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

18–22 March 2019
Manila, Philippines
Eighth Meeting of Vaccine-Preventable Diseases Laboratory Networks in the Western Pacific Polio Session
20–21 March 2019
Manila, Philippines

Eighth Meeting of Vaccine-Preventable Diseases Laboratory Networks in the Western Pacific Measles and Rubella Session
18–19 March 2019
Manila, Philippines

Workshop on Genetic Analysis of Measles and Rubella Molecular Data
20–22 March 2019
Manila, Philippines
MEETING REPORT

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

Convened by:

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR THE WESTERN PACIFIC

Manila, Philippines
18–22 March 2019

Not for sale

Printed and distributed by:

World Health Organization
Regional Office for the Western Pacific
Manila, Philippines

July 2019
### ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AFP</td>
<td>acute flaccid paralysis</td>
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<tr>
<td>cVDPV</td>
<td>circulating vaccine-derived poliovirus</td>
</tr>
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<td>CRS</td>
<td>congenital rubella syndrome</td>
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<td>EV</td>
<td>enterovirus</td>
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<tr>
<td>EPI</td>
<td>Expanded Programme on Immunization</td>
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<tr>
<td>EQA</td>
<td>external quality assessment</td>
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<td>ES</td>
<td>environmental surveillance</td>
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<tr>
<td>GAPIII</td>
<td><em>Global Action Plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of oral polio vaccine use</em></td>
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<tr>
<td>GMRLN</td>
<td>Global Measles and Rubella Laboratory Network</td>
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<td>GPLN</td>
<td>Global Polio Laboratory Network</td>
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<tr>
<td>GSL</td>
<td>global specialized laboratory</td>
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<tr>
<td>HFMD</td>
<td>hand, foot and mouth disease</td>
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<tr>
<td>IgG</td>
<td>immunoglobulin G</td>
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<tr>
<td>IgM</td>
<td>immunoglobulin M</td>
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<tr>
<td>IPV</td>
<td>inactivated poliovirus vaccine</td>
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<tr>
<td>ISO</td>
<td>International Organization for Standardization</td>
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<tr>
<td>ITD</td>
<td>intratypic differentiation</td>
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<tr>
<td>L20B</td>
<td>a mouse cell line (L-cells), genetically engineered to express the human poliovirus receptor</td>
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<tr>
<td>MCV</td>
<td>measles-containing vaccine</td>
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<tr>
<td>MeaNS</td>
<td>Measles Nucleotide Surveillance</td>
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<tr>
<td>MMR</td>
<td>measles, mumps and rubella</td>
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<td>NIID</td>
<td>National Institute of Infectious Diseases</td>
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<td>NMRL</td>
<td>national measles and rubella laboratory</td>
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<tr>
<td>NPEV</td>
<td>non-polio enterovirus</td>
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<tr>
<td>NPL</td>
<td>national polio laboratory</td>
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<td>OPV</td>
<td>oral polio vaccine</td>
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<td>PASRS</td>
<td>Polio AFP Surveillance and Reporting System</td>
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<tr>
<td>PCR</td>
<td>polymerase chain reaction</td>
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<tr>
<td>PEF</td>
<td>poliovirus-essential facility</td>
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<tr>
<td>PIM</td>
<td>potentially infectious material</td>
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<tr>
<td>PRN</td>
<td>plaque reduction neutralization</td>
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<tr>
<td>PT</td>
<td>proficiency test</td>
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<td>PV</td>
<td>poliovirus</td>
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<tr>
<td>RCV</td>
<td>rubella-containing vaccine</td>
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<tr>
<td>RD</td>
<td>human rhabdomyosarcoma</td>
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<tr>
<td>RNA</td>
<td>ribonucleic acid</td>
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<tr>
<td>RT-PCR</td>
<td>reverse transcriptase polymerase chain reaction</td>
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<tr>
<td>RITM</td>
<td>Research Institute for Tropical Medicine (Philippines)</td>
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<tr>
<td>RLC</td>
<td>regional laboratory coordinator</td>
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<td>RRL</td>
<td>regional reference laboratory</td>
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<td>RVC</td>
<td>Regional Verification Commission for Measles Elimination</td>
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<td>RubeNS</td>
<td>Rubella Nucleotide Surveillance</td>
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<tr>
<td>SL</td>
<td>Sabin-like</td>
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<tr>
<td>UNICEF</td>
<td>United Nations Children’s Fund</td>
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<tr>
<td>US CDC</td>
<td>United States Centers for Disease Control and Prevention</td>
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<tr>
<td>VDPV</td>
<td>vaccine-derived poliovirus</td>
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<tr>
<td>VIDRL</td>
<td>Victorian Infectious Diseases Reference Laboratory</td>
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<td>VPD</td>
<td>vaccine-preventable disease</td>
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<td>WHO</td>
<td>World Health Organization</td>
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<td>WPV</td>
<td>wild poliovirus</td>
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The Eighth Meeting of Vaccine-Preventable Diseases Laboratory Networks in the Western Pacific Region was held in Manila, Philippines from 18 to 22 March 2019 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 Seventh Meeting of Vaccine-Preventable Diseases Laboratory Networks in September 2017. 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. Also discussed were: 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 surveillance.
1. INTRODUCTION

1.1 Meeting organization

The Eighth Meeting of Vaccine-Preventable Diseases Laboratory Networks in the Western Pacific Region was held in Manila, Philippines from 18 to 22 March 2019. Fifty-one participants from network laboratories (18 measles and rubella network laboratories and 12 poliomyelitis (polio) network laboratories), temporary advisers, observers, and WHO staff attended the meeting. The list of participants is available in Annex 1. The meeting was organized in two sessions over five days to cover measles and rubella (18–22 March) and polio (20–21 March). The meeting programme is available in Annex 2.

1.2 Meeting objectives

The objectives of the meeting were:

For the measles and rubella laboratory network:

1) to review the progress in the implementation of quality assurance systems and to identify challenges of the laboratories in support of measles and rubella elimination programmes;

2) to discuss improvement strategies to obtain continuous genotype data of measles and rubella viruses, and further improve the molecular detection capacity and data reporting; and

3) to enhance knowledge and skills of participants in performing intensive genetic analysis of the molecular data of measles and rubella viruses.

For the polio laboratory network:

4) to review the progress in the implementation of quality assurance systems and to identify challenges of the polio laboratories in support of polio eradication programmes; and

5) to identify challenges and define the way forward for 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).

2. PROCEEDINGS

2.1 Measles and rubella laboratory network

2.1.1 Overview of global and regional measles and rubella elimination

Substantial progress in measles control has been achieved since 2000 when global measles elimination goals were established. All WHO regions have established measles elimination goals, and three regions have established goals of rubella elimination, to be achieved by 2020. Currently, only the countries of the Pan American Health Organization (PAHO) have achieved measles elimination (2002) and rubella elimination (2009), although the reestablishment of endemic measles in Venezuela has resulted in the region having lost its measles elimination status. In 2017, measles deaths were estimated to be 109,638, down 80% from the 2000 estimates, and measles vaccination has averted about 21 million deaths since 2000, with 5.5 billion doses of measles-containing vaccine (MCV) administered during this time.

In 2017, the global coverage was 85% for the first dose of measles-containing vaccine (MCV1) and 67% for the second dose (MCV2). A total of 118 countries (61%) had achieved at least 90% coverage with
MCV1, and 169 countries (87%) had introduced or planned to introduce MCV2 in 2019. A total of 162 countries had introduced rubella-containing vaccine (RCV) by 2017.

Very large measles outbreaks have occurred recently in countries in nearly all WHO regions: Madagascar (N=67,422), Ukraine (N=53,918), Philippines (N=20,755), Yemen (N=12,617) and Brazil (N=10,262). As of 1 March 2019, 324,277 measles cases were reported globally for 2018, compared with 138,719 reported for 2017 at the same time last year. Measles is grossly under-reported, and it is estimated that 6.7 million measles cases occurred globally in 2017 compared with 173,330 cases reported through the WHO–UNICEF Joint Reporting Form.

Countries in the Western Pacific Region reported 26,157 measles cases in 2018, but there has been a resurgence of endemic measles with a prolonged outbreak in the Philippines since late 2017 with over 16,000 cases and 260 deaths in the first quarter of 2019. There is an ongoing nationwide outbreak in Malaysia despite high reported MCV coverage. There have also been import-related outbreaks in countries and areas that had achieved elimination or low incidence such as Cambodia, the Lao People’s Democratic Republic, New Zealand, Hong Kong SAR (China) and Japan. However, prompt and well-coordinated, targeted outbreak responses in Mongolia, the Lao People’s Democratic Republic and Cambodia successfully limited spread of measles outbreaks, and China has reported its lowest incidence ever in 2018. Reported regionwide coverage is 96% for MCV1 and 93% for MCV2.

Some of the challenges for measles and rubella elimination in the Region include: reviewing and updating national response plans, identifying high-risk areas and vulnerable populations, assessing and enhancing quality of surveillance, identifying and filling immunity gaps, and developing protocols to coordinate rapid and effective outbreak investigations and response.

2.1.2 Global Measles and Rubella Laboratory Network

The Global Measles and Rubella Laboratory Network (GMRLN) is the largest coordinated laboratory network globally and provide 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. Global workload for both measles and rubella cases tested increased in 2018 with more than 178,000 measles immunoglobulin M (IgM) and 135,000 rubella IgM tests performed. Molecular surveillance for measles has improved over the years, and 5336 measles virus sequences and 374 rubella virus sequences were reported to the WHO sequence databases in 2018. Molecular surveillance gaps still exist, especially for rubella; however, the Western Pacific is one of the better reporting regions. The discontinuation of the production of Siemens IgM assays has disrupted reporting timeliness in many regions due to kit stock-outs prior to substitute assays being evaluated and implemented. A comprehensive IgM kit evaluation is in the process of being developed. The new Measles and Rubella Laboratory Manual is now available online with methods now available as annexes. New technologies and strategies are being developed by the GMRLN to support the measles and rubella programme and include: e-learning; next generation, extended window and whole genome sequencing (NEW); point-of-care testing (POCT); and multi-antigen immunoassays (MIA) identification of secondary vaccine failure/reinfection cases. The accreditation checklists have been comprehensively revised, and the WHO surveillance guidelines, with algorithms for case classification, have been published recently. Further financial support for the continued expansion of the GMRLN is required to provide laboratory support for surveillance, not only for measles and rubella, but also for other vaccine-preventable diseases and emerging pathogens.
2.1.3 Regional measles and rubella laboratory network

The regional measles and rubella laboratory network in the Western Pacific comprises 385 laboratories: one global specialized laboratory (GSL) in Japan; three regional reference laboratories (RRLs) in Australia, China and Hong Kong SAR (China); 16 national measles and rubella laboratories (NMRLs); 31 provincial and 331 prefectural laboratories in China; and one subnational laboratory in Malaysia and two in Viet Nam. The workload in 2018 for non-China laboratories in the Western Pacific Region was 44,860 serum samples received, more than two times the amount received in 2017 and mostly contributed to by the ongoing outbreak in the Philippines. Chinese laboratories experienced a declining workload due to the marked and continuing reduction in measles and rubella cases since 2015; in 2018, China had the lowest ever reported incidence rate of 2.9 million.

Genotype and sequence information for measles viruses submitted to the Measles Nucleotide Surveillance (MeaNS) WHO sequence database was received from 12 countries in the Region. Genotype D8 predominated in 2018 (N=11 countries), with H1 (N=4 countries) and B3 (N=10 countries) also detected. Genotype D9 was not detected in the Region in 2018 after being detected in four countries in 2017. The convention and convenience of using “named strains” to identify genetic clusters of measles viruses has yet to be fully incorporated in the Region. For rubella viruses, sequences were submitted to the Rubella Nucleotide Surveillance (RubeNS) genotype database for seven countries in the Region with genotype 2B (N=6 countries) and 1E (N=5 countries) being reported.

All 54 laboratories in the Region that participated in the annual global serology quality assurance programme in 2018 passed. All 13 molecular testing laboratories passed the molecular quality assurance proficiency test (PT) in 2017, and 12 laboratories have received the 2018 panel with final results still pending. Laboratory accreditation reviews for the past 18 months have largely utilized the format of desk reviews rather than on-site visits due to the Regional Office Measles and Rubella Laboratory coordinator position being vacant for more than 12 months.

The laboratory network has an important role to play in the confirmation of congenital rubella syndrome (CRS) cases. However, of the estimated 4000–21,000 CRS cases per year expected in the Region, none was reported in 2018. CRS surveillance has yet to be implemented in five countries, representing 82% of the Region’s population.

The regional measles and rubella laboratory network has made considerable progress since establishment began in 1998. The network laboratories all follow WHO-recommended methods and procedures with strong overarching quality assurance. The strong capability of molecular detection in many laboratories in the Region has resulted in 980 measles virus sequences and 359 rubella sequences being reported to the WHO genotype databases in 2018, allowing informed decisions on the molecular surveillance of measles and rubella globally and in the Region. They also provided evidence for determining the verification status of countries. Challenges include identifying sufficient funding to support procurement and shipment and sustaining the high quality of the laboratory network. The Philippines and Malaysia are considering expanding their number of subnational laboratories to combat logistic challenges in getting samples to the central laboratories from remote areas.

2.1.4 Global Specialized Laboratory and Regional Reference Laboratory reports

Japan as GSL

The GSL at NIID, Japan, continues to be involved in strengthening the capacity of the regional laboratory network. 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. Conclusions of a study on alternate cell lines to Vero/hSLAM were that none was better, although A549/hSLAM-C or -NS1 can be a second choice. NIID has collaborated with the National Institutes of Biomedical Innovation, Health and Nutrition in Japan for them to maintain the Vero/hSLAM cells and complete the importation documentation and transport on request for any laboratories in the network for a moderate additional cost. NIID has developed a molecular external quality assessment (EQA) programme for Japanese public health laboratories conducting measles and rubella reverse transcriptase polymerase chain reaction (RT-PCR) (N=68), all of which achieved 100% accuracy. An IgM panel for commercial diagnostic laboratories (N=4) was also developed, and all laboratories passed. In 2017, 181/185 (97.8%) of measles cases reported were confirmed by PCR. Of these, 164 could be sequenced, and 155 (94.5%) were genotype D8, two (1.2%) H1 and seven (4.3%) B3.

