Meeting Report

The Fourth Meeting of the National Influenza Centres in the Western Pacific Region

3–6 May 2010
Manila, Philippines

World Health Organization
Western Pacific Region

WPDCC1002859/HES/DCC/CSR English only

Report series number: RS/2010/GE/16(PHL)

REPORT

REPORT ON THE FOURTH MEETING OF THE NATIONAL INFLUENZA CENTRES IN THE WESTERN PACIFIC REGION

Convened by:

WORLD HEALTH ORGANIZATION

Not for sale

Printed and distributed by:

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

June 2010

NOTE

The views expressed in this report are those of the participants of the fourth meeting of the National Influenza Centres in the Western Pacific and do not necessarily reflect the policies of the World Health Organization.

This report has been prepared by the WHO Regional Office for the Western Pacific for the Member States in the Region and for those who participated in the fourth meeting of the National Influenza Centres in the Western Pacific Region held in Manila, the Philippines, from 3 to 6 May 2010.

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Key words

Influenza, Human – Epidemiology/Influenza in birds/Influenza vaccines
Vaccination/Disease outbreaks – prevention and control

SUMMARY

The fourth meeting of the National Influenza Centres (NICs) in the Western Pacific Region was held in Manila, the Philippines, from 3 to 6 May 2010. The meeting was attended by 43 participants from 15 countries and areas.

Participants from the Western Pacific Region included country representatives from Australia, Cambodia, China, Hong Kong (China), Fiji, Japan, the Republic of Korea, the Lao People's Democratic Republic, Malaysia, Mongolia, New Caledonia, Papua New Guinea, the Philippines, Singapore and Viet Nam.

There were 10 temporary advisers and 14 observers.

Temporary advisers included representatives from the WHO Collaborating Centre for Reference and Research on Influenza (Australia), Centers for Disease Control and Prevention (the United States of America), the Public Health Laboratory Centre (Hong Kong, China) and the National Institute of Infectious Diseases (Japan).

Observers included representatives from the Centers for Disease Control and Prevention (the United States of America), the Regional Emerging Disease Intervention (REDI) Centre (Singapore), the Secretariat of the Pacific Community and the WHO Collaborating Centre for Reference and Research on Influenza (Australia).

The WHO Secretariat consisted of 12 representatives from Headquarters, Western Pacific Regional Office and Country Offices including Cambodia, China, the Lao People's Democratic Republic, Mongolia, the Philippines and Viet Nam.

The objectives of the meeting were:

(1) to review the progress and lessons learnt on pandemic preparedness planning by ministries of health and contingency planning by NICs;

(2) to assess the progress and discuss the next steps on influenza disease burden studies;

(3) to update the progress in research and development of pandemic and seasonal influenza; and

(4) to provide training on influenza vaccine and vaccination policy developments.

The meeting consisted of four plenary sessions: Regional and global updates, influenza surveillance, avian influenza updates and pandemic planning and laboratory contingency planning. The meeting also included a workshop on recent advances in vaccine development and vaccination policy, a panel discussion on training and support from WHO Collaborating Centres, presentations on influenza sero survey studies and new developments in virus detection and analysis.

1. INTRODUCTION

The Global Influenza Surveillance Network (GISN), established in 1953, contributes to global public health by gathering and analysing information on the appearance of novel strains of influenza virus and reporting to WHO to enable a prompt and appropriate public health response. It also collates data on circulating influenza viruses, which are used to make recommendations on the strain composition of seasonal influenza vaccines. The network consists of five WHO Collaborating Centres and 130 NICs in 101 countries. In WHO's Western Pacific Region, there are 19 NICs in 14 countries and two WHO Collaborating Centres for Reference and Research on Influenza, one each in Australia and Japan.

Since 2007, the annual NICs meetings have provided an opportunity for NICs, Ministry of Health officials and WHO to meet and share experiences, successes and challenges.

The first meeting of the NICs in the Western Pacific Region and South-East Asia Region was held in Melbourne, Australia, from 1 to 4 May 2007. A biregional four-year workplan for strengthening national influenza surveillance capacity was formulated during the meeting and subsequently was endorsed by the biregional Technical Advisory Group (TAG) as a sub-workplan of the Asia Pacific Strategy for Emerging Diseases (APSED). The workplan requires WHO to take actions in strengthening the capacity of NICs, including organizing their annual meetings.

The second meeting was held in Tokyo, Japan, from 21 to 24 April 2008. During the meeting, comprehensive influenza surveillance guidelines, guidelines for conducting an influenza disease burden studies and database software for NICs were introduced.

The third biregional NIC meeting was hosted by the China National Influenza Centre (CNIC), Beijing, China, from 18 to 20 August 2009, and reviewed lessons learnt from pandemic response and determined appropriate measures for mitigating the impact of the pandemic.

The pandemic influenza A (H1N1) 2009 placed major strains on the institutions responsible for laboratory testing and analysis of influenza surveillance data. Recommendations from previous NIC meetings emphasized the need for continued preparedness planning by governments and contingency planning by laboratories. In addition to the current pandemic strain of influenza, influenza A (H5N1) continues to pose a risk to human health, and the possibility remains of reassortments of other influenza viruses to produce a new virus with pandemic potential. The Region remains a possible source of pandemic influenza viruses because of the high population density of both people and livestock with the capacity for transmitting influenza viruses with pandemic potential. There is a continuing need for pandemic preparedness activities.

The fourth meeting of the NICs in the Western Pacific Region was held in Manila, Philippines, from 3 to 6 May 2010. Participants were encouraged to share their experiences during pandemic (H1N1) 2009, assisting those countries formulating preparedness plans and laboratory contingency plans.

1.1 Objectives

(1) To review the progress and lessons learnt on pandemic preparedness planning by ministries of health and contingency planning by NICs.
(2) To assess the progress and discuss the next steps on influenza disease burden studies.
(3) To update the progress in research and development of pandemic and seasonal influenza viruses.
(4) To provide training on influenza vaccine and vaccination policy formulation.

1.2 Opening Remarks

Dr Esperanza Cabral, Department of Health, the Philippines

Dr Esperanza Cabral welcomed participants to the fourth meeting of NICs in the Western Pacific Region. We live with constant fear of when and where the next epidemic will manifest itself and should use this fear to fuel needed responses and actions. We are under an obligation during lulls to use that time to continue with our preparations.

It is now easier than ever before for diseases to travel from one country to another. Stopping an influenza pandemic, or mitigating the harm, is no longer the responsibility of an individual country but a regional and global responsibility. Since the first meeting of NICs in 2007, we have pulled together resources: NICs have been established where they did not exist, and the initiative has functioned well.

The Philippines provides a good example of the success of this regional effort. The pandemic (H1N1) 2009 virus was staved off as long as possible. When it entered, the NIC became the focal point of the national response to the crisis. This would not have been possible without support from friends in the Region, particularly WHO. In particular, the Philippines appreciates donations of the pandemic (H1N1) 2009 vaccine, which was being administered to vulnerable populations.

Dr Cabral reiterated the call for international cooperation and expressed the hope that this meeting of NICs will translate into being better equipped, better prepared and better motivated to address pandemic influenza.

Dr Takeshi Kasai, on behalf of Dr Shin Young-Soo, Regional Director, Western Pacific Regional Office

The first pandemic of the new millennium emerged last year. To date, there have been 268 000 confirmed cases; most suffered only mild illness. The GISN played a central role in the response to the pandemic. Each component played its part. NICs detected the arrival of the virus in country and tracked its spread. Sending isolates to the network contributed to selecting the most appropriate strains for vaccine.

