

National Influenza Centres and Influenza Surveillance in the WHO's South-East Asia and Western Pacific Regions

Report of the eighth bi-regional meeting
Jakarta, Indonesia, 12–15 August 2014



**World Health
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Regional Office for South-East Asia



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Western Pacific Region

SEA-Immun-94
Distribution: General

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Printed in India

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Acronyms

APSED	Asia-Pacific Strategy for Emerging Diseases
ARI	acute respiratory infection
BSL	biosafety level
CC	collaborating centre
EID	emerging infectious disease
EQA	external quality assurance
EWARS	early warning and response system
GISAID	Global Initiative on Sharing All Influenza Data
GISRS	Global Influenza Surveillance and Response System
HA	haemagglutinin
HAI	haemagglutination inhibition
IEDCR	Institute of Epidemiology, Disease Control and Research
IHR	International Health Regulations
ILI	influenza-like illness
JRF	joint reporting form
MERS-CoV	Middle Eastern respiratory syndrome coronavirus
NA	neuraminidase
NHL	national health laboratory
NIC	national influenza centre
NIH	National Institute of Health
NRA	national regulatory authority
PC	partnership contribution
PCR	polymerase chain reaction
PIP	pandemic influenza preparedness

RIRL	regional influenza reference laboratory
SAGE	Strategic Advisory Group of Experts
SARI	severe acute respiratory infection
SMTA	Standard Material Transfer Agreement
SOP	standard operating procedure
TIV	trivalent influenza vaccine
UNICEF	United Nations Children’s Fund
US CDC	United States Centers for Disease Control and Prevention
WHO	World Health Organization

Executive Summary

The Eighth bi-regional meeting of national influenza centres and influenza surveillance in the World Health Organization (WHO)'s South-East Asia and Western Pacific Regions was held in Jakarta, Indonesia from 12 to 15 August 2014.

The general objective of the meeting was to further strengthen influenza surveillance, preparedness and response in WHO's South-East Asia and Western Pacific Regions. The primary objectives of this meeting were (1) to update participants on the current global and regional status of seasonal, avian and other novel influenza subtypes; (2) to discuss ways by which to further strengthen national influenza surveillance systems, data reporting and response within the framework of national pandemic influenza preparedness plans; (3) to discuss challenges faced by national influenza centres (NICs) in specimen referral, laboratory detection and characterization of novel influenza and other emerging respiratory viruses; and (4) to decide on actions to overcome them and provide updates on influenza vaccine virus selection, seasonal influenza vaccines and the regional status of seasonal influenza vaccine use.

There were 50 participants from 24 Member States in the WHO South-East Asia and Western Pacific Regions, 11 temporary advisers, 23 observers from partner agencies and 31 participants representing WHO headquarters, the two regional offices and country offices. The meeting was inaugurated by the WHO representative to Indonesia and Director General of the National Institute of Health Research and Development of the Ministry of Health. The meeting consisted of sessions on the following: (1) Update on the current global and regional status of seasonal, avian and other novel influenza virus subtypes; (2) Strengthening national influenza surveillance systems, data reporting and response in the Asia-Pacific Region; (3) Pandemic influenza preparedness (PIP) Framework: a platform for strengthening influenza surveillance and response; (4) Strengthening laboratory systems for surveillance of, and response to, influenza and other emerging respiratory infections; and (5) New influenza activities. The participants visited the National Influenza Centre and the avian influenza A/H5N1 reference hospital in Jakarta.

Meeting recommendations to the Member States included that (1) Influenza surveillance programmes and NICs should actively advocate for utilization of influenza surveillance and disease burden data to guide public health action and seasonal influenza vaccination policies, (2) design and conduct joint training and workshops on influenza surveillance for epidemiologists and laboratory scientists in influenza surveillance (3) continue to report novel/non-seasonal influenza virus sub-types, including those that do not cause severe human illness, to WHO under the International Health Regulations (IHR) (2005) (4) NIC s should subtype all influenza A viruses, (5) strengthen, use and maintain viral isolation and Haemagglutination Inhibition (HAI) techniques to increase and sustain viral isolation levels.

The meeting recommended to the WHO to (1) work with selected Member States to overcome challenges to the uptake of FluID, including providing more information about the platform and technical assistance for using it (2) conduct a survey to identify gaps in influenza surveillance capacity to guide technical assistance, (3) facilitate and coordinate the design and implementation of multi-country studies to determine the appropriate timing and type of seasonal influenza vaccines (southern and northern hemispheres) to be used for pilgrimage and (4) disseminate clear guidance to NICs on their obligations under the PIP Framework and (5) include updates on the PIP Framework in subsequent bi-regional NIC meetings.

1. Introduction

The Asia-Pacific Region is an epicentre for the emergence of novel influenza viruses of pandemic potential, which could impact global health security and the integrated global economy. Large numbers of avian influenza A(H5N1) cases in the Asia-Pacific Region and the emergence of clusters of influenza A(H7N9) in China are recent examples that highlight this particular risk in the region. It is therefore important to have systems in place for the early detection of, preparedness for and rapid response to novel influenza threats. Emergence of other novel respiratory infections with epidemic potential, such as the recent Middle East respiratory syndrome coronavirus (MERS-CoV) further underscore the value of these systems and their linkage to a global network in detecting not only novel influenza strains but also other respiratory pathogens of epidemic potential.

Despite the establishment and strengthening of systems for influenza surveillance, preparedness and response to influenza pandemics in the Asia-Pacific Region, numerous gaps remain in terms of implementing the standards of the World Health Organization (WHO)'s pandemic influenza preparedness (PIP) framework. Recent reviews have indicated surveillance gaps in relation to detecting novel influenza virus strains, their diagnostics and resultant inadequate response. These reviews have also highlighted capacity gaps in influenza surveillance and response at subnational levels. Gaps also exist in translating generated evidence from influenza surveillance to decision-making on introducing seasonal influenza vaccines in some Member States.

Emerging novel influenza subtypes and other emerging respiratory pathogens such as MERS-CoV have highlighted gaps, issues and challenges in the prompt and accurate diagnosis of these at 15 national influenza centres (NICs) in 21 Member States of the Western Pacific Region, and 10 NICs in eight Member States of the South-East Asia Region. Assessments of national laboratories not designated as NICs in the Asia-Pacific Region have

identified current gaps that do not allow these laboratories to be designated as NICs.

Regardless of the significant contribution of NICs in the Asia-Pacific Region in sharing influenza virus strains for further characterization and selection of candidate vaccine virus strains, the use of influenza vaccine for selected high-risk groups is very low in the South-East Asia Region and relatively low in the Western Pacific Region. In this context, there are several specific areas that require focused attention in order to identify how NICs and agencies conducting influenza surveillance can help the decision-making process of Member States on introduction of seasonal influenza vaccines at the country level in the Asia-Pacific Region.

WHO regional offices (South-East Asia and Western Pacific Regions), in alignment with the Global Influenza Surveillance and Response System (GISRS), need to provide strategic guidance and technical support, and coordinate activities essential to address the above gaps, issues and challenges. They also need to make health systems better prepared for seasonal, zoonotic and pandemic influenza threats to populations and individuals. The annual bi-regional meeting of the NICs and influenza surveillance is a platform to discuss collectively how these issues can be better addressed. The annual bi-regional meeting provides the opportunity for the following:

- Participants from Member States of the two WHO regions come together at one venue to share and learn from each other's experiences.
- They annually interact with experts from the WHO collaborating centres and discuss issues, challenges and mutually acceptable solutions pertinent to specimen sharing, diagnosis and laboratory capacity development.
- They have an annual platform for interacting with and learning from global multidisciplinary experts involved in different influenza-related areas.
- They jointly review the implementation status of recommendations of the previous bi-regional meeting.

- They jointly formulate new recommendations for the coming year based on existing gaps in surveillance and laboratory diagnostics.

The previous seven meetings were held in Member States of the Western Pacific Region. The Eighth bi-regional meeting was hosted by the WHO Regional Office for South-East Asia in collaboration with the Regional Office for the Western Pacific and the WHO country office in Jakarta, Indonesia, which is the most preferred venue, given the status of influenza A(H5N1) in Indonesia. It provided the opportunity for Indonesia to learn from global and regional experts, and for participants to share experiences with and learn good practices from the host Member State.

2. Objectives and expected outcomes

The general objective of the meeting was to further strengthen influenza surveillance, preparedness and response in WHO's South-East Asia and Western Pacific Regions.

The primary objectives of this meeting were:

- (1) To update participants on the current global and regional status of seasonal, avian and other novel influenza subtypes;
- (2) To discuss ways by which to further strengthen national influenza surveillance systems, data reporting and response within the framework of national pandemic influenza preparedness plans;
- (3) To discuss challenges faced by NICs in specimen referral, laboratory detection and characterization of novel influenza and other emerging respiratory viruses, and decide on actions to overcome them;
- (4) To provide updates on influenza vaccine virus selection, seasonal influenza vaccines and the regional status of seasonal influenza vaccine use.

The main outcome of the Eighth bi-regional meeting was the generation of a set of recommendations for Member States, WHO and other stakeholders. These would be implemented over a period of

12 months or longer, if necessary, with a view to further strengthening influenza surveillance, preparedness and response in the Asia-Pacific Region.

3. Proceedings of the meeting

The bi-regional meeting was attended by representatives from Member States of the WHO South-East Asia and Western Pacific Regions, WHO collaborating centres (CCs), WHO country offices, and other partners. The list of participants and the programme are given in Annexes I and II. The meeting was inaugurated by the WHO country representative to Indonesia, Dr Kanchit Limpakarnjanarat. He read out the message of the Regional Director of the WHO South-East Asia Region, Dr Poonam Khetrpal Singh (Annex III). Professor Dr Tjandra Yoga Aditama, Director-General of the National Institute of Health Research and Development, spoke on behalf of the Ministry of Health, Indonesia. Dr Rana Bardan Jung, Acting Regional Advisor, Disease Surveillance and Epidemiology unit of the South-East Asia Region, provided a brief overview of the objectives and expected outcomes of the meeting. Professor Mahmudur Rahman from Bangladesh and Dr Masato Tashiro from Japan were elected co-chairs of the meeting while Dr Sonam Wangchuk of Bhutan, Dr Janice Lo of the Hong Kong Special Administrative Region of China and Dr Anne Kelso of Australia were chosen as rapporteurs.