Australia as RRL

The epidemiology of measles in Australia shows the characteristic of an eliminated country with multiple sporadic outbreaks from importations and minimal spread. In 2018, a total of 82 PCR positive cases were identified with 78 genotyped as either B3 (N=26) or D8 (N=52), and they were associated with importations from multiple countries, with Philippines B3 heavily represented. Eight “named strains” were identified, and this naming convention proved highly beneficial in determining importation. The Victorian Infectious Diseases Reference Laboratory (VIDRL) supports the sequencing of viruses for other countries in the Western Pacific Region and confirmed B3 and D8 from isolates sent from New Zealand in 2018.

Only one rubella case was confirmed in 2018. It was identified as genotype 2B and linked to importation. Australia was verified as having eliminated rubella in 2018, with molecular epidemiological information from VIDRL providing critical evidence of importation of rubella viruses from 2008 to 2017.

VIDRL 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. Serological confirmatory testing was done on samples referred by Brunei Darussalam, Malaysia, Fiji and New Zealand.

China measles laboratory network (with 31 provincial laboratories)

China’s measles case numbers have continued to decline since 2014. In 2018, a total of 4,025 cases were confirmed, with an incidence of 2.9/million, the lowest ever reported. Five provinces reported incidence of less than 1/million during 2017–2018. Measles virus genotype H1 continues to be predominant, although small numbers of imported genotypes, B3 (N=3) in two provinces and D8 (N=10) in six provinces, were detected in 2018. The China NMRL plays a key reference and quality assurance role for the measles and rubella laboratory network in China. In 2018, the NMRL and 32 provincial laboratories passed the WHO serology PT panel, and the NMRL, 32 provincial and 30 prefecture laboratories participated in a molecular external quality assessment (mEQA) panel generated by the Chinese Center for Disease Control and Prevention (China CDC). Six provincial laboratories underwent on-site accreditation in 2017, and all participants passed with high scores. A translated version of the latest WHO checklist was used for desk accreditation reviews in 2018, and on-site reviews for several provincial laboratories are planned for 2019. Training in molecular data analysis is planned for later in 2019.
**Hong Kong SAR (China) as RRL**

Hong Kong SAR (China) experienced an increase in measles activity in 2018. In 2018, 12 measles cases were confirmed from 428 suspected cases compared with three measles cases confirmed from 242 suspected cases investigated in 2017. Measles genotypes H1, D8 and B3 were identified, and all viruses were considered imported. For rubella, in 2018, six cases were confirmed from 346 suspected cases, and genotypes 2B and 1E were detected compared with no rubella cases confirmed in 2017 from 222 cases investigated. Measles virus genotypes were detected in serum samples sent from Cambodia, Macao SAR (China), the Philippines, Singapore and Viet Nam (Hanoi and Ho Chi Minh City) for confirmatory testing in 2018 and 2019. Rubella genotype information was also found in sera from the Philippines (2B) and Viet Nam (Ho Chi Minh City) (2B) received in 2018. The RRL is undertaking an evaluation of alternative suppliers of measles and rubella IgM assays as replacements for Siemens kits.

**2.1.5 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 operates under the umbrella of Clinical Laboratory Services. The Ministry of Health is responsible for the laboratory component of measles surveillance and serological testing and is now part of the WHO measles laboratory network in the Western Pacific Region. The laboratory obtained ISO15189 accreditation in 2011 and achieved 100% for the 2018 global IgM measles and rubella PT. Confirmatory testing of samples sent to VIDRL resulted in 100% concordance for measles IgM but 88% (15/17) for rubella.

The Regional Verification Commission for Measles Elimination (RVC) verified Brunei Darussalam as having achieved measles elimination in March 2015. From 2004 to 2018, 64 measles confirmed cases were notified to the Disease Control Division. In 2018, one of 24 specimens tested was a laboratory-confirmed case (genotype D8) and determined to be imported. A total of 12 rubella cases were reported in the country between 2007 and 2013 but none since.

**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 aged over 1 year have blood collected and those below 1 year have dried blood spot collected. From January 2016 to December 2017, 66 measles cases were confirmed. A further three were confirmed in 2018, and 12 cases were identified from 1 January to 15 March 2019. All cases were considered imported or import related, with genotype B3 and D8 identified with some having epidemiologic links (epi-links) to neighbouring countries. Prior to elimination, measles genotypes D9 and H1 were identified. A total of three rubella cases were confirmed in 2018 compared with seven in 2017. The NMRL is now using Euroimmun IgM assays as a replacement for Siemens. Challenges include: samples received in the laboratory more than five days after collection; stock-outs of reagents; specimen inadequacy (especially dried blood spot); and poorly filled case investigation forms.

**Macao SAR (China)**

Macao SAR (China) has a population of 640,000 but receives more than 35 million visitors per year and has 188,000 non-resident workers. The NMRL provides a full testing service for the public sector and
also a limited service for the private sector hospitals, clinics and laboratories. Private sector testing makes up about 1% of workload. Siemens assays have been replaced with Serion Virion since early 2018 for measles IgM; for rubella IgM, Roche Cobas has been used since April 2018. IgG tests are routinely used for assisting both measles and rubella diagnosis as well as for serosurveys, which are completed annually on 500 random samples collected from routine samples.

Measles-positive cases were detected in 2018 (N=3) and February 2019 (N=3). Genotypes were either B3 or D8 and considered imported. The 2018 measles serosurvey identified detectable antibody in only 57% of under 2-year-olds. Other age groups (2–40+) ranged from 97% to 100%. One positive rubella case was detected in 2018 (1E), although many false positive rubella IgM results occur through the antenatal TORCH screening programme, which also tests for rubella IgM.

**Fiji**

The NMRL in Mataiaka House received a total of 91 samples in 2018 from Fiji, and all were tested for both measles and rubella IgM. None was positive, although five dried blood spots were measles equivocal and three were rubella equivocal. Thirteen dried blood spots and 71 sera were received in 2018. Siemens assays were replaced with Euroimmun in January 2019. There are challenges with inadequate sample volumes being received and dried blood spot giving equivocal results. A new enzyme-linked immunosorbert assay (ELISA) reader needs to be repaired.

**French Polynesia**

French Polynesia is an autonomous French territory with 118 islands, 76 of which are inhabited, over an area of 4167 square kilometres. MCV coverage is above 95% for 2017 and 2018, and in common with France, measles vaccination has been mandatory since 2018. A total of 107 suspected cases were reported in 2018, but the NMRL in Tahiti received no samples. The only samples tested in 2018 were the global PT samples for which Institut Louis Malardé achieved 100%. The current procedure for confirmatory testing is sending samples to CNR Rougeole in Caen, France. Molecular detection is not currently available.

**Guam**

Guam reported zero cases for the past 10 years. The NMRL at Guam Public Health Laboratory reported one suspected measles sample received in 2018 from a 4-year-old Chuuk patient referred to Guam. A serum sample tested negative for both measles and rubella IgM. No molecular testing is performed. Challenges include identifying resources for procurement of their own laboratory test kits. MR test kits (Siemens) are currently provided by the WHO Regional Office for the Western Pacific. The NMRL performs the global PT annually and are CLIA accredited.

**Lao People’s Democratic Republic**

In 2018, several outbreaks occurred of both measles and rubella. A total of 500 suspected measles cases were reported: two laboratory confirmed and five epi-linked. For 2019 (January–March), 294 suspected cases were reported and 40 laboratory confirmed and 47 epi-linked, an incidence rate of 12.4/million. Seven rubella cases were laboratory confirmed and one epi-linked for 2018. Molecular capacity has been established in the National Centre for Laboratory and Epidemiology, and nasopharyngeal or throat swabs are collected if within five days of rash. No CRS surveillance and/or sentinel surveillance system has been established.
**Malaysia**

Measles incidence in Malaysia has plateaued at 40–60/million since 2015. In 2018, 1,968 cases were confirmed from 10,378 samples tested, with 65% of cases under 7 years of age. For rubella, 314 cases were laboratory confirmed from 7,554 samples tested in 2018. Measles genotypes detected included D8 (N=105) and B3 (N=115) for 2018. One 2B rubella virus genotype was confirmed for 2018, detected in eastern mainland Malaysia. An online, case-based reporting system has been established in Malaysia with clinicians and health officers able to report any suspected case of measles within 48 hours, and the process has reduced the number of under-reported cases.

**Mongolia**

Mongolia was verified as having achieved measles elimination by the RVC in 2014. However, a large outbreak between 2015 and 2016 with genotype H1 virus resulted in more than 16,000 cases being confirmed by the NMRL. In 2018, no cases were confirmed from 244 suspected measles cases tested at the NMRL. In 2019 (March), two cases were confirmed (genotype D8) from 138 suspected cases tested. The first case had recently arrived from India, and the second case was a Mongolian boy vaccinated three times – two doses through routine immunization in 2007 and a third dose during a supplementary immunization activity in 2017. There was no obvious epidemiologic linkage between the two cases.

**New Caledonia**

Between 2015 and 2019, two cases of measles have been identified in the country. One in 2015, an unknown vaccination status man returning from Vanuatu; the second, in 2017, a 33-year-old unvaccinated individual after contact with recent visitors from France. A total of 21 cases were tested in 2018 with none positive. No data are available on rubella incidence as it is not a mandatory reportable disease. Both IgM and IgG tests are performed for measles and rubella. A positive measles reaction is sent to VIDRL for confirmation. Positive rubella samples are sent to France (Caen) for confirmation. A number of false positive rubella IgMs were reported.

**New Zealand**

New Zealand was verified as having achieved the interruption of endemic measles and rubella at the RVC meeting in September 2017. The NMRL in Canterbury Heath uses PCR and serology, IgM, and IgG for case confirmation. In 2018, 281 samples were tested by real-time RT-PCR and 87 serum samples by IgM EIA (Siemens). Thirty-one measles cases were reported in 2018, 28 laboratories confirmed and three epidemiologically linked. Genotypes identified were B3 and D8. Most of the small outbreaks were imported or linked to imported cases. In 2018, no rubella cases were confirmed; in 2017, one case was confirmed in a visitor to the country. There have been no cases of CRS reported in New Zealand since 1998.

**Papua New Guinea**

Papua New Guinea has a population of 8.5 million people and a reported MCV coverage of less than 50%. In 2018, 93 suspected measles cases were tested at the NMRL in Port Moresby, and 16 were confirmed measles IgM positive and three rubella IgM positive. Positive IgM serum samples from 2017 and 2018 will be sent to VIDRL for possible genotyping. CRS sentinel surveillance detected no CRS cases in 2018. Quality performance indicators for the laboratory are good.

**Philippines**

In 2018 and first quarter of 2019, there was an increase in measles referrals to the NMRL at the Research Institute for Tropical Medicine (RITM), Philippines. A measles outbreak was first identified in Luzon in the National Capital Region and then spread to most of the country. By the end of 2018, 13,285
compatible cases had been reported for the year and a further 3,466 laboratory-confirmed cases, making a total of 18,405 confirmed and compatible cases. In 2019, case numbers increased with the laboratory being overwhelmed with samples being received from 3,500 suspected cases in January and 6,250 in February. By mid-February 2019, 803 serum samples had been tested, of which 77% were positive for measles IgM. RT-PCR tests on 532 pharyngeal swabs over the same period identified 95% as measles virus positive. All strains genotyped from the 2018–2019 outbreaks have been B3 and closely related to the 2009 named strain from Harare, Zimbabwe (MVI/Harare.ZWE/38.09), which had been also found in the Philippines prior to 2018. In response to the heavy workload in 2018 and 2019, RITM has activated its surge capacity system and employed extra staff. It has also instigated daily testing, from three times a week, and surveillance is identifying cases which have epi-linkages to laboratory confirmed cases. RITM has switched from Siemens to Euroimmun. It has maintained its quality with passes in the annual WHO serology and molecular EQA programmes and was accredited in May 2018. However, timeliness of reporting has been negatively impacted in 2019 due to the heavy workload. Challenges brought about by the large outbreak have included: insufficient specimen storage space and incomplete case investigation forms. Plans for developing a subnational laboratory network in the country are being considered.

Republic of Korea

The Republic of Korea was verified as having eliminated measles in 2014. Vaccination rates of MCV2, through two doses of measles, mumps and rubella (MMR) vaccine, have exceeded 97% in the country, and this has been enhanced through the introduction of the school entry requirement of MMR2 between 2013 to 2016. The NMRL at the Korea Centers for Disease Control and Prevention (KCDC) uses Siemens IgM and IgG assays for both measles and rubella. Vero-hSLAM cell culture and real-time RT-PCR and sequencing are used for identifying virus sequences. From 2015 to 2018, 46 measles cases were confirmed with genotypes B3, D8 and H1 detected. In common with other countries in the region, the Republic of Korea has experienced a resurgence of cases in 2019. In January and February 2019, 63 cases have been confirmed and genotypes B3 and D8 detected. Travel history and importation were associated with 23 of the 63 cases in 2019. In late 2018 and early 2019, two hospital-based outbreaks were reported, one with 16 cases (B3) and the other with 22 cases (D8). Health-care workers were reported to belong to age groups with higher susceptibility. One rubella case belonging to the 1E genotype was confirmed during the period 2018 to February 2019. KCDC plans to establish measles and rubella avidity tests and to implement sequencing of the matrix–fusion non-coding region (M-F NCR) of the N gene and the H gene to gain further resolution for measles molecular epidemiology.

