Fifth Meeting of National Influenza Centres in the Western Pacific and South-East Asia Regions

7–10 June 2011
Vientiane, Lao People’s Democratic Republic
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Key words: Influenza, Human - prevention and control/ Epidemiology/ Pandemics / Regional health planning/ Disease outbreaks – prevention and control
1. INTRODUCTION

The introduction of global influenza surveillance in 1948 was one of the first actions of the newly created World Health Organization, and in 1952, the Global Influenza Surveillance Network (GISN) was established. In 2011, GISN was re-named the Global Influenza Surveillance and Response System (GISRS) in recognition of increasing expectation from Member States, together with strong institutional and governmental support. The GISRS contributes to global public health by gathering and analyzing information on the appearance of novel strains of influenza virus and reporting to WHO to enable a prompt and appropriate public health response. It also collates data on circulating influenza viruses, which are used to make recommendations on strain composition of seasonal influenza vaccines. The GISRS currently consists of six WHO Collaborating Centres for Reference and Research on Influenza and 135 National Influenza Centres (NICs) in 105 countries. There are 21 NICs in 15 countries in the Western Pacific Region and 10 NICs in eight countries in the South-East Asia Region. There are three WHO Collaborating Centres in the Western Pacific Region, one each in Australia, China and Japan.

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 four 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 bi-regional 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, Philippines, from 3 to 6 May 2010. Participants were encouraged to share their experiences during pandemic (H1N1) 2009 to assist those countries developing preparedness plans and laboratory contingency plans.

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.
1.1 Objectives

(1) To review current capacity of the network in the regions and develop the next five-year plan (2012–2016) for national influenza surveillance.

(2) To finalize a regional review paper of seasonal influenza.

(3) To develop a prioritized region-specific research agenda based upon the WHO Public Health Research Agenda for Influenza, and develop the plan for implementation.

1.2 Welcome and opening remarks

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

On behalf of the WHO Regional Director, Dr Kasai welcomed participants to the Fifth Meeting of the National Influenza Centres in the Western Pacific and South-East Asia Regions. He conveyed appreciation to the Government of the Lao People's Democratic Republic for hosting the meeting. The venue of the meeting was purposely determined in light of the Lao People's Democratic Republic being home to the newest National Influenza Centre in the Western Pacific Region.

Participants were encouraged to think strategically to develop innovative ways to improve collaboration and information sharing between organizations, both within their own countries and within the regions. Cooperation between virologists, epidemiologists, researchers and policy-makers will continue to facilitate the link between disease surveillance and virological information and improve regional and global communicable disease response.

Dr Kasai highlighted the importance of the meeting objectives and said he was pleased to have a gathering of influenza experts from the two regions to share experiences and knowledge, thereby moving forward in the battle against influenza while strengthening the regions' core capacities to address emerging diseases and other public health events.
His Excellency Dr Bounkouang Phichit, Vice-Minister, Ministry of Health, Lao People's Democratic Republic

His Excellency Dr Bounkouang Phichit welcomed all participants to the Lao People's Democratic Republic. He emphasized the importance of the Asia Pacific Strategy for Emerging Diseases (APSED) in controlling emerging diseases. He highlighted the significant influenza events of the past, including severe acute respiratory syndrome, influenza H5N1, and the 2009 influenza pandemic, and cautioned about unknown future events.

On 6 August 2010, WHO recognized the new National Influenza Centre in the Lao People's Democratic Republic. With the NIC in place, the Lao People's Democratic Republic has an increased capacity in science and technology that has the potential to improve the quality of life of its citizens. Dr Phichit thanked the partners for contributing to the success of the meeting.

Dr Ann Moen, Associate Director for Extramural Program, United States Centers for Disease Control and Prevention

Last year’s meeting focused on reviewing lessons learnt from the 2009 influenza pandemic. This year, the focus of the meeting was on looking forward and planning for the next five years. Dr Moen highlighted the importance of the gathering to develop friendships and partnerships to continue to learn from each other. She suggested that the meeting should act as a catalyst for improvements for the recognition, prevention and control of influenza and other emerging infectious diseases.

2. PROCEEDINGS

2.1 Plenary 1: Regional and global updates

Chair: Dr Anne Kelso, Co-chair: Dr Chong Chee Kheong

2.1.1 Presentation 1: Asia Pacific Strategy for Emerging Diseases

Dr Takeshi Kasai, WHO Western Pacific Regional Office

An update on the Asia Pacific Strategy for Emerging Diseases (APSED) was delivered. Based on the fourth meeting of the Technical Advisory Group and the biregional consultation on "APSED and Beyond" held in May 2010, it has been recommended that APSED (2010) will continue to focus primarily on building national and local capacities for emerging infectious diseases. The ongoing objectives are to reduce the risk of emerging diseases by strengthening early detection, rapid response and effective preparedness and building technical partnerships.

