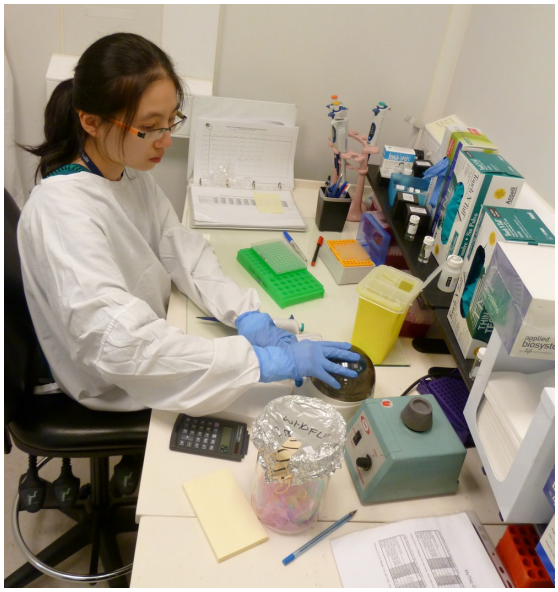
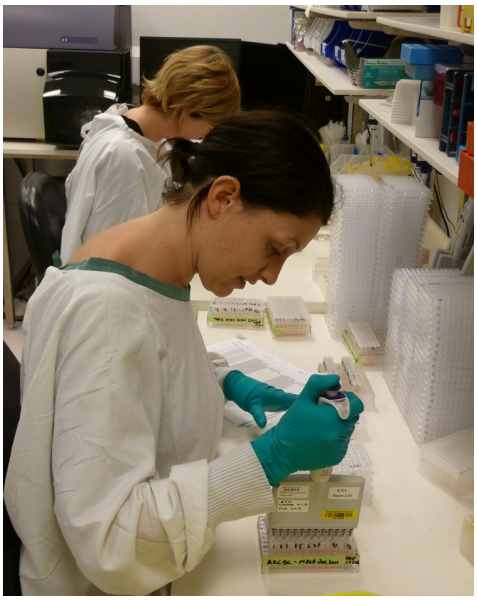
Annual Report 2013





WHO Collaborating Centre
for Reference and
Research on Influenza
VIDRL

Contents

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About the Centre

The WHO Collaborating Centre for Reference and Research on Influenza at the Victorian Infectious Diseases Reference Laboratory (VIDRL) in Melbourne is part of the World Health Organisation Global Influenza Surveillance and Response System (WHO GISRS). The network was established in 1952 to monitor the frequent changes in influenza viruses with the aim of reducing the impact of influenza through the use of vaccines containing currently circulating strains. Together with WHO Collaborating Centres in Atlanta, Beijing, London and Tokyo, the Centre is responsible for analysing influenza viruses currently circulating in the human population in different countries around the world. The Centre in Melbourne was first designated as a Collaborating Centre in 1992, the third such Centre in the world.

Terms of Reference

Under its designation as a WHO Collaborating Centre for Reference and Research on Influenza, the Centre's Terms of Reference (for 2011-2015) are:

i. to obtain, isolate and preserve representative viruses from outbreaks and sporadic cases of influenza, and characterise their antigenic and other relevant properties, including resistance to anti-influenza drugs;
ii. to exchange information and new antigenic variants of influenza viruses with other WHO Collaborating Centres for Reference and Research on Influenza and with Essential Regulatory Laboratories;
iii. to assist WHO in developing recommendations on viruses to be included in influenza vaccines;
iv. to provide training and laboratory support to WHO National Influenza Centres and other laboratories, especially those in the developing world, in specialised techniques for diagnosis, isolation and characterisation of influenza viruses, according to their needs;
v. to collect epidemiological information on the prevalence of influenza, especially in countries and areas in the Region;
vi. to undertake research to improve the detection, prevention and treatment of influenza; and
vii. to assist WHO and national health authorities in developing and implementing plans for responding to pandemic influenza.