Session I: Update on the current global and regional status of seasonal, avian and other novel influenza virus subtypes

*Global update on seasonal, avian and other novel influenza subtypes
Dr Katelijn Vandemaële, Medical Officer (Influenza, Hepatitis and PIP Framework), WHO headquarters*

In the winter of 2013–14, in areas where the influenza A(H1N1) pdm09 strain predominantly circulated, the disease was of a high intensity with associated morbidity and mortality. The antigenic match between circulating viruses and the vaccine viruses was good. Less than 1% of over 10 000 viruses tested, demonstrated reduced sensitivity to the neuraminidase (NA) inhibitors oseltamivir and zanamivir. However,

detection of a community cluster of influenza A(H1N1) pdm09 strain of virus (with H275Y substitution) with reduced sensitivity to NA inhibitors in Japan warranted continued vigilance.

In the temperate zones of the southern hemisphere, the observed strains were mainly influenza A(H3N2) in South America and South Africa, while in Oceania it was influenza A(H1N1) pdm09. In the temperate zones of the northern hemisphere and tropical Americas, the predominant strain was influenza A(H1N1) pdm09 followed by non-subtyped influenza A virus. In tropical Africa, South and South-East Asia, influenza A(H1N1) pdm09 and A(H3N2) were predominant.

As of August 2014, 667 sporadic cases of influenza A(H5N1) with 393 deaths (case fatality rate 59%) were reported from 15 countries. There was no sustained human-to-human transmission. Most often, exposure was due to direct or indirect contact with poultry. Isolated viruses in humans were clade 1.1.2 (Cambodia and Viet Nam), clade 2.2.1(Egypt), clade 2.1.3.2a (Indonesia), 2.3.4 (China), and 2.3.2.1c (Canada and Viet Nam). There was no evidence of increasing antiviral resistance to oseltamivir or reassortment with any of the circulating seasonal human influenza viruses.

The number of laboratory-confirmed influenza A(H7N9) cases was 451 with 171 fatalities. All exposures occurred in mainland China. Eighty per cent were exposed to live poultry or a contaminated environment. Despite the availability of family clusters, sustained human-to-human transmission was not reported. The seroprevalence of anti-A(H7N9) antibody in poultry workers was 6–14%, with no antibodies in the general population.

Improved surveillance leads to increased detection of non-seasonal influenza viruses. Therefore, increased vigilance and strengthened epidemiological and laboratory capacity are of particular importance. All human infections with non-seasonal influenza viruses should be reported under the International Health Regulations (IHR). These non-seasonal influenzas have the potential to impact hugely on public health and the economy, even without human-to-human transmission.

Regional update on avian influenza virus subtypes and other novel respiratory infections in the Western Pacific Region
Dr Angela Merianos, Medical Officer (Influenza), Emerging Disease Surveillance and Response, WHO Regional Office for the Western Pacific Region

The Western Pacific Region is considered one of the world's epicentres for the emergence of novel influenza subtypes with pandemic potential. A high density of humans, swine and avian species living in close proximity, and behavioural factors that increase human exposure create frequent opportunities for interspecies transmission. The Region has also contributed most of the seed strains for seasonal and pandemic influenza vaccine production in the past 20 years.

Since 1997, both highly pathogenic avian influenza and low pathogenic viruses have been detected in patients with severe pneumonia in the Western Pacific Region, causing either prolonged human outbreaks (A[H5N1] and A[H7N9]) or sporadic human infections (A[H10N8] and A[H5N6]). These influenza subtypes highlight the importance of fully characterizing novel influenza viruses in reference laboratories for human or animal influenza viruses.

The objectives of preparing for response are to decrease disease transmission, reduce the number of preventable deaths, and mitigate the adverse social and economic consequences of disease outbreaks. Components of response include early case or cluster detection, diagnosis and source investigation; appropriate case management; implementation of behavioural and social interventions; transmission-based precautions; laboratory biosafety; public health control actions; and timely risk communication. Readiness to respond requires an adaptable, multi-hazard incident management system, based on pandemic preparedness, which provides the operational platform for disease-specific responses to novel influenza subtypes and other emerging infectious disease (EID) risks to the Western Pacific Region such as MERS-CoV. The framework for action on emergency risk managements of EIDs highlights the importance of establishing and sustaining links among clinicians, laboratories and public health agencies for early case detection, investigation, risk assessment and reporting, and include the need for clinical, testing and reporting

algorithms, and health-care facility preparedness and emergency response plans.

Continued interspecies transmission of influenza A viruses and, more recently MERS-CoV, reinforce the importance of having multidisciplinary and multisectoral relationships in place at the local, national and international levels before an emergency.

Regional update on seasonal, avian and other novel influenza subtypes in the South-East Asia Region

Dr Pushpa Ranjan Wijesinghe, Dr Rana Bardan and Dr Aparna Singh Shah, WHO Regional Office for the South-East Asia Region

All Member States except for Timor-Leste have established surveillance for influenza-like illness (ILI) or/and severe acute respiratory infections (SARI) to varying degrees. Ten NICs are functional in eight Member States. The reported monthly test positivity rate for influenza virus in the Region ranged from 10% to 15% in 2014. The predominantly circulating influenza virus strains were influenza A(H1N1) pdm09, the lineage undetermined influenza B and influenza A(H3N1) viruses.

Capacity-building, providing consultant support and appraisal of national influenza laboratories still not designated as NICs were some key activities performed regionally. Regional challenges include establishing and strengthening SARI surveillance in all Member States, capturing temperature zone-dependent regional variation in seasonality and circulating strains of influenza, and expanding human influenza surveillance to the human–animal interface. Additional issues for resolution are enhancing the national capacity for high-quality influenza virus detection in all Member States, sharing influenza viruses with the GISRS in a timely manner, sharing information with different stakeholders, generating representative disease burden estimates for large Member States, utilizing local evidence for public health response and building adequate capacity of the national regulatory authorities (NRAs).

Focusing on priority countries, technical/financial collaboration with different partners and optimum utilization of PIP partner contribution funds are essential for addressing the regional inequity in national capacity. Countries need to establish mechanisms to share information with the

veterinary sector and Expanded Programmes on Immunization. Gap analysis in public health laboratories not still designated as NICs, linking of virological data with epidemiological data, possibly through web-based interfaces, and identifying the training needs of laboratory staff involved in influenza diagnostic activities were highlighted as essential for the way forward in strengthening regional laboratory capacity. The Region expects to utilize PIP partnership funding for strengthening NRAs in selected countries.

Influenza activity in the northern hemisphere

Dr Takato Odagiri, Director, Influenza Virus Research Centre, National Institute of Infectious Diseases, Japan and WHO Collaborating Centre for Reference and Research on Influenza

At the time of the meeting, the overall influenza activity of the 2013/14 season was in decline in the northern hemisphere. In some areas, it was at the interseasonal level. Influenza A (H1N1) pdm09, A (H3N2) and B viruses co-circulated in varying proportions in many countries. The majority of influenza A(H1N1) pdm09 viruses were antigenically related to the influenza A/California/07/2009 vaccine strain and belonged to genetic clade 6B. In Japan, a community outbreak with oseltamivir-resistant influenza A(H1N1) pdm09 virus carrying the H275Y substitution occurred in Hokkaido from December 2013 to January 2014. As a result, the proportion of resistant viruses in the area was 28%. The resistant viruses, however, did not spread and the outbreak declined by the end of January. The proportion of viruses carrying the same resistant marker detected outside Hokkaido was as low as 2.7%.

The majority of influenza A(H3N2) viruses were antigenically related to the influenza A/Texas/50/2012 virus. However, two genetic groups (3C.3a and 3C.2a), which may have been associated with antigenic drift, have emerged recently. They show a four- to eightfold reduction in Hemagglutination-inhibition[HAI]/Plaque reduction neutralization assay(PRNA) titres to ferret antiserum raised against influenza A/Texas/50/2012 virus. These two genetic groups have increased proportionately among viruses sequenced in three WHO CCs (Atlanta, Tokyo and London) from February to August 2014 as compared to that from September 2013 to January 2014. Both the Yamagata and Victoria lineages of influenza B viruses were co-circulating worldwide, with the

influenza B/Yamagata lineage being the predominant strain. Influenza B/Yamagata lineage viruses belonging to both the Influenza B/Wisconsin/1/2010 (clade 3) and influenza B/Massachusetts/2/2012 (clade 2) genetic groups co-circulated with clade 3 predominant in the 2013–14 season. Influenza B Victoria lineage viruses were antigenically and genetically similar to the influenza B/Brisbane/60/2008.

Influenza activity in the southern hemisphere

Dr Ian Barr, Deputy Director, WHO Collaborating Centre for Reference and Research on Influenza, Victorian Infectious Diseases Reference Laboratory, Australia

By the time of the Eighth bi-regional meeting (mid-August 2014), the influenza season in the southern hemisphere was at its peak in the temperate regions of Australia, New Zealand and South Africa, while in similar climatic regions of South America (such as Argentina, Chile), their season was coming to an end. The 2014 influenza season in Australia and New Zealand recorded a large number of confirmed cases of influenza. In fact, in Australia, it documented the second highest number of influenza cases in the past decade after the 2009 pandemic year by the end of the season. In 2014, both influenza A subtypes (A[H3N2] and A[H1N1] pdm09) and influenza B viruses circulated widely, with A(H1N1) pdm09 being predominant in Australia and New Zealand, and A(H3N2) viruses in South Africa and South America. A(H3N2) viruses were also commonly seen in the Australian state of New South Wales where they were responsible for a large number of outbreaks in nursing homes. The impact of the 2014 season on admissions to hospitals and intensive care units and deaths was similar to the 2013 season. Google Flutrends (<http://www.google.org/flutrends>) showed high seasonal influenza patterns. The Google Flutrends findings in Australia were similar to data originated from traditional systems such as ILI surveillance. However in New Zealand, Google Flutrends data were higher than those derived from traditional influenza surveillance. The reasons for these differences are not clear.

In terms of the influenza vaccine match against influenza viruses circulating in 2014 in the southern hemisphere, there was an excellent match with the A(H1N1) pdm viruses and a reasonable match with the A(H3N2) and B viruses. Like the vaccine B component, most of the B viruses circulating were of the B/Yamagata lineage. However, in Australia

and New Zealand, there were some subtle differences in the types of Yamagata viruses circulating in 2014 as compared to 2013. Very few B/Victoria lineage viruses were seen in Australia and New Zealand, with small numbers of viruses seen in samples from Singapore, Cambodia and the Philippines. The number of NICs sending samples to the WHO CC in Melbourne in 2014 was 14, the same as in 2013 and 2012. The majority of samples received up to mid-August consisted of clinical samples (44%) with the rest (56%) being viral isolates. Resistance to the NA inhibitors oseltamivir and zanamivir was very low in 2014 in all influenza types and subtypes. In contrast, high levels of resistance were seen to amantadine and rimantadine for both influenza A(H3N2) and A(H1N1) viruses.

