Sixth Meeting on National Influenza Centres and Influenza Surveillance for the Western Pacific and South-East Asia Regions

Hanoi, Viet Nam
29-31 May 2012
REPORT
SIXTH MEETING OF NATIONAL INFLUENZA CENTRES
AND INFLUENZA SURVEILLANCE IN THE
WESTERN PACIFIC AND SOUTH-EAST ASIA REGIONS

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NOTE

The views expressed in this report are those of the participants of the Sixth Meeting of the National Influenza Centres and Influenza Surveillance in the Western Pacific and South-East Asia Regions and do not necessarily reflect the policies of the Organization.

This report has been prepared by the WHO Regional Offices for the Western Pacific and South-East Asia for the Member States in the Regions and for those who participated in the Sixth Meeting of the National Influenza Centres and Influenza Surveillance held in Hanoi, Viet Nam, from 29 to 31 May 2012.
The Sixth Meeting of the National Influenza Centres (NICs) and Influenza Surveillance in the Western Pacific and South-East Asia Regions was held in Hanoi, Viet Nam, from 29 to 31 May 2012. Participants discussed progress, activities and technical updates occurring in the year following the 5th Meeting in 2011, reviewed new technical guidance on influenza surveillance developed by WHO Headquarters, and discussed the role of the Global Influenza Surveillance and Response System (GISRS) in providing data for vaccine policy development. In addition, the meeting initiated multi-country collaborations for the development of scientific manuscript(s) to document current influenza vaccine use and to provide epidemiological details to guide future influenza vaccine use in the Regions.

Forty-one participants from 21 countries and areas attended the meeting. Participants included directors of NICs, epidemiologists, public health officials and influenza researchers from Australia, Bangladesh, Cambodia, China, Fiji, Hong Kong SAR (China), Indonesia, the Lao People's Democratic Republic, Malaysia, Mongolia, Myanmar, Nepal, New Caledonia (France), New Zealand, Papua New Guinea, the Philippines, the Republic of Korea, Singapore, Sri Lanka, Thailand and Viet Nam.

Temporary advisers to the meeting included 11 experts from four World Health Organization (WHO) Collaborating Centres for Reference and Research on Influenza (United States Centers for Disease Control and Prevention, Atlanta; Victorian Infectious Diseases Reference Laboratory, Melbourne, Australia; National Institute of Infectious Diseases, Tokyo, Japan; Chinese National Influenza Center, National Institute for Viral Disease Control and Prevention, Beijing, China). The WHO Secretariat consisted of 12 representatives from Headquarters, the Regional Offices for the Western Pacific and South-East Asia and Country Offices in Cambodia, the Lao People's Democratic Republic, and Viet Nam.

The three-day programme consisted of six plenary sessions. The sessions covered regional and global updates, reports on influenza activity in the northern and southern hemispheres, and country experiences from Viet Nam, Thailand, Papua New Guinea and Australia on the use of data to inform vaccine use/guidance. There were also discussions on the future of the GISRS and its role in providing data for national decision-making for influenza vaccine introduction, and discussions on multi-country collaborations. A poster session was held for NICs to showcase their recent influenza work. A total of 11 posters were presented and discussed. In addition, the meeting included a presentation and workshop session on revisiting national influenza surveillance. The meeting ended with a site visit to National Institute of Hygiene and Epidemiology, a national influenza centre, in Hanoi.

The meeting was an excellent opportunity for participants to meet and share experiences. From the meeting it was agreed that countries and areas should review the new global guidance for influenza surveillance vis-à-vis the implementation of the five-year Biregional Plan for Further Strengthening National Influenza Surveillance. It was also agreed that multi-country collaborations for the development of scientific manuscript(s) should be pursued, starting with the documentation of current influenza vaccine use across the region. It was recommended that the next biregional meeting be structured in a way that allows both combined and separate laboratory-oriented and epidemiology-oriented technical sessions.
1. INTRODUCTION

Influenza surveillance has been established in many countries in World Health Organization’s (WHO) Western Pacific and South-East Asia Regions. The WHO Global Influenza Surveillance and Response System (GISRS) in these two Regions currently include 31 National Influenza Centres (NICs) in 23 countries and areas and three WHO Collaborating Centres for Reference and Research on Influenza. The GISRS monitors the occurrence and evolution of influenza viruses and informs global vaccine strain selection.

Between 1998 and 2010, more than 76% of the virus isolates selected for influenza vaccine strains was provided by GISRS members in the Western Pacific and South-East Asia Regions. However, despite the major contributions to the global vaccine composition effort, seasonal influenza vaccination programmes grounded by national policy have been limited to a few countries and areas in these Regions.

Since 2007, annual NIC meetings have provided an opportunity for NICs, Ministry of Health officials, WHO and partners to meet and share experiences, successes and challenges. The five previous meetings have been successful in contributing to strengthening GISRS in the Asia Pacific region.

(1) The first meeting of NICs in the Western Pacific and South-East Asia Regions 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.

(2) The second meeting was held in Tokyo, Japan, from 21 to 24 April 2008. Guidelines on comprehensive influenza surveillance and influenza disease burden studies were introduced. A software database for NICs was also presented.

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

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

(5) The Fifth Meeting of National Influenza Centres in the Western Pacific and South-East Asia Regions was held in Vientiane, the Lao People's Democratic Republic, from 7 to 10 June 2011. The capacity of the network in the Regions was reviewed and the next five-year plan (2012–2016) for national influenza surveillance was developed.

The Sixth Meeting of the National Influenza Centres (NICs) and Influenza Surveillance in the Western Pacific and South-East Asia Regions was held in Hanoi, Viet Nam, from 29 to 31 May 2012.
1.1 Objectives

The objectives of the Sixth Meeting were:

(1) to develop a checklist of minimum requirements for comprehensive influenza surveillance in line with the five-year plan (2012–2016) for national influenza surveillance;

(2) to review the draft influenza research agenda and discuss the role of GISRS in providing research data for vaccine policy development; and

(3) to initiate multi-country collaborations for the development of scientific manuscript(s) to document current influenza vaccine use and to provide epidemiological details to guide future influenza vaccine use in the Regions.

1.2 Welcome and opening remarks

Dr Takeshi Kasai, WHO Representative in Viet Nam, on behalf of Dr Shin Young-soo, Regional Director, WHO Regional Office for the Western Pacific

On behalf of the WHO Regional Director, Dr Takeshi Kasai welcomed the participants to the meeting and expressed his sincere appreciation to the Government of Viet Nam for hosting the meeting. He emphasized that Viet Nam, as a country on the frontline of the battle against influenza with pandemic potential, reminded us of the importance of continued vigilance and strengthening of influenza programmes.

Dr Kasai acknowledged that the Sixth Meeting was an important opportunity to work together to build capacity and reduce the burden and threat of influenza in the Regions. The discussions would assist countries and areas to review their influenza surveillance systems, and ensure the breadth and quality of data collected meet the health needs of each country for detection, response and disease control policy development. To continue to move forward, he encouraged the countries and areas to: (i) undertake special studies; (ii) fill gaps in data required for the development of influenza vaccine introduction policy; and (iii) explore opportunities for multi-country collaborations to maximize efforts and resource utilization.
Dr Kasai expressed his appreciation for the many representatives from national influenza centres and national epidemiological surveillance systems in both the South-East Asia and the Western Pacific Regions as well as the observers from partner organizations. He wished everyone success in the work that lay ahead and looked forward to seeing the outcome of the meeting.

Dr Tran Thanh Duong, Deputy Director, General Department of Preventive Medicine, Ministry of Health, Viet Nam

On behalf of the General Department of Preventive Medicine, Ministry of Health of the Socialist Republic of Viet Nam, Dr Tran Thanh Duong expressed thanks for the honour accorded to Viet Nam for hosting the meeting.

With support from WHO and the United States Centers for Disease Control and Prevention (CDC), Viet Nam has set up two national influenza centres and has participated in the Global Influenza Surveillance and Response System (GISRS) since 2006. The national influenza centres in Viet Nam have made remarkable contributions towards monitoring circulation and changes of influenza viruses in Viet Nam. Dr Tran Thanh Duong expressed sincere thanks to the international agencies that had helped in setting up and implementing the influenza surveillance sentinel sites, and hoped to continue receiving support for maintaining and expanding the surveillance system to make an even greater contribution to the GISRS system.

In light of the continuous changes of influenza viruses as well as of the occurrence of emerging diseases in recent times, there is a need for closer cooperation among scientists in national influenza centres around the world. Dr Tran Thanh Duong noted that the Sixth Meeting of the National Influenza Centers and Influenza Surveillance in the Western Pacific Region and South-East Asia Regions offered an opportunity to share results from many influenza surveillance and research across the two Regions and discuss the biregional five-year master plan for influenza surveillance and guidelines on influenza vaccines.

Dr Tran Thanh Duong wished all delegates good health. He hoped that the meeting would be a success and that everyone would enjoy a happy time in the peaceful city of Hanoi, Viet Nam.

Dr Michael Shaw, Influenza Division, Centers for Disease Control and Prevention, United States of America

Dr Michael Shaw highlighted the importance of the collected data and encouraged the participants to discuss priorities. There is no way to predict where and when a new strain would strike; therefore, it is important for participants to identify new strains in their countries and share the information. The meeting was a useful occasion to reflect on what was being done, how it was being done and why, particularly in the difficult current economic climate.
2. PROCEEDINGS

2.1 Plenary Session One: Regional and global updates

Chair: Dr Masato Tashiro, Co-chair: Dr Le Thi Quynh Mai

2.1.1 Presentation 1: National Influenza Centres in the South-East Asia Region

Dr Richard Brown, WHO Regional Office for South-East Asia

The countries of the South-East Asia Region are Bangladesh, Bhutan, the Democratic People’s Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Thailand, Timor-Leste, and Sri Lanka. All have established National Influenza Centres except Bhutan, Maldives and Timor-Leste. The Region is characterized by significant differences in size, climate, political and organizational structures and socio-cultural norms. There is also a changing context, with increasing travel, trade and industrialization and effects of climate change. Good data are available on the burden of influenza in some countries, but most countries do not have programmes for influenza vaccination, the notable exception being Thailand. Capacity for influenza vaccine manufacturing is being established in some countries (India, Indonesia and Thailand).

The Region has a relatively high burden of human infections with highly pathogenic avian influenza A (H5N1), with cases reported in Bangladesh, Indonesia, Myanmar and Thailand. The cases peaked in 2006 when nearly 60 cases were notified. Since then, numbers have decreased and have not exceeded 15 notified cases since 2010. Most cases have been identified in Indonesia.

At the beginning of the pandemic caused by the pandemic influenza A(H1N1)pdm09 virus, all South-East Asia Region Member States already had influenza pandemic plans. Formal reviews of the pandemic response have since been undertaken in several countries and many plans are now being revised.

A Regional Consultation on implementation of the Pandemic Influenza Preparedness (PIP) Framework was held in New Delhi, India, 5-6 March 2012. Consensus was reached by South-East Asia Region countries on the following issues:

1. Advocacy should be undertaken for laboratories that are part of GISRS, in consultation with policy/decision makers to adopt the Terms of Reference (TORs) defined by the Framework.

2. Concerned laboratories should continue to share influenza viruses, including those with pandemic potential, in a timely manner.

3. The process for prioritization of benefits through Partnership Contribution should be reviewed to allow input from Member States.

4. The process for negotiation of Standard Material Transfer Agreement (SMTA) type 2 should be accelerated.
Consideration should be given also to developing a mechanism to allow Member States to provide input into the process of negotiation of SMTA type 2 arrangements for non-financial contributions, e.g. ‘in kind’ benefits /technology transfer.