Governance

The Centre is supported by the Australian Government Department of Health through a funding agreement between the Commonwealth and Melbourne Health, and reports directly to the Department as well as to WHO. An Australian Government Advisory Committee (AGAC) reviewed the Centre's work program and progress, provided advice to assist the Centre and the Commonwealth with its objectives under the work program, and monitored and advised on the scientific performance and direction of the Centre. AGAC was disbanded in 2013.

AUSTRALIAN GOVERNMENT ADVISORY COMMITTEE 2013

Prof Chris Baggoley, Chair (Commonwealth Chief Medical Officer)

Dr Gary Lum AM, Deputy Chair (Assistant Secretary, Health Emergency Management Branch)

Prof Michael Richards (Director, Victorian Infectious Diseases Service, Royal Melbourne Hospital)

Prof Peter Doherty AC FAA FRS (Laureate Professor, Department of Microbiology and Immunology, The University of Melbourne)

Prof John Horvath AO (Principal Medical Consultant for the Department of Health and Ageing)

Prof John Mackenzie AO (Professor of Tropical Infectious Diseases, Curtin University of Technology)

Dr Greg Stewart (Director Operations, Ambulatory and Primary Health Care, South East Sydney Local Health District)

Dr Heather Wellington (Consultant, Health Law Team, DLA Piper Australia)

Dr Martyn Jeggo, observer (Director, Australian Animal Health Laboratory, CSIRO)

Dr Mike Catton (Director, Victorian Infectious Diseases Reference Laboratory)

Prof Anne Kelso AO (Director of the Centre)

Highlights of 2013

Surveillance

The Centre received 3990 samples from 13 countries during 2013. Of the samples tested, 32% were A(H1N1) pdm09 and 27% were B/Yamagata lineage viruses.

Response to Potential Pandemic Viruses

Following the emergence of avian influenza A(H7N9) in early 2013, the Centre worked closely with WHO and the GISRS network to prepare reagents for viral detection and monitor developments in response to the outbreak.

Sequencing and Phylogenetic Analysis Workshop

The Centre hosted a week-long Regional Workshop on Sequencing and Phylogenetic Analysis of Influenza Viruses in April. The workshop was attended by 16 participants from National Influenza Centres in the Asia Pacific region, who undertook training in practical laboratory and computational analysis methods.

Research

The Centre continued to expand and develop its range of research interests during 2013, including a seroepidemiological study of infants in Vietnam, further developing relationships with influenza sentinel surveillance systems within Australia and investigating the effectiveness of antiviral drugs in animal models. Together with collaborators at the Bioinformatics Institute in Singapore, Centre researchers received a joint A*STAR/NHMRC grant.

Publications

Centre staff were authors on a total of 45 original research papers, reviews, reports and book chapters, the largest number of annual publications by the Centre to date.

Director's Report

It is a great pleasure to present the 2013 Annual Report. During the year, our Centre made a major contribution to influenza virological surveillance and capacity building in the Asia-Pacific region and continued to expand its collaborative and in-house research activities. We also saw the completion of the Doherty Institute building project and preparation for the Centre's move into its new premises in 2014.

Surveillance remains at the heart of the Centre's work. Many WHO National Influenza Centres and other reference and diagnostic laboratories throughout Australia and the region send us clinical specimens and virus isolates to enable the monitoring of antigenic and genetic evolution of influenza viruses through the year. The twice-yearly collation and review of these data with those from the other four WHO Collaborating Centres for Influenza form the basis of WHO's recommendations on the updating of seasonal influenza vaccines for use around the world. We and other Centres then provide candidate vaccine viruses to the manufacturers. This important global system depends on the contributions of many National Influenza Centres and other submitting laboratories and we thank them for their outstanding support in 2013.

The Centre is very pleased to offer technical support to National Influenza Centres through staff training in their own laboratories or in ours, and a number of such activities were undertaken in 2013. This year the Centre also ran a regional workshop on sequencing and phylogenetic analysis for 16 students from 9 countries, with instruction by several international experts as well as our own staff.