But the response also revealed challenges such as increasingly high expectations from governments. Human resources were pushed to the limit. Many public health laboratories took on the role of diagnostic laboratories. This meeting will consider some of these challenges and enable us to prepare better for the next epidemic, keeping in mind the threat posed by avian influenza.

Dr Kasai also welcomed two new NICs within the Western Pacific Region (the Institute Pasteur in Ho Chi Minh City, Viet Nam, and the Public Health Laboratory in Singapore) as members of the network. The China Centers for Disease Control was in the process of being designated as the third WHO Collaborating Centre on Research and Reference in Influenza in the Western Pacific Region, further enhancing the Region's capacity.

Dr Wenqing Zhang, World Health Organization, Geneva

It is almost a year since the emergence of pandemic (H1N1) 2009 and a good time to reflect on the role of the NICs. It was NICs that diagnosed and confirmed the virus and triggered responses in each country. Over the last 50 years, the GISN has worked to build its capacity, and this network proved its value during the pandemic response. Laboratory diagnostics, monitoring of the virus and vaccine support were all key areas of work delivered by network. The response to the pandemic also provided an opportunity for the network to identify gaps and areas for future development. Never before has network spirit been so important in handling public health emergencies.

1.3 Appointment of Chairperson, Vice-Chairperson and Rapporteur

The following representatives were selected as chairs and vice-chairs respectively:

Plenary 1 -- Regional and global updates: Dr Anne Kelso and Dr Takato Odagiri. Plenary 2 -- Influenza surveillance: Ms Ann Moen and Dr Aeron Hurt. Plenary 3 -- Avian influenza updates: Dr Wilina Lim and Dr Xu Xiyan. Plenary 4 -- Pandemic planning and laboratory contingency planning: Dr Masato Tashiro and Dr Ian Barr. Workshop on recent advances in vaccine development and vaccination policy: Dr Alexander Klimov and Dr Julia Fitzner. Influenza serology survey results: Dr Ian Barr and Patrick Reading.

Photo: Participants at the fourth meeting of the National Influenza Centres in the Western Pacific Region, 3 to 6 May 2010 Manila, Philippines.

2. PROCEEDINGS

2.1 Plenary 1: Regional and global updates

2.1.1 **Western Pacific Region**
Dr Takeshi Kasai, Western Pacific Regional Office

Dr Takeshi Kasai spoke about the regional situation and response to pandemic (H1N1) 2009. Currently, levels of influenza-like illness (ILI) in the Western Pacific Region remain low. In the Republic of Korea, there has been an increase in seasonal influenza and in Malaysia there has been some increase in the levels of pandemic (H1N1) 2009. In the southern hemisphere, ILI activities have been closely monitored for elevated levels occurring earlier than the normal influenza session, but this has not yet been seen.

Dr Kasai also reflected on the progress made globally and within the Region in preparing for a pandemic. Countries have formulated national plans, tested these plans with exercises, gained experience in responding to avian influenza and established stockpiles of antiviral. However, the more we do, the more questions we have. There is still another potential pandemic ahead.

The annual NIC meetings grew out of an identified need to build capacity for comprehensive National Influenza Surveillance Systems (NISS). Over the last three years, a step-by-step approach to training has strengthened the capacities of the NICs and associated epidemiology programmes. This has been supported by the publication of guidelines, including *"A Practical Guide for Harmonizing Virological and Epidemiological Surveillance Data"* and *"A Practical Guide for Designing and Conducting Influenza Disease Burden Studies"*.

Dr Kasai concluded by asking three questions to consider during the fourth meeting of NICs: Can we lower our guard? If not, what do we need to do? And what will be our future direction?

2.1.2 **APSED and Beyond**
Dr Li Ailan, Western Pacific Regional Office

Dr Li Ailan updated participants on the Asia Pacific Strategy for Emerging Diseases (APSED) and spoke about the planning process now under way to formulate a new strategy. APSED is a biregional strategy for countries to strengthen the capacity required for managing emerging disease and was endorsed by Member States through the Regional Committee Meeting (RCM) in 2005. Strengthening NIC capacity has been a key APSED priority.

APSED incorporates three agendas: general capacity-building, meeting the International Health Regulations (IHR) (2005) minimum core capacity requirements and pandemic preparedness and response. The presentation outlined the approach taken by each of APSED's five programme areas: surveillance and response, laboratory, infection control, zoonoses and risk communications.

The fourth meeting of the TAG recommended that an updated five-year strategy be formulated. The scope of the next strategy will continue to focus on emerging infectious disease threats but also will address the capacity and mechanisms to respond to noninfectious disease events. A comprehensive consultation process was under way and a revised strategy will be submitted to the RCM in October.

2.1.3 **WHO Geneva**
Dr Wenqing Zhang, WHO

Dr Zhang gave an overview of the response to the pandemic (H1N1) 2009, with particular focus on the role of the GISN.

As in previous pandemics, pandemic (H1N1) 2009 emerged from animals, became capable of sustained community transmission among people and many people had no immunity to the virus. Some epidemiological characteristics also were similar to previous pandemics, including the virus's disproportionate impact on young, healthy adults.

There have been 17 700 laboratory-confirmed deaths, but this figure is difficult to compare with past pandemics and represents the tip of the iceberg. Although most cases were resolved without special treatment, some countries observed higher than normal outpatient visits. Hospital admissions were not excessive, but greatest stress was placed on intensive care units. The pandemic's overall impact remains to be determined, but the greatest burden has been on the young.

Many WHO efforts have focused on strengthening broad public health systems. Others have focused on building specific influenza capacities such as access to antiviral drugs and vaccines. Substantial efforts to improve preparedness have paid off. But the global context is becoming increasingly complex. Handling future pandemics and global public health events will become more challenging.

The GISN played a key role in the global response. The same day a Public Health Event of International Concern (PHEIC) was announced, gene sequences for diagnostics were made available. The first diagnostic protocol was available within three days and the first RT-PCR kits were sent within a week.

The network's role incorporated supporting laboratory diagnostics and virus monitoring, identification of vaccine viruses, development of vaccine reagents and capacity-building. WHO's technical leadership on laboratory diagnostics and virological surveillance was well-accepted and well-appreciated. Sustaining this leadership is key.

The pandemic (H1N1) 2009 also helped identify areas for further strengthening. Coverage should be expanded, particularly in Africa, and capacity-building in sequencing and antiviral susceptibility testing is needed. There is also a need to better understand influenza viruses, including genetic markers related to growth property, pathogenicity and antigenicity.

2.1.4 **External Quality Assessment (EQA) programmes**

Dr Wilina Lim, Public Health Laboratory Centre, China

External Quality Assessment (EQA) is a system for objectively testing a laboratory's performance using an external agency or facility. WHO's EQA programme for the detection of influenza virus type A by PCR began in 2006. The aims of the programme are to monitor quality and standards of performance, facilitate information-sharing, identify problems and help establish testing strategies and provide mechanisms to address any deficiencies revealed. It is also a requirement of lab accreditation with international standards.