Current challenges in the South-East Asia Region include:

(1) standardizing and expanding the scope of influenza surveillance to make data obtained more valid and representative;

(2) generating better information on disease burden to inform discussion about national policies on vaccination); and

(3) integrating influenza surveillance within programmes for other vaccine preventable diseases.

A number of initiatives are currently being planned. Bhutan has formally declared its intention to start the process of designating an NIC and work has commenced to establish a WHO Collaborating Centre (CC) in Indonesia for influenza at the animal-human interface. A workshop on influenza data management is also being planned to be held in Bangkok, 14-18 August, organized in collaboration with new WHO CC for epidemiology in Prince Songkhla University and supported by US CDC.

2.1.2 Presentation 2: Summary of influenza activity in the Western Pacific Region

Dr Jeffrey Partridge, WHO Regional Office for the Western Pacific

The Global Influenza Surveillance and Response System (GISRS) in the Western Pacific Region currently includes 21 national influenza centres (NICs) in 15 countries and three WHO Collaborating Centres for Reference and Research on Influenza in the Western Pacific Region—one each in Australia, China and Japan.

The following documents have been published since the 2011 NIC meeting:

(1) Fifth Meeting of National Influenza Centres - Western Pacific and South-East Asia Regions. Weekly Epidemiological Record, February 2012.


(http://www.wpro.who.int/topics/influenza/InfluenzaSurveillanceFiveYearWorkplan_website.pdf.)


Activities since the 2011 NIC meeting included the following:

(1) training of 45 participants from 10 countries in shipping of infectious materials (IATA) in workshops in Phnom Penh, Cambodia, in September 2011, and in Hanoi, Viet Nam, in December 2011;

(2) conducting of a review at NIC, Institute of Medical Research, Papua New Guinea, from 27 to 29 June 2011 (in collaboration with the WHO Collaborating Centres in Atlanta and Melbourne), and drafting of a one-year workplan for improvement of NIC; and
(3) WHO Western Pacific Regional Office-supported training in molecular techniques and virus culture, at the WHO Collaborating Centre in Melbourne, for two Laboratory Specialists from the NIC in Papua New Guinea and one Laboratory Specialist from the NIC in Fiji.

Activities planned for the second half of 2012 include the following:

(1) a meeting on influenza vaccines in October;

(2) planning of a workshop on sequencing and phylogenetic analysis (to be conducted in 2013);

(3) a technical writing workshop in November;

(4) a survey of influenza vaccine use in the Western Pacific Region;

(5) the publication of a literature review of influenza research in the Western Pacific Region; and

(6) the publication of a survey of global influenza vaccine production capacity done in collaboration with WHO Headquarters.

Update from the Influenza Reagents Resource: Web ordering will begin soon following website registration by eligible laboratories. Web ordering will eventually replace ordering through the email address (FluOrder@CDC.Gov). A webinar is available at: https://www.influenzareagentresource.org/IRRWebsiteWebinar.aspx

2.1.3 Presentation 3: An update from WHO Headquarters

Dr Wenqing Zhang, WHO Headquarters, Geneva

As of June 2012, the WHO GISRS continues to be a key global mechanism for global health security, comprising 147 laboratories in 108 Member States (111 countries, areas or territories). In the past year, two new NICs; one in Qatar and the other in Jordan, joined GISRS. However, GISRS coverage is still uneven globally with the biggest gaps remaining in Africa and the Middle East. Dr Zhang congratulated the South-East Asia and Western Pacific Regions, which cover 99.9% of their populations through GISRS and have 50% of the world’s resources in terms of WHO CCs, WHO Essential Regulatory Laboratories (ERLs) and WHO avian influenza A (H5) Reference Laboratories of GISRS.

GISRS is a dynamic network. Development of GISRS is on-going, including the development of new CCs, such as VECTOR Russia and the National Institute of Health Research and Development (NIHRD), Indonesia, though they are at different stages of the process. Pasteur Institute Paris has withdrawn its application for becoming a WHO CC of GISRS due to financial considerations. NICs continued to be engaged in WHO activities/meetings including the biannual WHO vaccine composition consultations and the global consultation on improving influenza vaccine selection in December 2011.

The communication platform has been used actively. The GISRS platform based on EZCollab, an interactive and informal communication tool managed by WHO Headquarters, has 258 registered users from GISRS receiving timely information from WHO or other GISRS members.
Virus monitoring and laboratory diagnosis have been the key roles of GISRS with functions by CCs, NICs and H5 reference laboratories under the coordination of WHO. The annual polymerase chain reaction (PCR) working group (WG) meetings took place in June 2011 and June 2012 to review issues related to the use of PCR, in the context of broad surveillance role of GISRS, reagents and the WHO external quality assessment project (EQAP). WHO EQAP is in its 6th year in 2012. For panels 9 and 10 in 2011, the percentage of participating laboratories with 100% correct performance in the South-East Asia Region remained as high as 75%; however, in the Western Pacific Region, it dropped from 91.3% to 83.3%. Emerging needs have also been taken into consideration, e.g. antiviral susceptibility surveillance. A working group (WG) meeting took place in November 2011, finalizing protocols, guidance and advice, while practical approaches for NICs were discussed in the WG meeting in June 2012 (to be posted on WHO website). FluNet reporting is efficient, although there are two NICs in the South-East Asia Region and one in the Western Pacific Region that did not report anything since 1 May 2011. WHO Shipping Fund Project unfortunately has to be scaled down due to shrinking resources available in WHO Headquarters. Interim measures are being put in place while intensive efforts on fundraising are on-going.

Vaccine support is another key area of work for GISRS. WHO updated its recommendations on vaccine composition in September 2011 and February 2012 and continued playing a key role connecting CCs, ERLs, reasserting laboratories, International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) and other vaccine manufacturers on the development, evaluation and availability of high-growth reassortants and potency reagents. Due to financial constraints, the planned third consultation on improving influenza vaccine virus selection, planned for 2012, will be postponed to 2013.

Implementation of the PIP Framework since the adoption of World Health Assembly resolution WHA 64.5 has been ongoing with an Advisory Group set up to advise the WHO Director-General. Terms of reference (TORs) of GISRS laboratories, in the context of addition of the Pandemic Influenza Programme (PIP) TORs, are being reviewed engaging all members of GISRS. The influenza virus tracking mechanism (IVTM) has been functioning with educational models nearly finished.

WHO Headquarters, through an epidemiological group, continues its work on risk assessment, disease monitoring, clinical management and other activities, e.g. burden studies, pandemic mortality estimates and research agenda.

WHO, through its GISRS team in Headquarters, has broad collaboration and partnership within various units, departments and clusters in WHO Headquarters, Regional Offices and Country Offices. It also has built close collaboration with external partners from both public and private sectors. The GISRS team continues to be the interface of WHO with GISRS laboratories and coordinating body of GISRS associated activities.

2.1.4 Presentation 4: WHO External Quality Assessment Programme for the detection of influenza virus type A by polymerase chain reaction (PCR)

Dr Janice Lo, Public Health Laboratory Centre, Hong Kong

The “External quality assessment programme (EQAP) for the detection of influenza virus type A by PCR” was initiated in 2007, coordinated by the WHO Global Influenza Programme, and implemented by the H5 Reference Laboratory and NIC in Hong Kong. The background for undertaking this programme was varied, including the continually evolving pandemic and avian influenza situation as a global issue; recognition that efficient and reliable detection of novel influenza infections in humans is extremely important for global pandemic influenza outbreak response; and usefulness of PCR as the first choice
laboratory test for detection of potential pandemic infections, due to biosafety requirements on virus culture and the absence of higher containment facilities of many NICs.

Since the establishment of the programme in 2007, with two dispatches per year, the programme has evolved over time. The initial dispatch comprised ten ribonucleic acid (RNA) samples, including influenza A H1, H3 and H5 viruses, where 64 laboratories returned results and 77% of them reported all correct H5 results. Since then, changes in the programme included addition of influenza A(H1N1)pdm09 and influenza B (Victoria and Yamagata lineages) viruses, and removal of the seasonal influenza A H1 virus. In 2011, two gamma-ray inactivated viruses were included in addition to the RNA samples to evaluate nucleic acid extraction. In the last dispatch in 2011, 159 laboratories returned results and 89% reported all correct H5 results. A Good Laboratory Practice (GLP) Survey was undertaken in 2010, and another would be undertaken in 2012. From 2012 onwards, there would be one dispatch per year, and all samples would comprise gamma-ray inactivated viruses.

The number of participants in the EQAP has steadily increased over the years. The performance also has improved with time, even when new strains were included to provide continuous challenges, and gamma-ray inactivated viruses were introduced in addition to RNA samples. Continued provision of the EQAP is necessary to monitor the quality and comparability of laboratories that perform PCR diagnosis, since emergence of multiple genetic groups and continuous virus mutation requires continued review, update and validation of different primers and protocols and help to identify gaps of PCR testing in these laboratories.

2.1.5 Presentation 5: Influenza activity in the northern hemisphere

Dr Takato Odagiri, WHO Collaborating Centre, Japan

Influenza activity in most countries in the northern hemisphere (NH) started relatively later than the usual season. A(H3N2) and B were the predominantly co-circulating viruses, as A(H1N1)pdm09 activity was low in many counties. By antigenic and genetic analyses, A(H3N2) viruses tended to change from A/Perth/16/2009 vaccine-like virus to the current representative virus A/Victoria/361/2011. The prevalence of B/Yamagata-lineage viruses has been increasing in many countries and co-circulated with B/Victoria-lineage viruses in similar proportion. Due to the low levels and low cross-reactivity of serum antibodies in individuals elicited by the 2011-12 season vaccine against B/Yamagata-lineage viruses, the B component for the upcoming seasonal vaccine was selected from the B/Yamagata-lineage to stimulate antibody responses. The composition of the NH vaccine for the 2012-13 season can be seen in Weekly Epidemiological Record (http://www.who.int/wer/2012/wer8710.pdf).

2.1.6 Presentation 6: Influenza activity in the southern hemisphere

Dr Ian Barr, WHO Collaborating Centre, Australia

The influenza season for most countries in the Southern hemisphere (SH) follows a temperate pattern with the peak of influenza activity between June and September each year. Hence to date there has been little activity either in Australia, New Zealand, South Africa or South America. Unfortunately, little information is available in real time from the tropical countries in the region such as Indonesia and Papua New Guinea, although the latter has recently reported outbreaks of A(H3) viruses in the northern regions. Data from FluNet show that in the majority of SH regions, viruses have been A(H3) and B, with a few A(H1N1)pdm09 viruses circulating. In Australia, an increase in B/Yamagata-lineage viruses has been seen in 2012; however, B/Victoria-lineage viruses still predominate.
Many other sources of information on influenza circulation are now available via the internet such as Google Flutrends (http://www.google.org/flutrends/), which gives an estimate of influenza activity in a number of countries in the SH (including data for the past six years) but, unfortunately, not yet for those in the South East Asian tropical/subtropical regions.

The WHO SH influenza vaccine recommendation for the 2012 season is the same as 2011, so it will be interesting to see if the SH vaccine effectiveness is reduced as the 2012-13 NH vaccine contains an updated A(H3) component and a change in the B lineage to a B/Yamagata virus.

Discussion

Plenary Session One triggered many questions followed by discussion. Many participants expressed concern over the WHO transmission zone as it did not appear to be set up in a systematic way. It was established during the pandemic to help summarize data, with the attempt to group countries together that had similar transmission. It was acknowledged that the definition of the zone needed revision and evaluation to determine if it reflected reality. If it did, it could be a useful means for countries that do not have the resources to collect critically significant amount of data.