APSED (2010) will continue to provide a common framework for countries to strengthen national and local capacities required for managing all emerging infectious diseases. In addition, with threats arising from other public health events and the requirements of the International Health Regulations (2005), the new strategy addresses other public health events, such as food safety events. The updated strategy seeks to build on the common approach and maximize the benefits achieved under APSED (2005).
2.1.2 Presentation 2: National Influenza Centres in the South-East Asia Region  

*Dr Oommen John, WHO South-East Asia Regional Office*

There are eight NICs in the South-East Asia Region, all with virus isolation and polymerase chain reaction (PCR) testing capacity. The Region is trying to overcome the following challenges: encouraging the establishment of NICs in the three countries that do not have them, expanding immunization and surveillance and increasing data sharing. The burden of influenza in the South-East Asia Region is still not fully understood; however, there have been numerous studies to learn more, particularly in Thailand, Myanmar and India.

To control influenza in the Region, WHO is aiming to strengthen preparedness and capacity to respond to influenza with pandemic potential, strengthen and integrate capacity to carry out surveillance and response, and strengthen laboratory infrastructure. This includes building laboratory and epidemiology capacity to accurately and promptly diagnose seasonal influenza and influenza with pandemic potential.

2.1.3 Presentation 3: Summary of influenza activity in the Western Pacific Region  

*Dr Jeffrey Partridge, WHO Western Pacific Regional Office*

Reports of influenza virus detection in the Western Pacific Region for the past year (30 May 2010 to 8 May 2011) have shown a predominance of influenza A(H1N1) 2009 (41%), followed by influenza A(H3) (34%) and influenza B (19%). Two peaks were observed during this period, the first in early September 2010, and the second, larger peak in the first month of 2011. Low influenza-like illness (ILI) activity in the northern hemisphere, tropics, and southern hemisphere has been observed for the current period (mid-April–mid-May). A mix of influenza viruses were reported from nine countries, but they were predominantly B viruses (>70% of positives) followed by influenza A(H3) and influenza A(H1N1) 2009 viruses. As of 3 June 2011, only Cambodia has reported cases of avian influenza H5N1 in the Western Pacific Region. Five cases have been reported; all were fatal.

Dr Partridge summarized the ongoing project to better define epidemiological and virological characteristics of influenza in the Western Pacific Region, as part of a collaborative effort to improve the understanding of disease burden in the Western Pacific Region and identify areas for improvement of surveillance and reporting. Influenza disease data were requested and collected by WHO from 16 countries and areas via survey. All 16 countries and areas responded to the survey by submitting weekly or monthly data by age group on influenza-like illness, acute respiratory infection (ARI), severe acute respiratory infection (SARI) and all-cause outpatient visits or hospital admissions data. Virological data were extracted from the GISRS database (FluNet) and validated and updated as required.

Surveillance systems and data collection methods, cases definitions and age categorizations varied across the Region. ILI, SARI and ARI were reported from 14, 5, and 4 countries or areas, respectively. Many challenges were observed, including data collection issues (timely and difficult collection, different case definitions, different methodologies in collection/sampling, missing data) and interpretation issues. The collection time period of three years was too difficult to determine patterns (especially since this period included the 2009 pandemic), and there was not enough data on ARI, SARI and age-specific categorizations to make solid conclusions related to these topics.
2.1.4 Presentation 4: An update from WHO Headquarters

*Dr Wenqing Zhang, WHO Headquarters, Geneva*

On 24 May 2011, the WHO Global Influenza Surveillance Network changed its name to the WHO Global Influenza Surveillance and Response System. WHO Headquarters supports GISRS in selected activities including coordination, virus surveillance, vaccine support, and development of the epidemiological surveillance strategy. Since the last biregional NIC meeting, WHO Headquarters conducted several activities related to these work areas, including: organizing two vaccine composition meetings; publishing the third NIC survey; updating/upgrading FluNet; organizing a meeting on improving the vaccine virus selection process; organizing the global NIC meeting; organizing two PCR working group meetings; publishing serological study protocols; updating guidance on use of rapid diagnostic tests; conducting trainings on sequencing and antiviral susceptibility surveillance; publishing guidance on using PCR versus virus isolation and the selection of representative viruses for shipping; and providing continuing support to the WHO Shipment Project.

Dr Zhang also provided overviews of the Pandemic influenza preparedness framework for the sharing of influenza viruses and access to vaccines and other benefits and the Report of the Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009. The full documents can be found at:

Framework: [http://apps.who.int/gb/ebwha/pdf_files/WHA64/A64_R5-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA64/A64_R5-en.pdf)

2.1.5 Presentation 5: WHO External Quality Assessment Programme for the detection of influenza virus type A by PCR

*Dr Wilina Lim, Centre for Health Protection, Hong Kong (China)*

External quality assessment is a critical component of a laboratory network. The objectives of the WHO External Quality Assessment Programme (EQAP) for the detection of influenza virus type A by PCR are to monitor quality and standards of performance, to facilitate information exchange, to identify problems with assays, to help develop testing strategies, and to provide mechanisms to remedy any deficiencies revealed.

In 2007, the GISRS sent its first panel of unknown specimens (Panel 1) as an external quality assessment to 64 participating NICs globally. The most recent panel, Panel 9, was sent to 160 laboratories. Results were reviewed at the WHO meeting in Tunisia in December 2010.

