region were H1, D8, B3 and D9. In 2017, D8 became more predominant than in previous years and occupied an almost similar proportion to H1 and was reported from eight countries in the Region. H1 has become less commonly detected and is mainly limited to the mainland of China. For rubella genotypes, 2B was found in six countries and 1E in three countries in 2016. In 2017, 2B was found in five countries and 1E in one country. Quality assurance performance remains high in the Region, with all 54 laboratories that participated in the global serological PT passing both measles and rubella components and 12 of 13 laboratories that underwent the molecular PT passed for both measles and rubella. One laboratory has pending results for measles. The 2017 PT panels have not been distributed due to funding delays, but will be distributed during the meeting. The sixth regional hands-on training workshop for the laboratory diagnosis of measles and rubella was held in Hong Kong SAR (China) in February 2016. On-site accreditation reviews were performed on six provincial laboratories in China and on VIDRL and NIID. Other laboratories are undergoing accreditation desk reviews and implementation of the global web-based database accreditation process is awaited. One challenge for the Region is that a funding delay in 2017 has impacted procurement of ELISA kits, the shipment of PTs and support for some laboratories. The WHO pouch can no longer be used for shipping supplies and the need to use an independent courier service adds considerable costs. To support verification of measles elimination, there is need for continuous genotype surveillance, especially for countries experiencing outbreaks close to or after verification of elimination.
2.2.4 GSL and RRL reports

**United States Centers for Disease Control and Prevention as GSL**

It is proposed that the measles and rubella functions carried out by US CDC will be reorganized into a new Viral Vaccine-Preventable Disease Branch. However, the measles and rubella teams will remain the same. The United States continues to experience outbreaks of measles due to importations. A total of 119 outbreaks were detected in 2017 (to September) due to D8 imported from Bali and B3 imported from Romania. Outbreaks in Los Angeles (D8) and Minnesota (B3) were from unknown sources although genetic linkages to the Bali outbreak for the D8 outbreak and to Shandong, China for the Minnesota cases were found. Increasing the resolution for the molecular epidemiology of measles can be helpful in determining transmission patterns. Sanger sequencing of the highly variable non-coding region between open reading frames (ORFs) for M and F protein (MF-NCR) is feasible for most laboratories that perform N-450 sequencing. Measles Nucleotide Surveillance (MeaNS) has been modified to accept these sequences and most reference strains have been sequenced for the MF-NCR. However, currently there is no large database for genetic comparison and MF-NCR is difficult to amplify. US CDC’s experience in testing in the measles elimination stage includes confirmation by IgM and RT-PCR, with IgG avidity and plaque reduction neutralization (PRN) used when the former are inconclusive or not available. In the investigation of the Mongolian measles outbreak, avidity and PRN testing provided helpful information. It was concluded that failure to vaccinate appears to have been the major cause of cases in Mongolian children younger than 14 years and 66% of adults aged 15–30 were considered reinfection cases (RIC) while in 34% of adults the disease could be attributed to primary vaccine failure (PVF) or failure to vaccinate. The 2014 Pohnpeii measles outbreak in the Federated States of Micronesia showed that a total of 49 of 82 (60%) cases could be confirmed as reinfection due to evidence of IgM positive/high avidity or high avidity/PRN> 40 000. Reinfection cases are reported to have a mild presentation with short duration rash and low fever, but some have full-blown measles symptoms. Useful next steps would be for GMRLN to validate commercial measles avidity assays and to develop a substitute for PRN such as enzyme immunoassay (EIA) or multi-antigen immunoassays. There is need to maintain capacity for high-quality laboratory surveillance for measles and rubella and the rapid confirmation of measles vaccine reactions is essential. It is important to describe the lineages in addition to the genotypes and to always include a phylogenetic tree and include matches with named strain on MeaNS or Rubella Nucleotide Surveillance (RubeNS) databases. Additional training in molecular methods including sequence analysis and database submission should be considered using webinars.

**Japan as GSL**

The position of head of the measles laboratory is currently vacant after Dr Komase’s recent retirement. The GSL at NIID, Japan continues to be involved in strengthening the capacity of the regional LabNet. The laboratory helped facilitate the Japan International Cooperation Agency’s Global Training Course for Laboratory Diagnosis Techniques for the Control of Vaccine Preventable Diseases, including polio, measles and rubella for participants from the African Region, Eastern Mediterranean Region and the Western Pacific Region. NIID investigated measles and rubella seroprevalence in the Lao People’s Democratic Republic following RCV introduction. Seroconversion for measles was lower than for rubella, which could be due to the higher sensitivity of measles virus to breakdown in the cold chain impacting its vaccine potency. Commercial laboratories in Japan mostly carry out measles and rubella surveillance but NIID is committed to the standardization of testing in these commercial labs. External quality assessment (EQA) is required by law in Japan and a molecular EQA for prefecture laboratories was started in 2016, and 51 prefecture public health laboratories will be tested in 2017. NIID is
investigating human cell lines permissive for the propagation of rubella virus. To date, only few cell lines have been found that allow efficient replication of rubella virus. Similarly, for finding cell lines useful for propagating measles virus, it has been challenging to establish a new cell line that is superior to Vero/SLAM.

In 2016 to July 2017, two major lineages of D8 were found in outbreaks in Osaka, one with linkages to Indonesia and the other to multiple importations from other countries.

**Australia as RRL**

Australia’s measles and rubella reference laboratory discussed the genetic characterization of measles and rubella importations over the previous 12 months and compared this to the previous 10 years. This included differentiation of wild-type and vaccine strain information, tracking of transmission pathways using phylogenetics, comparing this to global strains and showing evidence of interruption of transmission.

The epidemiology of measles in Australia shows the characteristic of an eliminated country with multiple sporadic outbreaks from importations and minimal spread. An example of this was shown following identification of seven different lineages of D8 viruses identified in 2016. Countries associated with the importation of D8 measles cases included: India, Indonesia, Nepal, New Zealand, Thailand and Viet Nam. B3 and D4 genotypes were also identified in a small number of cases. Two rubella cases were identified in 2016 as genotypes 2B and 1E and no rubella has been detected by molecular methods in 2017. VIDRL supports the sequencing of viruses for other countries in the Western Pacific Region and identified D8 (Osaka) in New Caledonia in 2017, genotype A in Fiji, and confirmed genotypes B3, D4 and D8 detected in New Zealand in 2016–2017. VIDRL reported a vaccine-related case with genotype A virus detectable by PCR 54 days post-vaccination. The previously longest detection reported was 37 days post-vaccination.

The laboratory participated in international EQA/PT such as by Quality Control for Molecular Diagnostics (QCMD) for measles and mumps, the Royal College of Pathologists of Australasia (RCPA) for respiratory pathogens, and the WHO EQA on measles and rubella molecular PT. Confirmatory testing was done on samples referred by Fiji and New Zealand.

**China measles LabNet (with 31 provincial laboratories)**

China’s measles cases have declined since 2014. In 2017 (to August), a total of 5084 cases were confirmed, with an incidence of 3.7 million, the lowest since 2014. A similar reduction in rubella cases has been reported and 922 cases were IgM confirmed by August 2017. Measles genotype H1 is predominant and has been the only endemic virus circulating in China for at least 20 years although multiple imported viruses have been detected since 2009. In 2017 (January–August), genotypes identified were: H1 (N=322), D8 (N=7) and B3 (N=1). D8 and B3 strains were confirmed as imported. The China NMRL plays a key reference and quality assurance role for the measles and rubella LabNet in China. In 2016, the NMRL and 32 provincial laboratories passed the serology WHO PT panel, and all participants passed the molecular PT. Six provincial laboratories underwent on-site accreditation in 2016, and all participants passed with high scores. The 13th national measles LabNet workshop was held in Kunming in November 2016 for all the network laboratories in China, and a hands-on training course for measles and rubella detection was held in July 2017. Some of the challenges identified for the China LabNet include: very heavy workload for serology diagnosis and molecular detection in the China measles and rubella LabNet; weak communication between the Expanded Programme on Immunization (EPI) and the laboratory in some provinces; poor timeliness of sample collection and
room for improvement of transportation; and need to continue to strengthen quality assurance for the molecular detection in the provincial and prefecture laboratories. Measles genotype surveillance is comprehensive with just one gap in Tibet, although alternative sampling techniques such as DBS or oral fluid are being considered to enhance surveillance.

**Hong Kong SAR (China) as RRL**

Hong Kong SAR (China) has achieved the interruption of endemic measles virus transmission as verified by the RVC in the Western Pacific Region in September 2016. In 2016, 510 cases were tested for measles with nine confirmed positive. In 2017 (September), three were found positive from 176 cases investigated. Measles genotypes H1, D8 and B3 were identified from January 2016 to August 2017 and viruses were considered to be imported. For rubella, in 2016, 501 cases were investigated and three found positive (genotypes 2B and 1E). No rubella cases were confirmed in 2017 (September) from 163 cases investigated. Measles genotype information was identified from Cambodia, Mongolia, the Philippines, Singapore, Viet Nam (Hanoi and Ho Chi Minh City) from serum samples sent for confirmatory testing in 2016 and 2017. Rubella genotype information was provided to Cambodia (2B), the Philippines (2B), Viet Nam (Hanoi and Ho Chi Minh City) (2B) and Singapore (1E) from serum samples received in 2016 and 2017.

**2.2.5 Country presentations**

All countries presented a summary of their achievements. All laboratories have passed the global PT, have acceptable concordance with their confirmatory tests and are fully accredited. Most countries presented their testing and reporting algorithms, which followed WHO recommendations.

**Brunei Darussalam**

The Virology Laboratory under the umbrella of Clinical Laboratory Services, Ministry of Health obtained ISO15189 accreditation in 2011 is responsible for the laboratory component of measles surveillance and serological testing. Since 2014, the Virology Laboratory has also been certified as the WHO NMRL for Brunei Darussalam and is now part of the WHO measles LabNet in the Western Pacific Region.

The RVC verified Brunei Darussalam as having achieved measles elimination in March 2015. From 2004 to 2016, 63 measles confirmed cases were notified to the Disease Control Division. In 2016, one from 13 specimens tested was a laboratory-confirmed case (genotype B3) and determined to be imported. A total of 12 rubella cases were reported in the country between 2007 and 2013. However, no CSR cases have been reported since 2014.

**Cambodia**

Cambodia was verified as having achieved measles elimination status in March 2015. All samples from suspected cases are sent to the National Institute of Public Health (NIPH) for testing, and confirmatory testing samples are sent to the RRL in Hong Kong SAR (China). Children over 1 year old have blood collected and those below 1 year old have DBS collected. In January 2016, two imported measles cases were confirmed and two further cases reported in May 2016 with a total 66 cases identified from 889 suspected measles cases from January 2016 to June 2017. All cases were considered imported or import related, with genotype B3 and D8 identified. The first cases were detected close to the Viet Nam border and subsequently spread to other parts of the country due to frequent internal movement, an
accumulation of susceptible children. Nosocomial infection also occurred and 40% of cases were below 9 months old.