Session II: Strengthening national influenza surveillance system, data reporting and response in the Asia-Pacific Region

Capacity strengthening of the influenza surveillance system: its role in detecting novel influenza viruses in China

Dr Yuelong Shu, Director, Chinese National Influenza Center and WHO Collaborating Centre for Reference and Research on Influenza

The influenza surveillance system in China comprises (1) the notifiable infectious diseases reporting system, (2) sentinel hospital-based surveillance for ILI and SARI, and (3) event surveillance (ILI outbreaks and unusual event reporting system). The goal of surveillance in China is monitoring (a) influenza activity and trends, (b) antiviral susceptibility, (c) unusual events, and (d) emerging influenza viruses for pandemic preparedness and response. Other outcomes of surveillance are providing laboratory diagnostic capacity for special clinical needs, providing viruses, genetic and antigenic information for vaccine virus selection, providing data for risk assessment, estimating the influenza burden, and helping decision-makers prioritize resources and plan public health interventions.

The functions of surveillance systems include the following: (a) collection, reporting, consolidation, regular analysis and interpretation of data; (b) providing data feedback to data providers and feed forward to decision-makers; (c) detection, evaluation and response to unusual data patterns; and (d) quality assurance. To achieve the goal of influenza surveillance, strategies used in China are adhering to national

guidelines/standard operating procedures (SOPs), providing continuous training, using standard reagents, building laboratory capacity, integrating epidemiological and laboratory information, using internet-based information systems, implementing an external quality assurance (EQA) programme and using a quality evaluation scoring system. China has 556 sentinel hospitals and 411 network laboratories. Specific tasks have been defined and assigned to sentinel hospitals, city influenza laboratories, provincial centres of disease control, provincial reference centres and the Chinese National Influenza Centre.

China has identified some activities that can be performed during influenza surveillance. These include viral isolation, virus detection by polymerase chain reaction (PCR) technique, genetic sequencing, performing serological assays, determining antiviral susceptibility and timely information sharing. Professional technicians, skilful technical platforms, monitoring influenza trends and resources for public health studies were required to improve the influenza surveillance network. China is expected to improve pathogen detection by employing the full spectrum of respiratory disease surveillance, expanding emerging disease surveillance and using the experience of surveillance for other infectious diseases. The subsequent plan is to detect novel pathogens from influenza-negative specimens. The Chinese NIC was able to identify in a timely manner the first three influenza A(H7N9) cases, human cases of avian influenza A(H₁₀N₈) and A(H₅N₆). In conclusion, China strives to ensure better influenza surveillance, leading to better risk assessment and vaccine development, with a view to better responding to the infection.

Strengthening the national influenza surveillance system in Bangladesh: application of lessons learned during the influenza A(H1N1) pandemic and influenza A(H5N1) outbreaks

Professor Mahmudur Rahman, Director, Institute of Epidemiology, Disease Control and Research, Bangladesh

The Institute of Epidemiology, Disease Control and Research (IEDCR) is a government-owned research facility for identifying and mitigating diseases in Bangladesh. It has developed several surveillance platforms to monitor influenza:

- An urban community surveillance site in Kamalapur, Dhaka monitors influenza circulation in the urban population.
- There is a hospital-based sentinel surveillance system that has a network of 12 tertiary-level hospitals spread evenly across the country; two more sites were added recently to enhance monitoring for influenza A(H7N9) and MERS-CoV.
- The national influenza surveillance, Bangladesh monitors the circulation of influenza and other respiratory viruses in seven districts. Three more sites were added recently to monitor influenza A(H7N9) and MERS-CoV activities in Bangladesh.
- The high-risk group avian influenza surveillance monitors contacts of all avian influenza events in sick poultry for 14 days to detect zoonosis.
- The wet market surveillance for influenza A(H5N1) in Dhaka city corporation area has been operational since 2010, and has detected three spillover cases.
- Web-based integrated disease surveillance monitors several high-priority diseases, including pneumonia, ILI and SARI. It lacks the capability for laboratory detection.
- The event-based surveillance platform triggers outbreak investigations to any kind of disease. It monitors 12 national newspapers and eight television channels to detect any report of diseases in the media. It can respond to any disease of national or international concern through formal and informal reports. Moreover, it has two hotline numbers where any unusual disease event can be directly reported to IEDCR round the clock.
- Cell phone-based surveillance monitors influenza, foodborne illnesses, and other communicable and noncommunicable diseases through telephone interviews.

IEDCR has the capacity to detect respiratory viruses, influenza type A and B viruses, and subtypes H1, H3, H5, H7 and H9. It provides all respiratory samples to the WHO CC at the United States Centers for Disease Control and Prevention (US CDC) for typing, subtyping and genome sequencing or viral cultures. By detecting many influenza and

other respiratory viruses, IEDCR has contributed to understanding the epidemiology, clinical presentations and molecular biology of these viruses. Influenza surveillance activities helped in establishing seasonal trends in the country, identifying novel strains, providing seeds for vaccine selection, monitoring influenza activities during epidemics and pandemics, and decision-making and policy developments.

Integrating laboratory and epidemiological data to detect influenza in Cambodia

Dr Paul Horwood, Deputy Head of Virology Unit, Acting Head of National Influenza Centre, Pasteur Institute, Cambodia; Dr Seng Heng, Chief of Surveillance, Bureau of the Communicable Disease Control, Ministry of Health, Cambodia

Influenza surveillance in Cambodia consists of (1) weekly syndromic surveillance, (2) event-based surveillance, and (3) sentinel surveillance. All hospitals report SARI cases weekly, including zero reporting. In event-based surveillance, unusual clusters of ILI/SARI cases are reported through hotlines to the central level. The laboratory immediately reports any influenza subtype of interest. Laboratory specimens from sentinel surveillance sites and animal specimens are referred to the NIC under the oversight of the Ministry of Health. Epidemiological investigation reports and laboratory data are shared with national and international partners. Other platforms for collaboration are ministerial briefings and the monthly national zoonotic technical working group sessions. Both epidemiological and laboratory data are published monthly in the National Respiratory Disease and Influenza bulletin.

In 2013, a new clade 1.1 genotype of influenza A(H5N1) was detected, in which haemagglutinin (HA) and NA genes belonged to clade 1.1, while all internal genes were of clade 2.3.2.1 origin. The NIC issued a rapid initial alert and prompted an investigation immediately. Contact tracing, sample collection, treatment of suspected cases and health education activities were initiated. All contacts were tested by serological assays. Most contacts had no evidence of exposure to cases of avian influenza A(H5N1) except for two cases. In the first case, three out of the 12 contacts tested and in the second case one out of 24 contacts tested demonstrated evidence of exposure to avian influenza A(H5N1). There was no evidence of person-to-person transmission.

During investigation of the community influenza A(H5N1) cluster, communication was strengthened between the investigation team and the laboratory with regard to sample collection and laboratory confirmation. Immediate quarantine was imposed and secondary cases were treated. No human-to-human transmission was established.

Genetic studies and sero-prevalence studies of avian influenza A(H5N1) among contacts and market vendors are worth mentioning as ongoing collaborations related to avian influenza. Challenges include the financial sustainability of surveillance, ensuring the quality of laboratory specimens, standardizing laboratory techniques, and coordinating and converging different public health and research goals of multiple organizations. The country is currently working towards NIC accreditation, continued collaboration, information-sharing, implementation of the pilot joint animal and human health standard operating project in two provinces, and conducting an avian influenza market intervention study.

Strengthening influenza surveillance for an effective response in Indonesia: current challenges, issues and way forward

Dr Selamat, Director of Direct Transmitted Diseases, Director General, Disease Control and Environmental Health, Ministry of Health, Indonesia

Indonesia is an archipelago with a 240 million population that is diverse in culture and geography. Indonesia has an NIC and a network of 44 laboratories with influenza PCR testing capacity. Due to the outbreaks of avian influenza A(H5N1), which started in 2005, influenza surveillance has become a priority.

Indonesia has surveillance systems with differing objectives, such as detecting influenza disease outbreaks and monitoring disease trends. Potential outbreaks of human avian influenza A(H5N1) cases are identified through the nationally notifiable disease surveillance, called early warning alert and response system (EWARS), as well as through event-based surveillance. The epidemiological and virological trends of seasonal influenza are monitored through three sentinel surveillance systems; the national ILI surveillance system operating in 26 health-care centres, the national SARI surveillance system operating in six hospitals, and the East Jakarta Project that has four ILI and six SARI sites in one urban area of Indonesia.

The information arising from public health surveillance, including information on virus characteristics, provides the necessary evidence base to enable policy development and aid in Indonesia's preparedness and effective response. The surveillance systems have previously detected cases of avian influenza A(H5N1) and triggered rapid response team investigations. All three sentinel systems have also been modified to enable detection of other emerging respiratory infectious diseases, such as MERS-CoV. These systems are also ready for surveillance during a future pandemic as they monitor disease severity, geographical spread and patient outcomes.

Implementation of disease control activities by the local governments is challenging. This is due to the limited capacity of local health authorities to respond to influenza-related disease alerts and their limited ability to commit resources to influenza disease control. Other challenges include sustaining the capacity of the laboratory network due to regular staff turnover and machine malfunctions.

Indonesia needs to continue to strengthen local public health and laboratory capacity, harmonize influenza surveillance systems to maximize epidemiological and virological data linkages, improve disease alert response options and use the influenza evidence base for policy development in the area of disease control.

*Multiple challenges to influenza surveillance at the human–animal interface
Dr Stacey Schultz-Cherry, Deputy Director, WHO Collaborating Centre for
Studies on the Ecology of Influenza Viruses in Lower Animals and Birds, USA*

Influenza viruses circulating in animals pose a threat to human health. Recent examples of animal viruses that have crossed the species barrier to cause human disease and even death include the avian H5, H6, H7, H9, and H10 subtypes, and swine H1 and H3 subtypes. Thus, monitoring influenza viruses at the animal–human interface is an important component of public health surveillance. This can include monitoring people who work or live in close contact with infected animals, people who handle or slaughter infected animals or work with the raw byproducts, and people who may come in contact with objects that have been in contact with infected animals, including housing areas, equipment, and even water sources. However, there are some challenges to conducting surveillance at

the human–animal interface. Multiple players at many levels, different and sometimes opposing mandates, differences in established mind-sets, institutional constraints and determining who is doing what are some of these challenges. However, collaboration between different stakeholders is definitely improving, at least at the global level.

Introduction to FluID

Dr Katelijn Vandemaële, Medical Officer (HIP, Influenza, Hepatitis and PIP Framework), WHO headquarters

Global influenza monitoring tools are the basis for real-time data collation for monitoring influenza activity, informed decision-making at the national, regional and global levels, and analysis of country data in a global context. Flunet is a web-based interactive reporting, query and mapping system of the GISRS. NICs of over 130 countries report weekly laboratory data, which include specimens collected/received, processed, influenza virus types and subtypes.