Another part of the EQAP is the Good Laboratory Practices (GLP) survey. The survey, first conducted in 2007 and composed of 73 questions, was sent to 64 laboratories. In 2010, it included 32 questions and was sent to 142 laboratories. Questions on the GLP survey addressed personnel, quality managements, design, equipment and consumables, pre-analytical procedures, analytical procedures, post-analytical procedures, reporting and record keeping and safety.

Discussion following the presentation recommended that EQAP would benefit from a review of materials for simulated specimens/scope, type/subtype/clade to include in the panel, and frequency of shipment.
2.2 Plenary 2: Influenza activity in the northern and southern hemispheres

Chair: Dr Xiyan Xu, Co-chair: Dr Ondri Dwi Sampurno

2.2.1 Presentation 1: Northern hemisphere

Dr Takato Odagiri, WHO Collaborating Centre, Japan

Influenza activity reports from the northern hemisphere for the previous few months (29 August 2010 to 29 January 2011) has shown a predominance of influenza A(H1N1) 2009 (31%), followed by influenza A(H3) (27%) and influenza B and influenza A (not subtyped). A peak in activity was observed during January 2011. The majority of influenza A(H1N1) 2009 viruses have remained antigenically homologous to influenza A/California/7/2009 vaccine virus. The 2011/2012 vaccine composition recommended by WHO for the northern hemisphere has not changed from the previous season.

Since January 2011, Japan has observed an increase of influenza A(H1N1) 2009 viruses with haemagglutination inhibition titres. Australia has also detected this phenomenon but at a lower proportion than Japan has found. China has not observed this, but are not detecting a lot of influenza A(H1N1) 2009 viruses at the moment.

2.2.2 Presentation 2: Southern hemisphere

Dr Ian Barr, WHO Collaborating Centre, Australia

It is still early for the 2011 influenza season in the southern hemisphere. There was increased out-of-season influenza activity in Australia in early 2011, with an increase in influenza A(H3N2) activity in 2011 compared to 2010. The A(H3N2) viruses were mostly related to influenza A/Perth/10/2010 genetically and influenza A/Perth/16/2009-like (antigenically). Pandemic A(H1N1) 2009 is still common in Australia and is mostly influenza A/Brisbane/70/2011 genetically and influenza A/California/7/2009-like antigenically. There are few influenza B viruses circulating (mainly B/Brisbane/60/2008-like – B/Victoria lineage). Currently 100% of influenza A(H3N2) and influenza A(H1N1) 2009 viruses are adamantine resistant. There are low levels of neuraminidase inhibitor resistance with <1% viruses currently oseltamivir (Tamiflu) resistant. There is little activity in New Zealand, South Africa or South America so far. The 2011 vaccine match so far appears good.

The discussions resulting from both the northern and southern hemisphere presentations highlighted the lack of major antigenic change in the three viruses circulating in the last few years.

2.3 Poster session

Facilitators: Dr Ann Moen, Dr Anne Kelso

A poster session was held to give NICs the opportunity to present information on how their influenza research or surveillance data are used for public health practice. Fourteen posters were displayed and discussed. Four posters were also selected for oral presentation.
2.3.1 Presentation 1: Characterization of human influenza virus circulation in Cambodia (2006–2010) and impact on national public health policies

Dr Ly Sovann, Ministry of Health, Cambodia
Dr Philippe Buchy, Institut Pasteur in Cambodia, Cambodia

The Cambodia National Influenza Centre characterized circulating influenza viruses from 2006 to 2010. Each year, influenza viruses generally circulate from June to December, which is during rainy season. Although Cambodia is geographically located in the northern hemisphere, influenza circulation has a southern hemisphere pattern. Therefore, while the northern hemisphere vaccine may provide some protection in Cambodia, the southern hemisphere vaccine is recommended.

2.3.2 Presentation 2: Epidemiological and virological characteristics of seasonal influenza in the Lao People's Democratic Republic, 2008–2010

Dr Bouaphanh Khamphaphongphane, Ministry of Health, the Lao People’s Democratic Republic

Information on influenza from the Lao People’s Democratic Republic is limited. Seasonal patterns of influenza have not been previously described. The epidemiology of ILI based on results of sentinel surveillance conducted by the National Centre for Laboratory and Epidemiology (NCLE) was presented.

Descriptive analysis was conducted on 2348 samples taken from ILI patients who presented at seven sentinel hospitals in three regions of the Lao People's Democratic Republic between 2008 and 2010. A large proportion of ILI patients in the Lao People's Democratic Republic, particularly younger children, did not have influenza. Influenza affects all ages but mostly older children. Similar to other countries in the Region, influenza season is from June to December and is dominated by a different virus each year. ILI surveillance is critical in recognizing changing patterns of seasonal occurrence and associated burden of disease as contributing to future influenza vaccination policy and strategy.