Singapore

Singapore was declared as having verified the elimination of measles in 2018. In 2018, the reported incidence rate was 0.6/million for measles and 0.2/million for rubella. A total of 33 measles cases were confirmed in 2018, with age distribution in two clusters: less than 4 years and 15–44 years. Measles virus genotypes B3 and D8 were detected in 2018 and some were identified as being import related. H1 and D9 genotypes were found in 2016 and 2017 but not in 2018. Ten rubella cases were confirmed in 2018, and all were in the 15–54 years age range. All four females with confirmed rubella were of childbearing age. Rubella genotypes 1E and 2B were detected, one of which was confirmed as imported. The NMRL is currently using Siemens IgM assays for measles and rubella and has passed the WHO latest global serology and molecular EQA panels.

Viet Nam

Hanoi

Measles vaccine coverage in Viet Nam was maintained at above 95% for the first dose since 2003 and 90% for the second dose since 2014. Numbers of confirmed measles cases did not exceed 200 in northern
Viet Nam between 2015 and 2017, but a resurgence of cases in 2018 saw 1 264 cases confirmed from 5 534 suspected cases tested by the NMRL at the National Institute of Hygiene and Epidemiology, Hanoi. Molecular testing of throat swabs identified 225 measles virus RT-PCR positive from 307 samples received. A total of 125 were sequenced and identified as D8 with two main clusters identified which were closely related to strains previously identified in India, Bangladesh and Viet Nam. Fifty-six rubella cases were confirmed in 2018, but no sequencing was completed. Sentinel CRS surveillance has been established at the National Paediatric Hospital, Hanoi. Five CRS cases were confirmed in 2018, from 145 suspected cases tested. The NMRL substituted Siemens kits for Virion-Serion. Dual measles and rubella IgM positives were identified in about 2.3% of positive cases, with strong measles and weak rubella reactions. Six of these dual reactions gave 100% concordant results with both Siemens and Virion-Serion.

**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 2018, a measles outbreak began in August and peaked December and January 2019 with more than 340 cases confirmed per month. The predominant age groups affected were: under 12 months (40%), 16–46 years (20%) and 3–5 years (19.4%). Genotype D8 was detected. Fifty rubella cases were confirmed in 2018, and 12 CRS cases were detected.

**Nha Trang**
The Virology Department of Pasteur Institute in Nha Trang is a subnational laboratory providing laboratory surveillance for measles and rubella in central Viet Nam. Siemens kits and IBL kits are used for measles and rubella IgM detection and the US CDC method for molecular testing. In 2018, 51 measles and four rubella cases were laboratory confirmed. For January and February 2019, 82 measles cases have been confirmed already, and none was identified for the same period in 2017 and 2018.

**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 76 measles cases were confirmed in 2018 from 173 suspected cases tested with a further 234 positive cases identified in the first two months of 2019. Dak Lak and Dak Nong provinces were the most affected.

### 2.1.6 Update from technical consultation of the GMRLN in January 2019

#### New Accreditation checklist

The Measles and Rubella WHO accreditation checklist has been revised and divided into four separate sections: 1) General Review & Overall Findings; 2) Serology Review; 3) Molecular Review; and 4) Virus Isolation Review. Each section has two parts: 1) Profile or Performance (self-filled by the laboratory for WHO desk review) and 2) Laboratory Operating Procedures and Work Practices (filled by WHO assessors during an on-site accreditation visits). The changes to the checklist include: a reduction in the number of repetitive questions in parts I and II; the review can focus on only the relevant sections; and the scoring system has changed to total 100% for each of the four sections with a laboratory assessed on each section separately. For example, a very good performance in one section may not influence a less than optimal performance in another section. Each laboratory is expected to undergo an annual accreditation desk review, and an on-site review will be held every 3–4 years or as decided by the regional or global laboratory coordinators.
Manual for the Laboratory-based Surveillance of Measles, Rubella and Congenital Rubella Syndrome

The third edition of the measles and rubella laboratory manual was published in June 2018 and is available at http://www.who.int/immunization/monitoring_surveillance/burden/laboratory/manual/en/.

The Manual provides a resource for the global network of laboratories that supports the surveillance for cases of measles, rubella and CRS. It outlines new approaches and challenges for the laboratory to provide increased diagnostic and analytic support for case classification in elimination settings, to accurately measure and interpret data for population immunity studies, and to meet the growing workload generated by the integration of measles and rubella surveillance. Topics include: the importance of accreditation and quality assurance programmes; guidelines and best practices for collecting suitable clinical specimens and methods for the laboratory confirmation of measles and rubella infection in different epidemiological settings; and guidelines, tools, forms and protocols for diagnosis of measles and rubella infection and molecular characterization of circulating viruses. Laboratory procedures and protocols are posted as annexes to the manual, enabling them to be revised and modified without requiring a revision of the whole manual.

Progress on measles and rubella kit comparison and evaluation

The Siemens Enzygnost IgM assays for measles and rubella has been the mainstay assay for GMRLN case confirmation for two decades. However, these assays will likely be no longer manufactured beyond the end of 2019. Multiple measles and rubella IgM assays are currently commercially available, but their performance has not been fully assessed. A study has been devised to evaluate the operational characteristics of potential commercial assays, and these will be assessed for ease of use, performance, reproducibility and suitability for use in the GMRLN. A reference panel of sera will be gathered to comprise a minimum of 300 globally represented measles and rubella IgM positive and negative specimens and will include well-characterized seroconversion panels and analytical specificity performance panels. Four or five different kits are expected to be evaluated with the panel with the expectation that the manufacturers will have the capacity and commitment to provide up to 70% of the global needs of the GMRLN. The Canadian RRL in Winnipeg has agreed to perform the assessment and will hopefully complete the one for measles IgM by the end of 2019.

Introduction to the International Reagent Resource

The International Reagent Resource (IRR) is a US CDC reagent distribution programme in operation since 2008. Originally designed to support production and distribution of influenza reagents for surveillance and research activities, it has been expanded to include many non-flu reagents since 2016. IRR currently distributes 13 000 reagents per year on request from the 700 laboratories in 150 countries that have registered with the resource. The current catalogue has over 800 reagents and includes diagnostic kits, PTs, positive controls, antigens and antisera. Laboratories must first register with IRR in consultation with their RLC. US CDC reviews all requests for reagents to ensure they meet the appropriate needs and anticipated workload of the laboratory concerned. Currently, the items of interest for the GMRLN are molecular kits and reagents for measles and rubella RT-PCR and also MR serological tests for selected laboratories.

2.1.7 Verifying elimination of measles and rubella

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

At the meeting in Kuala Lumpur in September 2018, 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 Verification Committee and Subregional Verification Committee
(21 Pacific island countries and areas) reports were reviewed: In addition to the eight countries and Member States previously verified, Singapore was verified as having achieved the interruption of endemic measles in 2018. Mongolia has yet to regain its measles elimination status after losing it due to two years of endemic circulation following the 2015–2016 outbreaks. Laboratory-specific recommendations from the RVC included: that all countries/areas that have achieved elimination should continue to obtain genotype information from all cases of measles and rubella, even sporadic cases, and submit to MeaNS/RubeNS databases; that WHO should provide clear instructions on how to best report genotype information in the annual elimination progress reports; that countries must develop appropriate criteria and procedures for laboratory testing versus epi-linking cases to laboratory confirmed cases; and that countries conducting serological surveys must use standardized validated methods.

**Experience from Singapore**

Singapore used five key approaches to eliminating measles: high immunization coverage; enhanced measles and rubella surveillance; high-quality laboratory surveillance; an initiative for using post-exposure prophylaxis (PEP); and establishing a National Verification Committee. As part of the enhanced surveillance, for all notified cases, information is collected on symptoms, travel history, exposure to sick contacts, vaccination records of cases and contacts, and health status of household contacts and exposure history. The PEP initiative offered MMR vaccination to all unvaccinated individuals and to high-risk close contacts. Singapore introduced mandatory measles vaccination for all children aged 12–24 months and used catch-up MMR vaccination at school. The National Public Health Laboratory was designated as the NMRL in 2016 and parallel tests residual samples from the public hospitals and private laboratories and performs RT-PCR and sequencing. In 2018, 559 samples were received for molecular testing compared with 63 for serological testing which provided a high resolution for determining the source of measles viruses detected and provided evidence as to whether viruses were being continuously imported or were part of an outbreak of the same strain. For the National Verification Committee, Singapore was able to determine that multiple lineages were identified and showed that transmission of imported cases was time limited and did not become established.

**Experience from New Zealand**

New Zealand was verified as having achieved the interruption of endemic measles and rubella transmission during the RVC meeting in 2017. The country identified the last measles endemic case in 2012, and in the subsequent six years no reintroduction of measles virus has led to transmission for more than six months. For rubella, the last national outbreak was 1995/96, and no CRS has been detected since 1998. Measles virus sequence of the N450 region between 2016 and 2018 showed that the 2016 D8 viruses circulated for a maximum of six months, and no identical strains were detected subsequently. Multiple importations of different strains of both B3 and D8 viruses were also detected in 2017 and 2018 and were associated with small outbreaks limited a maximum duration of three months. Investigation of several larger outbreaks leading to nosocomial transmission or transmission in large facilities such as universities or factories was facilitated using next-generation sequencing/whole genome sequencing to identify multiple imports of viruses with identical N450 regions but were up to 25 nucleotides different by next-generation sequencing. In 2019, New Zealand has experienced multiple imports, some of which have led to increased number of cases and outbreaks in hospitals and schools. Several strains detected have identical sequences to the current Philippines B3 outbreak. More than 28 cases have been confirmed by February 2019, compared with 32 for all of 2018.
2.1.8 Rubella and congenital rubella syndrome surveillance

The Western Pacific has developed a regional field guide for CRS surveillance after discussions with country representatives at various meetings in 2018. The document proposes minimum standards for CRS surveillance for verification of elimination and will be finalized later in 2019.

The estimated burden of CRS in the Western Pacific Region is between 4 000 and 21 000, but just five cases were reported in 2015. Rubella surveillance is not sensitive due to less than 50% of cases being detected by acute fever and rash surveillance. CRS surveillance provides a more complete picture of the immunity gaps among women of childbearing age and sometimes their male contacts. CRS surveillance can indicate changes in rubella epidemiology before it is evident in rubella surveillance and can monitor for potential paradoxical increase in CRS due to low RCV coverage.

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 utilizing retrospective records review, depending on each country’s purpose and health system structure. CRS surveillance can be integrated with measles and rubella surveillance, using the measles and rubella laboratory network and including the cases in the national surveillance system.

Rubella outbreak and CRS surveillance in Japan

Following the large 2013 rubella outbreak, Japan developed a national guideline for rubella to strengthen surveillance with a view to verification of elimination. The guidelines shortened the reporting timeliness of cases from seven days to immediately, required the active investigation of every case, and required viral surveillance for all suspected cases. Following years of low incidence of rubella and no reported CRS, Japan experienced an outbreak of almost 3 000 cases in 2018 and 650 in 2019 (February). One CRS case has been reported. The outbreak has been widespread over Japan, but higher incidence was reported in Tokyo, Aichi, Osaka and Fukuoka. Cases were predominantly male (81%) and aged 13–69 years. Most of the 553 cases in females were in the childbearing age group. A seroprevalence study in 2017 identified immunity gaps in the age and sex affected mostly by the current outbreak. Following the implementation of the revised guidelines, a higher percentage of cases were laboratory confirmed. Prior to 2018, 60–75% of cases were laboratory confirmed, compared with over 95% in 2018 and 2019. Molecular epidemiology has identified three unrelated clusters of genotype 1E and sporadic and unrelated 2B cases. To target the susceptible population identified by the seroprevalence study, supplementary immunization for adult males born between 1974 and 1979 will be started in 2019. Due to vaccine shortages, individuals will be screened at their annual health check-up, and those with no detectable immunity will be vaccinated.

Update of rubella virological surveillance in China

China reported the lowest level of rubella ever in 2017 (1.2/million), but incidence increased in 2018 (2.8/million). Cases in 2018 were concentrated in three provinces in Southern China (Guangxi, Guangdong and Fujian), and a large proportion (66.7%) was aged between 15 and 39 years who were unimmunized or of unknown immunization status. Rubella virus genotype surveillance has identified two genotypes since 2003: 1E and 2B. Circulation of endemic 1E rubella virus was interrupted in 2016 and subsequently replaced by an imported 1E, first detected at the start of 2018. This new strain has spread rapidly in China and has been found in 12 provinces simultaneously. Circulation of indigenous 2B genotype appeared to be interrupted in 2006, and multiple importations have been detected since. An imported genotype 2B virus in 2011 spread rapidly from east to west in China, and since then has been detected in 28 of 31 provinces. Multiple transmission chains of 2B viruses occurred during 2013–2015. Genetic diversity has gradually decreased since 2016, and genetically similar 2B viruses continue to
circulate. Challenges include: that the age of the majority of rubella cases is now in the age group 15–29 years, making it essential that national CRS surveillance is established, and that limited epidemiological data of cases have made it difficult to identify the source of imported viruses in index cases.

**Rubella and CRS in Brunei Darussalam**

Brunei Darussalam has a population of 437,000 and administers MMR at 12 months and 18 months. No laboratory confirmed rubella cases have been reported during 2015–2017, and no cases of CRS have been reported since 2007. The sensitivity of surveillance reached 4.5/100,000 in 2017 after the case definition was revised to fever and generalized maculopapular rash. The NMRL has capability for both serology and molecular testing and has passed the WHO serological and molecular EQA programme. It is accredited by WHO for measles and rubella and by ISO15819 for rubella serological testing. Brunei Darussalam was verified as having eliminated rubella by the RVC in October 2018.