2.2 Plenary Session Two: Multi-country collaborations

Chair: Dr Ian Barr, Co-chair: Dr Geethani Galagoda

2.2.1 Presentation 1: Seasonal influenza manuscript and potential collaborative influenza strain circulation manuscript

Dr Jeffrey Partridge, Epidemiological Surveillance and Response (ESR) Regional Office for the Western Pacific

Dr Partridge presented an article as the collaborative outcome of the previous meeting. “Epidemiological and virological characteristics of influenza in the Western Pacific Region of the World Health Organization, 2006 – 2010” was published by PLoS ONE in May 2012. He then initiated discussions on another potential collaborative manuscript on influenza strain circulation.

2.2.2 Presentation 2: Potential collaborations: Exploring strain circulation, match and hemispheres

Dr Ann Moen, WHO Collaborating Centre for Surveillance, Epidemiology and Control of Influenza, US CDC, United States of America

Dr Ann Moen began the session on potential collaborations on vaccine match and circulating strains in the Western Pacific Region by presenting data on a question posed by the US Department of Defense (DOD) several years ago. In her talk, she addressed the following two questions:

1. Are common circulating influenza viruses different enough to warrant separate northern and southern hemispheric vaccines?

2. Is there insufficient cross-reactivity between the two vaccines to actually warrant DOD procurement of the two different vaccines?

Since 1999, vaccine strain selection has been taking place twice annually. For the current discussion, all occurrences when the Southern hemisphere vaccine was updated prior
to the Northern hemisphere vaccine were considered. It happened six times between 1998 and 2007, the period covered in the discussion. Data on the predominantly circulating strains were extracted from WHO vaccine packages, and the percentage of time when the new vaccine (southern hemisphere vaccine in this case) covered the circulating strains better was examined. In the end, there was only one time when the newer vaccine was found not to be superior to the northern hemisphere vaccine. In 2000, about 69% of the circulating strains matched the prior northern hemisphere vaccine better. There was discussion about the two lineages of Bs and it was difficult to guess which strains might circulate more. However, this problem may soon be alleviated by the licensure of a quadrivalent vaccine. The conclusion of the DOD talk was that the most recent vaccine was always the better vaccine. For policy making on an individual basis, there was evidence to warrant purchase of the updated vaccine for deployment to the southern hemisphere. Dr Moen’s talk also examined two examples of tropical climate countries, India and Brazil, and how they have argued for using different vaccines based on seasonality of the viruses. These examples generated the topic of a regional vaccine strain match paper with examples from the two subsequent speakers.

2.2.3 Presentation 3: Strain circulation analysis

*Dr Jeffrey Partridge, ESR, Regional Office for the Western Pacific*

Twice annually, WHO organizes consultations to analyze influenza virus surveillance data generated by the WHO GISRS, and then issues recommendations on the composition of the influenza vaccine for the following influenza season. The two seasons for which vaccines are formulated are the "northern hemisphere winter" and the "southern hemisphere winter." When a country has well-defined influenza seasonality that coincides with one of these seasons, as is the case for temperate northern and southern hemisphere countries, the choice of which vaccine formulation to use is straightforward. However, for countries with less well-defined seasons or with seasons not coincidental with the seasons for which the vaccines are formulated, as is the case with many tropical countries, the choice of which vaccine formulation to use is less obvious. Dr Partridge presented a quantitative approach to inform the participants which influenza vaccine formulation (NH or SH) will prevent more influenza-associated diseases in a country by using influenza like illness data, virus type/subtype data with specific data on virus strain in comparison to the vaccine virus strains.

2.2.4 Presentation 4: Example from data at a WHO collaborating centre

*Dr Sheena Sullivan, WHO Collaborating Centre for Reference and Research on Influenza, Victorian Infectious Diseases Reference Laboratory (VIDRL), Australia*

Dr Sullivan’s presentation followed on from Dr Ann Moen’s description of the rationale for determining strain match in tropical regions and from Dr Jeff Partridge’s presentation of a spreadsheet to calculate a strain match index. An example was presented using data from the WHO CC in Melbourne for a country from the Western Pacific Region, which was chosen for having the most data (~230 results per year) for 2007 and 2008, the years when a vaccine change occurred. The data abstracted included haemagglutinin-inhibition (HI) assay results and a specimen collection date. A virus was considered matched to the vaccine when the HI titre was ≤8-fold, while a non-match was recorded when the titre was ≥8-fold. The proportion matched for each month was inputted into the spreadsheet. The example showed how, in order to get any value for the index, there needed to be several specimens per month with HI assay results. Options for increasing the data were discussed, including grouping samples into three-month groups or by regions (e.g. WHO influenza transmission zones). Other limitations included not knowing the representativeness of samples received by WHO CCs and the uncertainty of HI-titre results.
Discussions following the presentations demonstrated the group’s desire to undertake future research in collaboration. However, there are obvious challenges, such as a lack of data, different laboratory techniques, too much variation between countries and areas, and challenges in data interpretation.

2.2.5 Poster session

A poster session offered the different NICs an opportunity to present information on recent influenza work. Eleven posters were displayed and discussed.

2.3 Plenary Session Three: Country presentations

Chair: Dr Ann Moen, Co-chair: Dr Phengta Vongphrachanh

2.3.1 Presentation 1: Country presentation – Viet Nam

*Dr Nguyen Thi Thu Yen, National Institute of Hygiene and Epidemiology, Viet Nam*

In 2006, with US CDC support, a national influenza sentinel surveillance system (NISS) was established with 15 sentinel sites throughout the country. Since 2010, surveillance for Severe Acute Respiratory Infection (SARI) was set up at five sites. The WHO case definition is used to identify influenza-like illness (ILI) and SARI patients. Each day the first two ILI and first SARI patients are enrolled for investigation. Throat swab specimens are collected and tested by reverse transcriptase–polymerase chain reaction (RT-PCR).

During the six years of data collection, 3,644,241 outpatients were screened. A total of 436,770 (12%) were ILI cases, of which 35,047 were tested and 7,344 (21%) were found positive with influenza. Influenza viruses circulate throughout the year in Viet Nam. Influenza A(H1N1) activity that usually peaks in May predominated in 2006 and 2008, whereas influenza A(H3N2) predominated in 2007, 2009, 2010, remained low in 2011, but has again increased in 2012. Influenza B virus circulates widely every year regardless of influenza A subtype circulation. Influenza B activity was highest from January to March in 2012. A(H1N1)pdm09 was first isolated in June 2009, peaked in September-November 2009, remained low in 2010, but circulated again in 2011 as the predominant A subtype. From 2006-2011, 487 influenza viruses were isolated, which accounted for 6.6% of the RT-PCR positive cases. The rate of virus isolation was low and ranged from 3% to 13%.

Out of 1,587 SARI cases tested in 2011, 135 (8.4%) were influenza positive. Among the positive cases, one was confirmed as avian influenza A(H5N1), 63 as influenza B, 47 as A(H1N1)pdm09, and the remaining 24 as A(H3N2).

There have been many achievements in Viet Nam. Examples of which are: establishment of a national influenza surveillance network, standardization and high-quality performance in all regional laboratories, establishment of ongoing monitoring of circulating influenza types/subtypes, documentation of epidemiological and virological information to guide the control and prevention policies, and contribution to global influenza surveillance and provision of virus strains for vaccine virus selection.

Some challenges too have been encountered, such as the system’s reliance on external funds and high turnover of surveillance staff.
2.3.2 Presentation 2: Country presentation – Thailand

Dr Thitipong Yingyong, Ministry of Public Health, Thailand

In 1963, the Bureau of Epidemiology (BOE) of Thailand established the national disease surveillance system (R506). Data is collected from all health care centres, public hospitals and some private health-care facilities. The system monitors trends of influenza and pneumonia in Thailand and detects abnormal trends to warn epidemiologist/public health staff regarding outbreaks.

The outbreak notification system serves as an event-based surveillance system for all reports of outbreaks in Thailand. Suspected avian influenza (AI) and pandemic influenza outbreaks prompt an investigation by local staff. Until late 2003, avian influenza was found only in poultry. Highly pathogenic avian influenza (HPAI) surveillance was conducted across the country.

The AI surveillance was transformed to support monitoring of the A(H1N1)pdm09 pandemic in March-April 2009. The objectives were to detect outbreaks in humans and for rapid response and containment within 24 hours of a confirmed case. However, the R506 and AI systems were not timely, so an ILI surveillance system was launched to collect the aggregated data of ILI patients and all patients visiting out-patient departments (OPD). This system aimed to monitor the trend of the proportion of ILI cases that visited the OPD by week to reflect the trend of influenza cases more timely than the R506 data.

In 2004, the Department of Disease Control (DDC) decided to immunize health-care workers and poultry cullers to prevent re-assortment of HPAI and influenza. In February 2010, the National Vaccine Institute (NVI) introduced influenza A(H1N1)pdm09 vaccine for all high-risk groups. After the pandemic in 2009, NVI reviewed and/or conducted some studies on influenza and pneumonia burden, seasonality, risk groups, viral circulation strains, medical costs, vaccine effectiveness and the benefits of influenza vaccines before introducing the seasonal vaccine as a national programme. Subsequently, seasonal influenza vaccine was introduced to the national programme and immunization of high-risk groups commenced.

2.3.3 Presentation 3: Country presentation – Papua New Guinea

Dr Paul Horwood, Institute of Medical Research, Papua New Guinea

Influenza surveillance has been conducted in Papua New Guinea since 2008. The National Influenza Centre (NIC) currently receives nasopharyngeal swab samples from two sites. Papua New Guinea NIC has recently made improvements in the detection of influenza viruses in the laboratory by adopting a suite of real-time RT-PCR assays from the US CDC. The CDC real-time RT-PCR assays were successfully adopted by Papua New Guinea NIC which was evidenced by the 100% correct results from EQAP Panel 10. With assistance from WHO, Papua New Guinea NIC has also established a cell culture laboratory to enable the isolation of influenza viruses.

During 2011, Papua New Guinea NIC processed 491 samples from the sentinel surveillance sites. This is a significant increase on the number of samples processed in 2009 (n=254) and 2010 (n=293). Training opportunities for local scientists have greatly improved the laboratory capacity of Papua New Guinea NIC. In 2011, two Papua New Guinea scientists travelled to the WHO Collaborating Centre for Reference and Research on Influenza (Melbourne) for training in real-time PCR, cell culture and sequence analysis.
2.3.4 Presentation 4: Country presentation – Australia

Dr Dominic Dwyer, Westmead Hospital, New South Wales

The three Australian WHO NICs are located in Sydney (at the Institute for Clinical Pathology and Medical Research), Melbourne (Victorian Infectious Diseases Reference Laboratory) and Perth (PathWest Laboratory Medicine). The laboratories are part of the Australian Government’s Public Health Laboratory Network. All provide a wide range of influenza diagnostics and referral testing for both urban and rural locations: virus isolation and subtyping, nucleic acid testing (NAT, between 4000 and 10 000 annually), direct and rapid antigen testing, genotypic and phenotypic resistance, and serology. The three NICs send approximately 200 isolates annually to the WHO CC in Melbourne for detailed phenotypic and genotypic analyses, and report the numbers to their relevant State Departments of Health and to WHO via FluNet. The NICs participate in various community and hospital surveillance programmes for influenza and other respiratory viruses as well as undertake influenza-related research.