2.3.3 Presentation 3: Translating influenza research and surveillance into public health practice in New Zealand

Dr Q Sue Huang, National Centre for Biosecurity and Infectious Disease, New Zealand

National influenza surveillance and related research in New Zealand provide evidence for assessing and implementing public health strategies to control influenza. When population-based disease burden data were reviewed for the period 1992–1996, a greater influenza mortality rate was observed in the elderly compared to other age groups. This resulted in the introduction of free influenza vaccination to those 65 years and older in 1997.

A national seroprevalence study of influenza A(H1N1) 2009 indicated a higher infection rate in children (about one in every three) compared to other age groups. This led to the eligibility policy for pandemic vaccine to be extended to include children under 5 years old. In addition, annual virological surveillance in New Zealand identified predominant circulating strains and contributed annual virus strain selection for global vaccine production.

Public health measures have been associated with a significant decrease of influenza-related mortality, based on mortality surveillance data obtained during the post-vaccination period. Influenza research and surveillance in New Zealand is pivotal for guiding evidence-based public health measures to control influenza effectively.
2.3.4 Presentation 4: Seasonal pattern of influenza activity in the Philippines (2006–2008): research implications for recommendations for influenza vaccination

*Dr Remigio M. Olveda, Research Institute for Tropical Medicine, Philippines*

Influenza virus infection has been studied extensively in temperate countries but not in tropical countries like the Philippines. An influenza surveillance system was established in the Philippines in 2005 after creation of the NIC. A retrospective analysis of weekly trends in influenza virus infection was conducted using virological surveillance data collected from ILI cases reporting in health centres and outpatient clinics in hospitals in 11 regions in the Philippines from 2006 to 2008. Nasal and/or oropharyngeal swabs were collected from 40% to 50% of ILI cases and sent for viral isolation, typing and subtyping.

A distinct seasonal pattern of increased influenza activity was observed from the start of the rainy season in May (just before the opening of schools) to the end of November. This has important implications on the timing of influenza vaccination. Knowledge of existing influenza strains also helps determine the appropriateness of the vaccine strains recommended.

2.4 Group work 1: Quality assurance programmes

*Chair: Dr Wilina Lim, Co-chair: Dr Khin Yi Oo, National Health Laboratory, Myanmar*

Participants were divided into four groups to discuss quality assurance programmes, specifically, how they are used, if they are useful, and what more (if anything) is needed.

The importance of timely and accurate laboratory diagnosis of emerging diseases in a safe environment was highlighted in line with Focus Area 2 (laboratory) of the Asia Pacific Strategy for Emerging Diseases. APSED (2010) includes a component of strengthening external quality assurance for emerging disease diagnosis, and there is an opportunity to utilize influenza as a pathfinder. The expansion and coordination of laboratory networks is important in ensuring that the strategic directions of APSED (2010) are met.

While the current terms of reference of NICs do not require participation in the EQAP, a proposal to make participation mandatory was raised. A comparison was made to the EQAP requirement established as part of the Measles Laboratory Network, which is perceived to be a well-working model with laboratory accreditation conducted by WHO. However, it was noted that the perception of a punitive effect to a NIC as a consequence of poor results would need to be considered as the EQAP emphasizes an educational component and does not indicate the level of performance. Nonetheless, the EQAP provides an opportunity for laboratories to conduct self-assessment, identify challenges and find solutions to address them. The EQAP also provides staff with confidence in conducting their day-to-day work.

Several participants also requested that EQAP panels be more challenging, with inclusion of untypable influenza viruses. This could be addressed through, for example, inclusion of H9 and H7 strains, which not all laboratories have the PCR primers to detect. An alternative would be to use weak samples, such as those with low RNA titres, but temperature variations during shipment may render them unviable for testing.

While the importance of viral culture was highlighted by most countries, challenges such as shipment of live viruses were also raised. Lyophilized viruses, which are more stable than frozen viruses and can be shipped at room temperature, may provide a good alternative.

A proposal to establish an accreditation process for NICs was suggested as a way to support laboratories to operate using set standards. WHO was requested to pursue discussions with possible agencies to include areas of influenza laboratory requirements in an accreditation framework. WHO Headquarters is currently exploring this possibility.
2.5 Plenary 3: Influenza surveillance and reporting

*Chair: Dr Takato Odagiri, Co-chair: Dr Phengta Vongphrachanh, NCLE, Lao People's Democratic Republic*

2.5.1 Presentation 1: GISRS reporting and communication – FluNet and EZCollab

*Dr Wenqing Zhang, WHO Headquarters*

FluNet is a web-based interactive data reporting, query and mapping system for the support and coordination of national, regional and global influenza surveillance. The system houses data from 1997 to date for more than 80 countries.

FluNet was revamped in November 2010 to provide a more user-friendly platform for influenza data entry and generation of reports. In the Western Pacific Region, out of 21 NICs in 15 countries, 12 are currently using FluNet for reporting. NICs are encouraged to use the FluNet platform for influenza data reporting as it is instrumental in the semi-annual seasonal influenza strain selection for vaccine production.

EZcollab is an informal platform for information sharing. Its importance was highlighted during the A(H1N1) pandemic in 2009, when EZcollab was used for the rapid dissemination of information, guidelines and other useful information. All registered users of EZcollab receive e-mail notifications when updates are made on this website.