The Centre published its highest number of papers ever in 2013, reflecting the growth of collaborative and in-house research by many Centre staff members. Much of this work is undertaken with international collaborators in the WHO's Global Influenza Surveillance and Response System and shows how research can increase the value obtained from surveillance activities. The Centre was also successful in winning several competitive research grants with collaborators in Australia and Singapore. We are grateful to all our research colleagues for their continuing collaboration.

In March 2013, the Chinese Ministry of Health announced the detection of a new avian influenza A(H7N9) virus causing severe human disease in eastern China. The WHO Collaborating Centre for Reference and Research on Influenza at China CDC in Beijing immediately posted the sequences of the first H7N9 isolates in the GISAID database. Thanks to China's rapid sharing of information and viruses, we and the other WHO Collaborating Centres for Influenza were able to obtain reference H7N9 viruses, establish assays and provide reference material to National Influenza Centres and other diagnostic laboratories to assist them in preparing for diagnosis of possible human cases. I was also honoured to participate in a joint China-WHO Mission on H7N9 in Shanghai and Beijing in April 2013 to review and advise the Chinese Government on its response to the outbreak.

The Centre, with the rest of VIDRL, will move into the new Peter Doherty Institute for Infection and Immunity in early 2014. This presents an extraordinary opportunity for the Centre to be part of a new collaborative enterprise which is bringing together research, teaching, clinical and public health laboratory activities in infectious disease and immunology from Melbourne Health and the University of Melbourne. Centre staff members have been actively involved throughout the design and construction of the technically and architecturally sophisticated new Doherty Institute building and in strategic discussions on the Institute's future work. With practical completion of the building in November 2013, the focus has shifted to obtaining all the necessary regulatory approvals for the Centre's operation in its new BSL2 and BSL3 facilities and planning for relocation in 2014.

In early 2013, we successfully applied for funding of the Centre by the Australian Government through the Health Protection Fund for a further four years from 1 July 2013. The strong and sustained support we receive from the Australian Government underpins all of the Centre's work for WHO and provides the foundation from which we can leverage research funding for specific projects from other sources. We are extremely grateful for the Department of Health's long-term commitment to the Centre.

I would like to thank all the staff and students of the Centre for the high quality of their work in 2013. In VIDRL, Dr Mike Catton as Director, Renato Raimondi as Business Manager and Anna Ayres as Human Resources Manager have been unfailing in their support of the Centre. Finally, I would like to express my deep appreciation to the members of our Australian Government Advisory Committee whose wise counsel I have found invaluable from 2007 until early 2013 when the Committee completed its work.

Professor Anne Kelso *AO*
Director

Surveillance

Introduction

The WHO Collaborating Centre at VIDRL in Melbourne is one of five Collaborating Centres in the world that conduct human influenza surveillance for WHO by analysing samples submitted by WHO National Influenza Centres and other laboratories. Most of the samples received at the Centre in Melbourne come from the Asia-Pacific region.

Twice a year (once each for the northern and southern hemispheres) WHO makes recommendations on suitable influenza strains to be included in the next seasonal vaccine based on data and advice from the five Collaborating Centres and other experts.

Two types of influenza virus, Type A and Type B, cause significant disease in humans. The surface of influenza viruses is coated with two proteins, haemagglutinin (HA) and neuraminidase (NA). There are many subtypes of influenza A viruses originally of avian origin, with various combinations of 16 antigenically different HA variants and 9 NA variants. Although influenza B viruses are not classified into subtypes, there are two co-circulating lineages, B/Victoria and B/Yamagata. Currently there are three families of influenza viruses circulating in the human population — influenza A (H1N1), influenza A(H3N2) and influenza B. Since the emergence of the pandemic A(H1N1) strain in 2009 [A(H1N1)pdm09], circulation of the former seasonal A(H1N1) virus has ceased.