FluID is a web-based, epidemiological data collection platform through which data from over 60 countries are entered. FluID complements virological information and makes epidemiological information more comparable. Countries with formal surveillance systems may report ILI, acute respiratory infection (ARI), SARI, pneumonia and mortality data. The age groups can be defined for each reporting country. FluID is flexible in setting up data-reporting variables, depending on what is collected systematically.

FluID generates qualitative indicators, such as the geographical spread, disease trend, intensity and impact. The data input options for FluID and FluNet are many. Data are uploaded to FluNet by the NICs themselves or by the WHO regional offices or headquarters. Data to FluID can be uploaded by the national influenza surveillance focal points. Regional databases such as EUROFLU or Pan American Health Organization spreadsheets are directly linked to FluID. Meanwhile, some NICs provide data by e-mail to WHO headquarters. High country participation in both platforms is vital as integrated data from FluID and FluNet provide a comprehensive picture of the epidemiological and virological situation of influenza.

In future, WHO intends to add “built-in analysis tools” and user-friendly, interactive maps and graphs to the global influenza monitoring tools. With the prospect of more countries joining the platform, the opportunity will be available for linking country data to the regional databases. Combining the outputs of global influenza monitoring tools with other information sources enables regular risk assessments, conducting seasonal reviews, generating bi-weekly situation updates and publications such as the Weekly Epidemiological Record. Local ILI and SARI surveillance data are important for local decision-making and creating a global picture of influenza. The generated global picture is required to predict possible influenza scenarios for countries.

Discussion on the potential for country reporting to FluID and how we can make this happen

FluID is a useful tool for having epidemiological and laboratory data together. The discussion revolved around the reasons for the low reporting behaviour of countries. WHO headquarters suggested the need to work with regional offices to explore reasons for non-reporting in selected countries. Pilot implementation in one or two countries from each region of WHO was suggested as a means to help better understanding of country-specific reasons for not reporting. WHO was requested to disseminate the aim and objectives of FluID as many Member States do not have a good understanding of it. The regional offices were advised to select one or two Member States to enter data in FluID and provide technical support to them. It was decided to consider providing general recommendations to all Member States after analysing the experience of selected countries by the regional offices.

Session III: PIP framework: a platform for strengthening influenza surveillance and response

Introduction to the PIP framework, including virus sharing and access to benefits

*Dr Wenqing Zhang, Scientist, (HIV, Influenza, Hepatitis and PIP framework)
WHO headquarters*

Two objectives of the PIP framework are to improve sharing of influenza viruses with pandemic potential, and achieve predictable, efficient and

equitable access to benefits arising from the virus-sharing, notably vaccines and antiviral medicines. The framework applies to influenza viruses with pandemic potential but not to seasonal influenza viruses. The main elements of the framework are virus-sharing, benefit-sharing, governance and review. Influenza viruses with pandemic potential shared through the GISRS are used for risk assessment, development of candidate vaccine viruses and other activities described in the terms of reference for GISRS.

Benefit-sharing provides equitable access to vaccines and other pandemic response-related products, surveillance and risk assessment information, technical assistance and support to strengthen national pandemic influenza response capacities. There are two benefit-sharing systems:

- (1) Standard Material Transfer Agreement (SMTA)-2 between WHO and non-GISRS recipients of PIP biological materials,
- (2) Partnership contribution made up of annual payments from manufacturers to WHO.

The oversight mechanism of the PIP framework consists of three pillars. The World Health Assembly oversees its implementation. The Director-General promotes implementation, and the advisory group advises the Director-General on the use of the partnership contribution, monitors and assesses implementation of the framework, and interacts with industry and other stakeholders. Sharing of influenza viruses A(H5N1) and A(H7N9) is ongoing and recorded under the Influenza Virus Traceability Mechanism on the WHO website. Six SMTAs have been signed and several more are pending. So far, 25 contributors have contributed US\$ 23 million to the partnership contribution. The implementation plan of the partnership contribution for 2013–2016 has been signed by the Director-General, and 26 countries have focused on strengthening laboratory and surveillance capacity. A subsequent meeting and the first rotation of advisory group members was due in October 2014. The report of the Technical Expert Working Group on Genetic Sequence Data was submitted to the Advisory Group and it is expected to provide advice and recommendations to the Director-General on the best process for handling genetic sequence data. Ramping up implementation of the partnership contribution and SMTA-2 negotiations, improving and increasing communications, and preparing for the full framework review scheduled in 2016 are the next steps to be performed.

PIP framework: optimizing the use of partnership contribution implementation for strengthening the capacity of laboratory, surveillance and response for seasonal and pandemic influenza

Professor Dr Tjandra Yoga Aditama, Director General, National Institute of Health Research and Development, Indonesia

The plan of implementation of the partnership contribution (2013–2016) expects to estimate the influenza burden, strengthen (a) laboratory and surveillance capacity, (b) the capacity to regulate influenza-related pharmaceutical products, (c) risk-communication capacity, and (d) deployment of pandemic influenza supplies. The partnership contribution implementation plan has specified three major outputs, namely (1) strengthening national capacities to detect respiratory disease outbreaks due to novel viruses, (2) strengthening national capacities to monitor trends in circulating influenza viruses, and (3) strengthening global collaboration through sharing of information and viruses, and assuring the quality of PCR testing. It has also detailed key deliverables under each output.

Indonesia intends to optimize implementation of the partnership contribution to strengthen the capacity of laboratories, surveillance, and pandemic preparedness and response. Currently, the NIC has identified five pillars of research: reducing the risk of emergence of pandemic influenza, limiting its spread, minimizing the impact, optimizing patient treatment and promoting the application of modern public health tools. Surveillance activities of the NIC entail laboratory surveillance, outbreak investigation and pandemic response. Laboratory-related activities include biosafety, laboratory network coordination and enhancing laboratory diagnostic capacity.

Under the partnership contribution implementation plan, the NIC focuses on the major output 2. Specific activities have been planned under three key deliverables of output 2. Under deliverable 1 (strengthening influenza laboratory surveillance and the link with epidemiological surveillance), Indonesia intends to review existing sentinel surveillance sites, strengthen them through training, provide technical support, strengthen the NIC and revamp the surveillance network.

Under deliverable 2 (strengthening influenza disease surveillance), reviewing national influenza data management, conducting a gap analysis, establishing/strengthening/expanding the web-based data management system to share data, and improving data-sharing with national and international stakeholders have been proposed.

Under deliverable 3 (enhancing national data-sharing capacity to ensure monitoring and assessment of influenza events of international concern), Indonesia expects to enhance influenza surveillance, develop a data-sharing framework, and improve sharing of surveillance data at the animal–human interface.

Using the partnership contribution plan and with international collaboration, Indonesia directs its efforts towards strengthening pandemic preparedness as a means of mitigating the impact of future influenza pandemics.

Results of the fourth WHO survey of NICs

Dr Aeron Hurt, Research Scientist, WHO Collaborating Centre for Reference and Research on Influenza, Victorian Infectious Diseases Reference Laboratory, Australia

The purpose of the fourth global survey of NICs was to better understand the NIC capacity with a view to identifying gaps to further develop the GISRS. The survey was confined to activities performed during 2010–2013. Major topics included were (1) laboratory diagnosis, (2) virological surveillance, (3) pandemic preparedness and response, (4) laboratory practices, (5) information technology, (6) terms of reference of NICs, and (7) national policies and surveillance. Twenty-four (80%) NICs from 20 countries in the South-East Asia and Western Pacific Regions participated. Some key results relevant to the NICs of both regions are given below.

Of the 24 NICs that responded, 21 played a role in collecting seasonal influenza specimens. Overall, both regions contributed 22–28% of samples received globally. All NICs used a real-time PCR technique and 86% performed virus isolation. Fifteen NICs performed serological analyses of influenza viruses. Of these, 13 used HAI tests. The proportion of laboratories performing HAI tests (73%) and sequencing (68%) is higher in the Asia-Pacific Region than across all WHO regions. Fifteen NICs

performed antiviral susceptibility analyses, 10 conducted both genotypic and phenotypic assays, three conducted only genotypic assays, and two carried out only phenotypic assays.

Twenty NICs reported shipping isolates or specimens to one of the WHO CCs. Six NICs had shipped H5, H7 or H9 specimens or isolates to a WHO CC or reference laboratory. Thirteen NICs shipped both isolates and specimens. Nine NICs detected and/or isolated an influenza virus with human pandemic potential, and all were sent to a WHO CC, H5 reference laboratory or other GISRS laboratory. Ten NICs used the WHO influenza shipping fund during 2010–2013. Subject to the availability of funds, nine NICs would prefer to send more shipments to WHO laboratories. Regarding funding, the proportion of NICs with a specific budget for influenza was 86% in 2013. The budget has decreased in a third of NICs, while in 40%, the budget remained the same during the study period.

Twenty-two NICs had a standard procedure to determine the further course of action in the event of identifying an unusual influenza virus or a new subtype. Of these, 21 had procedures to inform the IHR focal point in the country. Ten NICs found that implementation of the PIP framework has affected the work of the laboratory.

Twelve NICs reported that their country conducts surveillance of humans for new introduction of animal influenza viruses. Nineteen NICs responded that their country performs specific surveillance of animals for influenza viruses, while 17 reported virus information exchange between the human health laboratory and the veterinary sector. Twenty NICs could detect A(H7N9) or A(H5N1) avian influenza viruses, while 12 NICs could detect A(H3N2) variant swine influenza viruses.

All NICs had real-time PCR machines and biological safety cabinets. A third of NICs possessed laboratories classified at biosafety level (BSL)-2; half had BSL-3 facilities while four NICs had BSL-4 facilities. Around 80% of NICs conducted continuous training programmes for the laboratory staff, while nearly 70% of NICs had annual competency assessments for the staff.

Three NICs reported a loss of expertise in their staff over the past 4 years, most commonly due to retirement or budget cuts. Laboratory technicians were the most needed personnel for NICs. Sixteen NICs had

mechanisms to rapidly increase staff numbers in the event of an outbreak of a novel influenza virus or a pandemic.

Nine NICs reported entering weekly data while two NICs reported entering data monthly to FluNet. Seventeen NICs were aware of the EZcollab GISRS information centre and 13 used it regularly. Eight of these NICs knew how to share information with other GISRS members via EZcollab. Nine NICs had their own website for reporting influenza activities/information. Nine countries reported epidemiological data to FluID. Thirteen NICs reported that their country had a national vaccination policy. According to the survey, all NICs reported the availability of antiviral medications in the country while 10 reported their use for routine treatment. Nineteen NICs reported that their country has a stockpile of antivirals for use in a pandemic.

In summary, survey findings were of considerable value in understanding and improving the capacity of NICs. Comparison of responses from NICs in the Asia-Pacific with all NICs demonstrates the strong network and capacity within these two regions for influenza surveillance, diagnosis and analysis.