2.5.2 Presentation 2: Integration of epidemiological and laboratory data – challenges and perspectives in China

*Dr Zhen Xu, Center for Disease Control and Prevention, China*

China has 556 sentinel hospitals and 411 laboratories to support ILI surveillance. There is a real-time database for ILI, PCR and virus isolation results, which allows efficient reporting functions. To encourage timely reporting of data, quality monitoring is regularly conducted.

In addition to this, training workshops are conducted regularly. Feedback is provided through weekly reports posted on the official website and in the reporting system, allowing stakeholders to review weekly reports and provide comments. With this system, China is working towards improving sentinel SARI surveillance and modelling the seasonal pattern of ILI. They also hope to use it as an early warning system, as a tool to describe disease burden and for vaccination policy-making.

2.5.3 Presentation 3: Integrated epidemiological and laboratory surveillance and reporting system in the National Influenza Centre in Mongolia

*Dr Alyeksandr Burmaa, National Center for Communicable Diseases, Mongolia*

Mongolia has three network laboratories and 197 influenza surveillance sentinel sites. Since October 2010, Mongolia has used a web-based system for reporting that has proven to be efficient for timely data collection. The sentinel sites share the same database and feedback of surveillance results is posted online in real-time. There is on-the-job training for health staff and statisticians in sentinel surveillance sites nationwide. Some functions of the system are still under development, particularly within the laboratory and epidemiology component. Future plans to overcome challenges and implement a better system include development of more comprehensive data analyses and reports, improvement of Internet access for sentinel sites and development of an English version of the website.
2.5.4 Presentation 4: Laboratory integration in influenza surveillance

**Dr Geethani Wickramasinghe, National Influenza Centre, Sri Lanka**

Sri Lanka is a developing country with limited resources. Until 2007 there was no organized continuous influenza surveillance. Influenza surveillance was initiated under the avian influenza preparedness plan of the GISN. The national network of laboratories consists of one NIC and two provincial laboratories. Training programmes were conducted to improve collection and transport of specimens and to introduce case definitions. The national influenza network consists of 20 ILI sites and three SARI sites. Each site sends 30 specimens per month to the NIC. In the future, Sri Lanka aims to improve subnational laboratories, improve routine surveillance, conduct disease burden studies, and initiate drug resistance monitoring.

2.6 Group work 2a: Summary of seasonal influenza in the Western Pacific Region

Participants were divided into four groups to discuss the draft summary of seasonal influenza in the Western Pacific Region and to make suggestions for improving the draft and developing it into a manuscript for publication. Challenges were noted and suggestions were made to improve the summary, including approaching countries and areas to obtain another two years of data, possibly linking ILI and virological data to determine if ILI is an indicator of influenza activity and including antigenic strains by zones (if incorporating vaccination strain matching data into the manuscript).

Overall, it was noted that while preparing the summary was challenging, there is value in presenting the data as a Region. For example, it can be used to put forward recommendations for future data improvements, such as annual NIC reports using a standardized format, introduction templates and harmonized case definitions. It was also noted that the process of reviewing the draft summary was useful in recognizing that while a great deal of progress has been made in the Region in terms of influenza surveillance, there is still work to be done to improve data collection and reporting.

2.7 Group work 2b: Strengthening NICs in the South-East Asia Region

Participants from the South-East Asia Region discussed the capacity of NICs in the Region, reviewed influenza surveillance activities and developed a summary of influenza surveillance challenges.

Discussions highlighted the following:

1. the importance of sending people to workshops and conferences who will share their new knowledge with others in their respective countries or areas;

2. the challenges associated with shipping and transport of specimens due to logistic difficulties;

3. the challenges associated with persuading some countries to share data in a timely manner (discussions with government officials have shown good support to overcome this issue and FluNet was identified as a good way to share information on a global level); and

4. the importance of purchasing good-quality laboratory equipment and ensuring you have timely service support in case equipment requires repair. Cheap equipment may cost more in the long term.
2.8 Plenary 4: Antiviral resistance surveillance

This session began with a presentation by Dr Aeron Hurt from the WHO Collaborating Centre in Melbourne, Australia. He presented factors that should be taken into consideration when establishing antiviral resistance surveillance. Participants were then invited to discuss antiviral resistance surveillance in their countries and areas.

Five broad questions should be considered before implementing antiviral resistance surveillance:

1. Which drugs are being used in your country or area?
2. Do you have a pandemic stockpile of antiviral drugs?
3. What type of samples will you be testing?
4. What is the current level of resistance in circulating strains?
5. Will other laboratories be testing strains from your region for resistance?

The most appropriate methodology for antiviral susceptibility testing will depend on the needs of the laboratory. The choice of methodology will be based on various factors such as requirements for adamantane or neuraminidase-inhibitor resistance testing, source of testing samples, i.e. from patients being treated with antivirals or from community samples, availability of resources and budget, and staff expertise. Regardless of the methodology chosen, it is essential that there is an understanding of the limitations of assays and that staff can interpret data appropriately.