Receipt of Influenza Viruses

During 2013 the Centre received 3990 clinical specimens and/or virus isolates from 33 laboratories in 13 countries (Figures 1 and 2, Table 1). A total of 3936 samples (99%) were cultured and analysed by haemagglutination inhibition (HI) assay and/or real-time reverse-transcription polymerase chain reaction (RT-PCR) reaction. Of the samples tested, 32% were identified as A(H1N1)pdm09 and 27% were B/Yamagata lineage viruses (Table 1). For reporting purposes, subtypes and lineages are based on antigenic analysis of the HA and in some cases are confirmed by genetic analysis of NA. Amongst samples received by the Centre for which the age of the patient was known, a broad range of age groups was represented (Figure 3).

Isolation of viruses

Original clinical specimens received by the Centre can be genetically analysed by sequencing or real-time RT-PCR and are also required for direct isolation into eggs as potential vaccine strains. For more extensive analyses, viruses from original clinical specimens are cultured and isolated in Madin-Darby Canine Kidney (MDCK) cells.

Figure 1. Samples received and analysed at the Centre, 2009-2013.

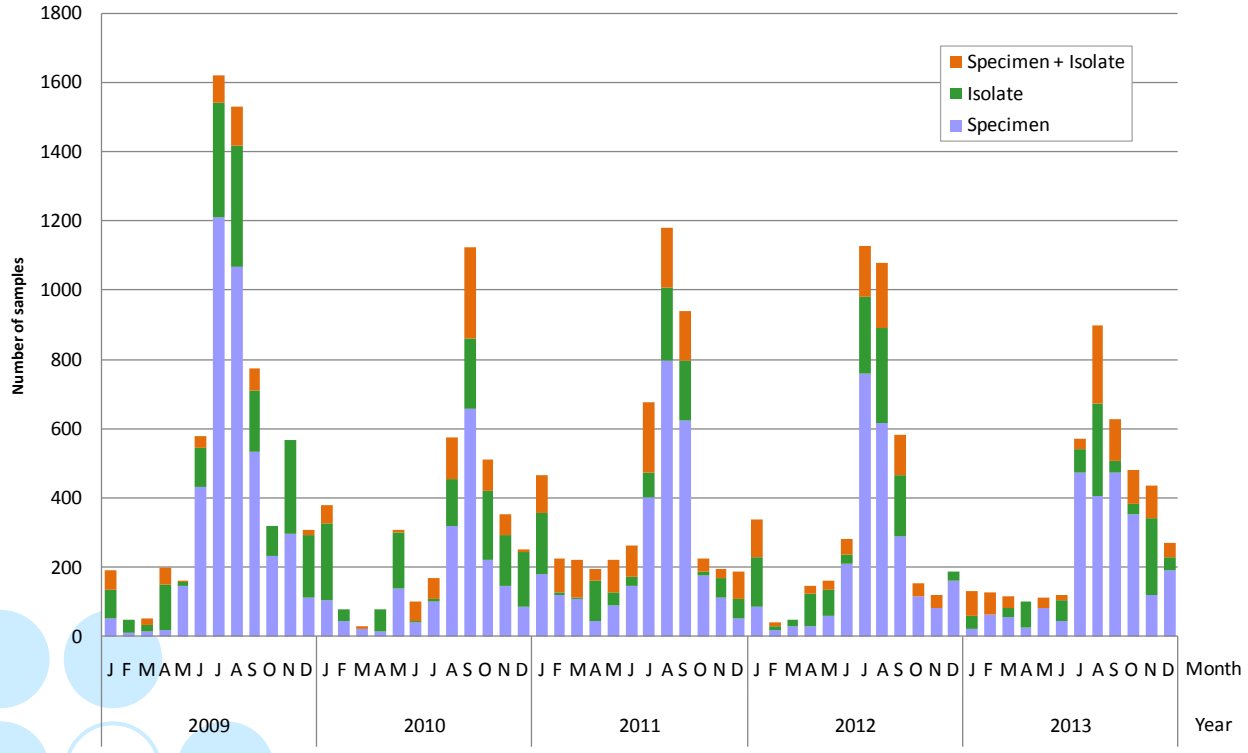


Figure 2. Geographic spread of influenza laboratories sending viruses to the Centre during 2013.