Cambodia implemented the following strategies in response to the outbreak: strengthened surveillance activities; reinvestigation of all confirmed cases; maintenance of high coverage of routine vaccination and application of a new measles and rubella strategy (MR0, MR1, MR2 and MR extra). Challenges include: samples are received in the laboratory more than five days after collection, stock-outs of reagents, and specimen inadequacy (especially DBS).

**Fiji**

The Fiji NMRL also supports Kiribati, Tuvalu and Vanuatu. The NMRL in Mataika House received a total of 259 samples in 2016 and 53 in 2017 (August) from Fiji. All were tested for both measles and rubella IgM. DBS (N=25) were received in 2016 and the remainder were sera. In 2016, five measles and seven rubella IgM positive samples were reported; in 2017 (as of September), one measles and one rubella positive IgM samples were reported. Establishing CRS surveillance proves to be a challenge.

**Lao People’s Democratic Republic**

The Lao People’s Democratic Republic is a landlocked country that shares borders with five countries: Thailand, Myanmar, China, Viet Nam and Cambodia. Measles and rubella vaccine was introduced in 2011, but coverage has not exceeded 88%. Acute fever and rash (AFR) surveillance was initiated at the same time. CRS surveillance has yet to start. In 2016, several small outbreaks occurred of both measles and rubella. A total of eight measles cases were reported: two laboratory confirmed and six epi-linked. For the same period, 40 rubella cases were reported: seven lab-confirmed and 33 epi-linked. However, only 40% of reported fever and rash cases have had samples collected. Some of the challenges identified include: no throat swab or urine samples collected for virus detection; most fever and rash cases are children, which leads to a limitation of collecting blood samples and thus DBS is being considered. No CRS surveillance and/or sentinel surveillance system established.

To support the achievement of measles–rubella elimination, a measles outbreak response preparedness plan needs to be developed. The NIP will use the existing measles elimination platform and strategies to initiate or accelerate activities for rubella elimination. Finally, in order to improve and achieve measles elimination, both the NIP and National Center for Laboratory and Epidemiology (NCLE) need to scale up immunization coverage and address the surveillance gap with the support from WHO and other development partners.

**Malaysia**

Laboratory data showed that in 2016, 5690 samples were tested for measles at the national public health laboratory and 1451 (25%) were IgM positive. In 2017 (as of July), 4357 samples were tested for measles and 727 (16.7%) were found to be measles IgM positive. Measles genotypes detected included: D8 (N=66), D9 (N=86) and B3 (N=64) for 2016, and D8 (N=46), D9 (N=22) and B3 (N=41) in 2017. For rubella, 1839 serum samples were tested in 2016 and three were positive. No rubella IgM positive samples were detected in 2017 (as of August). The rubella genotype detected in 2016 was 2B (N=2). The public health laboratory in Sabah has performed testing for measles IgM and rubella IgM since being appointed a subnational national measles laboratory in 2011. Samples for confirmatory testing from the public health laboratory in Sabah were sent to the national public health laboratory.
**Mongolia**

Mongolia was verified as having achieved measles elimination by the RVC in 2014. However, since mid-March 2015, a measles outbreak is still ongoing. The highest age-specific attack rate is reported among children under 1 year old, followed by young adults aged between 18 and 30 years. In 2015 and 2016, there were 8 and 132 deaths, respectively. The overall case fatality rate was 0.4%. The SIAs had shown positive results with a decreasing trend of cases seen as the activities were carried out extensively. In 2015 and 2016 (until August), a total of 14,462 samples were tested for measles IgM, and 6962 samples (48%) were confirmed positive. Measles genotype H1 was identified during the outbreak. Mongolia plans to develop and ensure implementation of the measles and rubella outbreak preparedness and response plan, improve infection prevention and control practices to prevent nosocomial transmission, establish a web-based immunization registry, and increase budget allocation for MCV SIAs every 4–5 years to ensure that herd immunity level reaches the standard level.

**New Zealand**

New Zealand was verified to have achieved the interruption of endemic measles and rubella at the 6th RVC meeting in September 2017. In 2016, three outbreaks with 103 notified cases were reported; all were genotype D8 but from different lineages and with epi-links to India (N=1), Indonesia (N=1) and unknown (N=1). The NMRL is using whole genome sequencing to better differentiate importation and endemic transmission. There have been no cases of CRS reported in New Zealand since 1998. In 2016, three laboratory rubella cases were confirmed. The cases were in non-immunized people and were linked to India as the source country. In 2017, one laboratory-confirmed rubella case was imported from the Philippines. All four cases were genotyped as 2B.

**Papua New Guinea**

Papua New Guinea has a population of 8.5 million people, cultural diversity and over 800 languages. Eighty-five per cent of the people live in rural areas with limited access to health services. This includes declining vaccination coverage in general with measles at 50% in 2016. Examples are multiple factors such as geographic challenges with difficult transportation in rural areas and funding issues.

A large measles outbreak in 2014 reported D9 along the Indonesian border and B3 in the rest of the country. This outbreak affected over 75,000 clinical cases with 2299 cases laboratory confirmed and caused 365 deaths (CFR of 0.46%). Much of 2015, 2016 and 2017 were quiet until August 2017 when another measles outbreak occurred in Vanimo Green District in Sandaun Province with 5 confirmed and 40 clinical cases reported. A response team has been on-site to assess and respond appropriately. Throat swabs and serum will be collected for genotyping in Hong Kong SAR (China). The laboratory recommends the following: strengthen routine immunization programmes in Papua New Guinea to improve herd immunity and reduce outbreaks; encourage sample collection for any acute fever and rash to match the national health information system and laboratory data; redistribute test kits in countries where there are no outbreaks to avoid expiry or limit stocks; and laboratory assessments to be conducted by independent assessors.

**Philippines**

The Philippines is using a devolved public health system where health programmes and implementation resides in the local government. Disease surveillance and the national laboratory still need further improvement and upgrade. A total of 1660 cases were referred to the NMRL in 2016 and 1787 cases in 2017 (as of August). Measles positive IgM cases totalled 41 and 43, respectively. In September 2017,
outbreaks of measles were seen in Region 3 (Central Luzon) and Region 9 (Zamboanga Peninsula). The positive cases for rubella also increased from 110 in 2016 to 282 in 2017. From September 2016 to August 2017, Region 4A (CALABARZON) has the highest referral rate and positive rubella cases, followed by the National Capital Region, which also has a few rubella positive cases. Rubella genotype 2B was confirmed from the rubella outbreak that affected most of the country. No measles genotype data were reported during this period.

**Singapore**

Singapore has a population of 5.6 million, of which 1.7 million are transient workers. Measles and rubella are mandatory notifiable diseases in Singapore. To reduce the number of measles and rubella cases seen in unvaccinated children aged 15 months and below, the Singapore Ministry of Health revised the age of vaccination in December 2011 that children would receive both doses of measles, mumps and rubella (MMR) vaccine at a younger age: 12 months and 15–18 months. Despite this effort, measles incidence rate among children aged 1–4 years remains highest among all age groups. MMR coverage (first dose) remained consistently above 95% during 2009–2015, with a slight drop in 2016 to 94.7%. In 2016, 71.3% cases were sporadic and the rest involved small outbreak clusters (average 2–3 cases) within unvaccinated family groups. Herd immunity against measles is high in the local population. As a result, no local cases with the same genotype were reported after an imported measles (H1 genotype) case from China in May. Rubella incidence fluctuated during 1991–1999. This was followed by a steady decline from 1999 (10.9 per 100 000 population) to 2016 (0.2 per 100 000 population). A total of eight cases of rubella were reported in 2016, a decrease of 53.3% compared to 15 cases reported in 2015. The incidence rate was highest in the 0–4 years age group contributing to 50% of all rubella cases. There were no cases of congenital rubella in 2016. Singapore General Hospital was the NMRL from 2001 to 2016, until the National Public Health Laboratory in Tan Tock Seng Hospital took over the responsibility from 2016 (overlapping) onwards.

**Viet Nam**

**Hanoi**

The measles vaccine coverage in Viet Nam was maintained at 95% for the first dose and 90% for the second dose since it was introduced in 2006. However, in 2011 and 2012, MCV2 coverage dropped to 80%, which contributed to the large outbreak in 2014 of more than 4000 confirmed cases. In 2016, 18 confirmed measles cases were reported with genotypes H1 (N=4) and D8 (N=11) identified, with evidence of importation from Mongolia, Indonesia and China. In 2017 (as of August), four measles confirmed cases were reported, with genotype D8 (N=1) identified and evidence of importation from Viet Nam, Myanmar and Thailand. Four cases of rubella were confirmed in 2016 and none in 2017 (as of August).

**Ho Chi Minh City**

The Pasteur Institute Laboratory in Ho Chi Minh City receives measles and rubella samples from 20 provinces in southern Viet Nam. It has established CRS surveillance in two sentinel sites at Children’s Hospital No. 1 and Children’s Hospital No. 2 in Ho Chi Minh City since 2011. In September 2016 to August 2017, 335 samples were tested for both measles and rubella. A total of 9 (2.7%) measles cases and 46 (13.7%) rubella cases were confirmed. More than 75% of rubella cases were in the 16–60 years age group and 26 CRS cases were detected from September 2016 to August 2017. The NMRL reported that stock-outs of kits contributed to problems with timely reporting of results.
Nha Trang
The Virology Department of Pasteur Institute in Nha Trang is a subnational laboratory (SNL) providing laboratory surveillance for measles and rubella in central Viet Nam from Quang Binh to Khanh Hoa Province. It has been ISO 15189:2012 accredited for influenza virus, HIV (serological testing), dengue virus and EV testing since 2013. The 11 provincial preventive medicine centres (PPMCs) collect and send samples to Pasteur Institute in Nha Trang for the diagnosis of measles and rubella. Serology diagnosis of measles and rubella is done using the Siemens kit and IBL kit (Germany). Central Viet Nam saw a significant decrease in both the number of samples and positive cases of measles and rubella in 2016 and 2017. In 2016, 185 samples were tested, but there was only one measles IgM positive and 10 rubella IgM positive. In the first eight months of 2017, 94 samples were tested both for measles and rubella, of which no sample was measles positive but two were rubella IgM positive. The laboratory has some challenges in collecting samples for VI including: a throat swab sample is rarely collected and PPCMs need to be trained on collecting and transporting samples. Also, ELISA kits such as Siemens and IBL are difficult to purchase in Viet Nam.

Tay Nguyen
The subnational measles and rubella laboratory for the Central Highlands Region of southern Viet Nam is situated in the Tay Nguyen Institute of Hygiene and Epidemiology (TIHE) and serves four provinces (Dak Lak, Dak Nong, Gia Lai and Kon Tum) with a total population of 4.3 million. A total of 222 suspected cases were reported to the Institute in 2016, with 12 tested for IgM. All were negative for measles and rubella. A total of 83 suspected cases were reported in 2017 (July), with 16 tested for IgM. All samples tested were negative for measles and rubella. The Institute reported challenges in obtaining adequate collection of samples from all cases.