2.1.9 New perspectives

**Genotyping requirement in support of measles and rubella elimination**

Two criteria are required to verify elimination of measles and rubella: 1) absence of endemic transmission for more than 36 months; and 2) a high-quality, laboratory supported surveillance system – and molecular epidemiology provides evidence required for both criteria. To provide evidence of interrupted endemic transmission, a country needs to determine the genetic characteristics of endemic strains during the endemic phase and further during the elimination process should thoroughly investigate cases detected and try to link the source of the infection as to whether it is vaccine associated, endemic, imported, importation related or unknown. When cases are found after elimination, it should be determined whether cases are linked to others in the country or neighbouring countries and when or whether transmission is interrupted. The performance indicators for determining high-quality surveillance include: samples should be collected from at least 5–10 cases early in a chain of transmission and every 2–3 months after if transmission continues; and at least 80% of laboratory-confirmed outbreaks have their genotype determined. Presentation of genotyping data is critical to clarify for non-laboratory personnel. One example is to display an epidemic curve of an outbreak by likely source of virus (import, import related, epi-link, unknown), week of onset and genotype. Another option is to display an epidemic curve of cases by source with supplemental mapping to highlight geographical distribution of cases. As the genetic diversity of measles and rubella viruses has decreased over time, more detail than genotype designation is required. Use of “named strains” of common lineages can be more informative and may be able to provide identification of possible source and transmission pattern. Additional information can be helpful such as phylogenetic trees with matches to named strains or other identical strains. Use of an expanded sequencing window can increase resolution where necessary. Laboratory staff must work with programme staff to encourage obtaining adequate samples for virus detection and sequencing from all cases, including sporadic ones.

**Point-of-care test for measles and rubella**

The point-of-care test (PoCT) device for measles was developed by Public Health England with support from the Bill & Melinda Gates Foundation. A similar device for rubella is currently under development. The advantages of the PoCT are that it is stable and can be stored before and after use at ambient temperature, it requires no electricity to run, and the end-point can be read by eye after 20 minutes. It has been assessed as usable with serum, capillary blood or oral fluid, and samples need minimal processing. The device is similar to many other PoCTs in the commercial market and can be used in the field by appropriately trained staff or in the laboratory. A performance documentation of the reading can be made by photographing the final result with a smartphone or by using an electronic reader. The PoCT device
traps cellular material from the patient sample and after completion positive devices can be sent to the laboratory for molecular testing with more than 90% of oral fluid samples and 50% of capillary blood samples collected in the first week after onset giving positive RT-PCR results.

In collaboration with US CDC, Public Health England and the Malaysian Ministry of Health, Malaysia plans to assess the feasibility of introducing a measles PoCT into the national surveillance programme with the objectives of: evaluating the acceptability, knowledge, attitudes and practices (KAP) of measles PoCT use; assessing the impact of PoCT use on measles surveillance and public health response; and documenting lessons learnt by the national measles surveillance program regarding logistics, training, quality assurance, reporting processes and regulatory issues. Ten health clinics have been selected in both urban and rural settings with an aim to recruit 450 cases for a pre-PoCT phase and then a further 450 over a six-month period in mid-2019 when PoCT samples will be collected. Changes in identification and response time will be determined between the pre- and post-PoCT introduction periods.

2.1.10 Quality assurance and control

Measles and rubella IgM EQA

Fifty-four laboratories in the Western Pacific Region participated in the 2018 IgM EQA (panel 01802), made and distributed by VIDRL. Siemens was the most commonly used kit in the Region for both measles and rubella IgM testing. In China, Haitai and Virion/Serion kits are mostly used. Other kits used were Euroimmun and Denka Seiken for measles and Kerunda, Euroimmun, Roche and Denka Seiken for rubella. All laboratories in the Region passed the measles PT, with 44 (81.5%) laboratories scoring 100%, and all laboratories scoring 90% or more. For the rubella PT component, 46 (85.2%) laboratories scored 100%, and all laboratories scored 90% or more. The small number of errors detected related to: transcription errors, incorrect placement of decimal point, insufficient data to determine validity of test and incorrect in-house control.

Measles and rubella molecular external quality assurance

The molecular EQA programme was developed by US CDC to assess the performance of laboratories that use measles and rubella molecular tests. The 2018 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 2018. For rubella, 11 laboratories have sent reports and two have results that are pending. One laboratory has yet to submit their rubella sequences to RubeNS. Of the 10 with completed results, all passed both detection and genotyping. For measles, 12 reports have been submitted and one is pending. Nine have passed and three are performing a retest for the genotyping component. A retest is permitted if a problem can be resolved by repeating a test, for example by re-analysing sequence data. Common problems detected in the submissions include: error in WHO name; incorrect WHO reference sequences when developing a phylogenetic tree; no cellular reference gene for real-time; no extraction control; and marker bands not labelled. For 2019, a new scoring scheme will be developed with points deducted if the common problems identified above are not resolved.

EQA for provincial laboratories in China

China’s NMRL and 32 provincial measles laboratories participated in the 2018 WHO measles and rubella IgM PT. Ten of the provincial laboratories received broken vials due to a transportation issue, but all but one was able to recover sufficient sample volume to test. Twenty-eight of the 32 provincial laboratories achieved a 100% score, and four lost marks due to incorrect results (N=2), incomplete form (N=1) or no in-house control (N=1) but achieved passing scores.
The NMRL performed the US CDC molecular EQA panel in 2018 and received a passing score. A measles and rubella molecular PT was developed by the National Laboratory at China CDC in December 2014 to evaluate the quality of the commercial real-time RT-PCR kit used in China. In 2018, all 32 provincial and 20 prefecture laboratories received the molecular EQA panel, which consisted of 16 virus cultures of measles, rubella and mumps. Laboratories received the viruses in different order and were required to report results within five working days. All laboratories passed the PT with scores of 100%. However, analysis of the laboratory data identified that some had issues with abnormally high or abnormally low cycle threshold (Ct) values which indicates that training in real-time RT-PCR testing is required.

**Standard operating procedure on confirmatory testing**

The Hong Kong SAR (China) RRL is a key laboratory in the Western Pacific Region for confirmatory testing and detecting virus sequences from serum samples in countries with suboptimal molecular surveillance. To facilitate the confirmatory testing procedures, the RRL 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; shipping specimens as “Biological Substance Category B”; volume of samples should be at least 0.3 ml; packaging should comply with UN650 regulations; and the standardized confirmatory worksheet should be used with details of case and specimen, kit name and batch number, the NMRL’s results, correction factor. RRLs performing confirmatory testing should acknowledge receipt of samples and test samples with a repeat in duplicate for samples with discordant results, classify results based in the confirmatory assessment algorithm, and report within 14 days of receipt. The RLC should follow up on discordant results with RRLs and NMRLs to determine the reason for the discrepancy and try to resolve any issue. 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 Pacific island countries and areas, by the 15th of every month – with 95% timeliness in both 2017 and 2018. 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. Important data for compiling indicators include: specimen received and tested with dates of receipt and reporting, and data on tests conducted for virus detection. Sequence data are currently received from different sources; laboratory reports, surveillance reports, and MeaNS and RubeNS, leading to inconsistencies. In the future, only data from MeaNS and RubeNS will be used to compile the genotype distribution table and maps in the Bulletin. Member States are currently using three different data reporting structures: Excel, Access and MRSRS. The Excel database has several formatting issues which can result in missing core variables, typos, or different formats or codes being used. It does not have an automatic reporting function and cannot be easily linked to surveillance data. The current Access database resolves most of the issues of the Excel database but only one user can enter data, and it cannot be easily linked to surveillance data. The MRSRS have surveillance and laboratory data entered in the same system, so cases and specimens
are already matched which makes it easy for fast investigation of cases. Further, automated reports can be generated and multiple users can use it at the same time. WHO has developed a common integrated platform for WHO immunization related data called the WHO Immunization Information System (WIISE). This system is able to streamline data collection, link into the Joint Reporting Form and surveillance and laboratory data, harmonize and validate processes, and improve overall access and analysis of data.

2.1.11 Polio transition and polio containment: impact on the measles and rubella laboratory network

Comprehensive vaccine-preventable disease surveillance

The Strategic Advisory Group of Experts has recommended surveillance for all vaccine-preventable diseases (VPDs), especially VPDs slated for global eradication or elimination: polio, measles and neonatal tetanus. When Member States decide whether to conduct surveillance for a particular VPD, they should consider whether surveillance will inform policy and immunization strategy decisions and whether resources and capacity are available. Prioritization of communicable disease surveillance should consider: disease burden and endemicity; severity and case fatality ratio; epidemic potential; prevention and control and elimination potential; and social and economic impact. A WHO working group with headquarters and Regional Office representatives has been convened to develop a global WHO strategy for comprehensive VPD surveillance. WIISE, a global and regional immunization programme and surveillance data management system, is under development and VPD surveillance modules are proposed. Being planned also is the development of a WHO country-level VPD surveillance costing guidance and global and regional costing of comprehensive and disease-specific VPD surveillance, including a current pilot in Nepal and other countries.

Polio containment-impact on measles and rubella laboratory network

The 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) has been developed to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of oral polio vaccine use and was endorsed by the Sixty-eighth World Health Assembly in May 2015. The Western Pacific Region has prepared the implementation of GAPIII through biorisk management training for poliovirus-essential facilities (PEFs) and national authorities for containment in 2015 and 2016 and has prepared auditor training in 2017 and for 2019. Strong advocacy from the Regional Office and commitment from Member States have reduced the number of PEFs in the Region. In phase I, more than 77 000 laboratories in 37 countries have been surveyed, including more than 55 000 in China and 14 000 in Japan. A World Health Assembly resolution from 2018 urges all members to intensify efforts to accelerate the progress of poliovirus containment certification and complete inventories for type 2 poliovirus (PV2) and destroy unneeded type 2 materials by 30 April 2019.

Laboratory testing in support of measles and rubella surveillance in elimination settings

Laboratory confirmation of measles and rubella cases is more challenging in elimination settings with increased false positivity due to decreased positive predictive value in low incidence of disease. Case history is critical, especially vaccination history, travel history and potential exposure to cases in ongoing outbreaks. Differential diagnosis for prevalent diseases with measles and rubella-like clinical symptoms can assist with discarding cases, and molecular testing (RT-qPCR) can rule in cases but not rule out cases. IgG and avidity tests may assist final case classification, and a second serum sample can be used to detect rising antibody levels indicative of recent infection.
Workshop on genetic analysis of the molecular data of measles and rubella viruses

A three-day workshop was held among 13 measles and rubella network laboratories with existing molecular infrastructure testing to enhance knowledge and skills of the staff in performing intensive genetic analysis of measles and rubella viruses, especially in those countries that have not yet verified measles and rubella elimination. In the verification process, countries should show the critical lines of evidence to demonstrate convincingly that these diseases are no longer endemic in the country. Hence, molecular surveillance for measles and rubella viruses is very important, and it is necessary for the laboratory staff to be able to compare sequence information in addition to the genotype information. Because genotypes contain multiple distinct lineages, comparing sequences is the most sensitive means to help identify and map transmission chains in a timely manner. Sequence and genotype information must be reported to centralized databases (MeaNS and RubeNS) in a timely manner, and this information must be available to members of the measles and rubella laboratory network.

During this workshop, the participants were able to analyse and upload sequences to MeaNS and RubeNS, create tables including MeaNS/RubeNS matches, and create epidemic curves with genotype information for the National Verification Committee.

2.2 Polio laboratory network

2.2.1 Polio endgame strategy and updates on maintaining polio-free status: global and regional

Polio endgame strategy: update on global and regional progress

In 2018, wild polioviruses (WPVs) from acute flaccid paralysis (AFP) cases were detected in only two countries globally: Pakistan and Afghanistan. A total of 33 wild poliovirus type 1 (WPV1) were confirmed, an increase on the 22 detected in the same two countries in 2017. In 2019 (March), six AFP and 56 environmental samples were found positive for WPV1, indicating ongoing circulation in three transmission zones: Karachi, Lahore/Punjab and Kandahar. No WPV1 has been found in Nigeria for 30 months after the re-emergence of cases in 2016. No WPV3 cases have been detected since November 2012, and the Global Certification Commission is considering certifying WPV3 as eradicated. In 2018, seven countries were found with circulating vaccine-derived polioviruses (cVDPVs) detected from AFP cases: cVDPV1 in Papua New Guinea and Indonesia; cVDPV2 in Nigeria, Niger, Mozambique and DRC; and cVDPV3 in Somalia. In response to the cVDPV2 outbreaks in Nigeria and Niger, monovalent oral polio vaccine (OPV) type 2 rounds have been used to combat low routine coverage and evidence of spread. In the Democratic Republic of the Congo, there was evidence of spread due to use of monovalent OPV type 2. The Papua province of Indonesia reported cVDPV1 in one AFP case and two healthy children in late 2018, with more than 60 nucleotides different to Sabin 1 indicating approximately 5–6 years of evolution. WHO/UNICEF coverage estimates report 29 countries have less than 50% coverage with inactivated poliovirus type 1 vaccine (IPV1), and approximately 43 million children are missed globally.

The Global Polio Laboratory Network (GPLN) has reclassified laboratories into three functions: 1) virus isolation only (N=15); 2) virus isolation and intratypic differentiation (ITD) (N=100); and 3) virus isolation, ITD and sequencing (N=29). The workload of AFP cases being tested by the GPLN remains almost constant despite the reduction in WPVs detected. Samples from contacts in the WHO African Region and Eastern Mediterranean Region contribute to a higher workload, and the number of environmental surveillance (ES) sites is increasing. Overall for the GPLN, timeliness and accuracy performance indicators for poliovirus (PV) detection and characterization remain good in all WHO regions, and there is a continuous capacity-building through training and orientation to meet the expanding programme needs. Some of the challenges for the GPLN include: a need to improve laboratory
data management for both AFP and ES in several regions; harmonizing the level of technical information between laboratories; and linking laboratory contingency planning to national contingency plans.