The number of laboratories reporting results has grown from 64 for panel 1in 2007 to 139 for panel 7 in 2010. The number of laboratories using real-time PCR has grown from 71% in panel 2 to 89% in panel 7. Globally, performance in correctly identifying specimens of influenza virus type A has improved. In the Western Pacific Region, 23 laboratories received specimens for panel 7, and all reported results. The proportion of laboratories identifying 100% of specimens correctly has grown from 57% in 2007 to 83% in 2010. Problems identified include inconsistent technical performance, positive control not used appropriately, lab contamination, misinterpretation of results and primers and probes mismatch.

The Good Laboratory Practice (GLP) survey asks questions on seven categories in areas from personnel, to procedures to equipment, safety and record-keeping. Those laboratories that did not return all correct results tend to meet fewer quality parameters. Analysis of the results of the EQA programme and the GLP survey are used to identify problems and correct deficiencies.

2.1.5 Plenary 1 discussions and questions

There was some discussion about pandemic fatigue and whether it will be difficult to convince governments to continue to pay attention to this issue. Some governments have not expressed this view and are still concerned about H5N1. It was suggested that the focus first should be on identifying needed action then working out the path ahead, given external contexts.

WHO was asked about how capacity-building under APSED contributed to the pandemic response. NICs played a vital role, providing laboratory confirmation of initial cases and monitoring drug resistance. ILI surveillance systems proved very helpful, as were event-based surveillance systems in detecting issues such as adverse events following vaccines.

How the next APSED strategy will coordinate with other partners addressing emerging diseases was discussed. Countries receive support from many different sources and there is often overlap and duplication. Member States are encouraged to fashion a national workplan based on APSED's five pillars and use this to coordinate efforts. At a regional level, donors can use the strategy to coordinate support with the same framework.

The observation also was made that initial classification of the pandemic H1N1 virus as BSL-3 posed severe limitations because most NICs did not have BSL-3 capacity. More communication with the biosafety group is needed.

2.2 Plenary 2: Influenza surveillance

2.2.1 **Philippines**

Dr Enrique Tayag, Department of Health, Philippines

During pandemic (H1N1) 2009, the Philippines used case definitions for ILI, laboratory-confirmed cases and severe acute respiratory infection (SARI) cases. Cases with a fever, a cough or sore throat, who had arrived in the Philippines from a pandemic (H1N1) 2009-affected country in the past 10 days were classified as Cases Under Investigation (later called Cases Under Observation, or CUOs). These cases initially were admitted to referral hospitals until laboratory results became available.

Surveillance information was collected from four data sources: a notifiable surveillance system, a laboratory system, an event-based system and a CUO system. Initially, not all data sources were harmonized.

The Philippines complied with WHO requirements, including using the IHR (2005) system, recording the first 100 cases and submitting weekly reports. The Department of Health released regular surveillance reports and, following the first death on June 21, mortality reports also were produced. By late 2009, the Philippines was ready to harmonize data from all influenza surveillance systems, although responding to several severe typhoons caused a shift in priorities.

2.2.2 **Northern Hemisphere**

Dr Takato Odagiri, National Institute for Infectious Diseases, Japan

Dr Takato Odagiri presented influenza virus surveillance findings from the period 2009-2010 season in the northern hemisphere. In Japan, peak ILI occurred two months earlier than the normal seasonal peak. Of the viruses isolated during the season, 97.5% were influenza A (H1N1) 2009. Currently, most states have little or no ILI activity. In the United States of America, most states also were experiencing low levels of ILI activity.

Antigenic cartography of influenza A (H1N1) 2009 viruses show limited antigenic variation, and the majority have been antigenically and genetically similar to the southern hemisphere vaccine virus A/California/7/2009. Low levels of resistance to oseltamivir have been detected and no resistance to zanamivir. All have been resistant to adamantine.

Globally, most countries are detecting little or no seasonal A (H1N1), while low levels of A (H3N3) have been reported. The majority of these closely were related to the southern hemisphere vaccine virus A/Perth/16/2009. Circulation of B viruses was limited, with low levels reported in several Asian countries. Data from the Chinese Centers for Disease Control and Prevention indicate that the majority were B/Victoria/2/87 lineage viruses, with an increase in B/Yamagata/16/88 lineage viruses between September 2009 and January 2010.

The influenza A (H1N1) 2009 virus is expected to circulate widely in the 2010-2011 influenza season in the northern hemisphere whereas seasonal A (H1N1) viruses is unlikely to circulate at significant levels and has not been recommended for inclusion in the vaccine composition for the 2010-2011 season. The WHO-recommended vaccine composition in the 2010-2011 northern hemisphere influenza season is an A/California/7/2998 (H1N1)-like virus, an A/Perth/16/2009 (H3N2)-like virus and a B/Brisbane/60/2008-like virus.

2.2.3 **China**

Dr Yuelong Shu, Chinese National Influenza Center, China

Since the onset of the pandemic, there have been 127 739 laboratory-confirmed cases, 7525 severe cases and 802 deaths in China. The first case was reported on 11 May and the first outbreak reported in a school on 18 June.

The median age for both severe cases and death cases was 24 years old. The two age groups most affected were children less than 1year old and young adults in their 20s. About 54% of severe cases and 73% of deaths had one of three risk factors. Of the severe cases and deaths, 86% and 80.5% received antiviral therapy, respectively, with a median interval between onset and antiviral treatment of four days for severe cases and five days for deaths.

China's National Influenza Surveillance Network includes 411 network laboratories and 556 sentinel hospitals. Influenza A (H1N1) 2009 was the predominant virus strain detected during the 2009 peak season. From January 2010, the influenza B virus has become the predominant circulating strain.

As of April 30, the China NIC has antigenically characterized 2219 influenza A (H1N1) 2009 viruses. Most are antigenically similar to the A/California/07/2009 (H1N1) reference virus. All influenza A (H1N1) 2009 viruses and all H3N2 viruses and 97% of seasonal H1N1 viruses have been resistant to adamantine. Of the influenza (H1N1) 2009 viruses isolated, only one (0.2%) was resistant to oseltamivir while 86% of seasonal H1N1 viruses isolated were resistant. No oseltamivir resistance was found in H3N2 and B viruses.

2.2.4 **Southern Hemisphere**

Dr Ian Barr, WHO Collaborating Centre for Reference and Research on Influenza, Melbourne

Current ILI activity in Australia is low. Googled flu trends also confirm low levels of ILI in Australia and New Zealand. Some countries in South America are showing regional or localized ILI activity. In Australia, laboratory-confirmed influenza data currently includes virus isolation and serodiagnosis. The majority of currently circulating viruses are influenza A (H1N1) 2009 with occasional B viruses. There is little resistance to NA Inhibitors (H3/H1N1pdm all resistant to M2 blockers). Viruses were being tested from Malaysia, the South Pacific, and were expected from Kenya. So far, vaccine matches look good.

There is never a quiet time with influenza, and several recent events show the need to prepare for the unexpected. The shelf lives of some vaccines recently were reduced and disruptions to air travel potentially could have caused delays in vaccine distribution.

In Australia, a number of adverse reactions to seasonal influenza vaccine have been reported and vaccination suspended for children under 5 years old. As of April 30, 77 cases of fever and convulsions following vaccination were reported, 57 of which were in WA. All recovered except for one unexplained death in Queensland, and one case was still in the ICU. It is not clear whether the adverse events occurred after one or two doses.

No similar issues were identified in the monovalent influenza A (H1N1) 2009 vaccine. In Australia, this is available free of charge and is recommended for all ages from 6 months old. For seasonal vaccine, no adverse events were reported in adults and children older than 5 years old. The investigation was continuing.