2.2.5 Strengthening coordination and cooperation between laboratory and epidemiology surveillance: lessons learnt

China
The National Immunization Programme, Chinese Center for Disease Control and Prevention, provided an overview and performance of the Chinese measles and rubella surveillance system. All provinces had implemented universal measles case-based surveillance with laboratory support by 2009. In 2014, rubella was incorporated into measles surveillance with a requirement for blood and throat swab specimens to be collected by hospital staff and shipped to the county CDC within 24 hours to arrive at the prefecture measles and rubella laboratory within three days of collection. RT-PCR is carried out on IgM negative samples to minimize false negative IgM results. In 2016, over 69 000 suspected measles and rubella cases were detected with 65 000 having blood specimen collected and more than 33 000 having throat swab collected. The county CDC makes the final case classification based on recorded EPI and lab data. Surveillance performance indicators have improved between 2010 and August 2017 and in 2016 all indicators reached the WHO Regional Office recommended target except for the percentage of second administrative level units reporting at least two of 100 000 discarded measles/rubella cases, which is slightly below the target by two percentage points. The key lessons for having established a strong measles and rubella case-based surveillance programme in China is: central government funding and policy support; strong national leadership by China CDC; strong cooperation between EPI and the laboratory at national, provincial, prefecture and county levels; continuous training workshops from national to local levels; effective quality control systems; and strategic collaboration with WHO, US CDC and other international partners.
**Malaysia**

Malaysia currently has a high incidence of measles (51.4 million, 2016) at levels not recorded since 2012. There are pockets of low MCV coverage and measles cases are found in all age groups with five deaths recorded in 2016. The immunization schedule was revised in 2016 with MCV1 now given at 9 months and MCV2 at 12 months. The current MCV2 administration schedule will continue until 2023. In Sabah State, monovalent measles vaccine will be given at 6 months and MMR at 9 and 12 months, with a second measles and rubella at 7 years until 2023. In 2017, a nationwide, targeted measles and rubella SIA will be held. Rubella incidence was 2.2 million in 2016 and has been below the target of 10 million since 2014. Most of the surveillance indicators meet the targets in the Western Pacific Region except for outbreak size (4 vs. 0) and samples collected from outbreaks for VI (3.5% vs. more than 80%). Strategies being implemented to meet the elimination goal include: undertaking regular risk assessments; closing the immunity gaps and standardizing the MCV schedule nationwide; and closing the surveillance gaps and implementing rapid response to measles cases/outbreaks.

**Mongolia**

Mongolia introduced measles vaccine (MCV1) into the EPI in 1973 for children aged 8–11 months with a second dose introduced in 1989 for children aged 12–23 months. MMR was introduced in September 2009 and the schedule was: MMR1 at 9 months and MMR2 at 2 years. Measles cases were not reported during 2004–2005 and 2011–2014, and Mongolia was declared to have met the criteria for measles elimination in June 2014. From 2015 to 2016, a very large measles outbreak (N=53 737) occurred in two phases. The first phase started in March 2015 and peaked in June 2015, and cases were reported mostly from Ulaanbaatar (83%) and Umnegovi Province. The second phase started in October 2015, with a peak in March 2016, and most cases were reported from the countryside outside Ulaanbaatar. Overall, 140 measles deaths were reported (CFR=0.26%) and 2.4% of cases were nosocomial. The laboratory tested 14 885 samples over the entire outbreak with 47.6% IgM positive. All viruses sequenced were genotype H1 and found to form two main clusters, one nucleotide apart.

In response to the outbreak, an SIA covering children 6 months to 5 years of age (94% coverage) was carried out in response to the first phase and an SIA covering adults 18–30 years of age (88.1% coverage) was carried out in response to the second phase. Training was conducted for VPD surveillance and response in all provinces and Ulaanbaatar. The Ministry of Health appointed an advisory team for surveillance, diagnosis and treatment during the outbreak, and an incidence management system was activated. With support from WHO and US CDC, studies were conducted to determine the risk factors for measles virus infection among adults during a large outbreak in a post-elimination era and the increase in infant measles mortality during a nationwide measles outbreak coincident with seasonal influenza. A seroprevalence study was also undertaken for measles and rubella in mothers and newborn infants in Ulaanbaatar.

The Ministry of Health faced many challenges, leading up to and during the outbreak, including: some indicators for the performance of case-based measles surveillance were inadequate; a large cohort of the susceptible population had developed but was undetected; coverage data quality was suspect; outbreak and case management problems arose in hospitals leading to nosocomial outbreaks; the laboratory was overwhelmed and not all samples needed to be tested with cases which could have been epi-linked instead; early collection of samples after rash onset led to some false-negative IgM results; and there was a lack of trained personnel, including health workers and laboratory specialists.
Cambodia

The RVC verified that Cambodia had achieved measles elimination in March 2015, noting that endemic measles virus transmission had been interrupted and sustained since November 2011 to March 2015. From January 2016 to June 2017, a total of 66 confirmed measles cases were reported from 16 provinces. Measles cases were found to be likely owing to multiple importations from neighbouring and/or other countries due to an open border and trade/free economy. Cases spread due to frequent internal movement, nosocomial infection and accumulation of susceptible children. In response to the outbreaks, the National Immunization Programme conducted detailed case investigation for all confirmed cases, local immunization responses immediately for most cases and several wide age-range SIAs. No cases have been found since June 2017. The coordination between the National Immunization Programme and the national measles laboratory was strengthened and the laboratory informed the National Immunization Programme immediately of any confirmed measles cases. The National Immunization Programme reviewed these data and provided final case classification in collaboration with the laboratory. The laboratory also provides information about any inadequate specimen collection and incomplete form and routinely participates in midterm and annual workshops and meetings of the National Immunization Programme. Joint field visits occur with support for training on sample collection and correct data entry form filling.

The lessons learnt from the improved coordination between the laboratory and epidemiology surveillance programme included: the immediate laboratory report of any measles case to the National Immunization Programme allowed for rapid response and to interrupt measles transmission immediately; the integration of laboratory and surveillance databases made significant improvements in the integration and matching of the data and improved timely reporting of lab results; and the coordination and collaboration between the National Institute of Public Health and the RRL in Hong Kong SAR (China) provided significant support to the National Immunization Programme to stop the chain of measles transmission which occurred in 2016–2017.

2.2.6 Update of the Sixth Meeting of the Regional Verification Commission for Measles and Rubella Elimination in the Western Pacific Region

At the sixth RVC meeting in Beijing in September 2017, RVC members discussed further refinement of the measles and rubella elimination process, particularly regarding how to better guide post-elimination countries. A total of 16 NVC and SRVC (21 PICs) reports were reviewed: New Zealand was verified to have achieved the interruption of endemic measles and rubella, and the Republic of Korea was verified to have achieved the interruption of endemic rubella virus transmission for more than 36 months. It was recommended that post-elimination countries develop a case confirmation algorithm to review all suspected cases in conjunction with an expert committee to make a determination of case confirmation status during an outbreak. The supplemental use of confirmation of serological results with PCR testing was commended and the use of well-conducted serosurveys, where feasible, is a complementary mechanism to identify population immunity gaps for corrective action. Data describing epidemiological and genotype details for all cases with an unknown source with summary outbreak descriptions that include epidemiological profile, risk factors and genotyping are recommended. Genotyping details from all cases (not only outbreaks) should be provided to distinguish endemic transmission from frequent importation. Genotype data should be used in a standard format so that the RVC can make informed determinations about importations, outbreaks and ongoing transmission.

For rubella, an assessment of CRS burden is required for verification of rubella elimination, but specific guidelines are not yet available. It is important to integrate rubella testing into existing syndromic
surveillance systems for congenital malformations. WHO will provide specific guidance to countries to implement CRS surveillance to support rubella elimination. The guidelines for verification of measles and rubella will be further refined and finalized. The rubella elimination guidelines are currently being worked on. These are similar to measles except for a description of CRS surveillance and there will be context-specific guidelines. Rubella virus is more heterogeneous than measles and has sufficient variability to be useful for aiding the monitoring of elimination progress.

2.2.7 Laboratory support experience from the European Region

The European RVC held its sixth meeting on 15–17 June 2017. Since 2014, the European Region started developing background laboratory documents to complement and clarify the information provided in annual status updates (ASUs) submitted annually by NVCs and support the RVC in their review and decision-making. These documents are regional and country charts and maps, country profiles, accreditation/verification databases, summaries and visuals on laboratory aspects. These data are not only based on laboratory data extracted from annual status updates, but also from MeaNS/RubeNS and European Region measles and rubella LabNet accreditation reviews. A critical piece of information collected in annual status updates is the MeaNS distinct ID for each chain of transmission or outbreak. It is important to emphasize that EPI–lab collaboration and EPI–lab data linkages are critical to make available high-quality information on molecular epidemiology. Currently the surveillance performance indicators of laboratory investigation and viral detection are satisfactory for measles but are still challenging for rubella.

2.2.8 Strengthening rubella and CRS surveillance

Regional rubella and CRS surveillance: progress, challenges and perspectives

The updated Measles and Rubella Elimination Strategy and Plan of Action for the Western Pacific Region defines five strategies to strengthen integrated measles and rubella, and CRS surveillance. The strategy to increase sensitivity of rubella surveillance to elimination standards is to adopt acute fever and rash as definition for suspected cases. For countries experiencing high incidence of measles, rubella or other disease characterized by acute fever and rash, this strategy may not be immediately implementable. Strategies to increase surveillance performance are: (i) assure suspected rubella cases are detected and reported by all facilities, including at the primary health care level, and private practitioners; and (ii) establish sufficient capacity for investigating suspected cases and for collecting/shipping specimens for serological and molecular testing from each outbreak or transmission. Securing sufficient resources is paramount. Linkage with existing surveillance networks (i.e. early warning and response, dengue) could be instrumental.

As all 36 countries in the Western Pacific Region have introduced RCV, establishing or expanding CRS surveillance is strategic to monitor the effectiveness of the rubella vaccination programme and to implement control measures. CRS surveillance could be sentinel or nationwide, active or passive, or retrospective records review, depending on each country’s purpose and health system structure.

Challenges in CRS surveillance with examples of imported cases into the United States

CRS is associated with significant morbidity and mortality and 30% of CRS patients die within the first 12 months after birth. CRS surveillance is challenging to implement as: clinical manifestations may not be apparent within the first year of life (after which laboratory confirmation is not currently possible), the health care system may not have the technology to detect the defect and chronic
disability, and death may be underestimated in infants/children with CRS. For the laboratory, confirmation for infants older than 6 months may be challenging, but adding viral isolation and RT-PCR to the CRS laboratory confirmation algorithms would enhance specificity. There is also a need to develop global CRS surveillance performance indicators.