2.4 Plenary Session Four: Revisiting national influenza surveillance

Chair: Dr Anne Kelso, Co-chair: Dr Narangerel Dorj

2.4.1 Presentation 1: New Technical guidance

Dr Katelijn Vandemaele, WHO/Headquarters

Historically, influenza surveillance focused on the collection of virus specimens to guide the selection of vaccine strains, to monitor drift and mutations and trends over time. The pandemic highlighted the need for more information on disease activity, especially information on the severe end, and the need for a standardized and international reporting mechanism. Therefore, WHO is now issuing global epidemiological surveillance standards. Influenza surveillance ideally consists of an early warning and a routine indicator based influenza surveillance component. The new guidance is providing a set of standards for the basic minimum routine influenza surveillance component. Sentinel surveillance for ILI and SARI is the surveillance method of choice. The following elements of influenza surveillance were presented: the recommended case definition for ILI and SARI, how to select sentinel sites, the minimum data elements to collect, recommended sampling methods, how to set baseline and thresholds, and the importance of monitoring and evaluation. The guidance will be posted for two months on the WHO influenza website for comments.

There was a lot of discussion around the change in the case definition. Many questions arose on how the definition was formulated and further information was requested on specific technical areas and the researched evidence. The definition will be put on the WHO website for three months for consultation.

2.4 Group work: Revisiting national influenza surveillance

When influenza surveillance data among countries are compared some differences often become apparent. However, these differences could be attributed to the way the individual surveillance systems are organized, and should not be taken as representing the actual situation, e.g. we can not necessarily conclude that Country A has a greater influenza burden than Country B just by looking at the surveillance data from the two countries. With respect to case finding, there could be differences related to the number and location of the sentinel sites and how representative the specimens collected at these sites are in terms of, for example, age groups and ethnicity. Additionally, the strategy for sampling or selecting the cases from whom specimens are collected for laboratory confirmation may also explain these
differences. Finally, it could depend on what type of data is being collected and how this is being used, e.g. the possibility of combining epidemiological and laboratory data.

To better understand and interpret surveillance data among different countries, group work was conducted. All participants were assigned to three break-out groups to separately discuss key elements of influenza surveillance, namely case finding (group A), sampling (group B), and data collection and reporting (group C). Each group had 1 hour and 15 minutes to discuss their topic. Afterwards, all three groups re-convened and the chairs of each group provided presentations of their findings followed by a brief discussion.

Discussions found that there were various methods for how sentinel sites are selected in each country or area with factors including region, population size and ease of access, e.g. proximity to airport. While there is a good representation of basic demographic data, including age and sex, it is difficult to determine if all ethnic groups are represented as information regarding ethnicity is not collected in most countries and areas.

The sampling strategies are dependent on each country’s or area’s objectives. It was generally agreed that to reduce bias on results the sampling strategy needs to be systematic. Selection bias could be introduced by location of sample collection, e.g. hospital vs. GP/private clinic, geographical location (urban vs. rural), and time of sample collection.

Common objectives of the sampling strategy included early detection of outbreaks, detection of new strains and collection of epidemiology/virology information about influenza virus circulation (including seasonality). Some countries list early warning as part of system objectives, but the systems are not designed to perform such functions (e.g. collect only small number of specimens per week or deal with timeliness issues). Quality of data needs improvement considering large number of sites. Type of analyses is dependent on funding capacity and resources.

Countries and areas expect information from regional and global levels to include type and subtypes circulating regionally and globally, severity of season, at-risk populations, drug sensitivity, vaccine availability, virus mutations, vaccine matching to circulating strains, specific tests and data for emerging strains, and burden of influenza including economic aspects. Participants expressed that they would also like to have a greater involvement in policy changes.

Overall, it is important for countries to be clear about the purpose of surveillance and what can be obtained from their systems. It is valuable to collect data in a systematic manner to meet the objectives of the surveillance system. The priority should be collecting good quality, useful data, rather than aiming to collect large quantities of data.

2.5 Plenary Session Five: Data to inform influenza vaccine use/guidance

Chair : Dr Michael Shaw  
Co-chair : Dr Ondri Dwi Sampurno

2.5.1 Presentation 1: Surveillance data to inform public health decision making – Australia

Dr Kate Pennington, Department of Health and Ageing, Australia

Dr Pennington’s presentation provided an overview of the various influenza surveillance systems that are used in Australia to inform public health decision making. The role of influenza surveillance in public health decision making was highlighted in the following functions: to provide an early alert; to characterise the season and the viruses circulating; to evaluate the impact of measures; to assess disease burden; and to provide data
in a timely manner. In terms of vaccination recommendations, it was noted that surveillance data play an essential role in informing not only vaccine composition, but also populations that should be targeted for vaccination under their National Immunisation Programme.

2.5.2 Presentation 2: Surveillance data to inform public health decision making – Malaysia

Dr Apandi bin Yusof, Institute for Medical Research, Malaysia

The virology unit in Institute for Medical Research, Kuala Lumpur was designated as NIC in 1968. Since then it has continued to carry out influenza surveillance activities for the Ministry of Health. ILI data were collected from >26 sentinel sites, which consist of outpatient departments of the government health clinics. Between 2004 and 2011, a total of 11,875 ILI and SARI clinical specimens were received. Among them, 10.8% (1279/11,875) were positive for influenza virus. Of the positive cases, 66.5% (850/1279) were influenza A and 33.5% (429/1279) were influenza B positive. Although influenza viruses circulate throughout the year, the peak is normally between May to August. This pattern is generally similar to countries in the southern hemisphere. Surveillance activities are important to ensure a good match between the vaccine strains and actual circulating strains. Therefore, the statistics emphasizes the importance of a local influenza surveillance programme not only as an early warning of upcoming epidemics but also as a means to develop appropriate annual influenza vaccines.

2.5.3 Presentation 3: Surveillance data to inform public health decision making – Republic of Korea

Ms Sunhee Park, Korea Centers for Disease Control, Republic of Korea

Republic of Korea's influenza surveillance is called the Korean Influenza Surveillance Scheme (KISS). The objectives of KISS are early detection of any increase in ILI in Korean communities, efficient performance for prevention and management of influenza epidemic, and strengthening of surveillance and management system preparing for pandemic influenza. The 840 weekly and 100 daily participating clinics operate in ILI, and 96 clinics participate in laboratory surveillance to monitor influenza virus types. Based on the surveillance data, the Korea Centers for Disease Control and Prevention (KCDC) decides the national baselines and declares nationally an "alert" for an influenza outbreak. Additionally, KCDC recommends influenza vaccines to high-risk groups who have not been vaccinated. KCDC recommends influenza vaccination from October to March the following year. During an outbreak, national health insurance covers at-risk groups for influenza antiviral drugs, for example, Tamiflu or Rerenza. KCDC publishes weekly and annual surveillance data by various ways, via website, email, and hard-copy.

2.5.4 Presentation 4: Surveillance data to inform public health decision making – New Zealand

Dr Sue Huang, Institute of Environmental Science and Research, New Zealand

Dr Huang described the impact of influenza surveillance and research data on vaccination policy in New Zealand. Three examples were used.

(1) The impact of the 1996 surveillance data on the vaccination policy:

There was no government policy on influenza vaccination before 1997. Overall, the international classification of diseases (ICD)-coded influenza mortality rates for hospital patients were quite high during 1990-1996. In 1996 in particular, 94 people died of influenza caused by AH3N2. Among them, 93 people were aged over 65 years.
In 1997, the government made a policy change. It arranged to provide free influenza vaccination for all people over 65 years of age. In 1999, this policy was extended to risk groups less than 65 years old. Since 1997, influenza mortality has decreased. Limited evaluation based on the surveillance and vaccine uptake data show an association of increase of vaccine uptake with the decrease of the mortality rate. But the surveillance data are not sufficient to prove the causation. Data from research such as vaccine effectiveness and better mortality estimate would help our understanding of the issue.

(2) The potential impact of the 2005 surveillance data on the vaccination policy:

Influenza B (Victoria-lineage) caused the biggest B epidemic in 2005 and school-aged children (5-19 years old) were affected the most, with high virus detection and rates of hospitalization. Three otherwise healthy children died from influenza B and many schools were closed during the epidemic. The proposal for vaccination for school-age children was raised but no decision was made. Other factors such as financial consideration, overall low hospitalization/mortality rate of the group compared to very old/very young age groups, and not being a priority group according to SAGE recommendations may also have influenced the decision-making process.

(3) The impact of the 2009 pandemic sero-survey and surveillance data on the vaccination policy:

Immediately after the first wave of the pandemic, a multistage, randomized, cross-sectional seroprevalence for the pandemic virus was conducted. One of the major aims was to inform vaccination policy. The largest increase in immunity between post-pandemic and pre-existing immunity was observed in school-aged children 5-19 and 1-4 years. However, no increase was observed in the oldest age group, but they had the highest pre-existing immunity. In addition, the pandemic hospitalization data showed that young children aged 0-4 years had much higher hospitalization rate than children aged 5-19 years. Considering the data from serosurvey and also from hospitalizations, the Ministry of Health extended eligibility policy for pandemic vaccine in 2010 by including all children aged less than 5 years.

2.6 Plenary Discussion: Is there a role for GISRS in providing data for national decision making for influenza vaccine introduction?

Facilitator: Dr Lance Jennings, Canterbury Health Laboratories, New Zealand

The discussion commenced by revisiting the process for influenza vaccine guideline development and vaccine introduction in countries within different climatic zones in the Asia-Pacific region. In New Zealand, although influenza vaccine had been available in the private sector for many years, government-funded vaccine for the elderly was not introduced until 1997 following a review of national surveillance and mortality data. Extension of this policy to include children >6 months and adults <65 years with certain medical conditions followed two years later after a systematic review of the literature and definition of the risk groups. A target was set for 75% coverage of the elderly and funding was allocated for education and pandemic preparedness planning. The National Influenza Strategy Group (NISG) was formed in 2000 as a public-private partnership involving influenza and public health experts, the Ministry of Health, and the contract vaccine supplier. NISG has been responsible for national influenza awareness education since.

The triggers for policy development in Australia were vaccine shortages in the early 1990s. Influenza, public health experts and key clinicians from each State were brought together to form a group now called the Influenza Specialist Group (ISG). This group was
industry funded and served to educate the key clinical opinion leaders, standardize the key messages on influenza, its severity and the benefits of vaccine nationally. The presence of the WHO CC in Melbourne and data from a General Practice Surveillance (GPS) and laboratory networks was an important part of the education process and public messaging strategy.

In tropical countries, influenza health priorities focused on influenza H5N1, and seasonal influenza other than for travellers to the Hajj and other religious pilgrimages. Indonesia encouraged the vaccination of pilgrims although had no recommendations for compulsory vaccination, although the country manufactured 200,000 doses of influenza vaccine annually for administration to these groups. Similarly, Singapore recommends vaccination for pilgrims although all vaccination is carried out by the private sector. Considerable discussion centred on the vaccination of pilgrims and the difficulty in accessing Halal influenza vaccine which would meet the criterion for such pilgrims.

A regional success story is Thailand which, since the formation of the Influenza Foundation of Thailand in 2005, has moved from seasonal vaccination focus on poultry workers to the introduction of the WHO guidelines and administration of 3.5 million doses of influenza vaccine in 2012. During this time, influenza hospitalization and burden of disease and cost-effectiveness studies have been carried out which have been used to support vaccine policy development.

The consensus on those countries in the tropical and subtropical zones was that few had countrywide influenza surveillance in place or influenza burden data available. None or few had a seasonal influenza vaccination programme in place. On the other hand, countries in temperate zones, where influenza surveillance was in place, winter influenza activity was seasonal and well-defined. Some countries had some burden of disease data available and had vaccine policies or guidelines and vaccination programmes in place. The challenge will be to understand the key drivers for vaccine policy development in countries in the tropical and subtropical zones within the SEA and Western Pacific Regions.