2.2.5 Plenary 2 discussions and questions

The Philippines was questioned about the reporting of the first 100 cases of pandemic (H1N1) 2009. This information was difficult to gather accurately with a bias in the data toward designated health facilities. More severe cases also were more likely to be recorded even though all early cases were admitted for isolation. While the notifiable disease system captured data from all age groups, sentinel sites were biased towards children. It was also observed that recording information about severe cases and deaths and communicating this to the medical community was very important. The data confirmed that a significant proportion of deaths did not have comorbidity.

The Philippines also was asked about current vaccination status. Fully 1.9 million doses were received by the end of April. The first priority for vaccination is front-line health workers. Other priorities include pregnant women, children and the elderly.

The role of the event-based surveillance system during the pandemic was discussed. Event-based surveillance enabled those cases not captured by other systems to be detected. It picked up a number of outbreaks and helped detect first community transmission, numerous school outbreaks and an outbreak among wedding participants. The information was used for the public health response.

Discussion raised the issue of whether clinicians in China experimented with using higher doses of antivirals or combinations of antivirals in severe cases. Oseltamivir treatment was used and some patients received antiviral along with traditional medicine.

The question also was raised whether laboratory-confirmed cases represent the tip of the iceberg and whether there was any seroprevalence data giving a more accurate indication of the population presented. This data was to be presented later in the meeting. Data confirms that young adults were infected at greater rates.

2.3 Plenary 3: Avian influenza updates

2.3.1 **Virology**
Dr Alexander Klimov, Centers for Disease Control and Prevention, the United States of America

Dr Klimov described the evolution of the influenza A (H1N1) 2009 viruses and the development of candidate H1N1 vaccine. Seven months before the pandemic, the United States of America's CDC's five-target RT-PCR assay had been approved. Double and triple reassortment of swine viruses in North America first started appearing during the period 1997-1998, and in March 2009 the CDC submitted an abstract on the universal detection of swine influenza viruses.

The first case samples arrived at the CDC on 15 April. RT-PCR suggested swine origin triple reassortment. The samples contained segments from classical and Eurasian swine flu, and on 17 April, the genome makeup was determined to belong to a novel virus.

By 21 April, the phylogenetic trees and genetic analyses were completed and gene sequences for A/CA/04/2009 were deposited into the Global Initiative on Sharing All Influenza Data (GISAID) database. Following antigenic testing of Mexican samples in Canada, there was recognition of a match between the Mexican and United States of America viruses. By February 2010, the CDC had distributed almost 2500 RT-PCR kits for detection of influenza A (H1N1) 2009 to 140 countries.

A suitable candidate vaccine virus was shipped to manufacturers about five weeks after the first case was identified. Two approaches to developing candidate vaccine viruses were used – classical reassortment and reverse genetics.

The influenza A (H1N1) 2009 virus has shown very little antigenic variation so far. Oseltamivir resistance has been detected in less than 1% of samples. Nearly all viruses have been found to be resistant to M2 blockers while all have been found to be sensitive to neuraminidase (NA) inhibitors.

Although overall variation is low, genome variants are emerging, but these have not been associated with increased morbidity or mortality. There are several scenarios that could occur. Influenza A (H1N1) 2009 may become a seasonal flu strain, an epidemic strain in pigs, reassort with other influenza strains, change its virulence due to mutation or acquire and transmit dual antiviral resistance.

Many aspects of the response were a tribute to preparedness, and in many ways we were lucky. There is a continuing need to monitor drug resistance and a need for the development of rapid tests for the detection of drug-resistant mutants. Holes in the surveillance systems – including geographic holes and at the animal-human interface – should be addressed. The pandemic (H1N1) 2009 also highlighted the need to pay more attention to swine as a source of influenza viruses.

2.3.2 **Epidemiology**

Dr Julia Fitzner, WHO, Geneva

To date there have been 496 cases of avian influenza reported in 15 countries with 293 deaths. The case fatality rate (CFR) is 59%. Four countries reported cases in 2010. The case fatality rate is lower than in previous years partly because of the lower CFR in Egypt, where many of the 2010 cases occurred. In Egypt this year, there have been 19 confirmed human cases, seven of which have been fatal. The age group affected has shifted, with a smaller proportion of recent cases in children under 10 years old. Sporadic cases are likely to continue, and reassortment of H5N1 with other influenza viruses is still a risk.

For global surveillance of influenza, FluNet data is used as well as the GISN. Other sources such as the IHR 2005 reporting mechanism and websites also contribute to epidemiological understanding. Four qualitative indicators for influenza are used: regional spread, intensity, impact and trend.

Most countries appear to have passed the peak of pandemic (H1N1) 2009. Influenza activity is currently low, with some pockets of higher transmission in tropical areas. In most countries, influenza A (H1N1) 2009 is the dominant influenza A virus, with seasonal H1N1 reported in very low quantities. H3N2 still is circulating.

Pandemic H1N1 (2009) mainly affected the young, and in terms of life time lost, the toll is quite high. Age and proportion of cases with comorbidity increased with severity (from hospitalization to ICU to death).

There is now more awareness of the need for a global influenza system, and it is a good opportunity to build on systems established during the pandemic to create national and global surveillance systems. There is also a need for epidemiological data that matches the robustness of the available virological data. Dr Fitzner described FluID, a web-based data collection tool, as potentially meeting this need.

2.3.3 **Impact of virus mutation – antiviral resistance**

Dr Aeron Hurt, WHO Collaborating Centre for Reference and Research on Influenza, Australia

There are two main classes of antiviral drugs – NA inhibitors and adamantanes. For isolates of seasonal A (H1N1), a high frequency of NA inhibitors has been observed and a low frequency of resistance to adamantanes. For influenza A (H1N1) 2009, this trend is reversed, with 100% resistance to adamantanes.

Oseltamivir-resistant isolates first were detected during the 2007-2008 European flu season. Globally, the prevalence of oseltamivir-resistant A (H1N1) mutants spread from 0% to 100% in one year. Oseltamivir usage in Europe is low, and it is likely that the spread was not driven by drug usage.

During the pandemic, very few oseltamivir-resistant strains were detected. A ll contained the H274Y NA mutation also present in resistant strains of seasonal A (H1N1). Two methods are used to test for antiviral resistance: NA enzyme inhibition assays and molecular-based assays. It is important to understand the limitations of each method. Enzyme inhibition assays detect changes regardless of the location and provide functional information about a mutation but require a cultured isolate. Molecular-based assays identify mutations at a desired target and give no information about how mutation may alter function. They can be performed on a clinical specimen and are better able to detect low proportions of mutant in a mixture. Ideally, laboratories would have access both methods.

Dr Hurt also outlined the Neruminidase Inhibitor Susceptibility Testing Workshop conducted by the WHO CC in November 2009 and attended by representatives from NICs in the South-East Asian and Western Pacific Regions.

2.3.4 **Impact of virus mutation – reassortment**

Dr Masato Tashiro, National Institute for Infectious Diseases, Japan

Dr Tashiro outlined factors affecting the risk that avian influenza could mutate into a virus with pandemic potential. This virus does not currently effectively infect humans. Adapting to humans across the species barrier would require changes to both receptor specificity and polymerase complex. The virus currently replicates most effectively at 36°C to 42°C, the body temperature of birds.