**Regional polio laboratory network**

The Western Pacific Region has been polio-free since a brief importation of WPV1 in China in 2011. As of February 2019, 38 out of 43 regional polio network laboratories have ITD functionality using molecular techniques, including 31 of 32 China’s provincial laboratories. In addition to AFP surveillance, many laboratories have been actively involved in supplementary enterovirus (EV) surveillance and/or ES. China has established an extensive hand, food and mouth disease (HFMD) laboratory network based on existing polio laboratories, and Japan and Viet Nam have also implemented HFMD surveillance. Six countries have implemented ES to expand sensitivity for detecting PVs. Viet Nam will additionally introduce ES in 2019, and the Lao People’s Democratic Republic and Cambodia are considering introducing ES in the near future. Papua New Guinea initiated ES following an outbreak of cVDPV1, which was identified in 26 AFP cases and eight community contacts in 2018. Five ES collection sites have been established and samples collected twice a month and shipped for processing and virus isolation to RITM in the Philippines. Isolates made by RITM are sent to NIID in Japan and VIDRL in Australia for further testing and identification. Some of the challenges for the regional network include: identifying long-term funding and managing the polio transition; difficulty of shipment of samples and reagents due to a long delay in receiving import permits in some countries; irregular and inconsistent ES reporting; and maintaining the preparedness of some laboratories.

**Regional update**

Key performance indicators for AFP surveillance for the Western Pacific Region have been maintained well above the targets for at least the past five years, but challenges with underperforming polio surveillance still remain in some countries such as Papua New Guinea and the Philippines. After the April 2016 OPV2 withdrawal, protection against PV2 is ensured by at least one dose of IPV in the countries that switched from trivalent OPV to bivalent OPV. In non-Pacific island countries, only Cambodia reported high coverage with one dose of IPV. The other three countries that switched reported low (Lao People’s Democratic Republic – 59%) to extremely low (Papua New Guinea – 10%) coverage. China did not report IPV coverage for 2016. In the Pacific, the majority of countries and areas reported more than 80% coverage and two less than 80% coverage. Due to the global shortage of IPV, Mongolia and Viet Nam were not able to introduce the vaccine as planned in 2016. However, as supply improved in 2018 Viet Nam introduced the vaccine in September 2018 and Mongolia will introduce in April 2019. As of January 2019 both countries accumulated around 3.5 million populations susceptible to PV2

There is a high susceptibility to polio infection in Papua New Guinea after persistently low-performing routine immunization coverage leading to emergence of cVDPV. The polio partners have provided a massive response to the outbreak and three rounds of OPV (national immunization days) have been administered and two supplemental immunization activities (subnational immunization days) have taken place.

Issues and challenges in the Region include: encouraging countries to actively look for ways and means to sustain essential functions with the likely polio eradication programme ramp-down post-certification; addressing the gaps at national and subnational levels in performance of AFP surveillance; and needing to further strengthen national capacities in outbreak preparedness and response.
2.2.2 GSL and RRL reports

Japan as GSL

Following outbreaks of HFMD and AFP/acute flaccid myelitis cases and other emerging and re-emerging EVs in Japan and other countries in the Western Pacific Region, Japan established national AFP surveillance in 2018 for polio and other EVs causing severe illness. Detailed guidance documents have been produced, and it is encouraged for various clinical samples to be collected, including stools, throat swabs, serum, cerebrospinal fluid and urine. From week 18 to 43 in 2018, 86 AFP cases were reported, all of which were negative for PV but EV D68 was identified in paralytic cases. Japan has also established ES with 16 public health institutes and two research public health institutes taking part. Since Japan switched to IPV in 2013, Sabin 3 (N=1) was identified in October 2014 and Sabin 3 (N=1) was identified in July 2016. Seroprevalence rates for under 5-year-olds have identified improving PV immunity due to greater acceptance of an inactivated vaccine once IPV was introduced. Challenges include: frequent leakage of samples received from the Lao People’s Democratic Republic and Cambodia with a risk of Japan Post suspending shipments in the future unless this issue is resolved. There is a plan for expanding PEFs in Japan from five to six, with Biken having an additional facility in Tokyo.

Australia as RRL

VIDRL supports the testing of AFP samples from Brunei Darussalam, Papua New Guinea, and Pacific island countries and areas. A total of 343 AFP cases were tested from these countries in 2018, including 57 cases identified from Australia. Combined non-polio enterovirus (NPEV) detection rates exceeded 38%. The cVDPV outbreak in Papua New Guinea boosted samples (N>600) and workload from AFP cases and contacts from that country.

VIDRL is fully accredited and achieved the following 2018 polio PT results: virus isolation PT: 100%; ITD/VDPV reverse transcriptase polymerase chain reaction (RT-PCR) PT: 80%; and sequencing PT: still pending. Two samples in the ITD/VDPV panel were incorrectly identified, a third sample was mislabelled, and a fourth was misinterpreted. The Laboratory instigated an internal review of the failure according to quality systems, a repeat panel was tested in January 2019, and a final score of 100% was obtained.

The Poliovirus Infection Outbreak Response Plan for Australia has been reviewed and published in January 2019 but will be edited to align with WHO’s Polio Outbreak Preparedness and Response Plan. A single confirmed or probable case of WPV or cVDPV infection is considered an outbreak and would trigger activation of the Plan.

China as RRL

The Chinese Center for Disease Control and Prevention (China CDC) National Laboratory and RRL received 134 polio isolates from the country’s provincial laboratories in 2018. Sabin-like (SL) type 1 was identified from 30 samples, SL3 from 92 samples and immunodeficiency-related VDPV3 from one case. No PV2 has been found since the switch to bivalent OPV. An NPEV rate of 7.1% was reported for 2018.

A total of 20 ES sites have been established in nine provinces considered at risk of PV or VDPV. All sampling sites are inlets to wastewater treatment plants. Three unrelated VDPV3s were detected from ES in 2018 in Guangdong, Xinjiang and Fujian provinces.

For containment, the national OPV2/Sabin 2 PV inventory has been 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 plan is to have the inventory completed by September 2019.
Currently, China cannot produce sufficient quantity of Sabin IPV for two routine doses to be administered, so currently one Sabin IPV and 2 bivalent OPV doses are used.

2.2.3 National polio laboratory reports

Hong Kong SAR (China)
The NPL in Hong Kong SAR (China) is located at the Public Health Laboratory Centre. Performance of AFP surveillance has been satisfactory, and all indicators above the target value have been achieved in 2018, though there are issues with physicians collecting rectal swabs rather than stools. Eleven AFP cases were investigated in 2018 and two NPEVs and no PVs were confirmed. More than 3 500 non-AFP stools and respiratory samples were also tested for EVs in 2018 and no PVs were detected. A serosurvey is conducted every five years on four different age groups. A trial using Luminex to detect antibodies proved to be not very successful, and this device will no longer be used. For containment, there will be no PEF established in Hong Kong SAR (China). All Sabin2/OPV2 viruses were destroyed in 2016, and a survey of PV potentially infectious materials (PIMs) in local laboratories in 2018–2019 is ongoing.

Malaysia
Malaysia performs AFP surveillance in addition to HFMD surveillance. The detection of a minimum of 95 AFP cases per year is required to meet the 1/100 000 indicator. A total of 179 cases were detected in 2018 with no PVs and 16 NPEVs detected from 374 specimens. Measures undertaken to improve the NPEV rate included: introducing new low passage cell lines from VIDRL; use of data loggers and temperature strips for monitoring temperature of specimen shipments; and requesting immediate delivery of samples after collection. The NPL has achieved a 100% score for the global virus isolation and sequencing PT for the past two years but has achieved a non-passing score of 85% on the ITD/VDPV PT for both years. No ES was conducted for the past 18 months, but due to an increase in funding ES is planned to restart in 2019. Four sampling sites, two in Sabah and two in Peninsular Malaysia (Selangor), have been identified.

Mongolia
Mongolia has a population of 3 177 899 with 967 896 (30.4%) under 15 years of age with a minimum AFP detection rate of nine cases per year. The AFP surveillance rate was 0.67/100 000 (N=6) for 2018 with adequate stool collection rates of 100%, although more than 400 samples from non-AFP, AFP contacts, healthy children and children with differential diagnosis were also tested. In 2018, the NPEV rate from AFP stools was 50%, compared with 0% in 2017, and 35% from healthy children samples. Plans are being developed to conduct a VPD serosurvey, and the NPL will send dried blood or serum to US CDC for PV immunity testing. Collection of samples should be completed by June 2019. A PV survey of 121 laboratories identified that none reported holding stocks of PV or PIM. Mongolia has completed their biorisk management, one of the first countries in the Region to do so. ES is not considered necessary due to existing AFP and healthy children surveillance and high immunization rates. Mongolia is considering introducing a birth dose for polio.

New Zealand
New Zealand has a minimum AFP detection rate of nine per year. In 2018, eight AFP cases were detected and one (12.5%) was NPEV positive. More than 10 000 non-AFP cases were also tested in 2018 with nine of 15 non-AFP stools being NPEV positive. No PVs have been detected since 2005 when a Sabin strain was confirmed. The annual progress report on sustaining polio-free status identified more than 700 individuals from high-risk countries for PV or VDPV transmission who were permanent or long-term arrivals in the country. The national response plan for WPV and VDPV importation was developed in
2009 and is constantly being reviewed by the National Certification Committee for the Eradication of Poliomyelitis. The NPL at the Institute of Environmental Science and Research Limited is accredited and passed the 2018 global virus isolation and ITD/VDPV PTs with the sequencing PT ongoing. For containment, a risk assessment approach using previous surveys to identify facilities at risk has been completed. A survey of facilities with potential of holding polio infectious materials or PIMs using WHO Form 1 is ongoing with a completion date of 31 March 2019 planned and a target date to send Form 2 to WHO by the end of April 2019.

Philippines

The Philippines NPL at RITM 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. The laboratory was accredited in 2015 and passed the 2018 WHO virus isolation PT and the ITD/VDPV PT after retesting.

In 2017, the Philippines reached 74% coverage with bivalent OPV3 while IPV coverage was 40%. National AFP detection rates were 0.93/100 000 for 2018 with a 60% stool adequacy rate. A national NPEV rate of 3.4% was reported for 2018 with just Region 8 and CARAGA reaching above 10%. From the 391 cases with 755 stool samples, 10 were L20B positive: PV1 and PV3 (N=2); PV3 only (N=7) and PV3 and NPEV (N=1). As the Philippines is assessed at high risk for PV transmission, ES has been performed since 2017 with 11 sites using the grab sampling method, once per month. For containment, the Philippines will be considered a non-PEF and has destroyed all stocks of PV2. OPV2 was withdrawn in April 2016. The national inventory of facilities with PIM and PVs is almost complete, and it is planned for the report to be submitted to WHO in April 2019.

Republic of Korea

IPV was introduced in 2005 into the Republic of Korea and coverage as of 2017 was reported as 97.7%. An AFP surveillance system has been established in 50 paediatric neurology hospitals, and national AFP detection rates were 1.04/100 000 for 2018 with a 90% stool collection rate. An NPEV rate of 8.6% was achieved in 2018. The NPL at KCDC achieved scores of 100% for both the WHO virus isolation and ITD/VDPV PTs for 2018 and was fully accredited in April 2018. A response plan for a possible polio outbreak has been developed. For containment, a national authority for containment was established in 2018 and national polio containment coordinators for implementation of WHO guidelines for PIM are in process.

Singapore

The NPL is situated in the Virology Laboratory, Department of Microbiology, Singapore General Hospital. In 1996, the 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. An AFP rate of 2.17/100 000 was reported for 2018. In addition to AFP samples, a further 391 samples from non-AFP, non-stool specimens and ES samples were tested. Eight NPEVs were detected and no PVs were found. The NPL achieved scores of 100% for the WHO virus isolation, real-time RT-PCR ITD/VDPV and sequencing PTs. 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 subsequently becoming very low.
Viet Nam

Hanoi

The NPL at the National Institute of Hygiene and Epidemiology is responsible for detecting PVs and NPEVs from specimens collected under AFP and HFMD surveillance programmes for 28 provinces in the north and six provinces in the centre of Viet Nam. The AFP rate is 1.5/100 000 overall with a range of 0 to 4. A total of 348 AFP stool samples were tested in 2018 with all meeting the timeliness indicators. A total of 503 samples for HFMD were tested in 2018. Overall, for AFP and non-AFP samples, 13.22% were EV positive, of which four were L20B positive (SL-1, N=2; SL-3, N=2). In 2018, the National Institute of Hygiene and Epidemiology achieved a score of 100% for both the WHO virus isolation and the real-time RT-PCR ITD/VDPV PTs. All PV2 containing samples were destroyed in October 2016 and the NPL is following the updated WHO Guidance to minimise the risk of sample collections potentially infectious for PVs. Plans for implementing ES in Hanoi are still underway.

Ho Chi Minh City

The Laboratory of Enteroviruses, Pasteur Institute (PI), Ho Chi Minh City, has been a member of the regional polio laboratory network in the Western Pacific Region since 1992 and serves the southern half of Viet Nam. The laboratory is ISO15189 compliant and has been accredited since 2011. A total of 346 AFP stool samples from 173 AFP cases were tested in 2018 with all meeting the timeliness indicators. The NPEV rate for 2018 was 13%, and four cases were L20B positive (SL-1, N=1; SL-3, N=3). A total of 1760 samples for HFMD were tested in 2018 with 682 (39%) found positive for EVs, predominantly EV71. In 2018, PI NPL achieved a score of 95% for the WHO virus isolation PT and 100% for the real-time RT-PCR ITD/VDPV PT. All PV2 samples were destroyed in late 2015.