Session IV: Strengthening laboratory systems for surveillance of, and response to, influenza and other emerging respiratory infections

Public health laboratory system for surveillance of, and response to, emerging infectious diseases

Dr Franciscus J.A. Konings, Technical Officer (Laboratory), Emerging Disease Surveillance and Response, WHO Regional Office for the Western Pacific

The Asia Pacific Strategy for Emerging Diseases (APSED) is a tool to support Member States to achieve IHR (2005) core capacities. APSED focus area 2, laboratory, supports both surveillance and response capabilities for emerging infectious diseases. This focus area is closely linked with others, including surveillance and zoonoses. National workplans are encouraged to promote engagement with subnational-level laboratories and, at a later stage, exercises are recommended to test the systems. Referral capabilities, either to national laboratories or to international reference laboratories, are a vital component of a fully functional laboratory system. The GISRS and

influenza laboratory network has been used to build laboratory capacity for emerging infectious diseases. For example, the influenza laboratory system was used to build testing capability for MERS-CoV

WHO has also facilitated EQA for dengue testing using lessons learned from the EQA for influenza. For dengue, the results from this assessment reveal good performance, with more than 80% of the 19 laboratories participating generating 100% accurate results. The next round will focus on other pathogens in addition to dengue. Using existing systems is an efficient and sustainable way to build laboratory capacity for emerging infectious diseases.

Using the influenza surveillance system as a platform for detecting other respiratory pathogens

Dr Raymond Lin Tzer Pin, Head and Senior Consultant, National Public Health Laboratory, Singapore

The presentation focused on the advantages and disadvantages of tapping into different sources of information for detecting new pathogens that cause respiratory tract infections. For example, routine testing of respiratory viruses from sentinel surveillance sites are useful only for showing seasonality and explaining trends, but are not sensitive enough to detect the emergence of novel pathogens. They may also not lead to any effective intervention. Taking into consideration local factors and limited resources, it was suggested that countries adopt a multipronged approach using their existing influenza surveillance mechanism to collect specimens from sentinel sites, and also include event-based surveillance, which requires clinician notification of clusters or unusual severe cases. Past and present challenges include linking clinico-epidemiological information with laboratory information, and providing support for laboratory development, including upgrading scientific and clinical expertise. To detect new unexpected agents or strains, it is useful to focus on severe hospitalized cases, unusual clinical presentations or clusters. New laboratory methods or referral laboratories are needed to detect novel pathogens. The WHO bi-regional NIC meeting should continue to focus on influenza, though relevant or useful information about other respiratory viruses can also be presented.

Country-level issues and challenges in specimen referral, laboratory detection and characterization of influenza and other emerging respiratory viruses

Dr Win Thin, Deputy Director, National Health Laboratory, Yangon, Myanmar

WHO assessed Myanmar's capacity for influenza surveillance in 2005. Subsequent to this assessment, the National Health Laboratory (NHL) was identified as appropriate for being designated as the NIC. WHO and donors supported the NHL with equipment and established laboratory facilities required for an NIC. The PCR laboratory at the NHL was renovated. The avian influenza mission comprising WHO and the National Institute of Health (NIH) of Thailand also helped to build the diagnostic capacity of and establish biosafety measures at the NHL. NIH also trained two microbiologists in the diagnosis of avian and seasonal influenza. In November 2007, the first human avian influenza case was correctly diagnosed at the NHL and was confirmed at the NIH, Thailand and WHO influenza A(H5N1) Reference Laboratory in Japan. The NHL was officially designated as the NIC by the Ministry of Health in November 2007, and it was recognized by WHO in January 2008.

At present, Myanmar faces a number of challenges in specimen referral, laboratory detection, and characterization of influenza and other emerging respiratory viruses. Overall, the country needs to strengthen the current influenza surveillance system. The major challenge is assuring financial sustainability for influenza surveillance, particularly in relation to accounting for specimen transport costs, costs of the viral transport media and costs of daily allowances for the staff. For better laboratory diagnosis of the etiology of influenza and other emerging infections, it is necessary to conduct refresher training programmes for the current staff, and training programmes for new recruits on specimen referral, laboratory detection, and characterization of influenza and other emerging respiratory viruses. Another area that needs focus in terms of training is specimen transportation according to international guidelines. In this regard, staff should be familiar with the requirements of the International Air Transport Association and IHR in shipping specimens.

Strengthening the capacity for SARI surveillance is complementary to the existing ILI surveillance platform. Specimen referral, diagnosis and reporting of detected pathogens causing SARI within the SARI surveillance

platform are other challenging areas. The laboratories require establishment of BSL-2, BSL-3 and BSL-4. Apart from the establishment of biosafety levels, the current staff and new recruits also require training in the biosafety aspect. Another area for intervention is quality. A key challenge in the long run in Myanmar is estimating the burden of disease to support policy decisions on influenza vaccine introduction so that the impact of seasonal and pandemic influenza can be mitigated.

*Laboratory detection and characterization of influenza and other emerging respiratory viruses: challenges to the Regional Influenza Reference Laboratory
Dr Malinee Chittaganpitch, Chief of Respiratory Virus section, National Institute of Health (NIH), Thailand*

The Thai NIC, under the Department of Medical Sciences, was recognized by WHO as a national influenza laboratory in 1972. In June 2010, it was designated by WHO as WHO's Regional Influenza Reference Laboratory (RIRL) for the South-East Asia Region. The three main objectives of the RIRL are (1) completing WHO's terms of reference, (2) providing laboratory services, and (3) conducting research activities. The Thai NIH has been supported since 2005 by WHO and US-CDC to strengthen the influenza surveillance network in Thailand. The capacity of the RIRL has also been gradually strengthened for detecting influenza and other emerging respiratory viruses such as influenza A(H7N9) and MERS-CoV. RIRL was able to transfer influenza A(H7N9) and MERS-CoV PCR diagnostics and provide proficiency testing panels for influenza and avian influenza viruses to all regional medical science centres under the EQA programme. However, the need for outbreak investigations of unusual events has necessitated the establishment of testing algorithms in order to determine the potential etiology of pathogens. Therefore, the RIRL needs to enhance its capacity to detect other respiratory viruses of EIDs so as to serve rapidly in a health emergency. At present, the RIRL has the capacity to characterize influenza by both phenotypic and genotypic assays, conduct virus susceptibility testing and detect six respiratory and other emerging viruses. However, the challenge that the RIRL will face in the near future is the sustainability of detection of other emerging respiratory viruses through the influenza surveillance system. The sustainability of a multiple pathogen detection system requires the management of resources such as human resources and funding. Possible support from WHO may entail funding for reagents, calibration cost of sequencers, cost of PCR machines, advance

technology transfer and coordination of EQA for other respiratory viruses of emerging infectious diseases.

Group work

Group work I: Major issues/challenges for implementing the WHO influenza surveillance standards in the Asia-Pacific Region and potential solutions

Participants identified several challenges in implementing the WHO Global Epidemiological Surveillance Standards for Influenza. These stemmed largely from difficulties in communication and collaboration between the different sectors and departments involved in surveillance, as well as from resource limitations. Coordination between the epidemiology and laboratory departments is variable and weaknesses in this area can lead to delays in batch submissions of laboratory specimens and diagnostic results. Collaboration is often lacking between public health practitioners and clinicians, who sometimes view influenza surveillance duties as extra work. Limited human resources pose another challenge, as high turnover and inconsistency in training impact the quality of surveillance staff. Professional development is often hampered by a lack of overall supervision and feedback. Laboratory facilities and staff are also limited in the Asia-Pacific Region. In addition, privacy issues affect patient tracking and identification of individual patients.

Several solutions to these challenges emerged in the discussion. To address the issue of resource limitations, participants suggested using existing surveillance structures such as that for poliomyelitis to better implement influenza standards. Another suggestion was reducing the number of sentinel sites to the minimum needed for geographical representativeness, and transitioning to computer-based data collection platforms. Telephone or Internet surveys of individuals or families could also be used to improve ILI surveillance. In order to bridge the gap between clinical and public health staff, creating opportunities for frequent interaction between influenza programme and clinical staff is vital. The need to train epidemiological and laboratory professionals together and provide a forum for both groups during key discussions was highlighted. Ensuring lateral and downward data flow and providing opportunities for enhanced data utilization are other areas of focus. Participants also highlighted the need for government policies to sustain surveillance

standards after current donor funds expire. The development of such policies would be furthered by ensuring the use of surveillance data for decision-making on influenza vaccine use. Including NICs under the government purview was another suggestion.

Group work II: Major issues/challenges to strengthening early warning alert and response systems in the Asia-Pacific region and potential solutions

Participants highlighted issues and challenges to strengthening EWARS in the Asia-Pacific region. Key issues highlighted were quality assurance and geographical representativeness of sentinel sites, sustainability of EWARS, low commitment of service providers, information-sharing within countries and globally, and intersectoral collaboration. Sustainability of EWARS is a challenge due to high staff turnover and donor-dependent financing of activities. Private sector providers contribute minimally to surveillance for influenza, especially as it is not a notifiable disease. In the animal sector, disincentives for influenza virus detection, including embargoes and economic losses, are an obstacle to reporting of events and collaboration with the human health sector.

Several priority training needs were identified to strengthen EWARS. Cross-disciplinary training is essential for multidisciplinary members of rapid response teams within the rapid response framework. Respiratory disease outbreak investigation should be an integral part of Field Epidemiology Training Programmes. Another important area for training is data management and analysis. Training should be coupled with multidisciplinary and multisectoral drills for effective action when it matters the most. Effective cross-border coordination of surveillance and response teams is indispensable for early warning and timely action.

The group made several recommendations to address these challenges. Surveillance systems should meet country-specific needs, as one size does not fit all for influenza surveillance. Member States, with the support of WHO, should consider reviewing their influenza surveillance and response systems by using existing evaluation tools. This should include capacity and skills appraisal of the multidisciplinary team members as per their job descriptions. There should be a mechanism to better engage clinicians, the private sector and use field epidemiology training for influenza surveillance and response. Interdisciplinary and intersectoral

coordination should be ongoing and further improved for event surveillance, outbreak investigations, data-sharing and response.

Group work III: Adapting influenza surveillance to detect other respiratory pathogens and support IHR and APSED implementation

Influenza surveillance platforms may be used to detect other emerging respiratory pathogens subject to adequate support by laboratory networks. Event-based surveillance may be more useful for detecting new or unknown pathogens, while existing syndromic surveillance systems are more useful for monitoring trends in such pathogens after their emergence. Member States could work towards integrating surveillance of other respiratory pathogens with existing systems to meet the IHR and APSED requirements.