Changes to the genetic determinants of H5N1 genes for host species may also mean changes to the genetic determinants for pathogenicity. Little is known about the biological properties of H5N1 viruses that may emerge following reassortment with contemporary human influenza viruses. Several studies show that reassortment can occur, and this has been associated with varying levels of replication and transmission.

Both humans and pigs are susceptible to both H5N1 and influenza A (H1N1) 2009. There is a continuing risk that dual infections may lead to gene reassortment resulting in a virus with pandemic potential.

2.3.5 **Plenary 3 discussion and questions**

There was discussion about whether the pandemic should be described as severe. Given that the pandemic affected the young, consideration needs to be given to the impact of life years lost.

Discussion raised the issue that there is not necessarily a relationship between those isolates identified as resistant using molecular-based assays and clinical drug resistance. It was suggested that these isolates would be better described as outliers or as exhibiting reduced susceptibility or sensitivity.

2.4 Country Presentations

On the afternoon of the second day, a representative from each country was given the opportunity to present his or her experiences in the surveillance of and response to pandemic (H1N1) 2009. The presentations showed the diversity of resources and circumstances among countries in the Western Pacific Region. Key points are summarized in table format at Annex 1.

2.5 Plenary 4: Pandemic planning and laboratory contingency planning

2.5.1 **Australia**

Georgina Papadakis, National Influenza Centre, Infectious Disease Reference Laboratory, Australia

Ms Papadakis described the experience of the Victorian Infectious Disease Reference Laboratory (VIDRL) during the pandemic (H1N1) 2009. VIDRL already had a pandemic plan which was adapted during the response.

A peak in testing burden was experienced during the contain phase (on the busiest day 1400 polymerase chain reaction (PCR) tests were performed). During the sustain and protect phases, numbers dropped to a more manageable level. The change in phase occurred before the peak in the epidemiological curve, suggesting that the number of cases would have surpassed the laboratory's capacity.

During the surge, staff worked 12 to 16 hours a day continuously for 15 days. Many staff previously had been cross-trained and volunteers from other laboratories were brought in. There also was a surge in the number of phone calls from doctors, the Department of Health, patients, other laboratories and the media. A significant issue was the slow data transfer because of a manual working system. Although reagents had been stockpiled, a shortage was experienced. A number of incorrect samples also were received. Other issues

were outside the laboratory's control, although they sometimes received the blame. These included delays in referral and transport and in the transmission of results.

The pandemic preparedness planning mean that there was an immediate scale-up of human resources to support testing, testing and outbreak equipment was available, plans were in place for a supply of reagents and result turnaround times averaged 18 hours for diagnostic samples.

2.5.2 **Malaysia**

National Influenza Centre Virology Unit, Institute for Medical Research (IMR)

In Malaysia, the NIC is also a public health laboratory and deals with all virological disease. There is a National Influenza Preparedness Plan and simulation exercises had been carried out. Preparation also included cross-training of staff, ensuring diagnostic quality, strengthening laboratory networks and stockpiling reagents and personal protective equipment (PPEs).

The NIC experienced a significant increase in workload during 2009. With the announcement of the pandemic, an operations room was established, teams were assigned functions and retraining on testing procedures and biosafety occurred. A positive control was received from the WHO CC in Melbourne, and all primers and probes in stockpile were aligned against influenza A (H1N1) 2009.

The testing strategies changed during the course of the pandemic, with viral isolation of all initial cases, and later only for severe and fatal cases. The number of PCR targets also was reduced. Staff initially were on call 24 hours a day, and staff from other units were called in to assist with data management and to answer phone calls and additional equipment was purchased. It was also important to continue the laboratory's other work and not to increase turnaround time of other diagnostic tests such as HIV confirmation. When the volume of samples increased, samples were prioritized based on severity, with colour-coded forms used for ease of processing.

Screening for H1N1 now has been decentralized to all major hospitals. The IMR plays a role in training and monitoring other centres and concentrates on antiviral resistance and sequencing for severe and fatal cases.

The main problem encountered was data management. Other problems included being sent repeated samples from confirmed cases and not being able to reject blank request forms. There were also inappropriate requests during the mitigation phase.

2.5.3 **The Lao People's Democratic Republic**

Ms Bouaphan Khamphaphonghane, National Centre for Laboratory and Epidemiology, the Lao People's Democratic Republic

The National Centre for Laboratory and Epidemiology (NCLE) received primers and reagents from USC DC and started testing for influenza A (H1N1) 2009 in April. Hospitals were encouraged to send samples for all suspect cases. The first case was identified on 13 June with a huge influx of samples received between July and August. The number of samples dropped from September because of a change in specimen collection and testing criteria.

During the busiest period, 40 samples were tested a day using two machines. Additional staff were trained to assist with influenza testing and an additional real-time PCR machine was purchased. A new testing algorithm also was developed. The Merieux Centre agreed to provide additional support if necessary, but this was not required.

The increase in workload led to a strain on human resources. Many staff worked long hours, seven days a week, for more than two months. Provincial laboratories have limited capacity and shipping specimens provided logistical challenges. There was a high demand for testing from public health workers and clinicians.

Lessons learnt included a need to prioritize testing. Personnel management is also vitally important. Monitoring of reagents and equipment needs to occur to ensure continuous supply. Collaboration with partners for technical support and assistance was a key to success. More staff should be trained in influenza testing techniques for surge capacity.

2.5.4 **Plenary 4 discussion and questions**

The issue was raised that in pandemic preparedness, reporting of results and data transfer was given limited consideration. It is a very sensitive issue and one that needs to be addressed. There is also a need to acknowledge the importance of reporting negative results. An example of an information technology (IT) solution was shared that enabled physicians to log on to receive results, which also was shared.

The point also was raised about whether rapid tests at point-of-care could be used to screen those samples sent for further testing.

The Lao's Peoples Democratic Republic was asked whether demands for laboratory results were linked to a limited supply of antivirals and a need for confirmation before treatment commenced. Hospital staff were encouraged to commence treatment based on clinical judgement, but there was a lack of confidence regarding the administration of antivirals in mild cases.

2.6 Workshop on recent advances in vaccine development and vaccination policy

2.6.1 **Analysis of isolates at WHO Collaborating Centres (WHO CC)**
Anne Kelso, Director, WHO Collaborating Centre for Reference and Research on Influenza, Australia

Samples submitted to the WHO CC are analysed to answer questions, including subtyping, whether it is different from known circulating influenza strains, whether it can be detected using current diagnostic tests, whether immunity to previous viruses or vaccines would be protective, whether it is sensitive to antiviral drugs and to determine what its geographic spread.

Isolates and clinical specimens received are logged in a database where every stage of analysis is tracked. Both types of samples are cultured in Madin-Darby canine kidney (MDCK) isolate and HI testing is carried out. Phylogenetic analysis is carried out on selected viruses and isolates are also tested for antiviral susceptibility. HI data is supplied to Cambridge University for antigenic cartography.

Clinical specimens are needed for isolation of vaccine candidates. Regulators require that influenza vaccine viruses are isolated and passaged exclusively in hen's eggs. WHO CCs obtain egg isolates as reference strains for provision to vaccine manufacturers.

WHO CCs also provide data to submitting laboratories to support local surveillance activities and policies. Dossiers of collated data are provided to WHO biannually and are used to provide information for the formulation of WHO recommendations on virus strains for seasonal and pandemic viruses.