**Rubella and CRS Surveillance in China**

Rubella was formally integrated into case-based measles surveillance in 2015 after rubella vaccine was introduced into EPI in 2008. Rubella incidence reached its lowest level in 2016 (N=4613 cases, 0.34/100,000). In 2017 (to August), the proportion of rubella cases among those below 15 years of age was 50.6%, and cases were mainly concentrated in those under 1 year of age (14.6%) and the 10–15 years age group (19.5%). Cases between the ages of 15 and 39 years accounted for 44% of all cases. Extensive molecular surveillance in China has allowed a genetic baseline database to be established. Two rubella genotype replacements have occurred since 1999. Genotype 2B has become predominant since 2014 and has been found in 26 of 31 provinces. Continuous virological surveillance occurs in all provinces although some surveillance gaps still exist in Xinjiang and Tibet autonomous regions and alternative specimens are being considered to enhance surveillance. CRS surveillance needs to be strengthened and is considered being integrated with a national birth defects surveillance system.

**Rubella and CRS Surveillance in Japan**

Japan has established 2020 as a target date for rubella elimination and a National Verification Committee for Measles and Rubella Elimination was launched in September 2017. The large rubella epidemic of 2012–2013 (N=16 730 cases) was caused by at least three genotypes/clusters of rubella virus strains. The geographical distribution of rubella viruses from 2010 to 2014 was classified into genotypes 2B and 1E, which were closely related to South-East Asian and South Asian strains. Rubella strains detected in 2015–2017 are also closely related to South-East Asian strains, but are not direct descendants of the epidemic strains between 2012 and 2013, and reflect importation. In 2016, 125 rubella cases were reported.

**2.2.9 New perspective and technique**

**Challenges in diagnosing measles and rubella cases in elimination phase – Cambodia**

During the elimination and post-elimination phases, the objectives of surveillance are to detect and accurately describe all cases, particularly to respond to cases, define source of infection (imported/import related), describe chains of transmission and exclude re-establishment of endemic transmission in case of longer outbreaks. Therefore, investigation of cases should provide an accurate history of cases to enable EPI linkage and genotype information, preferably including extended sequencing windows, to confirm and discard cases in a reliable manner.

The analysis of discarded non-measles cases during the 2016–2017 outbreaks in Cambodia supported the hypothesis that they were due to multiple importations, instead of re-establishment of endemic transmission. It also highlighted that Cambodia, as well as most countries in the Western Pacific Region, mostly relies on laboratory confirmation, predominantly through IgM testing, to confirm/discard cases. The majority of specimens are collected less than four days after onset of rash.

Criteria to confirm and discard measles and rubella cases should be revised, combining use of laboratory results from serological and molecular testing with EPI linkage and appraisal of clinical
compatibility. Case classification committees could be considered for measles and rubella, similar to AFP/polio.

**Challenges in diagnosing measles and rubella cases in elimination phase - China**

In 2017, China reported a record low incidence of measles and rubella. To reduce the chance of transmission through missing cases, China is increasing the sensitivity of measles detection and lowering the risk of false discards by introducing rRT-PCR at the prefecture level to supplement IgM detection. In an investigation of a measles outbreak at a high school, IgM was not detected within the first five days of rash onset. The investigation of several outbreaks of “mild” measles found that a combination of IgM on serum and rRT-PCR on throat swabs detected more cases. China CDC is considering introducing an IgM capture assay rather than indirect assay currently used, to improve IgM detection sensitivity. IgM detection is still considered the gold standard but rRT-PCR can be used as a complementary method to enhance the sensitivity of detecting real cases.

**Development of point-of-care test for measles and rubella**

As part of collaboration with Health Protection England and the Bill & Melinda Gates Foundation, a new oral fluid (OF) collector (Oralight) has been designed and evaluated as both a collection and extraction device under field settings. A point-of-care test has been developed with high sensitivity and specificity for measles IgM detection using serum. Evaluation of capillary blood and oral fluid in the test is currently under way in field trials in India. Uganda will be the site for another field trial planned for the next few months. The used point-of-care test can also be shipped to the laboratory, as can the blood filter pad used for molecular epidemiology studies using RT-PCR and sequencing of the trapped test blood cells. An EseQuant reader/smartphone combination is available for quality control purposes and to transmit results to the programme in real time. A rubella point-of-care test is also currently under development.

**2.2.10 Laboratory quality assurance**

**Update on quality assurance for molecular proficiency testing**

Molecular tests are becoming more and more important for case-based surveillance of measles and rubella, and the molecular external quality assessment (mEQA) programme was developed by US CDC to assess the performance of laboratories that use measles and rubella molecular tests. The 2016 molecular EQA panel was made and shipped by the Wisconsin State Laboratory of Hygiene and the measles and rubella teams at US CDC evaluated the returned reports and prepared a feedback report with the final score. For the Western Pacific Region, 13 laboratories participated in 2016: all passed the detection and genotyping components for rubella and 12 of 13 passed for measles, although two laboratories were required to perform a retest due to technical issues. One laboratory reported ambiguous nucleotides for measles. Overall, most countries produced sequences of high quality and all correctly identified the genotypes.

**Measles and rubella IgM PT and confirmatory testing**

The Western Pacific Region had 55 laboratories that participated in the 2016 IgM EQA (panel 01602), made and distributed by VIDRL. Siemens was the most commonly used kit in the Region for both measles and rubella IgM testing. In China, no Siemens kits are used and Haitai and Virion/Serion kits are mostly used. Other kits used were: Denka Seiken and Innovita (one lab each) for measles and also Kerunda, Roche and Innovita for rubella. All laboratories in the Western Pacific Region passed the
measles PT, with 46 (83.6%) laboratories scoring 100% and all laboratories scoring 90% or more. For the rubella PT component, 42 (76.3%) laboratories scored 100% and 54 (98.2%) laboratories scored 90% or more. One laboratory reported four incorrect rubella results, possibly due to a mix-up in the sampling order. Changes to the 2017 panel, such as new type of specimen tubes with a unique 2D barcode alphanumeric number, kit validation data changes for non-Siemens kits and the requirement to use the correction factor for Siemens, will be necessary. There are proposed changes to the website so that results using CSV files may be uploaded.

VIDRL supports the confirmatory testing for seven national laboratories in the Region: Brunei Darussalam, Fiji, Guam, Malaysia, New Zealand, Papua New Guinea and the Republic of Korea. In 2016 and 2017, six national laboratories referred samples for confirmation. All laboratories were found to have acceptable concordance rates (more than 90%) for both measles and rubella test results.

**China LabNet confirmatory testing and EQA for provincial laboratories**

China’s NMRL and 32 provincial measles laboratories participated in the 2016 WHO measles and rubella IgM proficiency test. The panel was composed of 20 samples. IgM tests for measles and rubella were performed and results were reported to WHO within 14 days from receipt of the samples. Assays used by provincial laboratories for the measles PT were: Haitai 19.6%; Virion/Serion 12.4% and Innovita 1.3%. For the rubella PT, assays used by the laboratories were: Haitai 16.5%, Virion/Serion 10.3%, Kerunda 5.2% and Innovita 1.3%. All laboratories passed the measles and rubella PT, with 28 (88%) achieving 100%. The NMRL performed the US CDC molecular EQA panel in 2016 and received a pass score. The rRT-PCR was introduced into the China LabNet in 2012 as a supplemental method for IgM serology and a measles and rubella molecular PT was developed in December 2014 to evaluate the quality of the commercial rRT-PCR kit used in China. The 2017 panel consisted of 10 virus cultures with each provincial laboratory receiving viruses in a different order. All the laboratories passed the PT with 100% scores, except for one laboratory from Xinjiang, which missed one rubella virus. In 2015, a serological survey was launched in China, with about 35,000 serum samples tested for measles and rubella IgG. The NMRL developed in-house control (IHC) samples and calibration reagents, provided standard operating procedures (SOPs) and performed training for those labs involved in the serosurvey. From 24 July to 5 August 2017, a hands-on training course was held at the NMRL in Beijing for 36 participants from 32 provincial laboratories.

**Standard operating procedure on confirmatory testing**

The Hong Kong SAR (China) RRL is a key confirmatory testing laboratory in the Western Pacific Region. It has developed a standard operating procedure for NMRLs to send samples to RRLs. The key points include: national measles laboratories need to coordinate with the Regional Laboratory Coordinator (RLC) on the number and type of specimens to be sent, with an agreed upon shipping schedule; packaging should comply with UN650 regulations; standardized documentation should be included, such as specimen details and NMRL results using the correction factor; an algorithm for testing (and retesting if discordant) and reporting should be used; and follow-up procedure for discordant results with RLC, NMRL and RRL is needed. For NMRLs requiring genotyping of serum samples, specimens should be collected within five days (measles) or three days (rubella) after onset. All sequence and genotype data will be forwarded to the NMRL and RLC within one month of specimen receipt and it will be a requirement for the NMRL to submit genotype data to MeaNS or RubeNS.
Data management and reporting

Measles and rubella surveillance and laboratory reports are being submitted to the WHO Regional Office for the Western Pacific on the 10th of every month – and for China and PICs, by the 15th of every month – with 92% timeliness in 2016 and 95% in 2017 (to August). Completeness of reporting has been 100% every year since 2015. Outputs produced by the Regional Office include: measles data exchange file (DEF) sent to WHO headquarters on a monthly basis; WHO Regional Office for the Western Pacific Measles and Rubella Bulletin issued once a month; measles and rubella country profiles issued at least once a year; and various ad hoc publications, reports and presentations. The current MS Access database allows only one user to enter data and cannot be easily linked to surveillance data. The number of lab-confirmed cases reported by the laboratories and surveillance teams are different and cases with positive lab results cannot be easily identified in the surveillance data. A web-based system has been designed to contain data from both surveillance and labs with surveillance and lab users entering information for each case, using the same form. The WHO Regional Office for the Western Pacific extracts data on the 10th of every month and the system can generate automated reports.

2.2.11 Polio transition and polio containment: impact on measles and rubella LabNet

Polio transition-impact on MR LabNet

The Seventieth World Health Assembly acknowledged that the GPEI ramp-down has started and highlighted the need for WHO to strategically manage the resulting impact on its human resources and other assets. It noted the reliance on GPEI funding of WHO at global, regional and country levels, involving many WHO programme activities, as well as the financial, organizational and programmatic risks that this reliance entails for WHO, including risks for the sustainability of WHO’s capacity to ensure effective delivery in key programmatic areas and to maintain essential continuing functions. It was recommended to develop a strategic polio transition action plan by the end of 2017 to sustain progress in other programmatic areas such as disease surveillance, immunization and health systems strengthening, early warning, emergency and outbreak response, including strengthening and maintenance of the International Health Regulations (IHR) core capacities and to maintain a polio-free world after eradication.