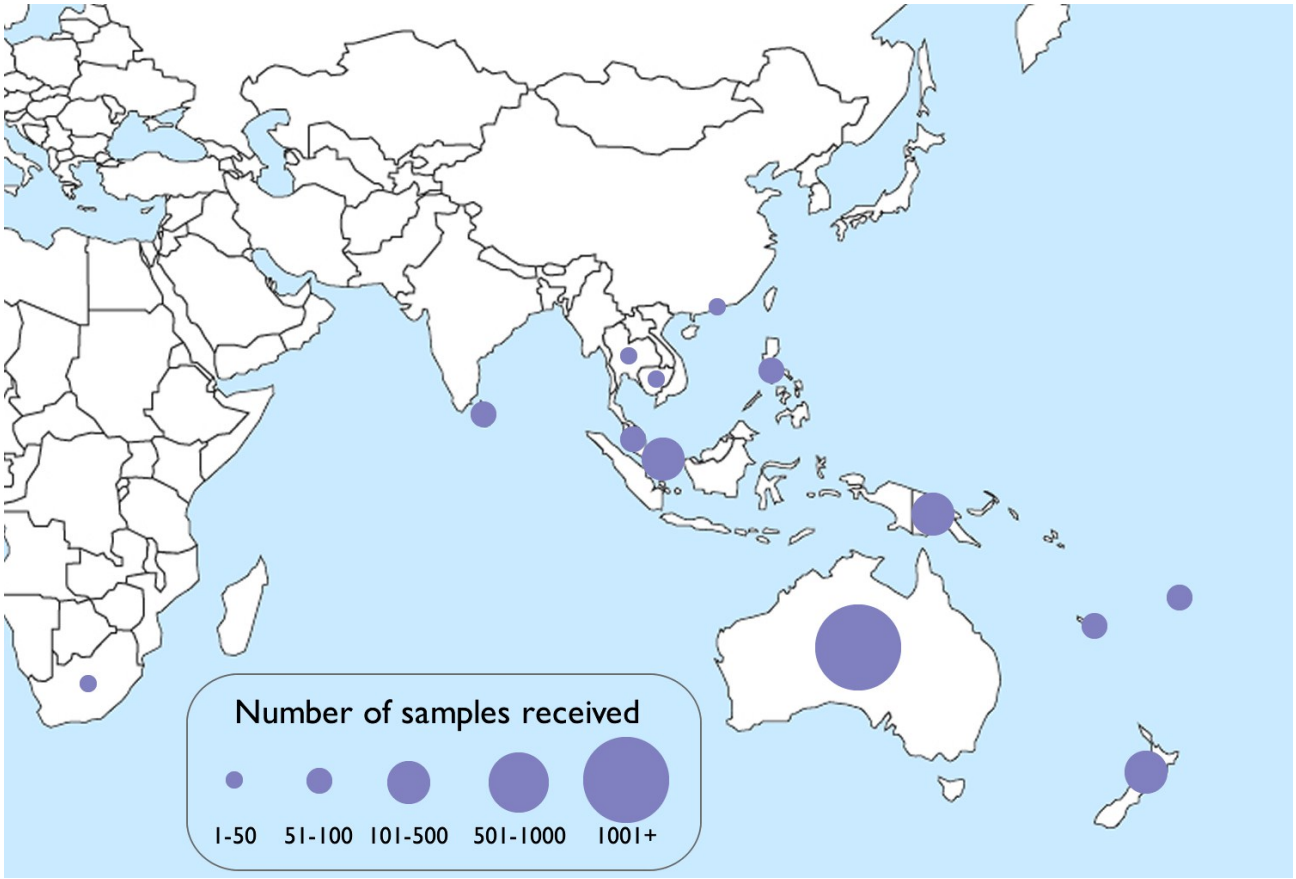


Figure 3. Age distribution of subjects from whom samples were received and the age is known at the Centre in 2013.