The processes carried out by the WHO CCs enable early detection of antigenic drift, the monitoring of the spread of antiviral drug resistance or other significant mutations and the matching of vaccines to circulating strains.

Ms Kelso also emphasized the importance of timely and regular submission of viruses throughout the influenza season and the provision of some high quality clinical specimens. Clinical and other information, such as antiviral treatment history, is also important.

2.6.2 **Vaccine composition selection process**

Dr Masato Tashiro, National Institute for Infectious Diseases, Japan

Dr Tashiro outlined the process of formulating recommendations on the composition of influenza vaccines. The WHO CCs perform detailed analysis of viruses sent by NICs, including HA antigenic analysis, genetic analysis and monitoring for neuraminidase inhibitors (NAI) susceptibility. Novel viruses are characterized in detail and assessed for risk as potential pandemic viruses.

At the WHO biannual consultations on the composition of influenza vaccines, epidemiological and virological trends are discussed and the epidemic viruses for the following season are predicted. Consideration is given to the adequacy of the current vaccine. Virus strains suitable for strains for vaccine production and immunization are selected and recommendations drafted.

Wild-type virus of vaccine-recommended strains is not always suitable for vaccine production and the development of high-growth reassortments as vaccine candidate viruses is necessary. These can be developed using classical gene reassortment or reverse genetics technology. Candidate viruses for vaccine production are evaluated for antigenic identity, genetic stability, growth efficiency in eggs and haemagglutinin (HA) protein recovery efficiency.

2.6.3 **Development of candidate strains**

Dr Ian Barr, WHO Collaborating Centre for Reference and Research on Influenza, Australia

There are three main processes used to develop vaccine candidate strains – egg-grown vaccines, reverse genetics and live attenuated viruses. More than 95% of viruses are still produced in eggs. Live attenuated vaccines are available in some countries whereas reverse genetic viruses have not yet been used for commercial seasonal or pandemic vaccines. This is because there are intellectual property issues, licensing issues, the process does not select for high growth viruses and yields have not been greater than conventional reassortment.

For the culture of influenza A (H1N1) 2009 viruses, WHO's safety recommendation was initially BSL3, but this was difficult for most manufacturers. This was partly because weight loss and lung pathology were more extensive than experienced with seasonal influenza and it was not known how influenza A (H1N1) 2009 flu gene segments contributed to pathogenicity.

There is growing interest in cell cultured-based vaccines, but these have yet to prove they can be the mainstay of influenza vaccines.

2.6.4 **Vaccine Policy Development**

Wenqing Zhang, WHO, Geneva

At the onset of pandemic (H1N1) 2009, WHO initiated a broad range of actions, one of which was to accelerate access to vaccines. The first teleconference with WHO CCs took place on 27 April, and on 26 May WHO recommended which viruses should be used in pandemic vaccine development and production.

In July, WHO also recommended priority groups for vaccination. Health care workers, (an estimated 1%-2% of the population) were recommended as a priority. An analysis of 48 national deployment plans found that 100% followed WHO recommendations for health care workers. Pregnant women were a priority in 92% of plans and people with chronic conditions in 69% of plans.

WHO also has monitored vaccine safety, with information from large-scale usage available from more than 50 countries. More than 350 million doses have been administered. There have been relatively few local and systemic reactions, with a small number of severe events, which have been mainly allergic reactions. No unexpected safety concerns have been identified for any of the pandemic (H1N1) 2009 vaccines used in population-level immunization programmes thus far.

Global influenza vaccine production capacity has grown from 350 million doses of trivalent seasonal vaccine in 2006 to over 800 million in 2010. During the period 2009-2010, actual vaccine production of seasonal trivalent vaccine was similar to planned production whereas actual production of pandemic virus vaccine is expected to be much lower than planned production. Although new manufacturers have been established in lower-income countries, production capacity is still lacking in some parts of the world.

The WHO vaccine deployment initiative aims to ensure access to vaccines to all low- and lower-middle-income countries. The donation target was 10% of population coverage for countries in need. Several donor governments and manufacturers pledged support, and WHO is coordinating deployment in collaboration with the United Nations System Influenza Coordinator (UNSIC).

All countries have indicated in their National Deployment Plans that the EPI infrastructure would be used for deployment and vaccination. Fully 10% of countries plan to vaccinate their priority groups beyond WHO-donated vaccine.

There are many time constraints on the vaccine development process, and although a vaccine was developed relatively quickly, influenza A (H1N1) 2009 was still widespread before the vaccine was available widely. Early detection of novel viruses in the laboratory could help reduce this gap.

2.6.5 Workshop discussion and questions

The development of an H5N1 vaccine was discussed. WHO has established a list of potential vaccine strains and this is reviewed regularly. H5 viruses are localized and it is therefore difficult to make a universal recommendation.

The screening of samples for mutations also was discussed. Although the H274Y mutation is currently the most commonly identified, it is also important to use both functional assays and pyrosequencing to screen for other mutations.

The issue also was raised about potential mismatches between WHO vaccine recommendations and circulating virus strains. Recommendations are made six months before the start of the influenza season and there is a need to shorten this time. Submitting samples in a timely manner is key to improving the match. WHO only recently began making biannual recommendations, and a new timeframe may be considered. There is a need for better understanding of seasonality and the speed of the evolution of viruses. It is also very important to understand the use of the terms "match" and "mismatch", and the clinical endpoint is most significant. Also, while WHO makes recommendations, these can be adapted by national authorities, but this would require local vaccine manufacturers.

2.7 Panel Discussion – Training and Support from WHO Collaborating Centres

The types of training and support provided to NICs include the organization of workshops, providing advice, training at collaborating centres, onsite visits, support in developing suitable processes and procedures and providing reagents, primers, kits and MBCK cells.

Training is vitally important for NICs. There is a big demand for the establishment of drug resistance monitoring. The issue of training in serology also was raised. For those laboratories that already have capacity, there is a need for standardized sera. These are available for some virus strains.

The issue of how best to identify the needs of NICs also was discussed. During the 2009 meeting, a survey was formulated identifying a broad range of needs. The idea was raised that this process could be repeated. Interaction with individual laboratories and in-house training is also valuable in identifying specific needs. At the global level, a number of surveys have been formulated to identify the current capacity of NICs, and a third survey will be drafted later this year. While regional training works well to address common capacity-building needs, there is a need for more tailor-made training and support as capacity builds.

2.8 Visit to the Research Institute for Tropical Medicine (RITM)

Participants were invited to visit the Research Institute for Tropical Medicine, which is also the Philippines National Influenza Centre.

2.9 Serology Survey Results

2.9.1 **Singapore**

Raymond Lin, National Public Health Laboratory, Ministry of Health, Singapore

Serological studies help to assess existing immunity in the population due to cross-reactivity and the proportion of the population infected. This helps predict the chance of

future outbreaks, informs the formulation of vaccine policy and the identification of at-risk groups and contributes to the understanding of future pandemics.

The findings of serological studies may appear to be conflicting, but geographical and population differences, selection bias and laboratory methods must all be taken into consideration.

The study outlined in this presentation studied seroconversion rates and risk factors in four adult cohorts in Singapore (the community, the military, hospital staff and residents in long-term care facilities). Samples were taken pre- or early pandemic four weeks after the peak and four weeks after decline. The results showed earlier seroconversion in the community and military cohorts and the highest rate of seroconversion among those between 20 years old and 24 years old. The final rates showed 13% of the community had seroconverted compared with 29% of the military cohort and 7% of hospital staff.