The impact on the measles and rubella programme could be considerable, as the percentage of GPEI support for EPI is considered to be the following: 23% of WHO polio-funded staff contribute to immunization and surveillance; 19% contribute to technical areas within EPI for laboratory support and data management; 56% provide critical operational support to implement surveillance and immunization activities through WHO country offices; and 90% of the WHO African Region immunization staff and infrastructure are funded by GPEI. It is considered that the measles and rubella elimination goal of the Global Vaccine Action Plan is fragile and could suffer from the withdrawal of polio support. For the LabNet, 84% (122 of 146) of polio laboratories/institutes are also measles and rubella laboratories and these could be at risk of being losing critical resources when polio funding declines.

Polio transition planning is a process of analysing infrastructure, knowledge and functions of the polio programme and managing their scale-down or transfer to other health programmes. There will be a requirement to map assets at country, regional and global levels, and to analyse against national and global health and development needs. Some of the challenges include: donors/partners/governments often fail to recognize the critical role of surveillance in disease control and monitoring vaccine impact,
and imminent reduction of resources supporting polio eradication is a major risk to continuing and expanding global VPD surveillance. There is an urgent need to communicate to donors the important role that disease surveillance plays and to mitigate threat of static or decreasing resources, particularly once polio eradication is achieved.

The contribution of the polio LabNet is considerable as the parallel functions of other VPD LabNets are sufficiently common enough to allow smooth transition in their establishment and maintenance where the facilities and/or personnel are shared. The laboratory coordinator activities are critical for the functioning of the LabNet and 3 of 18 RLCs are fully supported by polio funds and in addition coordinate measles and rubella and other VPD LabNets. In contrast, three RLCs are funded by measles programmes and in addition coordinate polio and other VPD LabNets. Minimal crossover of funding streams for polio and measles laboratory activities occur in the Eastern Mediterranean and European regions, and in-kind support is critical for the functioning of all the VPD LabNets. The support of US CDC and partners for the GMRLN, Japanese encephalitis and yellow fever, and Gavi, the Vaccine Alliance and the Bill & Melinda Gates Foundation for IB-VPD and rotavirus LabNets is critical. However, there is no guarantee that this support will continue in the future. There is a need to address the long-term funding concerns and continue to advocate and encourage new partners to support the LabNets, especially as the improvement in surveillance in some regions requires the development of new laboratories. The impact of diminishing polio funding will have an impact on the functioning of the measles and rubella LabNet but the level of this is still unknown.

Polio containment-impact on measles and rubella LabNet

Phase 1a containment of polio under GAPIII has been completed, but several cVDPV2 outbreaks in the period post switch has required a response with mOPV2. Phase 1b of GAPIII requires guidance for the completion of phase 1 of GAPIII by assisting non-PV facilities to assess the risk of PV PIM in their possession and to implement appropriate risk reduction consistent with GAPIII. PIMs are considered as faecal or respiratory secretion samples collected for any purpose in a time and a geographic area where WPV (including cVDPV) were in circulation or OPV was in use and products of such materials that were propagated in PV permissive cells or animals. Examples of non-PV facilities at risk include laboratories responsible for testing samples for: measles, rotavirus, EVs, enteric bacteria, hepatitis, influenza and other respiratory illnesses, sewage, and water. Strategies consistent with GAPIII include that risk elimination and the scientific value of retaining PIM should outweigh the public health value of its destruction. In addition, if the decision is that PIMs are maintained in a facility, then strong risk reduction and oversight requirements are required of the Member State. It was recommended by the containment advisory group that GAPIII be amended so that PV nucleic acid can be handled outside of containment under certain conditions.

3. CONCLUSIONS AND RECOMMENDATIONS

3.1 Conclusions

3.1.1 Polio LabNet

A two-day series of 11 sessions for the polio LabNet in the Western Pacific Region was organized to discuss global progress towards polio eradication, to identify challenges in maintaining polio-free status in the Western Pacific Region, to share updates on global and regional polio LabNets, to review the performances of the polio network laboratories and to discuss the implementation of new polio
containment requirements following the implementation of GAPIII. The sessions included updates on
the global transmission of wild and VDPV, new methods and perspectives which includes direct
detection of PVs, next-generation sequencing, possible alternatives to microneutralization assays for
immunity assessments and a review of the new enhanced intratypic differentiation techniques
introduced in the past 12 months. Laboratory containment and the implementation of the WHO global
action plan to minimize inadvertent release of PVs, quality assurance, detection of PVs from ES, post-
certification planning, data management and country reports completed the extent of the sessions
covered.

The meeting concluded that the performance of the regional polio LabNet has been sustained at polio-
free-certification standard and that AFP surveillance activities have been efficiently supported. The
network laboratories provided critical evidence in support of the continued polio-free status of the
Region. As of August 2017, all 43 network laboratories are accredited, including all 38 polio
laboratories with ITD function. Of the five VI-only laboratories, three will undergo ITD accreditation in
the near future. A total of 42 laboratories tested and passed the VI PT in 2016 with a 100% score;
however, two laboratories required a second attempt after an initial failure. Forty-one laboratories
performed the 2016 ITD/VDPV PT in January 2017. A total of 29 laboratories passed the first attempt;
however, 8 of the 12 that did not pass, achieved 100% on the second attempt and four laboratories are
pending due to delays in shipment of new panels. Two of the seven laboratories performing the
sequencing PT did not reach the passing score but did so on repeat testing. All laboratories that did not
pass their initial PTs have been provided with extensive support to strengthen their capability.

Since the WHO Regional Office for the Western Pacific Region has been polio free for more than
10 years, 43 network laboratories (12 national and 31 China provincial) have been actively involved in
supplementary EV or ES. China established an extensive HFMD LabNet based on existing polio
laboratories, and Japan and Viet Nam have also implemented HFMD surveillance. The polio
laboratories in Australia, China, Japan, Malaysia, the Philippines and Singapore are involved in testing
samples collected from ES in the Region in 2016 and 2017, with Viet Nam investigating the
introduction of ES by the end of 2017. A total of 7028 AFP cases with specimens were tested in the
Region in 2016 and 3849 were tested in 2017 (as of 13 September). The Lao People’s Democratic
Republic detected the most recent cVDPV cases during late 2015 and early 2016. No cases have been
detected since January 2016. China identified two VDPVs in AFP cases, one in 2016 and one in 2017,
both of which were determined to be “ambiguous”. None showed spread after extensive investigation.
After the switch from tOPV to bOPV in April 2016, Sabin type 1 and 3 viruses are being isolated from
both AFP cases and environmental samples. In the case of Sabin type 2, the last isolation was from
environmental samples in China in August 2016. Starting from September 2016, there have been no
Sabin type 2 viruses isolated either from AFP cases or environmental samples. The continued use of ES
and EV surveillance in a number of countries and areas in the Region has provided valuable data to
support evidence of the continued polio-free status of the Region.

The preparation for implementation of GAPIII is progressing in the Region and phase 1a containment
for WPV2 and VDPV2 has been completed. Biorisk management trainings for PEFs and for national
authorities of containment were carried out in 2015 and 2016, and an auditors’ training for the
Containment Certification Scheme occurred in 2017 with training in local languages (Chinese, Japanese
and Vietnamese). Strong advocacy from the WHO Regional Office for the Western Pacific and
commitment from countries have resulted in a reduced number of laboratories identifying themselves as
potential PEFs. Currently, five countries (Australia, China, Japan, the Republic of Korea and Viet Nam)
have identified that they will establish a total of 16 PEFs.
Considerable efforts have been made to achieve polio eradication in the Region with a critical contribution from the polio LabNet. Continuous strong quality assurance procedures and development of new technologies to enhance the sensitivity of detecting WPV and VDPV are being implemented in the Region, ensuring high-performance, high-quality laboratory support.

### 3.1.2 Measles and rubella LabNet

A two-day series of 12 sessions for the regional measles and rubella LabNet was organized to review progress, identify challenges, and develop plans to further strengthen the performance of network laboratories in support of measles and rubella elimination. The sessions included presentations on global and regional updates on progress with measles and rubella elimination, strengthening the coordination and cooperation between laboratory and epidemiology surveillance, the laboratories’ role in the verification process for the elimination of measles and rubella, strengthening rubella and CRS surveillance, new perspectives and technologies, quality assurance, data management, country reports, and the impact of polio transition and polio containment on the measles and rubella LabNet.

The meeting concluded that measles and rubella network laboratories have greatly contributed to the regional goal of measles and rubella elimination through the timely and accurate confirmation of suspected cases and identifying measles and rubella virus genotypes circulating in the Region. The measles and rubella LabNet has played a critical role in the recent verification of measles elimination of eight Member States by providing evidence that measles cases found in these countries are imported rather than due to endemic circulation. The network consists of a total of 386 laboratories: one GSL in Japan; three RRLs in Australia, China and Hong Kong SAR (China); 17 NMRLs; 31 provincial and 331 prefectural laboratories in China; and three subnational laboratories in Malaysia (N=1) and Viet Nam (N=2). Singapore has recently changed their national laboratory from the Singapore General Hospital to the National Public Health Laboratory. A total of 10 laboratories were assessed under the WHO accreditation process following on-site reviews, with desk reviews now taking precedence to reduce the workload of the RLC.

The role of molecular surveillance for confirming and maintaining verification of measles and rubella elimination is increasingly crucial for the LabNet. Countries are encouraged to collect samples for sequencing and genotyping for at least 80% of chains of infection for measles and especially rubella, but gaps still exist. Genotype and sequence information for measles submitted to the MeaNS WHO sequence database for measles was received from 12 countries. For rubella, sequences were submitted to the RubeNS genotype database for five countries in the Region. The RRL in Hong Kong SAR (China) greatly contributed to the regional measles and rubella genotype databases by sequencing serum samples from six countries that sent samples for confirmatory testing.

All 54 laboratories in the Region that participated in the annual global serology quality assurance programme passed in 2016, and all 13 laboratories passed the molecular quality assurance PT except for one result still pending for measles. Confirmatory testing samples were sent from 10 of 17 national laboratories in 2016 with all 10 laboratories achieving greater than 90% concordance for measles IgM results and nine for rubella.

Establishing CRS surveillance in countries in the Region continues to be a challenge. No country is sharing case-based CRS data with the WHO Regional Office for the Western Pacific yet. Surveillance officers from key countries shared their experiences in building linkages with their laboratory colleagues and thereby facilitating a more comprehensive surveillance programme for rubella/CRS and also measles.
Changes in the facilitation of shipping supplies from the Regional Office to national laboratories have negatively impacted the frequency and cost of distribution of PT panels and test kits in the Region. These changes, combined with delays in partner funding, have resulted in some stock-outs of kits in key countries and a reversion to hand-carrying of PT panels.