Participants discussed their current role in antiviral resistance surveillance, which is summarized below:

1. Cambodia, China, Hong Kong (China), Mongolia, New Zealand, the Republic of Korea, India and Thailand are all involved in antiviral resistance surveillance and test using both genotypic and phenotypic methods.
2. Fiji, New Caledonia and Singapore have found it more feasible to send samples to a collaborating centre for antiviral resistance surveillance, rather than doing internal testing.
3. The Lao People’s Democratic Republic and Sri Lanka send samples to a collaborating centre, and are also undertaking technical discussions and looking into the feasibility of conducting their own testing.
4. Malaysia and Nepal do not do routine antiviral resistance testing as it is currently a low priority.
5. Bangladesh, Myanmar and the Philippines have limited testing which is predominantly done in a research capacity.
6. Viet Nam conducts genotypic testing on select samples and plans to conduct phenotypic testing in the future.
7. Indonesia does not conduct antiviral resistance surveillance except on outbreak cases.
8. The Democratic People’s Republic of Korea does not currently conduct antiviral resistance surveillance.
2.9 Group work 3: Development of the NIC/national influenza surveillance system's five-year workplan

A draft of the *Biregional Plan for Further Strengthening National Influenza Surveillance: Guiding the Way towards Influenza Control Policy and Regional Surveillance* was presented to participants. Participants discussed the draft in four working groups. Recommendations and suggestions were put forward to improve the plan.

The groups acknowledged that a pandemic could occur at any time, and countries and areas would need to have technical capabilities to detect influenza and the appropriate systems and policies to respond rapidly to untypable viruses. They would also benefit from the skills and knowledge to effectively link animal health and human health, link epidemiological and virological surveillance at the earliest possible time and obtain better surveillance data that will inform on timing of vaccination.

It was agreed that Member States should develop workplans and monitor progress in three areas of work: (1) defining the epidemiology and burden of influenza by linking virological and epidemiological surveillance and strengthening national networks; (2) improving virological testing capacity in the National Influenza Centres in an environment where safe laboratory practices and quality assurance are ensured; and (3) supporting national efforts and improving communication and reporting through the development or strengthening of regional and global networks.

WHO can assist with the development and implementation of workplans by:

1. continuing to conduct annual NIC/National Influenza Surveillance System meetings to share experiences, address common issues, and improve communication between WHO NICs and collaborating centres;
2. identifying training needs through NIC capacity assessments;
3. supporting NICs to meet the minimum capacity requirements and quality standards;
4. supporting countries with the development of a national influenza reporting system;
5. developing a regional reporting platform;
6. providing practical guidelines or technical assistance for burden of disease studies;
7. developing a regional vaccine policy workgroup to look at regional vaccine introduction and use policies, the level of evidence or impact data by country, and vaccine production;
8. supporting national efforts for the development of seasonal influenza control policies;
9. supporting the development of national influenza awareness education strategies; and
10. establishing links with regional influenza awareness activities.

2.10 Summary and closing of the full plenary sessions

*Dr Jeffrey Partridge, WHO Western Pacific Regional Office*

Dr Partridge made closing remarks prior to the group breaking into parallel sessions on the final day. He acknowledged the fruitful discussion on the WHO External Quality Assessment Programme, which will be used to improve the programme. He also noted that the meeting was a good opportunity to learn more about antiviral resistance surveillance in the two WHO regions. Specifically, countries and areas discussed current initiatives and some of the challenges and barriers they experience.
The development of a summary of epidemiological and virological characteristics of influenza in the Western Pacific Region is a great example of collaboration within GISRS. The process of reviewing the draft summary was useful for recognizing that while a great deal of progress has been made in the Region in terms of influenza surveillance, there is still work to be done to improve data collection and reporting. Efforts to work together on the summary to develop it into a manuscript for publication will continue.

The five-year Biregional Plan for Further Strengthening National Influenza Surveillance: Guiding the Way towards Influenza Control Policy and Regional Surveillance provides direction for reaching the vision of reducing morbidity and mortality associated with influenza in all countries and areas of the two regions.

Participants were acknowledged for their participation in a successful meeting, and for the excellent work achieved by all countries and areas.

Dr Oommen John, WHO South-East Asia Regional Office

Dr John thanked the meeting organizers for inviting the South-East Asia Region to participate in the meeting. The meeting highlighted the need to continually work towards harmonization of data to translate it into public health policy. The South-East Asia Region looks forward to strengthening networks and sharing data and knowledge in the future. It also hopes to prepare a summary of epidemiological and virological characteristics of influenza in the South-East Asia Region, similar to the one drafted by the Western Pacific Region. He concluded by acknowledging the lessons learnt from discussions during the meeting, and expressing his appreciation for the informal networks built. He looks forward to ongoing collaboration.