Mr Lin also described a number of methods that can be used to predict the proportion of the population infected. Using clinical surveillance, it was estimated that 5% of the population would be infected by the end of September 2009, whereas using predictive modelling and sero-epidemiology methods, the estimated proportion infected was 13%.

2.9.2 **China**

Yuelong Shu, Chinese National Influenza Center, China

Dr Yuelong Shu described three serological studies conducted in China. The first was conducted to assess baseline immunity to pandemic (H1N1) in China. The cross-reactive antibody responses detected in all participants were significantly less than the antibody response to seasonal influenza viruses in China. The seroresponse in subjects born in and before 1925 was significantly higher than in younger subjects, suggesting that infection with the 1918 pandemic influenza virus or related H1N1 virus before 1925 or persistent and long-term exposure to H1N1 influenza viruses may have sustained some degree of cross-reactive antibody response to the current pandemic H1N1 virus.

A rapid serological study was conducted to provide information to inform vaccination strategies and other prevention and control measures in China. Samples were collected five times in 31 provinces. There was a significant increase in seroprevalence between the first and second surveys (pre- and post-pandemic peak), with no significant differences found in the following surveys. The rates of infection with 2009 pandemic H1N1 were greatest in schoolchildren 6 years old to 17 years old and lowest in those 56 years old or older.

A serological study using a random-sampling cross-section survey estimated the 2009 pandemic influenza H1N1 virus infection rate in China. More than 54 000 samples were collected and stratified into three geographical areas (big cities, small to medium cities and rural) and in five age groups. Based on the results, an estimated 220 million people were infected during the pandemic. Analysis of prevalence rates in different regions and age groups was continuing.

2.9.3 **Western Australia**

Dr Ian Barr, WHO Collaborating Centre for Reference and Research on Influenza, Australia

Dr Barr presented the results of serosurvey of influenza A (H1N1) 2009 infection in Western Australia in which samples were collected from children 1 year old to 19 years old (age stratified into 1 year old to 4 years old and 5 years old to 19 years old) and pregnant women. Samples were collected pre- and post-pandemic, but were not paired sera. Results showed the children 5 years old to 19 years old were most likely to have been infected with influenza A (H1N1) 2009, with up to 40% showing serological signs of infection whereas only 10.2% of pregnant women showed serological responses. These results are similar to the findings of other studies and suggest that as pregnant women and adults have the lowest level of serological evidence for exposure to the pandemic virus they should be prioritized in continuing vaccination programmes.

2.9.4 **Development in virus detection and analysis**

Dr Xiyan Xu, Centers for Disease Control and Prevention, the United States of America

Dr Xiyan Xu gave an overview of developments in influenza virus detection and analysis. Work was under way to improve current assays. Immunofluorescence has been used for viral antigen detection. For antigenic characterization, efforts have been made to improve HA and HI tests, including the development of semi-automated systems. Work also was under way on developing new assays to replace HA and HI tests. For nucleic acid detection, new developments include portable real-time PCR systems, linear-after-the exponential PCR (LATE-PCR) and light upon extension (LUX).

There is also an increase in the availability of large numbers of sequences, including publicly accessible influenza databases such as the GISAID.

A Rapid Influenza Immunity Test for rapid, point-of-care evaluation of H5 antibody status was also under development. Solid phase microarray technologies and glycan microarray analysis are other methods that also have been used. Other potential new technologies include mass spectrometry (MS), an analytical technique for determining the elemental composition of a sample or molecule and nanotechnology.

While the range of techniques for influenza virus detection is growing, virus isolation is essential for vaccine strain selection and virus isolation capacity is encouraged. Because influenza viruses are constantly evolving, test reagents may require periodic updates or modifications to maintain test specificity.

2.9.5 **Serology discussion and questions**

The reasons why the serological survey in Singapore showed that health care workers had lower levels of exposure to influenza A (H1N1) 2009 were discussed. The infection control practices in hospitals included wearing normal surgical masks as standard practice and the isolation of fever patients. It also was suggested that health care workers may have had a higher awareness of protective behaviours.

The purpose of a rapid test for antibody detection was discussed. If there was an outbreak of avian influenza, the test could rapidly assess the presence of influenza infections and could be supplementary to quick screening.

2.10 Closing Speech: Pandemic preparedness and response
Ms Anne Moen, Centers for Disease Control and Prevention

Ms Moen presented on pandemic preparedness and response from the WHO perspective. WHO preparedness guidance first was published in 1999 with revisions in 2005 and 2009 based on extensive input from global experts. The 2009 version included six pandemic phases and post-peak and post-pandemic. While the primary purpose for the phases was to assist in the preparation for a pandemic, some Member States have linked actions such as border control and screening, vaccine procurement and emergency licensing of drugs to the announcement of each phase in pandemic preparedness plans.

At the onset of the pandemic, 141 countries had publicly-available pandemic preparedness plans and many countries also had formulated intercountry plans. An analysis of these plans soon will be available.

Ms Moen also discussed some of the communication issues that occurred during the pandemic. The difference between phase 5 and phase 6 in current guidance is mostly geographic spread, but this led to significant communication challenges. Other simple and important issues included the name of the pandemic and the definition of severity.

It also has been argued that the definition of a pandemic should include a measure of severity, but this poses a challenge because it is difficult to predict beforehand and is a result of a complex interaction between the disease-causing agent, the host and the environmental and societal circumstances. However, it will be considered in the next revision of the guidelines. Vaccine deployment also posed challenges, and it was difficult to give clear public messages. Different patterns of vaccine uptake have been observed in different countries.

Lessons from the pandemic indicated that while the IHR 2005 worked for reporting newly detected cases and deaths, surveillance and monitoring still needs to be improved to overcome issues such as the manual collection of data and the lack of standardization of data. An IHR 2005 and pandemic review was under way and a final report and recommendations will be presented to the World Health Assembly in May 2011.

2.11 Questions and discussions

The issue of measures of severity were discussed. While WHO makes recommendations that are relevant worldwide, national governments have a very important role to play. For example, the impact may be much more severe in countries without well-developed health care facilities.

The use of rapid containment and border control measures also was discussed. While it is acknowledged generally that the effectiveness of border control measures is limited, they have been adapted for various reasons. For example, they can be a significant psychological deterrent against travelling when sick. The Western Pacific Regional Office has organized a series of meetings on how to respond at points of entry. Guidelines were being formulated and there were plans to pilot these towards the end of this year.

Rapid containment is based largely on modelling studies and relies strongly on assumptions. While it may be difficult to implement effectively, the Western Pacific Regional Office has found that conducting rapid containment exercises is a useful entry point to strengthen generic capacities and that emphasizing rapid containment encourages the strengthening of rapid response and surveillance capacity.

3. CONCLUSIONS

3.1 The main conclusions of the meeting were as follows:

(1) Currently in both hemispheres, influenza A (H1N1) 2009 and influenza B viruses are the most dominant circulating strains. Low levels of seasonal H3N2 and very little A/H1N1 virus were detected by the NICs.

(2) The vast majority of circulating pandemic viruses are antigenically similar to the current pandemic vaccine strain: A/California/7/2009.