The regional measles and rubella LabNet has made considerable progress since establishment began in 1998. The network laboratories all follow WHO-recommended methods and procedures under a strong environment of quality assurance. A total of 141,000 serum samples from suspected measles and rubella cases were reported in 2016 and they were reported timely and accurately. The high capacity of molecular detection in most laboratories in the Region has resulted in 3058 measles virus sequences and 102 rubella sequences being reported to the WHO genotype databases in 2016, allowing informed decisions on the molecular surveillance of measles and rubella globally and in the Region and contributing to the verification status of countries.

3.2 Recommendations

3.2.1 Polio LabNet

1) Following the Containment Advisory Group meeting in June 2017, PV nucleic acid that has been extracted/purified using methods demonstrated to inactivate PV can be handled outside of PV containment under the condition that they will not be introduced into polio-permissive cells or animals.

2) Only PEFs that are officially designated should handle and store WPV2, VDPV2 and oral polio vaccine/Sabin type 2 materials. Non-PEFs that will continue to receive diagnostic samples from AFP and supplemental surveillance samples (ES, EV surveillance) should implement safe and secure working practices based on a risk assessment and appropriate biorisk management systems as described in GAPIII, Annex 6.

3) All PV laboratories in the Western Pacific Region must follow the Global Polio Laboratory Network Guidance Paper 1 for PV2 sample referral.

   a) VI and ITD laboratories: all new identified PV2 isolates must be transferred (by FTA cards to a designated PEF that has the capacity for VI, ITD and sequencing (VIIS) for VP1 sequencing.

   b) Designated PEFs with capacity for VIIS in the regional polio LabNet are:

      • VIDRL, Australia: receiving PV2 for sequencing from Malaysia, New Zealand, the Philippines and Singapore;
      • China CDC: receiving PV2 for sequencing from provincial laboratories in China; and
      • NIID, Japan: receiving PV2 for sequencing from Hong Kong SAR (China), Mongolia (also for ITD), the Republic of Korea and Viet Nam (two laboratories).

   c) VIIS non-PEF laboratories are able to continue sequencing PV2 as usual if they inactivate RNA and destroy the original stool or ES sample.

4) All PV2-positive reactions identified by ITD must be sequenced. It will not be necessary to run an additional Sabin 2 VDPV assay. All polio laboratories are requested to report all PV2 detected from
any source within 24 hours after completing ITD and when sequencing results are available. The following steps, highlighted in GPLN Guidance Paper 1, should be implemented:

a) Report all new PV2 to the Ministry of Health and WHO within 24 hours.

b) All original stool samples, stool extracts and cell-culture harvests are to be packed, sealed and stored securely in a freezer at \(-20^\circ\)C, with access only to designated staff.

c) Send isolate using FTA cards as soon as possible and no later than seven days, for sequencing to a designated PEF and track the shipment.

d) When sequencing results are received from the PEF, immediately notify the Ministry of Health and WHO (country office, regional office and headquarters) within 24 hours (to get confirmation of receipt of message).

e) Destroy sealed packages under the guidance of the RLC and Global Laboratory Coordinator (GLC).

f) Document all procedures, to enable traceability, and share reports with the Ministry of Health and WHO.

5) Recognizing the historical suboptimal number of stool samples processed annually (by some laboratories), the WHO Regional Office for the Western Pacific will document and share with other polio laboratories and WHO headquarters the strategy used in Mongolia to have access to additional stool samples to be tested for PV to maintain the skills of trained staff in a context of very low workload.

6) All NPEVs growing on L20B cells should be typed and results shared with WHO RLCs and GLCs for compilation and drafting information note/guidance to all GPLN laboratories.

7) As previously recommended, it is important that a clear mapping of master and working cell banks be conducted in all laboratories to document origin, passage numbers and characterization (including cell sensitivity, authentication and mycoplasma testing as appropriate) of cell lines/RD and L20B used in polio laboratories, are shared with the WHO Regional Office and headquarters. A template will be developed by the Regional Office.

8) It is important to assess the PV serology status (including for type 2) of all polio laboratory staff and any personnel who can come across PV in a polio laboratory. It is therefore recommended that the WHO Regional Office for the Western Pacific: (i) nominate reference PEF laboratory(ies) able and willing to provide this service to polio laboratories in the Region, and (ii) provide support, in collaboration with WHO headquarters, to establish such laboratory(ies). For the meantime, US CDC has kindly agreed to receive DBS from polio laboratories as specified in GPLN Guidance Paper 3. Australia, China and Japan will test their own staff.

9) Polio laboratory personnel for whom suboptimal antibody titres are detected are requested to receive a booster dose and further polio antibodies testing to confirm adequate protection, according to local/national regulations.

10) As pilot-tested in 2017 in different laboratories, all ES laboratories in the Western Pacific Region can expect to undergo ES accreditation in 2018.
11) FTA cards have been validated for the shipment of sequencing PTs and have become a critical mechanism for referring samples within the GPLN. To test proficiency of RNA extraction from FTA cards and downstream sequencing of the extracted RNA, there will be three FTA card samples included in the 2017 sequencing PT. All results (three FTA cards and three RNA transcripts) will be graded this year and laboratories given seven days to report results. The WHO Regional Office for the Western Pacific Region polio laboratories are encouraged to practise sequencing FTA samples in advance of receiving the 2017 PT sequence panel. If no FTA samples are available, laboratories may spot their own cards with PV isolates and process them (RNA extraction and sequencing) as soon as possible.

12) VDPV classification should be a coordinated decision-making process. All laboratory personnel and national programme staff should be aware of the field investigation requirements described in the GPEI guidelines for the reporting and classification of VDPVs and the standard operating procedures for responding to PV2 detection (http://www.polioeradication.org/wp-content/uploads/2016/07/VDPV_ReportingClassification.pdf; http://polioeradication.org/wp-content/uploads/2017/05/POL-SOPs-Part-1-260517.pdf; http://polioeradication.org/wp-content/uploads/2017/05/POL-SOPs-Part-2-260517-.pdf). A sequencing laboratory should be familiar with the elements under the field investigation section of the guidelines when communicating a VDPV result so that it can advise field staff of the need to immediately conduct appropriate clinical and field investigations.

13) A standardized reporting text and table for email messages accompanying sequencing reports have been finalized and should be used in the GPLN. WHO in collaboration with the GSL at US CDC will provide a consensual guidance document on genetic characterization, categorization and reporting for VDPVs, after final clearance by the GPLN Small Working Group in October 2017. All laboratories are expected to comply with defined requirements starting January 2018.

14) It is reminded that all laboratories should share any ITD/VDPV rRT-PCR raw data file, for which there is a doubt in interpretation, with reference laboratories and WHO laboratory coordinators for troubleshooting and guidance before programme-wide reporting.

15) Several platforms have been validated for running CDC ITD/VDPV rRT-PCR assays. It is recommended that laboratories investigate their accessibility to such platforms, communicate the information with the WHO laboratory coordinators and validate the ITD assays in these platforms that can be used if necessary.

16) Annual accreditation desk reviews for the regional GPLN are to be submitted through annual reports to the GPLNMS and should be submitted no later than the end of the first week of February of each year. Laboratories will receive on-site visits every three years or as deemed necessary.

17) PASRS is up and running and all countries are strongly encouraged to submit their data to this web-based system, particularly countries that are still using Excel-based reporting and have weak linkage of surveillance and laboratory data. Use of PASRS requires coordination and agreement with AFP surveillance focal points. Laboratories and surveillance focal points who are having challenges using PASRS should contact the data management team in the Regional Office for the Western Pacific Region (wproepidata@who.int).
18) WHO headquarters is to provide examples of data dictionary of ES databases established/being established in other WHO regions to help build an ES component on the PASRS of the Regional Office for the Western Pacific.

19) All network laboratories (non-PEFs) should continue to use the laboratory self-assessment tools for GAPIII, Annex 6 for guidance in the safe handling of potentially infectious polio samples in their laboratories.

20) National polio laboratories that are designated as PEFs (China CDC, NIID and VIDRL) should work closely with their NAC to start the certification process as early as possible.

21) All network laboratories are urged to complete (by the first week of October at the latest), the GPLN survey launched by WHO/GPLN and Kid Risk, Inc. aiming to map the assets and requirements of polio laboratories to maintain a high standard level of polio surveillance, in order to inform the programme and maintain GPEI support to the GPLN.

22) It is extremely important that polio laboratory funds are utilized to complete global polio eradication and that they are not prematurely transitioned to any other VPD programme before global polio eradication certification is achieved and secured.

3.2.2 Measles and rubella LabNet

1) IgM detection and molecular testing for confirmation of both rubella and measles needs to be further strengthened in the Region. Laboratories will need to optimize the testing algorithm and develop flexibility when near to, or post elimination (e.g. for IgM test: parallel testing for both measles and rubella in low-incidence settings, or serial testing in high- incidence settings); and consider using rRT-PCR to complement IgM test information for serum collected within three days and to screen virological samples. IgG avidity testing may also be considered in countries that have reached elimination to help classify cases. Countries with arboviral acute fever and rash surveillance may consider using negative samples for measles and rubella to enhance surveillance.

2) Laboratories need to identify resource needs to cover the increased costs of the testing required for integration of measles and rubella testing and case-based surveillance. They should collaborate with their appropriate funding authority (e.g. Ministry of Health) to be allocated sufficient human and financial resources to support the increased activities associated with elimination-level surveillance.

3) It is recommended that all network laboratories work with epidemiological surveillance colleagues ensuring the collection of virological samples (throat swabs or urine), together with blood samples, during the first contact with suspected cases to supplement the IgM test and to obtain genotype data and also to obtain isolates for further analysis to provide better resolution. Throat swab samples may be shipped out using FTA cards at room temperature when challenges with cold chain occur.

4) Countries close to or having achieved elimination should generate genotype data for more than 80% of chains of transmission and should work in collaboration with their surveillance colleagues to identify the likely source of any new infection detected.

5) To provide better resolution of measles and rubella virus transmission patterns to support verification, it is important to describe the lineages in addition to the genotypes, and:
a) always include a phylogenetic tree;

b) always include matches with named strains on MeaNS;

c) consider using an expanded sequencing window to increase resolution when necessary; and

d) implement additional training in molecular methods including sequence analysis and database submission using web-based mechanisms where possible.

6) For sequences generated by a RRL for a national laboratory, it is recommended that the national laboratory submit their sequences to MeaNS or RubeNS, rather than the RRL. National measles and rubella reference laboratories without the knowledge to submit sequences to these databases should consult the RLC for support.

7) It is recommended that every sequence obtained from countries be submitted to MeaNS or RubeNS, even if they are 100% identical to other strains and/or all derived from the same outbreak. Vaccine strains should not be submitted to the databases.

8) NMRLs without the capacity for molecular analysis should send representative virological or serum samples or PCR products to their designated RRL after consulting with the RLC and RRL so that the country can obtain genetic information on both outbreaks and sporadic cases. Serum samples should be collected from confirmed cases within the first three days after rash onset for rubella and within five days of rash onset for measles. A serum volume of more than 300 microliters is required for molecular testing and should be shipped under the appropriate cold chain.