2.7 Plenary Session Six: Technical presentations and discussions

Chairs: Dr Babatunde Olowokure, WHO Viet Nam, and Dr Nora Chea, WHO Cambodia

2.7.1 Presentation 1: Overview of swine origin influenza virus infection in the United States

Dr Xiyan Xu, WHO Collaborating Centre for Surveillance, Epidemiology and Control of Influenza, US CDC, United States of America

Swine influenza viruses have been recognized as important pathogens for pigs. Occasional human infections with swine origin influenza viruses (SOIV) have been reported previously. During the past two decades, more than 40 human cases of SOIV infections have been identified in the United States. Six viruses isolated from 1990 to 1995 were recognized as classical SOIV A(H1N1). After 1998, SOIVs recovered from human cases were characterized as triple reassortant (trSOIV) inheriting genes from classical swine, avian and human influenza viruses. Of those trSOIVs, thirteen viruses collected between 1998-2009 were A(H1N1); the majority of trSOIVs collected since 2010 were A(H3N2). A (H3N2) trSOIVs or variant H3N2 viruses (H3N2v), identified in 2011, obtained their M gene from a human A(H1N1)pdm09 virus. SOIVs characterized were antigenically and genetically closely related to the subtypes of influenza viruses circulating in pigs but distinct from contemporary influenza viruses circulating in humans. Although such infections appear to be infrequent, isolation of swine origin viruses from humans repeatedly demonstrate the potential of further reassortment of such virus with other viruses which may result in efficient
transmission of novel viruses among humans. Strengthening influenza surveillance, therefore, plays a key role in early detection and identification of novel influenza virus.

2.7.2 Presentation 2: A widespread community cluster of H275Y oseltamivir-resistant A(H1N1)pdm09 influenza in Australia

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

Since the emergence of the pandemic A(H1N1)pdm09 influenza viruses, oseltamivir-resistant A(H1N1)pdm09 viruses have been detected at a low frequency (≈1%). However, data from the UK, USA and the Asia-Pacific region between 2009 and 2011 show that an increased proportion of resistant viruses are being taken from untreated patients, suggesting increased transmission of these viruses. In 2011, oseltamivir-resistant A(H1N1)pdm09 viruses caused a cluster of community influenza cases in the Newcastle region of Australia. Twenty nine (15%) of 191 A(H1N1)pdm09 viruses collected between May and September 2011 from Hunter New England (HNE), Australia, contained the H275Y neuraminidase substitution responsible for oseltamivir resistance. Only one patient had received oseltamivir before specimen collection. The resistant strains were genetically very closely related, suggesting the spread of a single variant. Ninety percent of cases lived within 50 km. Three genetically similar oseltamivir-resistant variants were detected outside of HNE, including one strain from Perth, approximately 4000 km away. Computational analysis predicted that neuraminidase substitutions V241I, N369K and N386S in these viruses may offset the destabilizing effect of the H275Y substitution. This cluster represents the first widespread community-transmission of H275Y oseltamivir-resistant A(H1N1)pdm09 influenza. These cases and data on potential permissive mutations suggest that currently circulating A(H1N1)pdm09 viruses retain viral fitness in the presence of the H275Y mutation and that widespread emergence of oseltamivir-resistant strains may now be more likely.

2.7.3 Presentation 3: Antiviral-resistant B virus with a novel mutation detection by antiviral resistance surveillance in Japan

Dr Masaki Imai, WHO Collaborating Centre for Reference and Research on Influenza, NIID, Japan

An influenza B virus, designated B/Kochi/59/2011, was isolated using Mardin-Darby canine kidney (MDCK) cells at the public health laboratory in Kochi prefecture during the 2010-2011 influenza season in Japan. Neuraminidase (NA) inhibition assays revealed that this virus exhibited reduced susceptibility to NA inhibitors, oseltamivir, zanamivir, peramivir, and laninamivir. Sequence analysis showed that the resistant B virus contained a mutation in NA (G140R) not previously reported as NA inhibitor resistance. However, an influenza B virus possessing the G140R mutation was not recovered from the same clinical specimens in MDCK cells maintained in the National Institute of Infectious Diseases (NIID). In addition, the G140R mutation was not detected in the original clinical specimens using either conventional sequencing or pyrosequencing. These results suggest that the resistant B virus with the G140R mutation may be present in very low proportions in clinical specimens and preferentially propagated only in MDCK cells at the local laboratory. Thus, the study highlights that proper maintenance of MDCK cell cultures is crucial to precision surveillance and monitoring for the emergence of antiviral resistance.
2.7.4 Presentation 4: Models for influenza surveillance and early warning

*Dr Wang Dayan, WHO Collaborating Centre for Reference and Research on Influenza, China CDC, China*

One of the primary efforts in influenza vaccine strain recommendation is to monitor through gene sequencing the viral surface protein haemagglutinin (HA) variants that lead to viral antigenic changes. In the study in China, a computational method, denoted as PREDAC, to predict antigenic clusters of influenza A (H3N2) viruses with high accuracy from viral HA sequences was used. Application of PREDAC to large-scale HA sequence data of H3N2 viruses isolated from diverse regions of mainland China identified 17 antigenic clusters that had dominated for at least one season between 1968 and 2010. The coupling of large-scale HA sequencing with PREDAC can significantly improve vaccine strain recommendation for China. There are also other published models, including models for HI data analysis, and sequence-based models for antigenic change, disease burden of influenza virus, et al. We should make full use of models to benefit our surveillance work and improve our capacity on early warning.

2.8 Panel discussion: The future of GISRS

*Moderator: Dr Wenqing Zhang*

**Highlights of Dr Wenqing Zhang’s discussion:**

The year 2012 is the 60th anniversary of GISRS. Looking back, from a network of limited resources and capacity ten years ago to a global mechanism for health security with well-equipped and functioning laboratories covering 108 countries, the value of GISRS has been demonstrated through its responses to the avian influenza A(H5N1) outbreaks since 2003. Since 2007, GISRS was under scrutiny of intergovernmental (IGM) process on virus sharing and benefit sharing, which concluded its debate in May 2011 with a WHA resolution 64.5. Indeed GISRS was highly acknowledged in the formal report of International Health Regulations (IHR) review of response to the pandemic A(H1N1)pdm09.

With increased awareness of influenza as a disease, but declining global economy and subsequent shrinking of resources, GISRS is facing a major challenge: timeliness and quality of global surveillance and response vs. reduced financial resources. Sustainability is an increasingly serious challenge for GISRS in the coming future, in particular in resource-scarce countries. WHO will work with members of GISRS on how to best use the available resources to deliver key products of public health entrusted to GISRS.

Another big challenge is issues associated with the implementation of PIP Framework, officially in effect since May 2011. Workload, perceptions of collaborators outside of GISRS, ongoing collaboration within and outside of the network, adjustment of structure/cooperation of GISRS etc. are all elements that should be taken into consideration from the perspective of the role of public health of GISRS.

An advantage of GISRS is the continuous public health needs arising from the constantly-evolving influenza viruses - the nature of influenza viruses decides. A strength GISRS has is the high technical capacity, dedicated staff and collaborative institutions, as one united global team. GISRS, with its open mind, passion and inspiration, will continue to meet the expectation of public health needs in the future.
Highlights of Dr Anne Kelso’s discussion:

From the perspective of one of the WHO Collaborating Centres, GISRS has several outstanding strengths. It is a truly global network of laboratories which now cover most member states and has extensive collaborative links within and outside of GISRS. The CCs receive good financial support from their national governments and GISRS, overall, has received extraordinary support from the US CDC. Most countries contribute strongly to GISRS through their NICs and other laboratories, and there is sharing of technical expertise among CCs and NICs to improve the capability of the overall network. There are, however, some challenges for the future. It is important to expand population coverage further by developing NICs in additional countries and achieving better coverage within countries. Financial resources are declining so new sustainable funding sources and greater technical efficiencies will be needed to maintain and expand laboratory surveillance and training activities. The collaboration also needs further strengthening through improved two-way communication of virological, epidemiological and other data between NICs and CCs. Finally, continuous improvement of the timeliness and quality of virus samples submitted to CCs will enable the greatest benefit to global health to flow from the work of the NICs.

Highlights of Dr Michael Shaw’s discussion:

Future of GISRS H5 Reference Laboratories:

There are many common issues affecting all GISRS laboratories in the current climate of budget concerns. However, because of their specific functions, the WHO H5 Reference Laboratories have some unique challenges and are especially impacted by the PIP Framework adopted by the WHA in May of 2011.

Shipping of specimens and isolates:

The sporadic and unpredictable nature of cases of human cases of highly-pathogenic avian H5N1 infection means that materials shipments cannot be planned in advance and must be arranged on short notice. WHO H5 Reference Laboratories can expect to be asked to cover the costs of shipping specimens for confirmation and analysis. Budget constraints make it impractical to rely on the WHO Shipping Fund used for the submission of surveillance specimens by NICs and it is not reasonable to expect the originating country to cover shipping expenses in many cases.

PIP Framework requirements for materials received and sent:

Essentially, all specimens and isolates handled by the H5 Reference Laboratories fall under the definition of PIP Biological Materials in the new PIP Framework. It means that time and personnel must be allocated to ensure compliance with the new requirements. This includes entry into Influenza Virus Traceability Mechanism (IVTM) and explanation of the new requirements to those requestors of materials that are not familiar with the Framework. For academic and institutional requestors accustomed to free and unencumbered exchange of research materials, the PIP Framework has generated concern over potential legal obligations requiring case-by-case explanations and referral to the WHO PIP Secretariat for interpretation.

Relationships with animal health ministries and authorities:

Knowledge of circulating nonhuman influenza viruses is needed to ensure that reagents for diagnostics and characterization of strains infecting humans are current and reliable. Exchange of information between human and animal health organizations is required which means the differing interests must be recognized. Because agricultural ministries in particular
are often focused on economic impact with human health a secondary consideration, agreements to share surveillance and virologic data must be put in place to ensure that business interests are protected without compromising our public health mission. Progress in establishing agreements with partner organizations and ministries has been encouraging but more efforts are needed to educate policy makers on the importance of the human-animal interface for decisions affecting public health.

Highlights of Dr Masato Tashiro’s discussion:

Essential Regulatory Laboratory (ERL) is an important component and a core member of GISRS, although most NIC staff of member states is not familiar with its essential roles. Several issues of ERL should be solved.

(1) Terms of Reference (TOR) of ERL should be formalized.

Different from other components of GISRS, TOR of ERL remains yet to be defined. Current functions of ERL include i) production, calibration and standardization of test reagents for quality assurance (QA) and quality control (QC) of influenza vaccines and provision of them to national regulatory agencies of member states as well as vaccine manufactures in a timely manner; and ii) human serology studies to investigate immune responses induced by current influenza vaccines to reference viruses and vaccine candidate viruses for the next influenza season. During discussions of Pandemic Influenza Preparedness (PIP) Framework, TOR of ERL was discussed but did not reach a consensus. Formalization of TOR for ERL is an urgent issue for GISRS.

(2) Designation process of ERL

Currently, four ERLs are working in GISRS: the National Institute for Biological Standards and Control (NIBSC) of UK, the Center for Biologics Evaluation and Research/Federal Drug Administration (CBER/FDA) of USA, Therapeutic Goods Administration (TGA) of Australia and the National Institute of Infectious Diseases (NIID) of Japan. As influenza vaccine manufacturers are increasing in number, especially in middle-income countries, the responsibility of each ERL is increasing beyond current capacity. In the future, therefore, additional National Reference Libraries (NRLs) would be needed to cover the global demand. In that case, designation process of NRLs should be formalized beforehand.

(3) Collaboration with national regulatory authorities (NRAs) of Member States

NRL is responsible for quality assurance/quality control (QA/QC) of influenza vaccines by NRA of member countries which produce or/and use influenza vaccines. Intimate collaboration with NRAs is, therefore, essential. Collaborations should include information sharing, technical transfer and international harmonization and standardization of reference materials and reagents. Furthermore, a pre-qualification of influenza vaccine system would be established to avoid unnecessary duplication and to save time in case of emergency response in a pandemic.