2.11 Plenary 5: Presentations and discussions with WHO collaborating centres

Chairs: Dr Harpal Singh, Dr Dapeng Luo

2.11.1 Presentation 1: A collaborating centre's perspective on the three Cs: collaboration, communication and capacity-building

Dr Anne Kelso, Dr Patrick Reading, WHO Collaborating Centre, Australia

To enhance collaboration in virological surveillance and isolation of vaccine viruses, collaborating centres request NICs to submit novel or unsubtypable viruses, recently circulating viruses, some clinical specimens for isolation of vaccine candidates and relevant clinical or epidemiological information. With timely virus submission, collaborating centres hope to provide NICs with urgent identification of novel or unsubtypable viruses, rapid reporting of results for circulating viruses and information on availability of vaccines matched to circulating viruses. Collaborating centres also hope to collaborate on research projects of mutual interest.

Collaborative networks can be strengthened through sharing of virological, technical and other information. This can be done effectively through meetings, telephone calls, e-mail and reports. WHO collaborating centres are committed to assisting NICs in laboratory-based detection of influenza viruses, particularly through training.

There were discussions surrounding the criteria for sending specimens from NICs to WHO collaborating centres. While there are no set criteria, the decision is often dependent on factors such as geographical feasibility, shipping and other logistical costs, permits and customs clearances. WHO was requested to provide guidance to NICs on how to select WHO collaborating centres for sending of specimens based on factors such as cost and logistics. There was notably good collaboration between WHO collaborating centres and NICs.
2.11.2 Presentation 2: Laboratory strategies and challenges for detection and characterization of influenza

Dr Xiyan Xu, WHO Collaborating Centre, United States of America

The strategies for detection of influenza, including detection of viral antigen, viral nucleic acid and live virus, were discussed, including the advantages and disadvantages of each strategy. An explanation of virus submission (why, when, what) was covered, including the steps involved in virus characterization at WHO collaborating centres.

A brief explanation of the challenges faced in the South Pacific was given. Rapid influenza diagnostic tests were initially seen as a feasible option in areas that were remote and where more technologically advanced methods were not available. However, the low sensitivity of the tests and over reliance by physicians were notable problems. While immunofluorescence assays are gaining popularity, it was noted that they are highly operator dependent and require skills with microscopy for interpretation. This has resulted in laboratory staff being less comfortable and confident with the results. PCR has now become the mainstay and is perceived to be straightforward.

The lack of dry ice for packing and shipping of viruses could be addressed by using virus lysis buffers, which enable viruses to be shipped at room temperature for PCR. However, virus culture is not possible when lysis buffers are added.

2.11.3 Presentation 3: Improving influenza vaccine virus selection process – report from a WHO informal consultation, 14–16 June 2010

Dr Wenqing Zhang, WHO Headquarters

Retrospective studies have shown that WHO recommendations for influenza vaccine virus selection closely match the circulating viruses during the targeted season. However, since a decision on vaccine composition must be made almost one full year in advance of the peak of the targeted season, it is crucial for NICs to collect and forward representative samples to WHO collaborating centres in a timely manner for this continued public health benefit.

While the process is highly technical and complex, with numerous collaborative efforts, vaccine virus selection lies at the heart of global efforts against influenza. WHO will maintain its central role of coordinating worldwide expertise to meet increasing public health needs and work with the GISRS and its partners to identify improvements, harness new technologies, and strengthen and sustain collaboration.

2.11.4 Presentation 4: Efficacy of influenza A(H3N2) and B vaccines

Dr Takato Odagiri, WHO Collaborating Centre, Japan

This presentation discussed recent research into the efficacy of influenza A(H3N2) and B vaccines conducted by the WHO Collaborating Centre in Japan. The results from this study are expected to be published in the near future.

2.11.5 Presentation 5: Management and quality evaluation of influenza surveillance network in China

Dr Dayan Wang, WHO Collaborating Centre, China

In 1952, the Chinese Center for Disease Control and Prevention commenced influenza surveillance, and in 1957, the Chinese National Influenza Centre was established. In 1981, the Chinese NIC joined the GISN network.
The surveillance network in China is very extensive. The network covers not only all provinces, but also all prefectures and some counties. The surveillance objectives are:

1. to monitor influenza activity in mainland China;
2. to determine which influenza viruses are circulating;
3. to detect changes in antigenic and genetic characteristics, and provide evidence for recommending circulating strain and vaccine strain; and
4. to monitor for novel influenza viruses with pandemic potential.

China NIC is willing to share a simplified version of their information system; however, it should be noted that while the system is very good, ongoing improvement is necessary to address issues such as software bugs, slow processing speed and the generation of analytical reports.

3. MEETING OF INFLUENZA PUBLIC HEALTH RESEARCH AGENDA

The Fourth Meeting of the National Influenza Centres in the Western Pacific Region held in June 2010 commended countries that were advancing the research agenda and made a categorical recommendation for vaccine development and disease-burden studies on influenza. In order to develop strategies that will reduce the burden of influenza and to strengthen regional public health preparedness and response, a public health research agenda for influenza must be developed. This consultative meeting with expert researchers on influenza aimed to develop a five-year research agenda for national vaccine policy development. The objectives were:

1. to facilitate discussion about research activities that would augment a five-year vaccine policy development plan;
2. to develop a road map with listed research activities for vaccine policy development; and
3. to discuss the necessary facilities and resources for the purpose of developing vaccine policy.