9) One of the lines of evidence for the verification of elimination is determining population immunity through analysis of data on routine immunization activities and SIAs. Alternatively, countries may include other sources of immunity data such as well-conducted seroprevalence studies. WHO is currently developing guidelines for the assessment of population immunity against measles and rubella through seroprevalence studies. However, countries should carefully consider implementing such activities as they are complicated, costly and time-consuming, and the use of high-quality serology assays is critical.

10) All NMRLs in the Region should submit samples for confirmatory testing to their designated RRL in a timely manner (1–2 times a year). A schedule of suitable shipping dates can be arranged in consultation with the RLC, RRL and NMRLs. To avoid delays to the agreed schedule, the NMRLs should arrange timely accession of import/export permit, if required. Follow-up of discordant results should be made and findings shared with the RLC, RRL and NMRLs for future improvement. A standard operating procedure on confirmatory testing is being developed and NMRLs can request support from their RLC and RRL if there is any difficulty in following the standard operating procedure.

11) To ensure the timely arrival of samples for PT, NMRLs should secure an import permit and liaise with WHO country offices (where present) to facilitate receipt of PT samples in advance of the schedule of distribution of PT panels. Laboratories should work with the RRL and RLC to evaluate results and address any issues identified by the PT. Results should be submitted via the PT website within the required 14-day timeline.
12) Laboratories should have regular communication with the RLC and WHO country offices to update them on any changes in workload and identify potential shortfalls in supplies that may impact their testing turnaround time.

13) Where issues in quality are identified in subnational laboratories, the NMRL responsible for that country should monitor the performance of subnational laboratories and provide support where necessary.

14) All countries approaching or achieving elimination of measles or rubella should define an expert committee, composed of both laboratory and epidemiologic experts, and written algorithm to decide case classification, particularly during outbreaks. The composition of the case classification and case classification algorithm should be specified as part of the national measles and rubella elimination plan of action.

15) Good-quality data management and linkage between epidemiological and laboratory surveillance should be ensured to enable accurate analysis of measles and rubella outbreaks and transmissions. Countries, particularly those still using Excel-based reporting and having weak linkage of surveillance and laboratory data, may consider different approaches, including the use of the web-based Measles and Rubella Surveillance Reporting System (MRSRS). The use of the system requires coordination and agreement with measles and rubella surveillance focal points in the WHO Regional Office for the Western Pacific. Countries should strictly ensure that laboratory and epidemiologic surveillance databases are linked using unique identification codes. The Measles and Rubella Surveillance Reporting System is an ideal resource for improvement of surveillance data management including linkage of laboratory and epidemiologic surveillance data.

16) All non-polio laboratories including measles and rubella should review the draft document Guidance for Non-Poliovirus Facilities to Minimize Risk of Sample Collections Potentially Infectious for Polioviruses and provide input to the WHO Regional Office for the Western Pacific by 31 October 2017. Laboratories are also encouraged to pilot the guidance document and provide feedback on how useful the guidance was to categorize potentially infectious materials according to risk. Once the guidance is finalized (early 2018), all non-polio laboratories must:

   a) assess the risk of PV PIM in their possession;

   b) if facilities plan to retain OPV/Sabin PIM, declare their holdings and submit a report to the National Polio Containment Coordinator and maintain a working inventory of materials in their possession; and

   c) implement appropriate risk reduction consistent with GAPIII as described in the guidance document.

18) Following the Containment Advisory Group meeting in June 2017, nucleic acid that has been extracted/purified using methods demonstrated to inactivate PV can be handled outside of PV containment under the condition that they will not be introduced into polio-permissive cells or animals.

3.2.3 World Health Organization

1) The WHO Regional Office for the Western Pacific will continue to expand ES in the Region for priority countries: Cambodia, the Lao People’s Democratic Republic, Papua New Guinea and Viet Nam.
2) The WHO regional offices and headquarters will continue to support all Member States in the Region for maintaining strong polio, measles and rubella LabNets for the eradication of PV and elimination of measles and rubella.

3) The WHO Regional Office for the Western Pacific will continue to work with RRLs to provide technical advice to national laboratories to select the representative serum samples to be sent to the designated RRLs for confirmatory testing.

4) WHO will consider defining a resource committee of experts in rubella and surveillance, to guide countries in designing CRS surveillance systems or activities (including retrospective case finding) that are appropriate to their epidemiological and programmatic situation to support rubella elimination efforts.
ANNEXES

LIST OF PARTICIPANTS, TEMPORARY ADVISERS, OBSERVERS, AND SECRETARIAT

POLIOMYELITIS SESSION, 26 – 27 September 2017

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PROGRAMME OF ACTIVITIES

PART I. POLIO LABORATORY NETWORK MEETING
26-27 SEPTEMBER 2017

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity/Agenda Item/Subject of Presentation</th>
<th>Presenter</th>
</tr>
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<tbody>
<tr>
<td>Tuesday, 26 September 2017</td>
<td><strong>Registration</strong>&lt;br&gt;08:00–08:30</td>
<td>WHO Secretariat</td>
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<td></td>
<td><strong>Opening session</strong>&lt;br&gt;08:30–09:00</td>
<td>Dr Yoshihiro Takashima&lt;br&gt;&lt;br&gt;Participants&lt;br&gt;&lt;br&gt;Dr Yoshihiro Takashima&lt;br&gt;&lt;br&gt;Ms Varja Grabovac</td>
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<td></td>
<td>• Welcome and opening remarks&lt;br&gt;• Self-introduction&lt;br&gt;• Election of officers&lt;br&gt;• Administrative announcements&lt;br&gt;• Group photo</td>
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<td><strong>Session 1. Polio endgame strategy and updates on maintaining polio-free status: Global and Regional</strong>&lt;br&gt;09:00–09:20</td>
<td>Dr Tigran Avagyan</td>
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<td></td>
<td>a) Polio endgame strategy: update on global and regional progress</td>
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<td>b) Update of Global wild poliovirus (WPV) transmission and status of Global Polio Laboratory Network (GPLN)</td>
<td>Dr Ousmane Diop</td>
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<td>c) Update of Regional Polio Laboratory Network– expansion of Intratypic Differentiation (ITD) laboratories and environmental surveillance (ES)</td>
<td>Ms Varja Grabovac</td>
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<td><strong>Coffee break</strong>&lt;br&gt;10:00–10:20</td>
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<tr>
<td>Time</td>
<td>Activity/Agenda Item/Subject of Presentation</td>
<td>Presenter</td>
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<td>10:20–10:35</td>
<td>Session 2.  Report from global specialized laboratory (GSL), regional reference laboratories (RRL)</td>
<td>Dr Hiroyuki Shimizu</td>
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<td></td>
<td>a) Japan</td>
<td>Dr Bruce Thorley</td>
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<td></td>
<td>b) Australia</td>
<td>Dr Xu Wenbo</td>
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<tr>
<td>10:35–10:50</td>
<td>Discussion</td>
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<td>11:05–11:15</td>
<td>Session 3.  Report from the national polio laboratories in the Region</td>
<td>Mr Lau Chi Shan</td>
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<td></td>
<td>a) Hong Kong SAR (China)</td>
<td>Dr Mohd Apandi Yusof</td>
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<td>11:15–11:30</td>
<td>Discussion</td>
<td>Dr Ichinkhorloo Bonduush</td>
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<td>12:15–13:00</td>
<td>Lunch break</td>
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<td>11:45–12:00</td>
<td>b) Malaysia</td>
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<td>12:00–12:15</td>
<td>c) Mongolia</td>
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<td>12:15</td>
<td>1) Viet Nam, Hanoi</td>
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<td>13:00–13:15</td>
<td>d) New Zealand</td>
<td>Ms Judy Bocacao</td>
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<td></td>
<td>e) Philippines</td>
<td>Dr Lea Necitas Apostol</td>
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<tr>
<td>13:15–13:30</td>
<td>f) Republic of Korea</td>
<td>Dr Chun Kang</td>
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<tr>
<td>13:30–13:45</td>
<td>g) Singapore</td>
<td>Ms Puong Kim Yoong</td>
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<tr>
<td>13:45–14:00</td>
<td>h) Viet Nam, Ho Chi Minh City</td>
<td>Dr Tran Thi Nguyen Hoa</td>
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<tr>
<td>14:00–14:15</td>
<td>i) Viet Nam, Hanoi</td>
<td>Dr Nguyen Thi Thanh</td>
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<td>14:15–14:30</td>
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<td>14:30–14:50</td>
<td>Discussion</td>
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<td>14:50</td>
<td>2) Viet Nam, Hanoi</td>
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<tr>
<td>15:15–15:30</td>
<td>Session 4.  New methods and perspectives</td>
<td>Ms Analisa Bautista</td>
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<tr>
<td></td>
<td>a) Progress on direct detection of poliovirus (PV) in stool samples/ laboratory detection without virus isolation</td>
<td>Dr Cara Burns</td>
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<tr>
<td>15:30–15:45</td>
<td>b) Progress on Rotor Gene/Bio Rad/Stratagene ITD 5.0 validation</td>
<td>Dr Cara Burns</td>
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<tr>
<td>15:45–16:00</td>
<td>c) Alternative method for microneutralization test (Luminex)</td>
<td>Mr Lau Chi Shan</td>
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<tr>
<td>16:00–16:15</td>
<td>d) Next Generation Sequencing</td>
<td>Dr Jason Roberts (via WebEx)</td>
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<td>16:15–16:45</td>
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<td></td>
<td>Session 5.  Laboratory Quality Assurance</td>
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<tr>
<td>16:45-17:00</td>
<td>a) Report on 2016 virus isolation proficiency testing from the National Institute for Public Health and the Environment (RIVM)</td>
<td>Ms Analisa Bautista</td>
</tr>
<tr>
<td>17:00–17:15</td>
<td>b) Report on 2016 ITD and report on 2015/16 sequencing</td>
<td>Dr Cara Burns</td>
</tr>
<tr>
<td>17:15–17:30</td>
<td>c) Quality assurance/control (cell sensitivity and authenticity, mycoplasma testing, etc…)</td>
<td>Ms Analisa Bautista</td>
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<td>17:30-18:00</td>
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<tr>
<td>18:00</td>
<td>Wrap up and close of the first day</td>
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<td>Regional Director's Reception</td>
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<tr>
<td>Time</td>
<td>Activity/Agenda Item/Subject of Presentation</td>
<td>Presenter</td>
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<tr>
<td>08:30–08:50</td>
<td><strong>Session 6.  Polio laboratory containment - GAP III</strong>&lt;br&gt;a) Implementation of GAP III in the Western Pacific Region</td>
<td>Ms Varja Grabovac</td>
</tr>
<tr>
<td>08:50–09:05</td>
<td>b) Regional status of poliovirus containment activities in the European Region</td>
<td>Dr Eugene Gavrilin</td>
</tr>
<tr>
<td>09:05–09:25</td>
<td>c) Update from Global Certification Commission (GCC) and Containment Advisory Group (CAG) meetings</td>
<td>Dr Jacqueline Fournier-Carruana</td>
</tr>
<tr>
<td>09:25–09:40</td>
<td>d) WHO guidance on identification of potentially infectious materials – completion of Phase 1</td>
<td>Ms Varja Grabovac</td>
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<tr>
<td>09:40–10:00</td>
<td>e) Challenges with identification of National Authorities for Containment</td>
<td>Dr Zuo Shuyan</td>
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<tr>
<td>10:00–10:30</td>
<td><strong>Discussion</strong></td>
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<tr>
<td>08:30–08:50</td>
<td><strong>Session 7.  Impact of polio laboratory containment on GPLN</strong>&lt;br&gt;a) Laboratory performance strategies in the GPLN in the context of poliovirus containment</td>
<td>Dr Ousmane Diop</td>
</tr>
<tr>
<td>08:50–09:05</td>
<td>b) Preparing polio laboratory to become a poliovirus essential facility (PEF)</td>
<td>Dr Bruce Thorley</td>
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<tr>
<td>09:05–09:25</td>
<td>c) Preparing polio laboratory to become non-PEF</td>
<td>Dr Lea Necitas Apostol</td>
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<tr>
<td>10:00–10:30</td>
<td><strong>Discussion</strong></td>
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<td>10:30–10:50</td>
<td><strong>Coffee break</strong></td>
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<td>10:50–11:05</td>
<td><strong>Session 8.  Environmental Surveillance (ES)</strong>&lt;br&gt;a) Global Perspective on ES</td>
<td>Dr Ousmane Diop</td>
</tr>
<tr>
<td>11:05–11:20</td>
<td>b) ES in China</td>
<td>Ms Zhu Shuangli</td>
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<tr>
<td>11:20–11:35</td>
<td><strong>Discussion</strong></td>
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<td>11:35–12:00</td>
<td><strong>Lunch break</strong></td>
<td>WHO Secretariat, Temporary Advisers, Rapporteur</td>
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<tr>
<td>12:00–13:30</td>
<td>Working lunch for developing of recommendations</td>
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<tr>
<td>13:30–13:50</td>
<td><strong>Session 9.  Data management</strong>&lt;br&gt;Data management and reporting</td>
<td>Mr Benjamin Bayutas</td>
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<td>13:50–14:05</td>
<td><strong>Discussion</strong></td>
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<td>14:00–14:20</td>
<td><strong>Coffee break</strong></td>
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<tr>
<td>14:20–14:40</td>
<td><strong>Session 10.  Post-certification planning</strong>&lt;br&gt;Post-certification strategic plan: impact on the WPR</td>
<td>Dr Tigran Avagyan</td>
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<tr>
<td>14:40–15:00</td>
<td><strong>Discussion</strong></td>
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<td>15:00–15:30</td>
<td><strong>Coffee break</strong></td>
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<tr>
<td>15:30–15:50</td>
<td><strong>Session 11.  Conclusions and recommendations</strong>&lt;br&gt;Draft Conclusions and recommendations</td>
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<td>15:50–16:20</td>
<td><strong>Discussion</strong></td>
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<td>16:20–17:30</td>
<td><strong>Closing of the meeting</strong></td>
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PROVISIONAL PROGRAMME OF ACTIVITIES