(4) Improvement of vaccine potency testing

Potency of current influenza vaccines, except for live attenuated vaccines, has been determined by the single-radial immunodiffusion (SRID) test, for which ERLs develop and produce reagents and provide them to NRAs and vaccine manufactures. As it takes more than 6-8 weeks to prepare the reagents, especially sheep anti-sera against purified HA antigens, it is needed to develop more rapid, concise and reliable potency test methods to replace SRID to shorten the production period of influenza vaccines.
(5) Limitation of egg-based influenza vaccines and introduction of tissue culture cell-based vaccines

Most current influenza vaccines are produced in embryonated hen eggs because of convenience, low cost and affordable capacity. However, recent isolates of H3N2 and B viruses have been shown that once adapted to eggs, antigenicity of the viruses will change to such an extent that vaccine efficacy tends to reduce. To overcome this phenomenon, tissue culture cell-based vaccine production system has been developed by WHO CCs/ERLs in collaboration with vaccine industries. In parallel, seed viruses for cell-based vaccine productions and relevant QA/QC reagents should be established.

(6) Collaboration with vaccine manufactures

To develop, produce and supply efficient and safe vaccines in a timely manner, efficient collaboration with vaccine industries is essential, including information sharing and technical harmonization. WHO GISRS has developed a transparent and fair mechanism of collaboration with private influenza vaccine manufactures, based on PIP Framework. This should be implemented formally as soon as possible and, if needed, refined in the future. On the other hand, conflict of interest should be strictly controlled to avoid any doubt from outside and to keep member states’ trust.

Highlights of Dr LE Thi Quynh Mai’s discussion:

National Influenza Center (NIC) is a member of GISRS and plays a role as an essential part of national influenza surveillance. There are two main functions of NIC:

(1) National function: To use National Influenza Surveillance System (NISS) to monitor influenza viruses and provide scientifically valid information, including animal influenza viruses with human pandemic potential and technical guide for national preventive policy.

(2) Global function: To share epidemiological, virological data and materials to WHO reference laboratories and GISRS.

The NIC’s functions may not change much in the future. However, to sustain and enhance the activities of NICs, the following issues need to be addressed.

To sustain the sentinel surveillance system:

Sentinel sites are the core of influenza surveillance systems. The influenza sentinel sites should be selected by geography, climates (tropical, subtropical, temperate), societies (developed, developing countries) and sampling to be representative by ages, times, subtype etc.

To improve testing strategy:

Presently, the molecular tests (conventional RT-PCR, real-time RT-PCR) have been widely applied. They provide good sensitivity, specificity, and timely and convenient results for identification of influenza infections as well as basic genetic information. Furthermore, the EQAP has been set up and works well. It may help the NIC staff refine their skills as well as be more confident in their work. However, molecular tests are not being used for antigenic characterization, and viral isolation requires the next step of influenza testing. The viral isolation standards of operation are not available since inoculation systems (cell lines, eggs) are not standardized. EQAP of viral isolation is also not available.
To monitor viral susceptibility to antiviral drugs:

Since antigenic variants of avian influenza A/H5N1 virus has been affecting some countries, a common A/H5N1 vaccine is not available. The antiviral drug is the first tool of treatment. However, the number of influenza antiviral drugs is limited and drug resistance to human/avian influenza is being identified more often. The strategy of antiviral resistance monitoring should be better developed.

Discussions commenced with questions around the supply of reagents. If the reagents are used for surveillance purposes then the products are free of charge; however, there is some cost recovery, e.g. shipping costs, involved.

It is not known how long funding will last, so countries and areas are encouraged to put systems in place that they will be able to sustain. It is also important for country and areas to build their own system and develop ownership. There is every indication that the network will always be available to give technical advice.

3. SUMMARY AND CLOSING SESSION

Dr Jeffrey Partridge, Epidemiological Surveillance and Response (ESR) Regional Office for the Western Pacific

Dr Partridge presented a summary of the meeting and highlighted some of the positive results, including a better understanding of the role of GISRS in providing data for vaccine policy development. He referred to the initial work on a collaborative multicounty strain analysis paper. Dr Partridge thanked the participants, particularly the presenters and the chair persons, and concluded with a hope for the ongoing work and future collaboration.

Dr Patrick O’Connor, Immunization and Vaccines Development (IVD) Regional Office for South-East Asia

South-East Asia Region is well placed to provide regional technical support in the following areas: strengthening regional and national preparedness and response capacity for pandemic influenza; standardizing and harmonizing seasonal and pandemic influenza surveillance with the existing vaccine preventable diseases (VPD) surveillance networks; and supporting surveillance activities with a robust and extensive regional laboratory network. The Disease Surveillance and Epidemiology (DSE) unit of the Communicable Disease Surveillance (CDS) Department and the Immunization and Vaccines Development (IVD) unit of the Family Health and Research (FHR) Department have been jointly tasked with administering these activities. The future work over 2012-13 will concentrate to find synergies at the country level between the National Influenza Centers and the Vaccine Preventable Surveillance Programmes and look at the need for conducting burden of disease activities for national decision making. There are many opportunities for increased collaboration at the regional and national levels.

Dr Ann Moen, WHO Collaborating Centre for Surveillance, US CDC

The quality of the work presented in these meetings has grown over the years and is important for global prevention and control of influenza. Dr Moen encouraged participants to contribute to their own systems and advocate for the work they do. They were advised to consider how the data could benefit their own countries and to think broadly for public health
good. They should reach out and talk to other countries, initiate interactions in the area to bridge the gap between epidemiology and laboratory work.

*Dr Babatunde Olowokure, WHO Viet Nam*

Dr Olowokure spoke on behalf of Dr Takeshi Kasai and Dr Tran Thanh Duong to thank the participants for their attendance and contribution. He noted that the meeting had offered a valuable opportunity to discuss ideas and learn from each other.

He gave special thanks to Dr Partridge and the team for facilitating an excellent meeting. From his personal experience, he found the meeting to be a good event and knew that Viet Nam had been proud to host such a successful event. He declared the meeting closed.

A site visit to the National Institute of Hygiene and Epidemiology was conducted in the afternoon of the last day.

4. EVALUATION

Thirty-five people filled out the evaluation form. The majority said that the objectives of the meeting were met and that the meeting was well prepared. People felt that they had adequate opportunity to learn new skills, exchange knowledge, and have comprehensive discussions with other participants. All respondents agreed that the meeting was personally worthwhile to attend.

There was a range of new skills and concepts obtained during the meeting. Many people noted that they benefited from the information and discussions on the use of data to influence policy decision, the new technical guidance, and movement of viral strain across the Regions and the decision for vaccination. Respondents’ recommendations for the seventh meeting included more group work discussions, more involvement from NICs rather than from WHO CCs, and more time allocated for general discussion.

5. CONCLUSIONS AND RECOMMENDATIONS

Countries and areas have made significant progress in developing influenza surveillance. Moving forward, countries and areas need to review their influenza surveillance systems, in accordance with the five-year plan (2012-2016) for national influenza surveillance. In addition, as recommended at the Fifth Meeting of National Influenza Centres in the Western Pacific and South-East Asia Regions in 2011, GISRS in the Regions should further develop its role in supporting the development of vaccine policy, and countries and areas should explore opportunities for multi–country data analyses and research collaborations to combine and maximize efforts. This meeting strengthened influenza surveillance for detection and response as well as for vaccine policy development in the Western Pacific and South-East Asia Regions.

During the meeting, discussions arose regarding the minimum requirements for comprehensive influenza surveillance that would be compatible with the five-year plan (2012–2016) for national influenza surveillance. Overall, it is important that countries are clear about the purpose for surveillance and what can be obtained from their systems. It is
equally important to collect data in a systematic manner to meet the objectives of surveillance. There should be a greater focus on collecting good quality, useful data, rather than merely large quantities of data.

There was a discussion around the role of GISRS in providing research data for vaccine policy development. The process for influenza vaccine guideline development and vaccine introduction in countries within the different climatic zones in the Asia-Pacific region was discussed. Few countries in the tropical and subtropical zones had countrywide influenza surveillance programmes, vaccination programmes, or influenza burden data available. Countries in temperate zones, where influenza surveillance was in place, had vaccine policies or guidelines and vaccination programmes. The future challenge will be to understand the key drivers for vaccine policy development in countries in the tropical and subtropical zones within the Regions.

GISRS, a global network of laboratories, now covers most Member States in the Regions and has extensive collaborative links within and outside of its own structure. However, with increased awareness of influenza as a disease but declining global economy and subsequent shrinking of resources, GISRS is facing numerous challenges. Sustainability will be an increasingly serious challenge in the coming future, especially in resource-scarce countries. Countries and areas are, therefore, encouraged to put systems in place that they are able to sustain and build and develop ownership.

A multi-country collaboration was initiated to develop of scientific manuscript(s) to document current influenza vaccine use and to provide epidemiological details to guide future influenza vaccine use in the Regions. It was noted that this is a challenging task but useful to gain comprehensive knowledge of influenza in the Regions to be able to guide policy and prepare for future pandemics. It is particularly useful for those countries and areas that do not have adequate resources to conduct research at the country level.

The meeting was an excellent opportunity for participants to meet and share experiences. From the meeting it was agreed that countries and areas should review the new global guidance for influenza surveillance vis-à-vis the implementation of the five-year Biregional Plan for Further Strengthening National Influenza Surveillance. It was also agreed that multi-country collaborations for the development of scientific manuscript(s) should be pursued, starting with the documentation of current influenza vaccine use across the region. It was recommended that the next biregional meeting be structured in a way that allows both combined and separate laboratory-oriented and epidemiology-oriented technical sessions.
ABSTRACTS FOR POSTER PRESENTATIONS AT THE SIXTH MEETING OF NATIONAL INFLUENZA CENTRES IN THE WESTERN PACIFIC AND SOUTH-EAST ASIA REGIONS

MANAGEMENT AND QUALITY EVALUATION OF NATIONAL INFLUENZA SURVEILLANCE

Dayan Wang\textsuperscript{2,3}, Jiandong Zheng\textsuperscript{2}, Haijun Su\textsuperscript{1}

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2 Chinese Center for Disease Control and Prevention

3 WHO Collaborating Center for Reference and Research on Influenza

Background: The influenza surveillance system in mainland China includes the following: ILI surveillance in outpatients of sentinel hospitals; ILI/ARI outbreak report; SARI sentinel surveillance in inpatients; national notifiable communicable disease reporting; etiology-unknown pneumonia surveillance; and Sero-epidemic Surveillance of Highly Pathogenic Avian Influenza in Population with Occupational Exposure and Environmental Surveillance of Highly Pathogenic Avian Influenza. Quality evaluation is an essential part of the national surveillance for improvement and maintenance of capacity.

Methods: Every year, CNIC conducts EQAP evaluation of the influenza network labs. The panel includes 10 samples, which is \( \beta \)-propiolactone inactivated egg isolates. About 20 indicators were developed for quality evaluation of the Centers for Disease Control and prevention at different levels.

Results: All provincial level influenza network labs, except the ones in Tibet, can pass the EQAP with all samples detected correctly. For the county level influenza network labs, those established for more than three years performed better than those newly established within the past three years.

Conclusion: More efforts should be put on the newly-established network labs for improvement of the surveillance capacity of the whole country. The national influenza surveillance system is also the basis for capacity building of other respiratory diseases surveillance, and is essential for timely sharing of information of public concern.