Participants listed (a) travel history, (b) contact with a suspected/confirmed case, (c) animal contacts, (d) occupation, (e) current pregnancy status, (f) co-morbidities, and (g) history of cluster of cases as additional epidemiological or clinical variables that could be added to the existing ILI or SARI surveillance systems so that these platforms could be used to support preparedness and response to emerging respiratory diseases.

The sustainability of the current surveillance system and inadequate coordination between clinicians, epidemiologists and microbiologists, and between the human and animal health sectors were major issues. The possibility of missing cases with mild symptoms and different clinical features by syndromic surveillance was another issue. Current sentinel surveillance sites are limited in number, and have inadequate laboratory capacity to detect non-influenza respiratory pathogens. The need for timely reporting, data analysis, feedback and alerts were other flagged issues.

Participants highlighted the necessity for resources to sustain the existing surveillance system, and for improved linkages between the animal and human health sectors and clinicians, epidemiologists and laboratory networks. Strengthening advocacy and communication for current and other potential stakeholders was suggested. It was recommended that Member States add new variables as per specific needs; approach reference laboratories and WHO CCs in case of difficulty in

detecting/diagnosing newly emerging pathogens; sustain both epidemiological and laboratory capacity through training, monitoring, supervision; and by providing reagents and primers. Strengthening coordination and collaboration within surveillance programmes and between different sectors was also recommended, as well as immediate reporting of any diseases notifiable under IHR (2005). WHO CCs were recommended to continue their support to NICs through bilateral and multilateral approaches, especially in relation to newly emerging diseases, transfer of technology and techniques, promoting research and timely feedback. Meanwhile, WHO should continue to support capacity-building, networking, and provide guidance to and algorithms for NICs and Member States.

Group work IV: Issues/challenges for sample collection, referral and diagnosis of emerging respiratory pathogens using the influenza surveillance platform and potential solutions

Participants opined that the ILI/SARI definitions may not capture all emerging respiratory infections. They highlighted current issues in sample collection from patients with ILI/SARI. If more viruses are to be included in testing panels, participants raised the issue as to what the target for testing would be and how to prioritize this against the background of understaffed NICs.

Even in hospitalized pneumonia patients, not taking samples from the lower respiratory tract is an issue. Many samples are accompanied by limited or no information. Some laboratories receive small numbers while others are overwhelmed with the number of samples. Testing all of these when laboratories are overwhelmed is resource- and labour intensive. The issues related to sample transportation are improper timing, inadequate cold chain maintenance and cost.

In terms of detection and characterization of emerging respiratory pathogens, identification of new conditions and clusters is a challenge for clinicians. Use of available technology for identification of pathogens varies between laboratories and regions. Identification of novel pathogens is difficult for laboratories, and WHO CCs are only for referring influenza viruses. Therefore, how to capture novel non-influenza agents remains undetermined.

Participants recommended that NICs engage with clinicians and provincial health authorities to increase the number of samples referred to NICs. When NICs are overwhelmed with samples, the use of specific case definitions and prioritization of samples for testing was suggested. NICs will have to extend the range of testing from influenza to other respiratory pathogens by exploring the adoption of new testing panels/kits. However, this requires training. Other recommendations for the NICs are: (a) implementing appropriate SOPs for sample collection, transportation and testing; (b) determining targets for improvement of NICs; (c) understanding WHO shipment funds for possible utilization for sample transportation; (d) implementing the NIC assessment/accreditation process to improve skills, knowledge and understanding; (d) engaging with clinicians to better recognize ILI, SARI and other respiratory syndromes, and motivate sampling from appropriate sites.

Participants recommended that WHO CCs offer (a) staff training and technical support, (b) positive control materials and reagents, and (c) next-generation sequencing for influenza viruses that are untypeable to NICs.

Group work V: Issues/challenges related to the quality of epidemiological data and laboratory specimens sent to the NICs from ILI/SARI sites, integration of epidemiological and virological data in the Asia-Pacific Region and potential solutions

Difficulty in maintaining the cold chain, particularly in remote areas of countries and islands; lack of dry ice; inadequate funding to engage couriers for specimen transport, maintain surveillance and dedicated staff affect the quality of laboratory specimens sent to NICs. Inadequate coordination and communication between laboratory and hospital staff, having hospital doctors who are interested only during outbreaks, the low priority given by them to collection of surveillance specimens, and the lack of skilled and dedicated staff for taking specimens and completing request forms with the requisite demographic and epidemiological information are issues that affect the quality of epidemiological data.

Though laboratory and epidemiological data are mostly combined for ILI, this has not always been the case for SARI. The laboratory staff are not always fully aware of what happens to the test results they provide. Laboratory professionals are not always able to perform complex analysis

due to lack of epidemiological information. On the other hand, the data collected are not always reported, although several countries have either combined or separate epidemiological and laboratory web updates or mailing lists.

Laboratory challenges are sometimes hard to overcome, particularly in maintaining the cold chain (no electricity, insufficient funding). Therefore, inactivation of virus may be a solution in some situations by sacrificing virus isolation to preserve ribonucleic acid for molecular detection in inactivated viruses. As lack of Internet access has made it difficult to consolidate laboratory and epidemiological data, providing Internet access with a web-based data entry facility should be a priority. Conducting regular meetings between epidemiologists, laboratory professionals and hospital doctors, participation of epidemiologists in laboratory training and laboratory professionals in epidemiology training, and providing feedback to clinicians about their contributions are vital for common understanding. Regular training of staff to ensure adequate functioning is also recommended, especially with staff turnover.

In summary, while the overall laboratory and epidemiology sections are functioning well, some countries are faced with real challenges that are difficult to overcome (e.g. sample transportation). Integration of laboratory and epidemiological data is in place in some countries; however, ways to facilitate combining datasets (for example, web-based systems) could be explored. A better understanding between laboratory, epidemiological and hospital staff puts a context to their work and enables their enthusiastic participation.

Session V: Updates on influenza vaccine virus selection, seasonal influenza vaccines and the regional status of seasonal influenza vaccine use

Updates from the Third WHO informal consultation for improving influenza vaccine virus selection

Dr Wenqing Zhang, Scientist (HIP, Influenza, Hepatitis and PIP framework), WHO headquarters

The Third WHO informal consultation reviewed (1) global surveillance, (2) characterization of antigenicity and antibody response, (3) technologies and tools, and (4) manufacturing and regulatory perspectives.

The GISRS is the basis for the process of vaccine virus selection and development. There are challenges to vaccine virus selection and development in terms of sustainability, optimal size, timeliness and representativeness of surveillance, quality of viruses shared, information-sharing, timing of recommendations for WHO vaccine composition and virus evolution. Currently, the vaccine virus selection process is largely based on HAI. There are no viable alternatives to HAI as limited progress has been made in other technologies. NA and NA antibodies contribute to immunity. Efforts are ongoing to better understand the patterns of antigenic drift of NA and its impact on vaccine virus selection.

The “antibody landscape” approach has used antigenic mapping to understand the quality and breadth of the antibody response to HA (and NA), and influence of prior immunity on vaccination responses, known as the “back-boost” effect. Advances in the prediction of virus evolution, though still at a very early stage, can provide the potential for selecting the “optimum vaccine virus”.

High-throughput methodologies offer opportunities and challenges for surveillance. The consultation also reviewed the application of synthetic genomics technology and reverse genetics. Integrating antigenic and genetic data using mathematical modelling helps in understanding the factors that determine antigenic drift. The viral fitness concept predicts the evolution of HA sequence clades. System genetics and systems biology concepts have the potential to identify specific host-susceptibility genes, diagnostic and prognostic markers, understand pathogenic and virulence mechanisms, and evaluate vaccine performance and response. Efforts are ongoing to validate, map organizing principles and applications, and ensure the availability, accessibility and quality of the “big data” concept.

The capacity for influenza vaccine production has been increased in developing countries. The influenza vaccine cycle has an extremely tight timeframe. The ability to obtain high yields by optimizing “backbone” strains has been demonstrated and is of significance to a pandemic response. Regulatory demands on new influenza vaccine types are increasing. Continuous development of alternative potency assays to single radial immune diffusion assays is in progress.

Until “universal” influenza vaccines are available, vaccine virus selection remains a critical, challenging public health action. WHO

commits to continuing to provide the global platform to improve this process.

Selection of seasonal influenza vaccines in the tropics and subtropics: factors to be considered by Member States

Dr Nancy Cox, Director, Influenza Division, United States Centers for Disease Control and Prevention

US CDC and Asian collaborators attempted to generate a regional consensus on the seasonality of influenza, latitude gradient associated with seasonality and the best timing for vaccinations to help policy-makers/regulatory authorities approve the use of vaccines for both hemispheres.

Based on the analysis of weekly surveillance data from 2006 to 2011 in 10 countries in South-East Asia, the seasonality of influenza was determined. There were two groups of countries: (a) those with distinct influenza activity peaks; and (b) those without distinct influenza activity peaks. Bangladesh (Dhaka, July–August), India (Delhi, July–August), Lao People's Democratic Republic (Vientiane, August–September), Cambodia (Phnom Penh, August–September), Philippines (Manila, July–September), Thailand (Bangkok, August–September) and Viet Nam (Hanoi, May–July) belong to the first group, while Indonesia, Malaysia and Singapore belong to the second group.

The latitude gradient associated with discrete seasonality was seen in two locations in India. Srinagar, with influenza peaks in winter, was a case for northern hemisphere vaccines, while activity in Delhi peaked with the monsoon. This was a case for southern hemisphere vaccines.

For the seven countries with distinct influenza peaks, the best time of the year for vaccination was April to June. For countries without distinct influenza peaks, the best time needs to be decided based on national considerations. The South-East Asia region did not demonstrate temperate seasonality despite its location in the northern hemisphere. Influenza viruses circulated to some extent throughout the year. Countries between the equator and approximately 30 °N latitude have an influenza peak during the monsoon period (June–September). Countries closest to the equator have year-round circulation without discrete peaks. Most tropical

countries in Asia should consider vaccination in April–June each year, prior to the influenza peak, using the most recent WHO-recommended vaccine formulation.

India is translating this evidence into policy. A paradigm shift has occurred in the timing of the influenza vaccination, with the recommendation in April–May. The Indian Academy of Paediatrics recommended the change. Both northern and southern hemisphere vaccines are required at subregional levels. In future, it is necessary to explore in other Asian countries (1) whether influenza A has peaks and influenza B circulates most of the year, as was seen in India, (2) whether subtypes circulating in tropical Asia move to temperate regions, and (3) the implications of year-round circulation, such as persistent exposure to some level of influenza and natural priming for tropical Asia.