3.1 Module 1: Disease burden, vaccine target and effectiveness

Chairs: Dr Yoshio Hirota, Dr Lance Jennings

This module commenced with a presentation by Dr Sonja Olsen on "Influenza in Thailand: data for decision-making". She discussed how research in Thailand contributed to influenza vaccine policy changes. Prior to 2001, little was known about the burden of influenza in Thailand and the uptake of vaccine was minimal. Research studies identified susceptible populations, determined the burden and economic costs of influenza infections specific to Thailand, and influenced recommendations for vaccination policy changes, e.g. vaccinating the elderly and adults with chronic diseases.

In implementing an influenza vaccine programme in a country, it is important to know the burden of influenza in the community. Currently, many countries have implemented national influenza surveillance to monitor the trend of influenza activities, but few studies have been conducted on influenza disease burden. General discussion around disease burden and target audiences for vaccination highlighted the need for countries to know what data are collected, what
vital statistics are available, what health utilization surveys have been conducted, and what data are required.

Filling the gaps in knowledge research should begin with a literature review. After the literature review, two research paths should be considered: (1) identify core data requirements and ways to collect the data; and (2) undertake special studies to further understand influenza.

Burden of disease studies could focus on mortality, severity by age group, and hospitalization. The cost-effectiveness of a vaccination programme would help guide policy. Data need to be collected on basic demographics and denominator data. Studies should also consider target populations for vaccination, e.g. children, adults, the elderly, pregnant women, people living with chronic disease, and health workers.

3.2 Module 2: Vaccine selection, deployment and regulations

Chairs: Dr Myoung-don Oh, Dr Takato Odagiri

The meeting discussed the need for studies to address vaccine selection in prospects of influenza seasonality and vaccine manufacturing. Research in this area could identify influenza vaccines currently being used and production capacity in the Region, could identify seasonality/timing of vaccine use in tropical countries and could help determine which type of vaccine should be recommended based on cost, timing, availability, etc.

Vaccine deployment is a challenge in some countries. Issues associated with influenza vaccine deployment and administration should be identified to assist in the development of guidelines for deployment. Research could identify issues associated with influenza vaccine deployment and administration to develop guidelines.

3.3 Module 3: Design of research on disease burden, vaccine target and effectiveness

Chairs: Dr Hitoshi Oshitani, Dr Bonduush Ichinkhorloo

To move forward with the research agenda, it is possible to use a regional approach, i.e. data from a few countries could inform “all” countries. There is also a need to look for and validate “simplified” methods to define disease burden. Taking this approach is the simplest way to obtain the available core data for each country and area.

Some countries and areas have the capacity to conduct more sophisticated studies. Methods for moving from surveillance to disease burden studies are being developed by WHO Headquarters and Thailand. It was recommended that a regional practical guide for using surveillance systems for disease burden should be developed.
4. CONCLUSIONS

During the recent influenza A(H1N1) 2009 pandemic, when a novel virus strain was first reported, it became apparent that a global network of institutions was needed for influenza surveillance and the gathering, analysis and distribution of laboratory data. Throughout the pandemic, data availability and reporting was a testament to the great strides made by countries and areas in terms of strengthening surveillance systems, including establishment of laboratory facilities for case confirmation.

During the meeting, recommendations and suggestions were put forward to improve the draft *Biregional Plan for Further Strengthening National Influenza Surveillance: Guiding the Way towards Influenza Control Policy and Regional Surveillance*. It was agreed that countries and areas should develop workplans and monitor progress in three areas of work: (1) defining the epidemiology and burden of influenza, (2) improving virological testing capacity, and (3) improving communication and reporting through the development or strengthening of regional and global networks. WHO can assist in implementation by continuing its support and providing practical guidelines, tools, reporting platforms and forums for discussions.

Preparing the summary of epidemiological and virological characteristics of influenza in the Western Pacific Region was a greater challenge than first expected. However, it was agreed that the presentation of regional data was valuable. Further data collection was recommended to improve the understanding of disease burden in the Western Pacific Region and to identify areas for improvement in surveillance and reporting.

The research agenda meeting highlighted areas that need further research to better inform influenza vaccine introduction policy. It was recommended that research should begin with a literature review, followed by research to identify the core data required and special studies to fill knowledge gaps. To move forward with the research agenda, a regional approach to obtain data should be considered. A validated “simplified” method to define disease burden using surveillance systems was also recommend. Countries and areas that have the capacity could conduct studies to collect more sophisticated data.

The meeting was an excellent opportunity for participants to meet and share experiences. Several outcomes and actions were agreed upon.

(1) The five-year *Biregional Plan for Further Strengthening National Influenza Surveillance: Guiding the Way towards Influenza Control Policy and Regional Surveillance* will be finalized and disseminated after comments from participants have been addressed.

(2) Work on the summary of epidemiological and virological characteristics of influenza in the Western Pacific Region will continue with the collection of additional data from participating countries and areas.

(3) A regional influenza research agenda for the Western Pacific Region will be drafted based upon the deliberations of the meeting.
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