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MOLECULAR CHARACTERIZATION OF PANDEMIC INFLUENZA A(H1N1)PDM 09 VIRUS IN KOREA


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Background: Since the pandemic in 2009 of influenza A(H1N1)pdm 09, there have been many reports about the increasing emergence of influenza A(H1N1)pdm 09 variants. Mostly, the possibility of emergence of more virulent virus is the main concern in global public health perspective. We have performed genetic analysis of influenza A(H1N1)pdm 09 virus isolated in Korea to identify the possible correlation between molecular and clinical factors and also to understand the pandemic potential of influenza virus.

Methods: Sequence analysis of HA, NA and M gene of viruses collected from Korea Influenza and Respiratory Virus Surveillance Scheme (KINRESS), surveillance during 2009 pandemic and targeted surveillance for severe cases as a satellite system. The analyses have been focused on the detection of antigenic variant and antiviral drug resistant variant.

Results: Total 114 HA, 139 NA, 97 M sequences have been analyzed and compared with those of vaccine strain and other reference viruses. Although we could not find significant antigenic changes in Korean isolates compared to vaccine strain, the sequences have been consistently changed including specific amino acid change. Viruses isolated from severe or mild cases did not possess molecular features with virulence, implying that several factors might be related to virulence. All Korean isolates had amantadine-resistant genotype (S31N). However, 13 viruses were resistant to oseltamivir with H275Y variation, suggesting that neuraminidase inhibitors (NI) could be still effective for the treatment of influenza.

Conclusion: As other reports about foreign influenza A(H1N1)pdm 09 viruses, Korean influenza A(H1N1)pdm 09 isolates have not changed significantly. But considering the emergence of reassortants with changed characteristics in the virulence and transmission, comprehensive monitoring based on molecular characterization of influenza viruses prevailing in the country will be required.

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VIROLOGICAL CHARACTERISTICS OF SEASONAL INFLUENZA
IN LAO PDR, 2011

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3. Emerging Disease Surveillance and Response Unit, World Health Organization (WHO) Country Office, Lao People’s Democratic Republic

**Background:** Similar to other countries in the Region, influenza season is September to December in Lao PDR (analysis of 2008-10 data). We documented the epidemiology of seasonal influenza in 2011 based on the results of influenza surveillance and testing by the National Centre for Laboratory and Epidemiology (NCLE), Lao PDR.

**Methods:** We performed a descriptive analysis of data from ILI patients (fever >38°C with cough and/or sore throat) and SARI patients (ILI plus difficulty breathing or shortness of breath) from sentinel sites and outbreaks in 2011. A nasopharyngeal (NP) swab or combined nasal with oropharyngeal swab was collected from case-patients. NCLE conducted real-time PCR with US-CDC primers/probes. Isolates were identified by the haemagglutination inhibition assay using the WHO or National Institute of Infectious Diseases, Japan, influenza diagnostic kit.

**Results:** 1853 samples were received from all sources. Of these, 237 (12.8 %) were positive for influenza: 147 (62%) A/H3, 74 (31.2%) Flu B, 15 (6.4%) A/H1N1 2009 and 1(0.4%) Flu A untyped. 1,053 samples (57%) were received from ILI patients, median age 14 years (range: <1 to 84). Of these 169 (16%) were positive for influenza: 66.3% A/H3; 31.3% Flu B; 2.4% A/H1N1 2009; and the median age was 14 years (range: <1 to 65).

Influenza was detected year-round with the highest proportion of positive specimens in the 3rd and 4th quarters. Strains isolated in 2011 matched those in the southern (2011, 2012) and northern hemisphere (2011-12) vaccine strains.

**Conclusions:** Similar to previous years, influenza was detected year-round and influenza season was September to December. Three subtypes co-circulated in 2011 with A/H3 being predominant. ILI and SARI surveillance is critical in recognizing changing patterns of seasonal occurrence, and associated burden of disease as contributing to future influenza vaccination policy and strategy. Data collected and analysed helped inform a pilot seasonal influenza vaccination campaign conducted in April 2012.

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ISOLATION AND IDENTIFICATION OF INFLUENZA VIRUS STRAINS CIRCULATING IN MALAYSIA FROM 2004 TO 2011

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Background: The Virology Unit, Institute for Medical Research (IMR), Kuala Lumpur, was designated as one of the National Influenza Centre (NIC) for Malaysia in 1968. Since then, the Virology Unit continues carrying out influenza surveillance activities for Ministry of Health (MOH) involving participating government hospitals and outpatient clinics throughout the country as sentinel sites. This programme plays an important role in preparing for, and responding to, epidemics and pandemics.

Methods: All respiratory samples received were inoculated into Madin-Darby Canine Kidney (MDCK) cells and isolates were identified by the indirect immunofluorescence antibody technique (IFAT) using specific monoclonal antibody against influenza type A and B. Hemagglutination inhibition (HAI) assays were used to type and subtype the influenza isolates before sending to the WHO Collaborating Centre for Reference and Research on Influenza in Melbourne, Australia for further analysis.

Results: The Virology Unit received a total of 11,875 ILI and SARI clinical specimens from 1 Jan 2004 to 31 December 2011, of which 10.8% (1279/11875) were found to be positive for influenza virus. Of the 1279 positive cases, 66.5% (850/1279) were influenza A and 33.5% (429/1279) were influenza B.

Conclusions: Influenza virus was found to circulate throughout the year with higher occurrences in the middle part of the year. These patterns were generally similar to the countries in the southern hemisphere. However, the predominant strains found in Malaysia were not a perfect match with the strains used for southern hemisphere influenza vaccines. This study emphasizes the importance of local influenza surveillance programme not only as early warning for upcoming epidemics and potential pandemics but also in deciding the appropriate annual influenza vaccine needed for the population.

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ILI EPIDEMIOLOGICAL AND VIROLOGICAL SURVEILLANCE ACTIVITIES IN MONGOLIA IN 2011/12 SEASON

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Background: Mongolia is a landlocked country with the second-lowest population density in the world (1.74 people per square kilometer in 2010). Despite such low population density, influenza transmission occurs almost every year. Here we report the ILI activity in 2011/2012 season.

Methods: The epidemiological and virological data collected through sentinel surveillance system of NIC, NCCD, Mongolia were used for an analysis. Influenza viruses were detected by rt-RT-PCR and were isolated by inoculation of rt-RT-PCR-positive samples of MDCK cell culture according to the standard protocol.

Results: Cases registered during the period from 3 October 2011 to 1 April 2012 were 915.7 ILI per 10,000 population, which was 6.7% of all outpatient visits (3,739,992).

ILI events have decreased by 0.2% in outpatient visits and by 46.7 ILI per 10,000 population nationwide in comparison with the reported morbidities in the corresponding period of the previous season. In 2011/2012 season, influenza activity reached the peak in the 11th week, 2012.

In the hospital-based surveillance sites, 15,332 patients were hospitalized with pneumonia, which consisted of 7.0% of all inpatient visits (220,488). Of those, 34 (0.2%) patients died. 85% (13,019) of SARI and 94% (32) of death cases were in children aged less than four years old.

During 15 Sep 2011 to 1 April, 2012 the Virology Laboratory NIC, NCCD collected and processed 2,400 nasopharyngeal samples and detected 326 (13.6%) influenza viruses, of those 114 (35%) A (H3N2) and 212 (65%) B type, and isolated 80 (24.5%) strains, of those 78 (97.5%) B virus, 2 (2.5%) A (H3N2) subtype.

The susceptibility of 30 B and 2 A (H3N2) viruses to NA inhibitors was examined and all viruses were sensitive to Oseltamivir and Zanamivir.

Conclusions: In Mongolia, ILI activity was relatively mild in 2011/2012 influenza season and was dominated by influenza B viruses.
DYNAMIC PATTERN OF CIRCULATING SEASONAL AND PANDEMIC INFLUENZA VIRUSES FROM 2001 TO 2011 IN NEW CALEDONIA.

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Influenza surveillance is established in New Caledonia through sentinel sites sampling patients with influenza like illnesses (ILI) and systematic laboratory diagnosis.

From 2001 to 2011, Influenza diagnosis went from direct immunofluorescence to real time RT-PCR. Of the 6756 specimens tested in these 10 years, 1252 (19 %) were positive for influenza viruses, of which 549 (44%) were pandemic influenza A(H1N1)pdm09, 550 (44%) were seasonal influenza A and 153 (12%) were influenza B. While influenza viruses were detected every year, their type/subtype varied remarkably. Peaks of influenza activity coincided often with cold season and the known bimodal pattern due to migratory flows was minor. Pandemic A(H1N1) emergence in 2009 brought an important increase in laboratory activity and asked for technological adjustment.

Continued surveillance in New Caledonia will help detect introduction of new strains as its influences are multiple (Australia, New Zealand other Pacific Islands and France). It will allow optimal periods to implement influenza vaccination programs among priority populations.

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REFOCUSING THE NATIONAL SURVEILLANCE FOR INFLUENZA: TOWARD IMPROVED RESPONSIVENESS, PREPAREDNESS, AND SUSTAINABILITY

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After eight years of existence as a National Influenza Center, the Research Institute for Tropical Medicine, in coordination with the Department of Health National Epidemiology Center (DOH-NEC) and Infectious Disease Office of the National Center for Disease Prevention and Control (NCDPC-IDO), is reviewing its operations and is in the process of shifting its activities towards improved responsiveness, preparedness and sustainability.

**Refocusing Virological Surveillance** through a change in the algorithm of testing (utilization of molecular techniques to screen all ILI cases and selecting positive samples for virus isolation) to make it more rapid in reporting results, establishing criteria for selection and retention of surveillance sites and downsizing to fewer but high-quality sites to maximize fund utilization.

**Re-establishing/Strengthening links** with NEC and NCDPC-IDO to improve surveillance activities and data management for ILI and SARI cases in order to guide prevention/control strategies of the DOH and work towards full institutionalization of the NIC by 2015.

**Reinforcing the Subnational Laboratories** to make them all fully functional, quality-assured and sustainable, to start SARI surveillance in their respective institutions, and to potentially use these subnational laboratories as a platform for testing other epidemic-prone infectious diseases such as dengue, leptospirosis and others.

**Developing a National Influenza Surveillance Bulletin and Website**, jointly with the DOH to make available important and updated information to the country’s health practitioners and policy makers.

**Strengthening the NIC Research Agenda** to contribute to the global efforts to better understand the disease.

**Continued participation in the WHO Global Influenza Surveillance and Response Network** in terms of provision of viral isolates, timely reporting of cases, immediate notification of novel or unusual strains, increasing capacity for antiviral resistance testing, and implementing quality assurance.
The RITM NIC realizes the need to adopt a system that is responsive to the country’s needs and efficient and sustainable in its operations. Thus, its activities are now being refocused to contribute to the improvement of the National Influenza Surveillance. Crucial to the success of these steps is the commitment and support of the Philippine government and Department of Health.

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INFLUENZA SURVEILLANCE IN PAPUA NEW GUINEA

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**Background:** Influenza surveillance has been conducted in Papua New Guinea since 2008. The National Influenza Centre (NIC) currently receives nasopharyngeal swab samples from two sites in Papua New Guinea. In mid-2012, the NIC will begin receiving samples from two additional sites around the country.

**Methods:** The Papua New Guinea NIC has recently made improvements in the detection of influenza viruses in the laboratory by adopting a suite of real-time RT-PCR assays from the US Centres for Disease Control and Prevention (CDC). These assays have improved the sensitivity and rapidity of sample analysis. With assistance from the World Health Organization (WHO) we have also established a cell culture laboratory to enable the isolation of influenza viruses.

**Results:** During 2011 the PNG NIC processed 491 samples from the sentinel surveillance sites. This is a significant increase on the number of samples processed in 2009 (n=254) and 2010 (n=293). The CDC real-time RT-PCR assays were successfully adopted by the NIC which was evidenced by the 100% correct results from EQAP Panel 11.