Seasonal influenza vaccine use in the Western Pacific Region

Dr Kimberley Fox, Technical Officer (Vaccine-preventable Diseases) WHO, Regional Office for the Western Pacific

Data on seasonal influenza vaccination in the WHO Western Pacific Region comes from two main sources: the WHO/United Nations Children's Fund (UNICEF) Joint Reporting Form on Immunization (JRF) and a WHO Western Pacific Region survey on seasonal influenza vaccination policies, recommendations and practices in 2011. Of 36 countries and areas with data, 26 (72%) reported that influenza vaccine was available, 25 (69%) had influenza vaccination policies or recommendations, and 24 (67%) had introduced the vaccine in the national vaccination programme or schedule. However, introduction of influenza vaccine has slowed; only four countries or areas have introduced the vaccine since 2004. All the countries with recommendations for seasonal influenza vaccination target elderly persons and health-care workers, 76% target pregnant women, 60% target children, and 72% target those with chronic medical conditions. While all of these are appropriate target groups, they do not reflect the 2012 WHO recommendations to prioritize pregnant women. Most countries reported distributing enough doses of seasonal influenza vaccine to vaccinate less than 20% of their population. Only Japan, New Zealand, Palau, Tokelau and Pitcairn Islands exceeded 20% coverage. Among the 10 countries reporting coverage for specific target groups, coverage ranged from 10% to 93%. Most (22/26) countries reported using trivalent influenza vaccine

(TIV), one used adjuvanted TIV, two used TIV and adjuvanted TIV, and one used TIV and live-attenuated vaccine. Most (21/26) countries obtained influenza vaccine from international sources only; Australia, Japan, China and the Republic of Korea reported domestic sources of influenza vaccine. Most countries used the northern or southern hemisphere formulation of vaccine that matched the month of peak disease activity in that country. However, eight countries and areas, including five in the Pacific, had mismatches in vaccine formulation and peak disease activity. In summary, more than half of the countries in the Western Pacific Region have seasonal influenza vaccine policies or recommendations, and most target relevant risk groups but some do not include pregnant women. Coverage overall remains relatively low, and vaccine formulations are not always well matched to peak disease activity. Data are incomplete and need to be updated with a repeat survey or expanded JRF data collection.

Pregnant women as the highest priority target group for seasonal influenza vaccines: evidence for the Strategic Advisory Group of Experts (SAGE) decision

Dr Nancy Cox, Director, Influenza Division, United States Centers for Disease Control and Prevention

Pregnant women have a higher risk of influenza-associated hospitalization than non-pregnant women. This risk increases by trimester and when combined with other risk factors. In the United States, excess mortality attributable to influenza was observed among pregnant women, particularly in the third trimester. A case–control study of risk factors for hospitalization caused by influenza A(H1N1) pdm 2009 during the pandemic in Australia demonstrated that pregnancy was a significant risk factor for severe disease.

In Nova Scotia, infants born to mothers who had been hospitalized for respiratory illness during influenza seasons at any time during pregnancy were more likely to be small for gestational age (adjusted relative risk 1.66, 95% CI: 1.11–2.49) and had lower mean birth weight (3348.5 ± 498.2 g vs 3531.3 ± 504.1) than that of infants born to women without an influenza-season respiratory hospitalization during pregnancy. Though it varied from year to year, the incidence of laboratory-confirmed influenza in hospitalized children in the US has demonstrated the high burden in children aged <6 months.

Vaccinating pregnant women is effective in reducing influenza in infants <6 months of age. Evidence indicates that influenza vaccination of pregnant women can also result in higher birth weight of their children. The vaccines were as immunogenic in pregnant as in non-pregnant women in small clinical studies. Since the SAGE recommendation, a vaccine effectiveness study among pregnant women in the US demonstrated an efficacy of 42%.

Influenza vaccines have demonstrated an excellent safety profile in pregnancy. No study to date has shown vaccine-specific adverse consequences of inactivated influenza vaccine in pregnant women or their offspring. Data from an observational cohort study in Canada and from a birth and infant health registry in the US did not show any safety concerns related to pandemic vaccines among women during gestation or their offspring. Despite the lack of apparent safety issues, precautions and contraindications limiting vaccines' benefits to women during pregnancy and lactation are often included in product labelling.

In summary, pregnant women are at high risk for severe complications following influenza infection. Vaccination during pregnancy is likely to offer protection against the disease not only for pregnant women but also their infants during the first 6 months of life following maternal immunization.

Should the South-East Asia Region consider seasonal influenza vaccine for pregnant women? Maternal and Child Health perspective
Dr Martin Webber, Regional Advisor (Making Pregnancy Safer and Reproductive Health), WHO, Regional Office for South-East Asia

This presentation was built on the previous presentation, which gave an outline of the rationale for the recommendation by SAGE to vaccinate pregnant women as the highest priority group. It looked at the need for maternal immunization for influenza in the South-East Asia Region from a maternal and child health perspective. Given that influenza increases morbidity and mortality in pregnancy, affects the infant's birth weight, and causes a high disease burden among children less than five years of age with a significant burden in neonates, there is definitely a regional need. Opportunities are also available to provide maternal influenza immunization, given that the Region has a well-established antenatal care network with high coverage of antenatal visits, and the experience of

maternal tetanus vaccination. However, none of the countries in the Region has introduced it to date. There could be multiple reasons for this. These reasons could vary from “countries not convinced by the evidence”, “too small perceived burden”, “supply chain and logistics issues”, to the question of “programmatically feasibility of year-round vaccination in tropical climates”. At the end of the talk, the question was asked whether specific surveillance might produce data that might change these perceptions, possibly through targeted surveillance of pregnant women and young infants, or whether more research was needed to convince countries to consider maternal influenza vaccination.

Session VI: New influenza activities

“How much surveillance is enough surveillance?” Results from US right size project

Dr Nancy Cox, Director, Influenza Division, US-CDC

The “Right Size project” is a proactive effort to determine the level of surveillance required to provide a predetermined degree of detection accuracy. The objectives of the project are defining core capabilities and optimal “right-size” for virological surveillance of influenza to inform policy decisions and disease prevention efforts, providing a systematic, statistical approach to support evidence-based decisions, maximizing available resources, redirecting and building new capacity as needed for optimal surveillance, and creating a scalable approach to meeting outbreak/pandemic surge needs.

The “right-size project” roadmap describes virological surveillance requirements and associated functional requirements, implementation guidance/toolkit, and modelling tools to determine effective sample sizes. Virological surveillance requirements include the sampling strategy, laboratory testing, data management, partnerships, communications, quality systems, surge for outbreaks/pandemics and financial resources.

Sampling requirements include establishing a representative network of specimen submitters representing a subset of specimens of hospitalized patients, capturing influenza-positive samples that cannot be subtyped from clinical and commercial laboratories performing PCR tests, utilizing a

systematic, statistical approach to collecting an appropriate/adequate number of specimens for testing, and limiting sampling bias.

The project takes into account surveillance objectives and the surveillance question appropriate to surveillance objectives to calculate appropriate sample sizes for (a) situational awareness, (b) novel influenza detection, (c) novel influenza event investigation, (d) antiviral resistance, (e) vaccine strain selection/candidate vaccine virus development.

Full project implementation will take several years. The initial push is to get all jurisdictions participating at a level to meet national surveillance goals. The project encourages using existing data where appropriate. The biggest change is likely to be in the sample submission for vaccine strain selection.

Right sizing was much more complex and difficult than initially anticipated. However, now there is an in-depth understanding of the virological surveillance system. A single virological surveillance system is used to provide data and samples to answer multiple questions. Efficiency efforts can introduce new bias into surveillance. Therefore, understanding which subsets of data can be used to answer which questions is critical. Maintaining flexibility in the system is needed to respond to any situation that arises. The thresholds, time frames and the need for geographical details vary depending on changing risks. Subject matter expertise is required to determine the appropriate sensitivity corresponding to these variations in the context of changing risks.

New sequencing technologies and use of the Global Initiative on Sharing Avian Influenza Data (GISAID)

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With the advent of new sequencing technologies, it is becoming increasingly cheap and easy to obtain sequences and even whole genomes from influenza samples. The non-profit Global Initiative on Sharing Avian Influenza Data (GISAID) operates the publicly accessible EpiFlu™ database (hosted by the German government) on the guiding principle that those using its data must acknowledge the contribution of those providing the

data. Access to GISAID is free of charge and open to everyone, provided they identify themselves in order to allow fully transparent access and sharing. Data submitted to GISAID are publicly accessible and without any loss of ownership (in contrast to deposits made to archives in the public domain, e.g. GenBank). Submitters to GISAID do not lose their rights to the data that they deposit. GISAID's fair sharing principle is second to none for timely sharing of influenza sequences of public interest. GISAID is currently developing a new database version, EpiFlu™ 2.0, which also includes several new features that enhance the fair sharing experience. Uploaded isolates can be flagged by the submitters to be under a limited publication embargo, which is then visible to anyone accessing the data. All direct submissions to GISAID's database are verified, ensuring the highest quality standards. New analytical tools and user-friendly features, including single and batch uploads of sequence and metadata, automatic sequence annotation, data curation and validation, comprehensive searchable fields and catalogues, customizable query functions and data downloads, classification (H5 clade) tools and geo-referencing, sequence alignment, BLAST searches, phylogeny and analysis of mutation significance with FluSurver, are continuously added to facilitate the work of researchers. The latter allows quick identification of mutations relative to reference strains, providing information on the geographical and temporal occurrence patterns of variants as well as their protein structural position, and literature annotations for phenotypic interpretation.

*Future training needs and opportunities for national influenza centres
Dr M.S. Chadha, Deputy Director, WHO H5 Reference Laboratory National
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There are influenza A(H5N1) reference laboratories, designated NICs, and laboratories aspiring to be designated as NICs. NICs require training in surveillance, molecular detection, virus isolation and molecular characterization. All three groups of laboratories require training in the following specific areas.

Infrastructure: laboratory design and floor plan

Human resources management: staff training, working conditions

Laboratory equipment: choice, procurement, inventorization and maintenance

Supplies and reagents: procurement, management and preparation

Documentation: SOPs, equipment maintenance records, logbooks, quality control records

Other areas:

- Quality control and assurance of laboratory sampling procedures, request forms, specimen management and diagnostic tests
- Biosafety practices and documentation
- Waste management and security of the laboratory
- Computerized information management, data back-up, submission of data to the FLUNET.

In terms of pathogen detection for real-time PCR, training is required on protocol development, test kit/reagent selection criteria, and performance and interpretation of tests. For virus isolation, training is required on isolation in tissue cultures, in ovo and antigen detection. A well-established NIC, or H5 reference laboratory, can be the training venue. In addition, on-site training and troubleshooting workshops are needed.

For molecular detection, with the adaptation of more sensitive real-time PCR/multiplex PCR techniques, the need arises for developing/upgrading new protocols and point-of-care test protocols for outbreak response.