PART II. MEASLES AND RUBELLA LABORATORY NETWORK MEETING
28–29 SEPTEMBER 2017

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity/Agenda item/Subject of Presentation</th>
<th>Presenter</th>
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<tbody>
<tr>
<td>Thursday, 28 Sep 2017</td>
<td>Registration</td>
<td>WHO Secretariat</td>
</tr>
<tr>
<td>08:00–08:30</td>
<td>Registration</td>
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<tr>
<td>08:30–09:00</td>
<td>Opening session</td>
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<td></td>
<td>• Welcome remarks</td>
<td>Dr Zhang Yan</td>
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<tr>
<td></td>
<td>• Opening remarks</td>
<td>Dr Yoshihiro Takashima</td>
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<td></td>
<td>• Self-introduction</td>
<td>Participants</td>
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<td>• Election of officers</td>
<td>Dr Yoshihiro Takashima</td>
</tr>
<tr>
<td></td>
<td>• Administrative announcements</td>
<td>Dr Zhang Yan</td>
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<td>• Group photo</td>
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</tbody>
</table>
**Session 1. Overview of global and regional measles and rubella elimination**

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
<th>Presenter</th>
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<tbody>
<tr>
<td>09:00–09:20</td>
<td>a) Global and Regional updates on eliminating measles and rubella: progress in 2016–2017 and issues to be addressed in 2018–2020</td>
<td>Dr Jose Hagan</td>
</tr>
<tr>
<td>09:20–09:40</td>
<td>b) Update of Global measles and rubella laboratory network</td>
<td>Dr Mick Mulders</td>
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<tr>
<td>09:40–10:00</td>
<td>Update of Regional measles and rubella laboratory network</td>
<td>Dr Zhang Yan</td>
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<td>10:00–10:10</td>
<td>Discussion</td>
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**10:10–10:30** Coffee break

**Session 2. Reports from Global Specialized Laboratory (GSL) and Regional Reference Laboratories (RRL)**

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
<th>Presenter</th>
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<tbody>
<tr>
<td>10:30–10:50</td>
<td>a) US CDC</td>
<td>Dr Paul Rota (via WEBEX)</td>
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<td>10:50–11:05</td>
<td>b) Japan</td>
<td>Dr Yoshiro Mori/Dr Nakatsu Yuichiro</td>
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<tr>
<td>11:05–11:20</td>
<td>c) Australia</td>
<td>Mr Julian Druce</td>
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<td>11:20–11:35</td>
<td>d) China</td>
<td>Dr Wang Huiling</td>
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<td>11:35–11:50</td>
<td>e) Hong Kong SAR (China)</td>
<td>Dr Jasmine Kwong</td>
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<td>11:50–12:00</td>
<td>Discussion</td>
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**12:00–12:45** Lunch Break

**Session 3: Report from the National Laboratories in the Region (Part I)**

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
<th>Presenter</th>
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<tbody>
<tr>
<td>12:45–13:00</td>
<td>a) Brunei Darussalam</td>
<td>Dayang Hajah Mazmah</td>
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<td>Haji Ahmad Morshidi</td>
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<td>13:00–13:15</td>
<td>b) Cambodia</td>
<td>Mr Buth Sokhal</td>
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<td>13:15–13:30</td>
<td>c) Lao People's Democratic Republic</td>
<td>Ms Bouaphah</td>
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<td>Khamphaphongphane</td>
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<td>13:30–13:45</td>
<td>d) Malaysia</td>
<td>Ms Rashidah Mohammad</td>
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<td>13:45–14:00</td>
<td>e) Mongolia</td>
<td>Dr Altanchimeg Samdan</td>
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<tr>
<td>14:00–14:15</td>
<td>Discussion</td>
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</tbody>
</table>
Session 4: Strengthen coordination and cooperation between laboratory and epidemiology surveillance: lessons learned

14:15–14:30  a) China  Dr Ma Chao
14:30–14:45  b) Malaysia  Dr Faridah Kusnin
14:45–15:00  c) Cambodia  Mr Siphan Sovannara
15:00–15:30 Discussion
15:30–15:50 Coffee break

Session 5: Verifying elimination of measles and rubella

15:50–16:05 a) Update of the 6th Meeting of the Regional Verification Commission for Measles and rubella Elimination in WPR  Dr Jose Hagan
16:05–16:25 b) Laboratory support experience from European Region  Dr Myriam Mamou (via WEBEX)
16:25–16:40 Discussion

Session 6. Report from the national laboratories in the Region (Part II)

16:40–16:55  f) New Zealand  Dr Meik Dilcher
16:55–17:10  g) Papua New Guinea  Dr Evelyn Lavu
17:10–17:25  h) Fiji  Ms Taina Vadei
17:25–17:40  i) Singapore  Dr Ng Yi Kai
17:40–17:50 Discussion

Wrap up and close of the first day

18:00 Regional Director's Reception

Friday, 29 September 2017

Session 7: Strengthening Rubella and Congenital Rubella Syndrome (CRS) Surveillance

08:30–08:45  a) Regional Rubella and CRS surveillance: progress, challenges and perspectives  Dr Roberta Pastore
08:45–09:00  b) Challenges in CRS Surveillance with examples of imported CRS cases into the US  Dr Joseph Icenogle
09:00–09:15  c) Rubella and CRS surveillance in China  Dr Zhu Zhen
09:15–09:30  d) Rubella and CRS surveillance in Japan  Dr Yoshio Mori
09:30–09:45 Discussion

Session 8. New perspective and technique

09:45–10:00  a) Challenges in diagnosing measles rubella cases in elimination phase  Dr Roberta Pastore/ Dr Xu Wenbo
10:00–10:15  b) Development of a point of care test for measles and rubella - update and way forward Mr David Featherstone
10:15–10:30  Discussion

10:30–10:50  Coffee break

**Session 9: Report from the National and Subnational Laboratories in the Region (Part III)**

10:50–11:05   j) Philippines Mr Daniel Villarico
11:05–11:20   k) Republic of Korea Dr Chun Kang
11:20–11:30   l) Viet Nam, Hanoi Ms Trieu Thi Thanh Van
11:30–11:40   m) Viet Nam, Ho Chi Minh City Country participant
11:40–11:50   n) Viet Nam, Nha Trang Mrs Ngo Thi Quyet
11:50–12:00   o) Viet Nam, Dak Lak Dr Pham Tho Duoc

12:00–12:10  Discussion

12:10–13:40  Lunch break

Working lunch for developing of recommendations WHO Secretariat, Temporary Advisers, Rapporteur

**Session 10: Quality assurance (QA)**

13:40–13:55   a) Update on quality assurance for molecular proficiency test Dr Joseph Icenogle
13:55–14:15   b) Measles and rubella confirmatory testing and IgM proficiency test Dr Suellen Nicholson
14:15–14:30   c) China Laboratory Network: QA for provincial laboratories Dr Mao Naiying
14:30–14:45   d) SOP on confirmatory testing Dr Jason Chan
14:45–15:00   e) Data management and reporting Ms Kayla Mae Mariano
15:00–15:20   Discussion

15:20–15:45  Coffee break

**Session 11. Polio transition and Polio containment: impact on Measles and Rubella (MR) Laboratory Network (LabNet)**

15:45–16:00   a) Polio transition-impact on MR LabNet Dr Mick Mulders/
16:00–16:15   b) Polio containment-impact on MR LabNet Mr David Featherstone
16:15–16:30   Discussion Ms Varja Grabovac

16:30–17:30  Session 12: Conclusions and recommendations

17:30  Close of meeting