**Conclusion:** The Papua New Guinea NIC is making improvements in detection and isolation of influenza viruses in the laboratory. Training opportunities for local scientists have greatly improved the laboratory capacity of the Papua New Guinea NIC. In 2011, two PNG scientists travelled to the WHO Collaborating Centre for Reference and Research on Influenza (Melbourne) for training in real-time PCR, cell culture and sequence analysis. One staff member also travelled to the Centre of Excellence for Influenza Research and Surveillance (St Jude Children’s Research Hospital, Memphis USA) for training in detection of influenza viruses from animal samples.

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INFLUENZA SURVEILLANCE IN SINGAPORE

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In Singapore, influenza occurs throughout the year, with a bimodal increase in incidence during April-July and November-January. A sentinel virological surveillance system involving public primary health clinics and private general practitioner (GP) clinics enables the collection of samples from patients with influenza-like illness (ILI). Severe and fatal cases of influenza are notified to MOH. Our surveillance also includes acute respiratory infections and pneumonia attendances and admissions from the public primary health clinics and hospitals. The data are reviewed weekly for trends and the result is provided to healthcare practitioners through a web portal.

The isolation and typing of influenza viruses was done and influenza A(H1N1)pdm09 was the pre-dominant subtype in the early part of the year 2011. A switch to A(H3N2) as the pre-dominant subtype was seen in E-week 7-10 (four-week moving average). The prevalence of H3N2 generally declined from E-week 29-32, seeing an increase in the prevalence of influenza B which remained the pre-dominant subtype for the remainder of 2011 and early 2012.

Based on sequencing and HAI results, the majority of circulating A(H1N1)pdm09 and A(H3N2) viruses are similar to the A/California/7/2009-like and A/Perth/16/2009-like vaccine strains, but low reactors have also been detected in both subtypes.

Among influenza B positive cases of 2011, 74% of 493 samples were of B/Victoria lineage and 26% were of B/Yamagata lineage. Antigenically, 17 of 19 B/Victoria lineage isolates collected during the September-December period showed reduced titres with antiserum produced against B/Brisbane/60/2008, while all five Yamagata lineage isolates tested were characterized as B/Wisconsin/1/2010-like viruses. We also observed that more viruses of Yamagata lineages were detected in elder age groups (>35y).

In collaboration with Bioinformatics Institute, Singapore and WHO CC Melbourne, a novel influenza A/H1N1pdm09 variant with mildly reduced oseltamivir and zanamivir sensitivity has been detected in more than 10% of community samples in Singapore, which was also detected in more than 30% of samples from northern Australia during the early months of 2011. The variant (S247N in NA gene) had very high oseltamivir resistance when combined with the H275Y mutation.

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Background: Influenza-like illness (ILI) is a common cause of visits to health care facilities in Vietnam. In 2006, a national influenza sentinel surveillance system (NISS) was developed to assist in the control and prevention of influenza in Vietnam. A surveillance for Severe Acute Respiratory Infection (SARI) was developed since 2010 for early detection of A/H5N1 in human.

Methods: The WHO case definition is used to identify ILI/SARI patients. The first two ILI and first SARI patients each day are enrolled for investigation. Throat swabs specimens were tested by reverse transcription polymerase chain reaction (RT-PCR) using WHO primers and procedures. The total numbers of visits, the total visits for ILI/SARI, and the percentage of positive for influenza virus by RT-PCR are calculated weekly.

Results: During 2006 through April 2012, 436 770 ILI cases were identified accounting for 11.9% of 3 644 241 outpatients at 15 sentinel surveillance sites. Of 436 770 ILI cases, 3 5047 were tested and 7344 (20.9%) were positive with influenza by RT-PCR. Of the 7344 positive confirmed cases, 5650 (76.9%) were under 25 years old. Among the identified subtypes of influenza virus, influenza B, A/H3N2, A/H1N1 and pA/H1N1 2009 were mostly circulating in human population (34%, 31%, 18% and 17% respectively). There were 20 726 SARI cases that represented 30% hospitalized patients. Of 1587 sampled (7.6% of SARI patients), 135 (8.5%) were positive with influenza. In a graphical analysis, there was a fairly consistent pattern of each of the seasonal subtypes peaking every two years during the surveillance period.

Conclusion: ILI and SARI result in a common cause of visits to sentinel clinics. A high proportion of ILI cases was due to seasonal influenza viruses. Most ILI cases of influenza occur in people under 25 years old. Antigenic characterization and historic timing of influenza activity will be useful in determining Vietnam’s seasonal vaccine strategy.

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PROVISIONAL PROGRAMME OF ACTIVITIES

Day 1 – Tuesday, 29 May 2012

08:00 – 08:30 Registration

08:30 – 10:00 Opening session

Welcome and opening remarks
Dr Takeshi Kasai, WHO Representative, Viet Nam

Dr Tran Thanh Duong, Deputy Director, General Department of Preventive Medicine
Ministry of Health, Viet Nam

Dr Michael Shaw, Influenza Division, Centers for Disease Control and Prevention
United States of America

Overview of the agenda
Dr Jeffrey Partridge, Emerging Disease Surveillance and Response (ESR),
WHO Western Pacific Regional Office (WPRO)

Group photo

09:00 – 09:30 Coffee break

09:30 – 10:00 Self-introductions

Administrative announcements
Annex 1

10:00 – 12:30  Plenary 1: Regional and global updates

Chair: Dr Masato Tashiro, WHO Collaborating Centre, National Institute for Infectious Diseases, Japan

WHO SEARO Dr Richard Brown, DSE/SEARO
WHO WPRO Dr Jeffrey Partridge, ESR/WPRO
WHO HQ Dr Wenqing Zhang, WHO/HQ
WHO EQA Programme Dr Janice Lo, Public Health Laboratory Centre, Hong Kong

Influenza activity in the Northern and Southern Hemispheres

Northern Hemisphere
Dr Takato Odagiri, WHO Collaborating Centre, National Institute for Infectious Diseases (NIID), Japan

WHO SEARO Dr Richard Brown, DSE/SEARO
WHO WPRO Dr Jeffrey Partridge, ESR/WPRO
WHO HQ Dr Wenqing Zhang, WHO/HQ
WHO EQA Programme Dr Janice Lo, Public Health Laboratory Centre, Hong Kong

Southern Hemisphere
Dr Ian Barr, WHO Collaborating Centre for Reference and Research on Influenza, Victorian Infectious Diseases Reference Laboratory (VIDRL), Australia

12:00 – 12:30 Question and answer
12:30 – 13:30 Lunch break

13:30 – 15:00  Plenary 2: Multi-country collaborations
Chair: Dr Ian Barr, WHO Collaborating Centre, VIDRL, Australia

Seasonal Influenza Manuscript
- Dr Jeffrey Partridge, ESR/WPRO

Potential Collaborative Influenza Strain Circulation Manuscript

Introduction
- Dr Ann Moen, WHO Collaborating Centre for Surveillance, Epidemiology and Control of Influenza, US CDC, United States of America

Strain circulation analysis
- Dr Jeffrey Partridge, ESR/WPRO

Example from data at a WHO collaborating centre
- Dr Sheena Sullivan, WHO Collaborating Centre for Reference and Research on Influenza, Victorian Infectious Diseases Reference Laboratory (VIDRL), Australia

Discussion

15:00 – 16:00 Coffee break and Poster viewing
16:00 – 17:30  **Plenary 3: Country presentations**  
*Chair: Dr Ann Moen, WHO Collaborating Centre, US CDC, United States of America*

Viet Nam  
*Dr Nguyen Thi Thu Yen, National Institute of Hygiene and Epidemiology, Viet Nam*

Thailand  
*Dr Thitipong Yingyong, Ministry of Public Health, Thailand*

Papua New Guinea  
*Dr Paul Horwood, Institute of Medical Research, Papua New Guinea*

Australia  
*Dr Dominic Dwyer, Westmead Hospital, New South Wales*

17:00 – 17:30  **Question and answer**

18:00 – 20:00  **WHO welcome reception**

**Day 2 – Wednesday, 30 May 2012**

08:30 – 08:45  **Summary of Day 1 and administrative announcements**

08:45 – 09:45  **Plenary 4: Revisiting national influenza surveillance**  
*Chair: Dr Anne Kelso, WHO Collaborating Centre for Reference and Research on Influenza, VIDRL, Australia*

New Technical Guidance  
- *Dr Katelijn Vandemaele, WHO/HQ*

Explanation of Group Work  
- *Dr Frank Konings, ESR/WPRO*

09:45 – 10:15  **Coffee break**

10:15 – 11:30  **Group Work: Revisiting national influenza surveillance**

Group A – Case finding (e.g. case definition, sentinel site selection)  
Group B – Sampling (e.g. case selection, sampling strategy)  
Group C – Data collection and reporting (e.g. minimum data, analysis and reports)

11:30 – 12:30  **Feedback from Group Work**  
(10-minute presentations + 5-minute discussion for each group)

12:30 – 13:30  **Lunch break**

13:30 – 15:00  **Plenary 5: Data to inform influenza vaccine use/guidance**  
*Chair: Dr Michael Shaw, WHO Collaborating Centre for Surveillance, Epidemiology and Control of Influenza, US CDC, United States of America*

Examples of surveillance data for public health decision-making:

Australia  
*Dr Kate Pennington, Department of Health and Ageing, Australia*

Malaysia  
*Dr Apandi bin Yusof, Institute for Medical Research, Malaysia*
Annex 1

Korea
Ms Sunhee Park, Korea Centers for Disease Control, Republic of Korea

New Zealand
Dr Sue Huang, Institute of Environmental Science and Research, New Zealand

15:00 – 15:30 Coffee break

15:30 – 17:00 Plenary Discussion: Is there a role for GISRS in providing data for national decision-making for influenza vaccine introduction?
Facilitator: Dr Lance Jennings, Canterbury Health Laboratories, New Zealand

Day 3 – Thursday, 31 May 2012

08:20 – 08:30 Administrative announcements

08:30 – 12:00 Plenary 6: Technical presentations and discussions
Chairs: Dr Babatunde Olowokure, WHO Viet Nam
Dr Nora Chea, WHO Cambodia

08:30 – 09:00 Overview of swine origin influenza virus infection in the United States
Dr Xiyan Xu, WHO Collaborating Centre for Surveillance, Epidemiology and Control of Influenza, US CDC, United States of America

09:00 – 09:30 A widespread community cluster of H275Y oseltamivir-resistant A(H1N1)pdm09 influenza in Australia
- Dr Aeron Hurt, WHO Collaborating Centre for Reference and Research on Influenza, VIDRL, Australia

09:30 – 10:00 Coffee break

10:00 – 10:30 Antiviral-resistant B virus with a novel mutation detection by antiviral resistance surveillance in Japan
- Dr Masaki Imai, WHO Collaborating Centre for Reference and Research on Influenza, NIID, Japan

10:30 – 11:00 Models for influenza surveillance and early warning
- Dr Wang Dayan, WHO Collaborating Centre for Reference and Research on Influenza, China CDC, China

11:00 – 12:00 Panel Discussion: The future of GISRS
Moderator: Dr Wenqing Zhang, WHO/HQ

12:00 – 13:30 Lunch break

13:30 – 14:00 Summary and closing session
Dr Jeffrey Partridge, ESR/WPRO
Dr Patrick O’Connor, IVD/SEARO
Dr Takeshi Kasai, WHO Representative, Viet Nam
Dr Ann Moen, WHO Collaborating Centre, US CDC, United States of America
Dr Tran Thanh Duong, Deputy Director, GDPM, Ministry of Health, Viet Nam

14:00 – 14:30 Coffee break

14:30 – 16:30 Site visit to the National Institute of Hygiene and Epidemiology (NIHE)
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