For molecular characterization, training areas include sequencing and sequence analysis, next-generation sequencing platform, testing for antiviral susceptibility of influenza viruses, protocols for HA/NA amplification, gene sequencing, bioinformatics analysis and whole-genome analysis of influenza viruses using universal primers. Technical support for sero-surveillance is needed for study design, antibody detection through micro-neutralization assays and for emerging respiratory viruses. Capacity-building is required for the detection of emerging respiratory viruses with reagent support for diagnosis. Training is suggested for standardization of sensitive molecular tests to detect respiratory viruses other than influenza. NICs need capacity in conducting epidemiological, economic and vaccine efficacy studies, and

studies on host factors in relation to severe disease. H5 reference laboratories need guidance on the preparation of diagnostic reagents such as antigens/antibodies/standards, and development of a ferret colony. Most NICs participate in WHO's EQA programme. Additional voluntary participation in EQA is suggested for regional laboratories in larger countries.

4. Conclusions and Recommendations of the Eighth bi-regional meeting

Conclusions

- (1) Influenza surveillance and laboratory networks in the Western Pacific and South-East Asia Regions have enhanced their capacities and infrastructure. These have proven useful not only for the detection of novel influenza viruses but also for the detection of other EIDs.
- (2) Influenza surveillance networks in the Western Pacific and South-East Asia Regions play an important role in providing decision-makers in Member States with evidence required to formulate national influenza control policies, including seasonal influenza vaccination policies.
- (3) Long-term sustainability of the influenza surveillance programme is assisted by integration of influenza surveillance into existing national disease surveillance systems.
- (4) Recognizing the important implications of the PIP Framework for the functioning of NICs, awareness of the progress of implementation of the PIP Framework in the Western Pacific and South-East Asia Regions at regular intervals is essential for NICs.
- (5) Given the central role of clinicians in the frontline of disease detection and response, active clinician involvement in influenza surveillance systems and establishing clinician alert systems for the identification of human sentinels of unusual events are valuable components of the national influenza surveillance and other EID surveillance systems.

- (6) Levels of virus isolation and HAI have declined in previous years.
- (7) FluID for data-sharing is not universally used. Therefore, it is important to identify the challenges faced by Member States in reporting to FluID, and provide technical support to overcome these.
- (8) Recognizing the importance of the human–animal interface for influenza surveillance, outbreak investigation and response, it is critical to further promote collaboration between the human and animal health sectors in influenza surveillance in Member States and ensure reciprocal information-sharing.
- (9) Vaccine policies exist in some countries of the Asia-Pacific Region. However, the timing of vaccination needs further studies, given the mismatches related to disease peaks, timing of availability of northern and southern hemisphere vaccines, and types of seasonal influenza vaccines used.
- (10) Areas of research that may address key issues include virus evolution, prediction of antigenic drift, and integration of data, available vaccine types and standardization of assays.

Recommendations

For Member States

- (1) Influenza surveillance programmes and NICs should actively advocate for utilization of influenza surveillance and disease burden data to guide public health action and seasonal influenza vaccination policies in Member States.
- (2) Recognizing the complementary roles of epidemiologists and laboratory scientists in influenza surveillance, Member States may consider designing and conducting joint training and workshops on influenza surveillance.
- (3) Member States should continue to report novel/non-seasonal influenza virus subtypes, including those that do not cause severe human illness, to WHO under the IHR (2005). Recognizing the critical role of NICs in detecting influenza A viruses that cannot be subtyped, NICs should be encouraged to subtype all influenza A viruses.

- (4) Noting the declining levels of virus isolation and HAI in the past year, NICs should strengthen, use and maintain viral isolation and HAI techniques to increase and sustain viral isolation levels.

For WHO

- (1) WHO should work with selected Member States to overcome challenges to the uptake of FluID, including providing more information about the platform and technical assistance for using it.
- (2) WHO should conduct a survey to identify gaps in influenza surveillance capacity to guide technical assistance.
- (3) WHO should facilitate and coordinate the design and implementation of multi-country studies to determine the appropriate timing and type of seasonal influenza vaccines (southern and northern hemispheres) to be used for pilgrimage.
- (4) WHO should disseminate clear guidance to NICs on their obligations under the PIP Framework and include updates on the PIP Framework in subsequent bi-regional NIC meetings.

Annex 1

Agenda

- (1) Opening session
- (2) Update on the current global and regional status of seasonal, avian and other novel influenza virus sub-types
- (3) Strengthening national influenza surveillance system, data reporting and response in Asia-Pacific
- (4) PIP Framework: a platform for strengthening influenza surveillance and response
- (5) Strengthening laboratory systems for surveillance of, and response to, influenza and other emerging respiratory infections
- (6) Group Work
- (7) Field Visit to the National Influenza Centre, Indonesia, and H5N1 Reference Hospital, Jakarta
- (8) Group Work: Feedback and Discussion
- (9) Updates on influenza vaccine virus selection, seasonal influenza vaccines and the regional status of seasonal influenza vaccine use
- (10) New influenza activities
- (11) Conclusions and recommendations
- (12) Closing session

Annex 2

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Annex 3

Opening remarks of Dr Poonam Khetrpal Singh, Regional Director, WHO South-East Asia Region

Director General of Health Services of the Republic of Indonesia, distinguished participants from Member States, WHO collaborating centres, international partner agencies, colleagues from WHO headquarters and from the WHO regional offices and country offices in the Western Pacific and the South-East Asia Regions, ladies and gentlemen;

It is with great pleasure that I welcome you all to the Eighth Bi-regional meeting of the national influenza centres and influenza surveillance in the Western Pacific and South-East Asia Regions. It is the first time that this bi-regional meeting is being held in the South-East Asia Region to deliberate on our plans for surveillance, preparedness and response for influenza epidemics and pandemics in both WHO regions.

On assuming office as the Regional Director earlier this year, I had outlined four key strategic directions to fulfil the mandate of providing appropriate policy guidance and quality technical support to our Member States to help reduce health-related morbidity and mortality, and associated disability. Of these four strategies, strengthening surveillance, preparedness and response for influenza epidemics and pandemics are in full harmony particularly with the strategies of “Addressing the persisting, emerging epidemiological and demographic challenges” and “Articulating a strong voice in the global health agenda”. The other two strategic directions are also linked to the outcome of this meeting.

The strategy of building robust health systems benefits the preparedness and response for emerging respiratory infections caused by new influenza strains or other newly detected respiratory pathogens. “Strengthening emergency risk management for sustainable development” will lay the foundation for responding to pandemics and epidemics in an efficient and effective manner.

In this context, I believe that focusing on the Asia-Pacific Region is meaningful, given that it is an epicentre for the emergence of novel

influenza viruses of pandemic potential. The large numbers of avian influenza A(H5N1) cases and the recent outbreak of influenza A(H7N9) in China highlight the importance of having systems in place for early detection, preparedness and rapid response to these novel influenza threats in the Asia-Pacific Region. Though numerous activities have taken place previously in this region, there are numerous gaps in terms of reaching the standards of WHO's pandemic influenza preparedness (PIP) framework.

In alignment with coordinating and implementing the five-year Asia-Pacific Strategy for Emerging Diseases (APSED), including seasonal and pandemic influenza, the annual bi-regional meeting of national influenza centres and influenza surveillance is an ideal platform to collectively identify these gaps, help bridge them by sharing experiences and good practices of Member States, WHO collaborating centres and global partners, and also to benefit from regional and global expertise in this area.

I take this opportunity to thank my colleagues from the Western Pacific Region for hosting the previous seven meetings, which were of great benefit to us. Similarly, by hosting the meeting in the South-East Asia Region, I believe that Member States in the Western Pacific Region, WHO collaborating centres and numerous partners will benefit from the good practices adopted in the South-East Asia Region and by sharing their experiences with participants from the South-East Asia Region.

The collaboration between the two WHO regional offices through this continued exercise synchronizes with the fourth strategic direction of articulating a global health agenda in this era of interdependency and cooperation, to build and sustain alliances and partnerships. Such collaboration helps to give us the collective strength in the battle against new influenza strains of pandemic potential and other respiratory pathogens such as Middle Eastern coronavirus infections, etc. This is possible only through stronger partnerships, both within and beyond the Region. The efforts of the department of Family Health and Research and Communicable Diseases in the Regional Office for South-East Asia and the Regional Office for the Western Pacific and international partners beyond our regions in this endeavor are highly commendable.

Jakarta offers the best possible venue in the South-East Asia Region to organize this important meeting, given that Indonesia is a global epicentre

of avian influenza A(H5N1). Thus, the opportunity of the field visit to the National Influenza Centre (NIC) and the Avian influenza A(H5N1) reference hospital for participants will mutually benefit Indonesia, the two WHO Regions and global partner agencies. This meeting in Jakarta will provide an opportunity to enhance the capacity of a large number of Indonesian participants and will also help WHO's efforts in establishing a WHO collaborating centre on zoonotic influenza in Indonesia.

I am also aware that many new innovative technologies of diagnostics and research are available in the global arena. The global agencies that are present here have been using these technologies and are keen to share their experience and impart the core knowledge to the participants to improve the laboratory capacity of Member States. There is also new evidence, developments and guidelines in the area of influenza vaccines. These will be most useful for Member States to update their knowledge about influenza vaccines, both as a means of reducing the morbidity and mortality due to seasonal influenza and in effectively responding to pandemic threats.

Therefore, in the above context, I would urge you to take this opportunity to discuss and review issues pertaining to infections due to influenza and other emerging respiratory viruses in the Asia-Pacific Region and provide pragmatic recommendations to strengthen our efforts in mounting an effective response.

I wish you all success in your deliberations and a pleasant stay in Jakarta.

The Eighth bi-regional meeting of the national influenza centres (NICs) and influenza surveillance in the South-East and Western Pacific Regions was held from 12 to 15 August 2014 at Jakarta, Indonesia. The objective of the meeting was to further strengthen influenza surveillance, preparedness and response in the Asia-Pacific region. The bi-regional meeting brought together participants from Member States in South-East Asia and Western Pacific Regions, World Health Organization (WHO) Collaborating Centres, regional reference laboratories, partner agencies and WHO.

Participants were provided updates on the current global and regional status of seasonal, avian and other novel influenza virus subtypes, the pandemic influenza preparedness (PIP) Framework and new influenza activities in the world. They also discussed ways to strengthen national influenza surveillance systems, including laboratories, data reporting, and response to influenza and other emerging respiratory infections in the Asia-Pacific region. In a group work session, they collectively identified major issues/challenges pertaining to selected technical areas and potential solutions. This report summarizes the proceedings of the technical sessions, outcome of the group work and recommendations made by participants to further strengthen influenza surveillance, preparedness and response in the WHO South-East Asia and Western Pacific Regions.



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