2.2.4 Progress on direct detection of PV in stool samples

In order to speed up the 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. Two direct detection procedures/workflows are being piloted at US CDC using 182 stool specimens in parallel with the standard WHO virus isolation 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 a real-time RT-PCR reaction. The other procedure uses a 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. The results show that both direct detection methods were significantly better than virus isolation, and a double extraction method was selected based on ease of use and logistics. A further 202 samples from Yemen were compared, with the direct detection double extraction method showing greater sensitivity than virus isolation. Virus isolation missed two SL-1 viruses in a mixture with SL-3 and a further four SL3 viruses. Important lessons learnt were that: in order to minimize the chance of cross-contamination, batch sizes of 10–12 at one time were recommended; ITD analysis is critical; and low signals and atypical results are more common, such as invalid results, indeterminates and high Ct values.

The Zen8 probe for PanPV was developed by US CDC and will be a direct replacement of the PanPV assay. It contains a double quencher that prevents detector saturation. A pilot test to determine the reliability and comparability of the Zen8 probe to the traditional PanPV assay was performed by five polio network laboratories in GPLN including the Philippines polio network laboratory. Results were variable but in aggregate, Zen8 had equivalent or lower Ct values compared with the PanPV assay. One laboratory found it easier to determine positives with Zen8 and one laboratory found them both to be equivalent.
A direct detection algorithm is under development, but challenges with mainstreaming the direct detection method remain. As all AFP samples will need to be undergo ITD, there will be extra workload, greater kit usage and more difficult ITD analysis required. More independent evaluation is needed.

2.2.5 Progress on sequencing (Sanger/next-generation sequencing) validation

A comparison of RT-PCR enzymes identified that the Invitrogen SuperScript III one-step method was 1–3 logs more sensitive than the Qiagen one-step method, and the Invitrogen one-step kit outperformed the Qiagen one-step kit in routine use with PV isolates. However, Invitrogen enzyme/ kits cost about 25% more than Qiagen kits, and the additional sensitivity provided by the Invitrogen kit will not be sufficient to detect all PVs in direct detection testing. Additional method improvements will be necessary for sequencing directly from stool RNA in direct detection testing of low titre stools.

Next-generation sequencing is being used by GSLs and some RRLs and is working well with viral isolates. However, direct sequencing from stools is proving challenging and even more for environmental samples. There are no plans for a more comprehensive roll-out yet.

2.2.6 Review of sewage concentration methodologies and Global Polio Laboratory Network standpoint

The GPLN has developed guidelines for determining ES site selection and methodologies for collection, concentration and detection. The time required for the concentration procedure is important to consider when comparing different methods of sewage concentration. A head-to-head comparison identified large variations of virus recovery for all methods and the GPLN has recommended the grab and double phase separation method, which more than 30 laboratories were able to implement since 2000. Recent amendments and improvements have been made with adding higher concentrations of antibiotics (gentamicin) and using plastic (polytetrafluoroethylene, or PTFE) funnels rather than the more delicate glass ones. The GPLN recommends the two-phase method, although the introduction of other methods is acceptable if there is an adequate evaluation by and a recommendation from the GPLN.

Monitoring cell line sensitivity and mycoplasma testing

Routine evaluation of the sensitivity of cell lines for virus isolation is an important component of a laboratory’s quality assurance programmes. It provides assurance that RD and L20B cell lines being used in the Region are sensitive to detecting PVs, even if present at low titre. Almost all (42/43) polio laboratories in the Region implement and report results of cell-line sensitivity and titration experiments to the Regional Laboratory Coordinator for review and for implementation of appropriate corrective actions. To ensure cell authenticity, cell lines are obtained from authenticated sources such as US CDC, NIID, VIDRL and China CDC. Mycoplasma testing is done by most laboratories although test kits are not available in all countries.

2.2.7 Laboratory quality management system

The GPLN Management System (GPLNMS) is a web-based system developed to replace paper-based annual reporting and accreditation assessments. Each laboratory in the network is required to maintain up-to-date information about their staffing, equipment, virus shipments, key activities and accreditation status. The system also supports the yearly submission and assessment of key performance indicators. For the Region, 41 of 43 laboratories submitted the 2018 accreditation annual report. One laboratory has yet to complete the ITD checklist, and one laboratory has not reported at all. Some issues arising from the accreditation reporting included incomplete documentation, missing information, incorrect interpretation, and completed but not submitted accreditation form.
Report on the 2018 virus isolation proficiency testing

The 2018 virus isolation proficiency testing panel (VIPT2018) was shipped directly to almost all laboratories from the National Institute for Public Health and the Environment (Netherlands) at ambient temperature. Laboratories in the Western Pacific Region received their panels with an average of 4.4 days after shipment, with a range of 2–10 days. For the first time, laboratories were required to submit PT reports directly to the GPLN Management System. The PT panel consisted of 10 samples of mixtures, NPEVs and monotype PVs and was usable for both virus isolation and direct detection. Some direct detection laboratories used only 1 μl of sample and missed the low titre viruses. Of the 43 laboratories in the Region, 35 achieved a score of 100% and seven achieved 95%. One laboratory did not receive the panel. It was reported that submission to the GPLN Management System was not always seamless, and several modifications were made to accommodate issues detected.

An ES proficiency testing pilot (ESQA) was evaluated to establish proficiency for PV/EV concentration. The samples consisted of sewage-surrogates spiked with PVs and/or NPEVs. It was determined that the testing samples need to be shipped frozen and that the lower limit for spiking should be approximately 500 PV/500 ml. It is likely that the pilot will be rolled out for all ES laboratories by the end of 2019 and results included as part of the accreditation process.

Report on the 2018 virus ITD proficiency testing panel

The 2018 ITD PT resulted in all but five laboratories achieving a passing score, of which two failed to detect PV2 and three failed to detect VDPVs. There was no sequencing PT for 2018, but a 2019 panel is ready for shipment (March 2019). A new scoring system will be implemented with the PT and only re-runs as per the regular algorithm will be acceptable without a laboratory having points deducted.

S19 Hyper-attenuated PV strains: plans and timelines

The National Institute for Biological Standards and Control has been working on novel strains of PV that are more attenuated, less pathogenic and safer than the OPV/Sabin strains. They have genetically manipulated the domain V of 5’NTR so that it will not grow at temperatures above 33 °C and not in humans. A trial in mice shows they do not grow in mice, are stable with low infectivity and do not replicate in non-human primates. No reversion was detected after more than 20 passages, and possible uses include as challenge strains for serology assays. They could also be used for IPV production, but the process for validation and regulation will take time.

2.2.8 Polio laboratory containment: GAPIII

Implementation of GAPIII in the Western Pacific Region

Progress is continuing within the Western Pacific Region for the implementation of GAPIII. Biorisk management training for PEFs and national authorities for containment was carried out in 2015 and 2016, and auditors training for the Containment Certification Scheme occurred in 2017 in the local language for China, Japan and Viet Nam. The Region is working with countries to establish national containment authorities and to include containment in certification reports for the Regional Certification Committee. Strong advocacy from the WHO Regional Office for the Western Pacific and commitment from countries has resulted in a reduced number of PEFs than originally proposed. Currently, 16 PEFs are proposed: Australia (N=1), China (N=8), Japan (N=5), Republic of Korea (N=1) and Viet Nam (N=1). China has yet to confirm their national containment authority and just one PEF (China CDC) has been validated. Viet Nam has yet to officially designate their PEF, which may delay the certificate of participation application
process. The Region is lacking auditing capacity and qualified auditors to conduct auditing once the certificate of participation has been approved by the Global Certification Committee. The next steps are to assist the national authorities for containment in the GAPIII Containment Certification Scheme process, start planning for containment of PV1 and PV3, and for PEFs to formally engage in the Containment Certification Scheme.

**Poliovirus containment in the European Region and feedback from a Polio Outbreak Simulation Exercise**

The WHO European Region has undergone a polio risk assessment and identified three countries at high risk, 21 at intermediate risk and 29 at low risk, based on surveillance, population immunity and outbreak preparedness. For the 42 countries without a PEF, all have destroyed PV2 materials, but three have yet to establish a national polio containment coordinator. Of the 11 planning to have PEFs, all but one has a NAC, 10 have designated PEFs but only one has a certificate of participation issued.

A Polio Outbreak Simulation Exercise (POSE) was held by the WHO Regional Office for Europe to increase the countries’ preparedness for a potential PV containment breach at a PEF and to understand the critical actions needed to respond to facility-associated incidents. The Exercise was based on previous experiences of PV breaches in the Region, and countries were provided with an opportunity to identify potential deficiencies in emergency response and contingency planning at PEFs.

**WHO guidance on identification of potentially infectious materials-completion of Phase I of GAPIII**

Following the recommendations of the Global Certification Committee in October 2017, the PIM guidance document was published in April 2018 and PIM guidance training for national polio containment coordinators in the Western Pacific Region was held in April 2018. The key Global Certification Committee recommendations were: the establishment of a standardized data collection and verification mechanism; the National/Regional Certification Committee reports need to clearly identify where and when activities in phase I have been completed; the deadline for completion of phase I for all PV2 is 30 April 2019; countries are urged to complete the identification, destruction, transfer or containment (phase I) of WPV1 and WPV3 by the end of phase II; and countries planning to retain WPV1 and WPV3 materials should weigh the risks and benefits of having such facilities and the commitments to comply with appropriate safeguards. The Region has made progress with the PIM guidance: a regional workshop for national polio containment coordinators was held in April 2018; support was provided to countries for the completion of PIM guidance; reporting forms and e-tools were distributed to all countries; reports have been submitted by Brunei Darussalam, Mongolia and Guam; and documents have been translated into local languages for China, Japan, the Lao People’s Democratic Republic and Viet Nam. Some of the challenges identified for the Region include: meeting the Global Certification Committee deadline of 30 April for PIM guidance; VDPV2 retained in provincial laboratories in China are not able to transfer to the PEF; and no validation mechanism for implementation of WPV/VDPV and risk assessment strategies for OPV/Sabin PIM.

**2.2.9 Contingency planning in polio-free region**

**Contingency planning in the Western Pacific Region for referral of samples in outbreak situation (PV2, ES)**

The Region has proven it has a sensitive surveillance programme for detecting VDPVs. Since 2015, four countries have identified VDPVs: 1) the Lao People’s Democratic Republic experienced an outbreak of cVDPV1 in 2015–2016 affecting 11 AFP cases and 25 contacts; 2) Papua New Guinea has detected an
outbreak of cVDPV1 in 2018 with 26 AFP cases, eight contacts and seven environmental samples identified as positive; 3) China reported limited ambiguous and immunodeficiency-related VDPVs, which were identified from routine AFP and EV surveillance between 2015 and 2018; and 4) Australia detected an ambiguous VDPV from an environmental sample in 2017. The Region has shown strong collaboration across all levels of the laboratory network as neither the Lao People’s Democratic Republic nor Papua New Guinea have NPLs and require samples to be tested in other network laboratories. For the Lao People’s Democratic Republic, all PV testing is provided by NIID, Japan, which provided timely results and shared data for the cVDPV outbreak in 2015–2016. For Papua New Guinea, AFP samples were tested at VIDRL, Australia, which quickly shared sequence information with US CDC and NIID for confirmation of the VDPV. ES was established within 10 weeks after the outbreak, with samples processed at RITM, Philippines, and ITD data shared with VIDRL for confirmation and with NIID for sequencing.

The first Polio Outbreak Simulation Exercise in the Region was successfully held in Manila in March 2019 for Viet Nam, the Lao People’s Democratic Republic, Cambodia and China. An Exercise for PEF-containing countries is proposed for August 2019.

**Contingency planning experience from Japan**

NIID, Japan, was the key laboratory supporting the cVDPV1 outbreak in the Lao People’s Democratic Republic in 2015–2016. A total of 11 AFP cases and 25 household contacts were confirmed from three provinces covering seven districts. All cases were among an ethnic minority community with persistently low levels of OPV uptake. In 2015, the Lao People’s Democratic Republic had more than 50% of AFP cases with zero doses OPV and a stool adequacy rate of 42%. The cVDPV sequence indicated a mean duration of circulation of approximately three years before detection. In response to the outbreak, four rounds of OPV supplementary immunization activity were implemented starting two weeks after the outbreak was confirmed and six weeks after the first case was detected. NIID experienced a considerable increase in workload which went from approximately 40 samples a year for the Lao People’s Democratic Republic to more than 100 per month during the outbreak. Also the consideration for starting ES in the Lao People’s Democratic Republic in 2019 will have an impact on NIID with additional workload for the laboratory.

**Experience from VIDRL**

The VIDRL RRL serves Australia, Brunei Darussalam, Papua New Guinea and the Pacific island countries and areas for AFP stool testing. Routine stool samples from Papua New Guinea were received on 11 May and inoculated the same day. By the fifth day, the ITD was positive. Sequencing at VIDRL identified VDPV1 10 days later which was confirmed by US CDC. The classification of VDPV stimulated stool collection from enhanced AFP surveillance and collected from community contacts of the primary case. Overall for 2018, 800 stools were received from Papua New Guinea, compared with 43 stools received in 2017. The challenges during the outbreak were the unusually large shipments which negatively impacted the laboratory’s processes, including: specimen reception, data entry, sample processing, cell cultures for inoculation and the limitation of having only two biological safety cabinets and a small number of staff for performing the required tasks. There was a very heavy throughput of samples for both cell culture and molecular testing requiring a high volume of reagents and PCR machine time. VIDRL convened a high-level meeting to discuss surge capacity which resulted in internal management changes with responsibilities for routine sample testing relegated to another section and extra staff allocated to support AFP testing. Some of the biggest challenges were the unpredictability of shipments and the lack of communication related to shipment size and frequency. This meant that
preparation of cells and media could not be accurately estimated leading to wasted reagents, time and funds, and it impacted the morale of overworked laboratory staff. In March 2019, one shipment had an incomplete dangerous good declaration leading it to be transported overland from Sydney to Melbourne and was more than 10 days in transit. Good communication at all levels and WHO guidance is critical under outbreak situations.