(3) Very little resistance to oseltamivir and no resistance to zanamivir has been seen among circulating influenza A (H1N1) 2009 viruses globally and sustained human-to-human transmission of such viruses has not been observed. However, the circulating virus is resistant to amantadine.

(4) Considering that A/H5N1 and H9N2 viruses are sporadically detected in humans, the possibility of reassortment of the influenza A (H1N1) 2009 virus with these viruses as well as seasonal viruses cannot be ruled out. The resulting virus could have much higher pathogenicity, transmissibility or gain resistance to existing antiviral medications. Such possible reassortments could also occur with different subtypes circulating in animals.

(5) Over the last four years, countries and laboratories in the Region have made major progress in fulfilling the recommendations made at the first NIC meeting and in building their capacity for influenza diagnosis, surveillance and response. During this period, two new NICs have joined the network and the designation of a third WHO CC in the Region was awaiting approval. These achievements have been largely due to efforts in pandemic preparedness that have taken place in Member States. The annual meeting of NICs has stimulated this process by creating a forum for formulating regional strategies and goals.

(6) There has been a significant increase in the number of laboratories participating in the WHO EQA programme and marked improvements in performance results. Some laboratories also were investigating the possibility of being internationally accredited.

(7) The meeting commends those Member States that are moving the research agenda forward by conducting and publishing influenza serosurveillance studies.

(8) Almost all NICs within the Region experienced a major increase in workload due to pandemic influenza. Although most had contingency plans in place, which dealt with issues such as stockpiling of reagents, other factors such as sample transfer time period, management of external demands, data entry and reporting were not taken into account and acted as bottlenecks in many laboratories.

(9) The meeting noted the previous biosafety level recommendation of BSL-3 for higher containment practices with influenza A (H1N1) 2009 viruses as advocated by the WHO biorisk reduction group. The meeting participants

felt that these recommendations were inappropriately restrictive and were impeding the work that can be carried out on the virus. It also was noted by several participants that in some countries such as the United States of America, the United Kingdom of Great Britain and Northern Ireland and Japan the culturing of influenza A (H1N1) viruses can take place in BSL-2 laboratories.

(10) The process of developing influenza vaccines was discussed in detail and the importance of frequent and timely sharing of viruses, clinical specimens and related information on locally circulating influenza strains with the WHO CCs was emphasized as an essential step to ensure that vaccine strains match circulating strains.

(11) The meeting acknowledged that as part of global pandemic response, there were gaps in the sharing of timely epidemiological data in a cohesive manner. Strengthening this process would help coordination of the global response in the future.

3.2 Recommendations

(1) Pandemic preparedness should continue even during the pandemic response. These efforts will benefit the response to the evolving situation of pandemic (H1N1) 2009 and other health threats and IHR 2005 reporting.

(2) Collaboration between animal and human health sectors within Member States should be encouraged such as influenza disease information exchange and specimen-sharing.

(3) Member States are encouraged to review their response to pandemic (H1N1) 2009 and global lessons learnt and revise their national pandemic preparedness plan based on all lessons learnt from the response and outcomes of the review.

(4) NICs are encouraged to share recent representative and unusual influenza specimens frequently and in a timely manner to support virological surveillance and vaccine development. Building virus isolation capacity should be encouraged.

(5) NICs should immediately share any unsubtypable influenza viruses with the WHO CCs.

(6) NICs are encouraged to continue to enhance National Influenza Surveillance Systems through strengthening the capacities of the NICs and associated epidemiology programmes. Influenza disease burden studies could be a tool for such an enhancement.

ANNEX 1

PROGRAMME OF ACTIVITIES

Day 1 – Monday, 3 May 2010

08:00-09:00	Registration
	Opening Session
09:00-09:20	Remarks *Dr Esperanza Cabral, Secretary, Department of Health* *Dr Takeshi Kasai* *Dr Wenqing Zhang*
09:20-09:40	Introduction and overview of meeting agenda
	Election of chairs for each session
09:40-09:50	Self-introductions
09:50-10:00	Group photo
10:00-10:30	*Coffee break*
10:30-12:00	**Plenary 1: Regional and global updates** • WPRO – *Dr Takeshi Kasai* • APSED and beyond – *Dr Ailan Li* • WHO HQ – *Dr Wenqing Zhang* • EQA Programme – *Dr Wilina Lim*
12:00-12:10	Discussion
12:10-13:30	*Lunch break*
13:30-15:30	NIC Poster presentations
15:30-15:50	*Coffee break*
15:50-17:10	**Plenary 2: Influenza surveillance** • Philippines – *Dr Enrique Tayag* • Northern Hemisphere – *Dr Takato Odagiri* • China – *Dr Yuelong Shu* • Southern Hemisphere – *Dr Ian Barr*
17:10-17:30	Discussion and wrap for the day
18:30-21:30	Welcome Reception

Day 2 – Tuesday, 4 May 2010

08:15-08:30 Announcements and introduction

Plenary 3: Avian influenza updates

08:30-09:15 **Virology**
- Overview of seasonal and pandemic virus evolution
- Update on H5 and other non-human influenza viruses – *Dr Alexander Klimov*

09:15-10:00 **Epidemiology**
- Seasonal/pandemic replacement of seasonal virus by pandemic virus
- H5 latest developments – *Dr Julia Fitzner*

10:00-10:10 Discussion

10:00-10:40 *Coffee break*

10:40-11:40 **Impact of virus mutation**
- Antiviral resistance – *Dr Aeron Hurt*
- Reassortment – *Dr Masato Tashiro*

11:40-12:00 Discussion

12:00-13:15 *Lunch break*

13:15-15:15 Country presentations

15:15-15:30 *Coffee break*

15:30-17:30 **Plenary 4: Pandemic planning and laboratory contingency planning**

Sharing experiences
- Australia
- Malaysia/Lao PDR

Discussion and wrap for the day

Day 3 – Wednesday, 5 May 2010

08:15-08:30 Announcements and introduction

Workshop on recent advances in vaccine development and vaccination policy

Seasonal vaccine selection –
08:30-09:00 1. Analysis of isolates at WHO CCs – *Dr Anne Kelso*
09:00-09:30 2. Vaccine composition selection process – *Dr Masato Tashiro*
09:30-10:00 3. Development of candidate strains – *Dr Ian Barr*

10:00-10:15 Discussion

10:15-10:45 *Coffee break*

Vaccine policy development

10:45-11:00	1. WHO vaccine policy – *Dr Wenqing Zhang*
11:00-11:15	Discussion
11:15-11:45	Panel discussion - Training and support from WHO CCs
11:45-12:00	Discussions and wrap for the day
12:00-12:45	*Lunch break*
12:45	Visit to Research Institute for Tropical Medicine (National Influenza Centre for the Philippines)

Day 4 – Thursday, 6 May 2010

08:45-09:00	Announcement and introduction
09:00-10:00	**Influenza sero survey results** - Singapore - China - Western Australia
	Discussion
10:00-10:30	**Developments in virus detection and analysis** - *Dr Xu Xiyan*
10:30-10:45	Discussion
10:45-11:15	*Coffee break*
11:15-11:35	Pandemic preparedness and response – *Dr Hande Harmanci*
11:35-12:00	Discussion
12:00-12:30	Wrap up/conclusions
	End of meeting

CDC cooperative agreement partner's meeting.

ANNEX 2

PROVISIONAL LIST OF PARTICIPANTS, TEMPORARY ADVISERS, OBSERVERS AND SECRETARIAT

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