**The national emergency technical guidelines for WPV, VDPV and type 2 related polioviruses: The China perspective**

China has prepared guidelines to provide technical support for the immediate detection, investigation and intervention related to WPV, VDPV and PV2. Evidence of these viruses is considered a public health emergency, and reporting requirements are strict and rapid. A field investigation is undertaken and, if any case is detected, faecal samples must be collected every seven days until multiple continuous negative results are obtained. For immunodeficiency-related VDPV, specimens must be collected every 14 days until three continuous negative results by culture and direct detection are found. As an example of the guidelines in action, a virus identified in Xinjiang from a sewage sample collected in April 2018 was reported as NSL PV2 in July 2018. China CDC confirmed the virus was VDPV2. An active AFP case search by Xinjiang and China CDC was initiated, and no suspected polio or AFP cases were detected. A dynamic risk assessment was carried out with vaccine coverage rates and polio antibody levels evaluated. After three months, no further type 2 PV was detected from 118 AFP specimens, 32 healthy children and the newly added sewage sampling sites, and the level 3 emergency responses was ended. The WPV1 outbreak in 2011 in Xinjiang as a result of importation from Pakistan resulted in a strengthening of AFP surveillance and expansion in the high-risk and neighbouring provinces. All cases were isolated for the duration of paralysis symptoms, and environmental surveillance was initiated in a mobile P3 laboratory with staff from China CDC assisting. Serological investigation of 2600 individuals was carried out prior to a targeted OPV response.

**2.2.10 GPLN performance tools**

**Environmental Surveillance accreditation checklist**

GPLN has established ES standardized protocols, and an accreditation checklist has been developed. The checklist consists of three sections: Concentration Lab; Virus Isolation Lab; and General requirements. The checklist was rolled out in January 2018 and the first assessment has highlighted areas for improvement to ensure consistency between regions and a common understanding of some questions. A revised checklist has been developed based on the feedback. The Western Pacific Regional Laboratory Coordinator (RLC) conveyed concerns about the requirements for minimum indicators such as 50 samples per year and 48-hour transportation from site to laboratory. For example, it is challenging to get samples from Papua New Guinea to the laboratory in the Philippines, and some laboratories have only a monthly sampling strategy (12 per year).

An ES PT is under development and is planned for roll-out by the end of 2019.

**GPLN Management System**

Eight GPLN Guidance Papers (GP1-8) have been developed to disseminate information to laboratories in the polio endgame era of changes. With the evolving epidemiology of polio, implementation of new immunization protocols and new surveillance and response protocols, there are frequent changes in the diagnostic algorithm, and information needs to be shared quickly with GPLN members. The Guidance Papers are not meant to replace the Polio Laboratory Manual but to address specific issues for which clear
guidance is needed. For example, GP1, which covers safe handling and storage of PV2 in GPLN laboratories, has been updated to reflect the GAPIII changes to the consideration of handling PV2 RNA. The main change is that polio laboratories that have sequencing capacities, but are not PEFs, are permitted to inactivate the PV isolates and perform sequencing on extracted nucleic acids.

The GPLN Management System has been upgraded to include: a stock management module that can be used for ordering reagents and kits; a collaboration site to foster linkages and promote discussions within the network; and a mechanism for reporting of viral isolation PT results.

2.2.11 Environmental surveillance

Progress on implementation of the global ES expansion plan

ES adds value to and supplements AFP surveillance. Progress has been made in implementing global ES expansion as part of the 2013–2019 Polio Eradication and Endgame Strategic Plan. The plan is to establish ES in countries with high risk of circulation of WPV and VDPVs, and 14 of the 23 recommended high-risk, high-priority countries have established ES and systematically report to WHO. Eight of the 11 medium- and low-priority countries have also established ES. Of the high-risk, high-priority countries in the Western Pacific Region, the Philippines and Papua New Guinea have established ES and Cambodia and the Lao People’s Democratic Republic are about to implement ES. ES adds value to global polio surveillance but implementation remains a tedious, lengthy and costly process. Ensuring quality of ES is critical, and the newly introduced accreditation checklist and the recently piloted PT will assist in monitoring the quality of the ES process.

ES in the Philippines and Papua New Guinea

ES in the Philippines started in April 2017 and is being carried out at the RITM NPL. The Philippines is considered high risk for PV transmission due to very low AFP surveillance performance and suboptimal immunization coverage, and ES can be helpful as a supplementary tool to enhance detection of PVs in the country. ES in the Philippines took two years to establish after initial training in March 2015, and a cascade of activities occurred, including: delivery of equipment and supplies, developing a memorandum of understanding with partner agencies, training of collectors, and training of laboratory staff on processing samples. Collection finally started April 2017. Currently, there are 11 sites spread over the whole country, and the WHO two-phase concentration method is used. In 2017, a total of 40 samples were collected from three sites with 60% EV isolation rate including SL1 and SL3 viruses. In 2018, 70 samples were collected from seven sites with an EV isolation rate of 36% (N=25) with two SL1 and two SL3 viruses identified. A challenge with bacterial contamination of samples was resolved by using gentamicin in addition to Pen/Strep.

RITM is supporting ES in Papua New Guinea following the cVDPV outbreak starting April 2018. WHO Papua New Guinea coordinates the collection of samples from five sites in Morobe Province (N=2) and Port Moresby (N=3), and samples are sent to RITM for concentration and testing. Grab samples are collected twice a month. Confirmation of viruses is carried out by NIID and VIDRL. An additional two staff member has been assigned to cover the Philippines and Papua New Guinea ES work at RITM. US CDC has coordinated an evaluation of the Café and the two-phase concentration methods at RITM. Of 90 samples tested in 2018 and 2019 by both methods, the Café method identified EVs in 60% of samples and the two-phase identified 40%. ES will continue in Papua New Guinea after the cVDPV outbreak is over, and due to workload and logistics issues it is planned to train Papua New Guinea laboratory staff to perform the sample concentration with the processed samples sent to RITM for testing.
Polio laboratory network data reporting to WHO

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. An additional four laboratories have transitioned to using PASRS for a total of five countries. The System has been enhanced by correcting all reported bugs, customizing data entry fields, based on country requirements, and filters added for generating Excel line lists. Data reporting by laboratories has showed an improvement in timeliness with 7 of 13 laboratories now reporting on the required weekly basis. Three laboratories are reporting biweekly and three monthly. Papua New Guinea is reporting non-AFP suspected VDPV cases through PASRS; an ES module in PASRS is under development.

Polio eradication, integration and certification: The endgame strategy 2019–2023 and post-certification planning

The Polio Eradication and Endgame Strategic Plan 2013–2018 was updated in 2015 and was extended through 2019. A new budget was approved by the Global Polio Eradication Initiative Polio Oversight Board in 2018 to support the programme’s work for the Polio Endgame Strategy 2019–2023: Eradication, Integration and Certification. The post-certification strategy will begin at the point of certification to define the future state and functions to protect a polio-free world. The structure of the endgame strategy has three themes: 1) Eradication: stopping transmission, 2) Integration: collaborating with immunization and emergency partners to eradicate polio and to protect population, and 3) Certification: certifying eradication and containment of all WPVs and ensuring long-term polio security. The post-certification transition planning’s main objective is to mainstream polio essential functions to sustain global eradication with three goals: 1) contain, 2) protect, and 3) detect and respond. For the Western Pacific Region, the Regional Office will provide guidance on: containment; IPV immunization schedule; possible bivalent OPV withdrawal; and AFP and ES standards according to country and virus risk.
ANNEXES

Annex 1. List of participants, temporary advisers, observers, and Secretariat

MEASLES AND RUBELLA SESSION, 18 – 19 March 2019

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Annex 2. Programme of activities

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

Manila, Philippines
18–19 March 2019

PROGRAMME OF ACTIVITIES

PART I. MEASLES AND RUBELLA LABORATORY NETWORK MEETING
18-19 March 2019

Monday, 18 March 2019

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity/Agenda Item/Subject of Presentation</th>
<th>Presenter</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:00–08:30</td>
<td>Registration</td>
<td>WHO Secretariat</td>
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<tr>
<td>08:30–09:00</td>
<td>Opening session</td>
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<tr>
<td></td>
<td>Welcome remarks</td>
<td>Ms Varja Grabovac</td>
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<tr>
<td></td>
<td>Opening remarks</td>
<td>Ms Varja Grabovac</td>
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<tr>
<td></td>
<td>Self-introduction</td>
<td>All</td>
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<tr>
<td></td>
<td>Election of Officers</td>
<td>Ms Varja Grabovac</td>
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<tr>
<td></td>
<td>Administrative announcements</td>
<td>Ms Varja Grabovac</td>
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<tr>
<td></td>
<td>Group photo</td>
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<tr>
<td></td>
<td><strong>Session 1: Overview of global and regional measles and rubella elimination</strong></td>
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<tr>
<td>09:00–09:20</td>
<td>a) Global and Regional updates on eliminating measles and rubella: progress in 2017–2018 and issues to be addressed in 2019–2020</td>
<td>Dr Jose Hagan</td>
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<tr>
<td>09:20–09:40</td>
<td>b) Update on Global Measles and Rubella Laboratory Network GMRLN</td>
<td>Dr Mick Mulders</td>
</tr>
<tr>
<td>09:40–10:00</td>
<td>c) Update of Regional Measles and Rubella Laboratory Network</td>
<td>Ms Varja Grabovac</td>
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<td>10:00–10:15</td>
<td>Discussion</td>
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<td>Time</td>
<td>Activity/Agenda item/Subject of Presentation</td>
<td>Presenter</td>
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<tr>
<td>10:15–10:35</td>
<td>Coffee break</td>
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<td></td>
<td>Session 2: Reports from Global Specialized Laboratory (GSL) and Regional Reference Laboratories (RRL)</td>
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<tr>
<td>10:35–10:55</td>
<td>a) Japan</td>
<td>Dr Makoto Takeda</td>
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<tr>
<td>10:55–11:10</td>
<td>b) Australia</td>
<td>Ms Vicki Stambos</td>
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<tr>
<td>11:10–11:25</td>
<td>c) China</td>
<td>Dr Zhang Yan</td>
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<tr>
<td>11:25–11:40</td>
<td>d) Hong Kong SAR (China)</td>
<td>Mr Woo Kei-sheng Gibson</td>
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<tr>
<td>11:40–12:00</td>
<td>Discussion</td>
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<td>12:00–12:45</td>
<td>Lunch Break</td>
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<td></td>
<td>Session 3: Report from the National Laboratories in the Region (Part I)</td>
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<tr>
<td>12:45–13:00</td>
<td>a) Brunei Darussalam</td>
<td>Ms Mazmah Ahmad Morshidi</td>
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<tr>
<td>13:00–13:15</td>
<td>b) Cambodia</td>
<td>Mr Buth Sokhal</td>
</tr>
<tr>
<td>13:15–13:30</td>
<td>c) Macao (China)</td>
<td>Mr Wong Kong Hong</td>
</tr>
<tr>
<td>13:30–13:45</td>
<td>d) Fiji</td>
<td>Ms Talica Vakacolata</td>
</tr>
<tr>
<td>13:45–14:00</td>
<td>e) French Polynesia</td>
<td>Dr Elsa Dumas Chastang</td>
</tr>
<tr>
<td>14:00–14:15</td>
<td>f) Guam</td>
<td>Ms Anne Marie Santos</td>
</tr>
<tr>
<td>14:15–14:30</td>
<td>g) Lao People’s Democratic Republic</td>
<td>Dr Onechanh Keosavanh</td>
</tr>
<tr>
<td>14:30–14:45</td>
<td>Discussion</td>
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<td></td>
<td>Session 4: Update from technical consultation of the GMRLN January 2019</td>
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<tr>
<td>14:45–14:55</td>
<td>a) New accreditation checklist</td>
<td>Ms Varja Grabovac</td>
</tr>
<tr>
<td>14:55–15:05</td>
<td>b) Laboratory manual</td>
<td>Dr Mick Mulders</td>
</tr>
<tr>
<td>15:05–15:15</td>
<td>c) Validation of kits</td>
<td>Dr Mick Mulders</td>
</tr>
<tr>
<td>15:25–15:45</td>
<td>Coffee break</td>
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<tr>
<td></td>
<td>Session 5: Verifying elimination of measles and rubella</td>
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</tr>
<tr>
<td>15:45–16:00</td>
<td>a) Update of the 7th Meeting of the Regional Verification Commission for Measles and rubella Elimination in WPR</td>
<td>Dr Jose Hagan</td>
</tr>
<tr>
<td>16:00–16:10</td>
<td>b) Experience from Singapore</td>
<td>Dr Ng Yi Kai</td>
</tr>
<tr>
<td>16:10–16:25</td>
<td>c) Experience from New Zealand</td>
<td>Ms Julie-Ann Ira</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>16:25–16:40</td>
<td>a)  Malaysia</td>
<td>Dr Selvanesan Sengol</td>
</tr>
<tr>
<td>16:40–17:05</td>
<td>b)  Mongolia</td>
<td>Dr Nyamaa Gunregjav</td>
</tr>
<tr>
<td>17:05–17:20</td>
<td>c)  New Caledonia</td>
<td>Dr Frédérique Ducrocq</td>
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<tr>
<td>17:20–17:35</td>
<td>d)  New Zealand</td>
<td>Ms Julie-Ann Ira</td>
</tr>
<tr>
<td>17:35–17:50</td>
<td>e)  Papua New Guinea</td>
<td>Ms Janlyn Kumbu</td>
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<tr>
<td>17:50–18:00</td>
<td>Discussion</td>
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<tr>
<td>18:00</td>
<td><strong>Wrap up and close of the first day</strong></td>
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**Session 7: Rubella and Congenital Rubella Syndrome (CRS) Surveillance**

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity/Agenda item/Subject of Presentation</th>
<th>Presenter</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:30–08:45</td>
<td>a)  Regional Rubella and CRS surveillance: draft guidelines</td>
<td>Dr Jose Hagan</td>
</tr>
<tr>
<td>08:45–09:00</td>
<td>b)  Rubella outbreak and CRS surveillance in Japan</td>
<td>Dr Yoshio Mori</td>
</tr>
<tr>
<td>09:00–09:15</td>
<td>c)  Rubella and CRS surveillance in China</td>
<td>Dr Zhu Zhen</td>
</tr>
<tr>
<td>09:15–09:30</td>
<td>d)  Rubella and CRS surveillance in Brunei Darussalam</td>
<td>Ms Mazmah Ahmad Morshidi</td>
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<tr>
<td>09:30–09:45</td>
<td>Discussion</td>
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**Session 8: New perspectives**

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<thead>
<tr>
<th>Time</th>
<th>Activity/Agenda item/Subject of Presentation</th>
<th>Presenter</th>
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</thead>
<tbody>
<tr>
<td>09:45–10:00</td>
<td>a)  Genotyping requirement in support of measles and rubella elimination</td>
<td>Dr Bettina Bankamp</td>
</tr>
<tr>
<td>10:00–10:15</td>
<td>b)  Point of care test for measles and rubella</td>
<td>Mr David Featherstone/Dr Selvanesan Sengol</td>
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<tr>
<td>10:15–10:30</td>
<td>Discussion</td>
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<tr>
<td>10:30–10:50</td>
<td><strong>Coffee break</strong></td>
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<td>Time</td>
<td>Activity/Agenda item/Subject of Presentation</td>
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<tr>
<td>10:50–11:05</td>
<td>a) Philippines</td>
<td>Ms Leonibel Reyes</td>
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<tr>
<td>11:05–11:20</td>
<td>b) Republic of Korea</td>
<td>Dr Yoon-Seok Chung</td>
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<tr>
<td>11:20–11:35</td>
<td>c) Singapore</td>
<td>Dr Ng Yi Kai</td>
</tr>
<tr>
<td>11:35–11:50</td>
<td>d) Viet Nam, Hanoi</td>
<td>Dr Do Phuong Loan</td>
</tr>
<tr>
<td>11:50–12:05</td>
<td>e) Viet Nam, Ho Chi Minh City</td>
<td>Dr Nguyen Thanh Long</td>
</tr>
<tr>
<td>12:05–12:15</td>
<td>f) Viet Nam, Nha Trang</td>
<td>Ms Tran Thi Nhu Anh</td>
</tr>
<tr>
<td>12:15–12:25</td>
<td>g) Viet Nam, Dak Lak</td>
<td>Ms Duong Thi Ngoc Thuy</td>
</tr>
<tr>
<td>12:25–12:40</td>
<td>Discussion</td>
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<tr>
<td>12:40–13:20</td>
<td>Lunch break</td>
<td>Participants</td>
</tr>
<tr>
<td>12:40–13:40</td>
<td>Working lunch for developing of recommendations</td>
<td>WHO Secretariat, Chair/Vice Chair, Temporary Advisers, Rapporteur</td>
</tr>
<tr>
<td>13:20–13:40</td>
<td><strong>Breakout groups:</strong> exchange of experiences in the verification process. Four groups are available and facilitated by:</td>
<td>Participants:</td>
</tr>
<tr>
<td></td>
<td>a) Australia</td>
<td>All who would like to learn more about verification process from the lab perspectives and how to prepare data for the NVC report</td>
</tr>
<tr>
<td></td>
<td>b) New Zealand</td>
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<tr>
<td></td>
<td>c) Singapore</td>
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<tr>
<td></td>
<td>d) Hong Kong (SAR China)</td>
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<tr>
<td>13:40–13:55</td>
<td>a) Measles and Rubella IgM EQA</td>
<td>Ms Vicki Stambos</td>
</tr>
<tr>
<td>13:55–14:15</td>
<td>b) Measles and Rubella molecular EQA</td>
<td>Ms Raydel Anderson</td>
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<tr>
<td>14:15–14:30</td>
<td>c) QA/QC for provincial laboratories in China</td>
<td>Dr Mao Naiying</td>
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<tr>
<td>14:30–14:45</td>
<td>d) SOP on confirmatory testing</td>
<td>Dr Lam Tin-keung Edman</td>
</tr>
<tr>
<td>14:45–15:00</td>
<td>e) Data management and reporting</td>
<td>Ms Kayla Mae Mariano</td>
</tr>
<tr>
<td>15:00–15:20</td>
<td>Discussion</td>
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<td>15:20–15:45</td>
<td><strong>Coffee break</strong></td>
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<tr>
<td>15:45–16:00</td>
<td>a) Comprehensive VPD surveillance</td>
<td>Dr Mick Mulders</td>
</tr>
<tr>
<td>16:00–16:15</td>
<td>b) Polio containment-impact on MR LabNet</td>
<td>Ms Varja Grabovac</td>
</tr>
<tr>
<td>16:15–16:30</td>
<td>Discussion</td>
<td></td>
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<tr>
<td>16:30–17:30</td>
<td><strong>Session 12: Conclusions and recommendations</strong></td>
<td></td>
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<tr>
<td><strong>17:30</strong></td>
<td>Close of the meeting</td>
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**PROGRAMME OF ACTIVITIES**

**PART II. POLIO LABORATORY NETWORK MEETING**

*20–21 March 2019*

**Wednesday, 20 March 2019**

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity/Agenda Item/Subject of Presentation</th>
<th>Presenter</th>
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</thead>
<tbody>
<tr>
<td>08:00–08:30</td>
<td><strong>Registration</strong></td>
<td>WHO Secretariat</td>
</tr>
<tr>
<td>08:30–09:00</td>
<td><strong>Opening session</strong></td>
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<tr>
<td></td>
<td>• Welcome remarks</td>
<td>Ms Varja Grabovac</td>
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<tr>
<td></td>
<td>• Opening remarks</td>
<td>Ms Varja Grabovac</td>
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<tr>
<td></td>
<td>• Self-introduction</td>
<td>All</td>
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<tr>
<td></td>
<td>• Election of officers</td>
<td>Ms Varja Grabovac</td>
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<td></td>
<td>• Administrative announcements</td>
<td>Ms Varja Grabovac</td>
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<td></td>
<td>• Group photo</td>
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<tr>
<td>09:00–09:20</td>
<td><strong>Session 1: Polio endgame strategy and updates on maintaining polio-free status: Global and Regional</strong></td>
<td></td>
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<tr>
<td></td>
<td>a) Polio endgame strategy: update on global and regional progress</td>
<td>Dr Ousmane Diop/</td>
</tr>
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<td></td>
<td>b) Global Polio Laboratory Network</td>
<td>Ms Varja Grabovac</td>
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<tr>
<td>09:20–09:40</td>
<td>c) Regional Polio Laboratory Network</td>
<td>Dr Ousmane Diop</td>
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<tr>
<td>09:40–10:00</td>
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<td>Ms Varja Grabovac</td>
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<td>10:00–10:20</td>
<td><strong>Coffee break</strong></td>
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<td>Time</td>
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<tr>
<td>10:20–10:35</td>
<td>Session 2: Report from global specialized laboratory (GSL) and regional reference laboratories (RRL)</td>
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<tr>
<td>10:20–10:35</td>
<td>a) Japan</td>
<td>Dr Hiroyuki Shimizu</td>
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<tr>
<td>10:35–10:50</td>
<td>b) Australia</td>
<td>Dr Linda Katherine Hobday</td>
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<tr>
<td>11:05–11:15</td>
<td>c) China</td>
<td>Dr Zhu Shuangli</td>
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<td>10:20–10:35</td>
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<td>11:05–11:15</td>
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<tr>
<td>11:15–11:30</td>
<td>Session 3: Report from the National Polio Laboratories in the Region</td>
<td>Dr KWONG Fung-ming</td>
</tr>
<tr>
<td>11:15–11:30</td>
<td>a) Hong Kong SAR (China)</td>
<td>Jasmine</td>
</tr>
<tr>
<td>11:30–11:45</td>
<td>b) Malaysia</td>
<td>Dr Kamal HAIKAL bin Mat Rabi</td>
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<tr>
<td>11:45–12:00</td>
<td>c) Mongolia</td>
<td>Dr Ichinkhorloo</td>
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<td>12:00–12:15</td>
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<tr>
<td>12:15–13:00</td>
<td>Lunch break</td>
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<tr>
<td>13:00–13:15</td>
<td>Session 3: Report from the National Polio Laboratories in the Region (continued)</td>
<td>Ms Judy Bocacao</td>
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<tr>
<td>13:15–13:30</td>
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<td>Dr Lea Necitas Apostol</td>
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<td>13:30–13:45</td>
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<td>Dr Wooyoung Choi</td>
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<td>13:45–14:00</td>
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<td>Ms Puong Kim Yoong</td>
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<td>14:00–14:15</td>
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<td>Dr Tran Thi Nguyen Hoa</td>
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<td>14:15–14:30</td>
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<td>Dr Nguyen Thi Thanh Thao</td>
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<td>14:30–14:55</td>
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<td>14:55–15:15</td>
<td>Coffee break</td>
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<tr>
<td>15:15–15:30</td>
<td>Session 4: New methods and perspectives</td>
<td>Dr Everardo Vega</td>
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<td>15:30–15:45</td>
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<td>Dr Everardo Vega</td>
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<td>15:45–16:00</td>
<td></td>
<td>Dr Ousmane Diop</td>
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<td>16:00–16:15</td>
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<td>Ms Analisa Bautista</td>
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<td>16:15–16:45</td>
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<tr>
<td>16:45-17:00</td>
<td>Session 5: Laboratory Quality Management System</td>
<td>Dr Erwin Duizer</td>
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<td>17:00–17:15</td>
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<td>Dr Everardo Vega</td>
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<tr>
<td>17:15–17:30</td>
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<td>Dr Javier Martin (call)</td>
</tr>
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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 day</td>
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18:00 Regional Director's Reception All
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<tr>
<th>Time</th>
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<th>Presenter</th>
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<tbody>
<tr>
<td>08:30–08:50</td>
<td><strong>Session 6: Polio laboratory containment - GAP III</strong></td>
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<tr>
<td>08:30–08:50</td>
<td>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) Poliovirus containment in the European Region and feedback from POSE</td>
<td>Dr Eugene Saxentoff</td>
</tr>
<tr>
<td>09:05–09:25</td>
<td>c) WHO guidance on identification of potentially infectious materials – completion of Phase 1/GAPIII</td>
<td>Dr Santosh Gurung</td>
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<tr>
<td>09:25–09:40</td>
<td>Discussion</td>
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<tr>
<td>09:40–10:00</td>
<td><strong>Coffee Break</strong></td>
<td></td>
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<tr>
<td>10:00–10:15</td>
<td><strong>Session 7: Contingency planning in polio free region</strong></td>
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<tr>
<td>10:00–10:15</td>
<td>a) Contingency plan in the WPR for referral of samples in outbreak situation (PV2, ES)</td>
<td>Ms Varja Grabovac</td>
</tr>
<tr>
<td>10:15–10:30</td>
<td>b) Experience from NIID</td>
<td>Dr Hiroyuki Shimizu</td>
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<tr>
<td>10:30–10:45</td>
<td>c) Experience from VIDRL</td>
<td>Dr Linda Hobday</td>
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<tr>
<td>10:45–11:00</td>
<td>d) Experience from ChinaCDC</td>
<td>Dr Wenbo Xu</td>
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<tr>
<td>11:00–11:15</td>
<td>Discussion</td>
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<tr>
<td>11:15–11:30</td>
<td><strong>Session 8: GPLN performance tools</strong></td>
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<tr>
<td>11:15–11:30</td>
<td>ES accreditation checklist</td>
<td>Dr Ousmane Diop</td>
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<tr>
<td>11:30–11:45</td>
<td>GPLN Management System</td>
<td>Dr Ousmane Diop</td>
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<tr>
<td>11:45–12:00</td>
<td>Review of Guidance Papers</td>
<td>Dr Ousmane Diop</td>
</tr>
<tr>
<td>12:00–12:15</td>
<td>Discussion</td>
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<tr>
<td>12:15–13:30</td>
<td><strong>Lunch break</strong></td>
<td>Participants</td>
</tr>
<tr>
<td>12:15–13:30</td>
<td><strong>Working lunch for developing of recommendations</strong></td>
<td>WHO Secretariat, Temporary Advisers, Rapporteur</td>
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<tr>
<td>13:30–13:45</td>
<td><strong>Session 9: Environmental Surveillance (ES)</strong></td>
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<tr>
<td>13:30–13:45</td>
<td>a) Global Perspective and expansion of ES</td>
<td>Dr Ousmane Diop</td>
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<tr>
<td>13:45–14:00</td>
<td>b) ES in Philippines and PNG</td>
<td>Dr Lea Apostol</td>
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<tr>
<td>14:00–14:20</td>
<td>Discussion</td>
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<tr>
<td>14:20–14:40</td>
<td><strong>Session 10: Data management</strong></td>
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<tr>
<td>14:20–14:40</td>
<td>Data management and reporting</td>
<td>Ms Kayla Mariano</td>
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<tr>
<td>14:40–15:00</td>
<td>Discussion</td>
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<tr>
<td>15:00–15:30</td>
<td><strong>Coffee break</strong></td>
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<tr>
<td>15:30–15:45</td>
<td><strong>Session 11: Post-certification planning</strong></td>
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<tr>
<td>15:30–15:45</td>
<td>GPEI strategic plan 2019-2023</td>
<td>Dr Santosh Gurung</td>
</tr>
<tr>
<td>15:45–16:00</td>
<td>Discussion</td>
<td></td>
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<tr>
<td>16:00–17:30</td>
<td><strong>Session 12: Conclusions and recommendations</strong></td>
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<tr>
<td>17:30</td>
<td>Closing of the meeting</td>
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