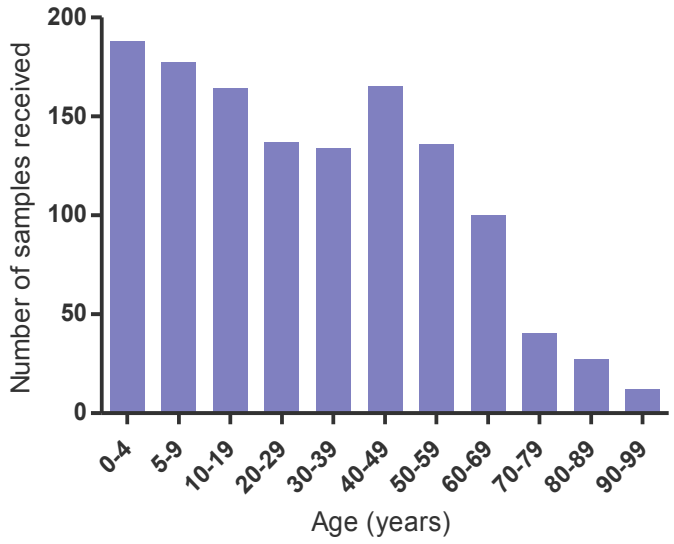


Table 1. Samples received and analysed at the Centre in 2013 by country, type and subtype/lineage.

Country	Samples received		Samples tested	Samples tested by HI and/or RT-PCR assay						
	Specimens	Isolates		A(H1N1) pdm09	A(H3N2)	A(unsub-typed)	Mixed type/ subtype	B/ Victoria	B/ Yamagata	C
AUSTRALASIA	**1758**	**1267**	**2991**	**985**	**591**	**145**	**1**	**863**	**59**	**29**
Australia	1678	733	2377	880	398	144	1	589	40	29
New Zealand	80	534	614	105	193	1	0	274	19	0
SOUTH PACIFIC	**427**	**0**	**407**	**82**	**16**	**6**	**1**	**5**	**1**	**0**
Fiji	70	0	70	5	8	0	0	5	1	**0**
New Caledonia	57	0	57	49	8	0	0	0	0	0
Papua New Guinea	300	0	280	28	0	6	1	0	0	0
SOUTH EAST ASIA	**31**	**361**	**392**	**108**	**129**	**20**	**3**	**67**	**43**	**0**
Cambodia	0	50	50	32	3	0	0	11	4	0
Malaysia	0	53	53	3	13	7	2	19	8	0
Philippines	21	44	65	11	20	13	1	0	0	0
Singapore	0	174	174	56	65	0	0	27	26	0
Thailand	10	40	50	6	28	0	0	10	5	0
EAST ASIA	**0**	**25**	**25**	**17**	**6**	**0**	**0**	**1**	**1**	**0**
Macau SAR	0	25	25	17	6	0	0	1	1	0
SOUTH ASIA	**100**	**0**	**100**	**35**	**25**	**11**	**0**	**8**	**1**	**0**
Sri Lanka	100	0	100	35	25	11	0	8	1	0
AFRICA	**0**	**21**	**21**	**17**	**2**	**0**	**0**	**2**	**0**	**0**
South Africa	0	21	21	17	2	0	0	2	0	0
TOTAL	**2316**	**1674**	**3936**	**1244**	**769**	**182**	**5**	**946**	**105**	**29**

Antigenic Analysis of Influenza Isolates

Background

The antigenic properties of influenza viral isolates are analysed using the HI assay, in which viruses are tested for their ability to agglutinate red blood cells in the presence of ferret antisera previously raised against reference viruses. Subtypes are based on analysis of the HA an in some cases are confirmed by genetic analysis of NA.

Antigenic analyses 2013

A total of 3548 isolates that were received at the Centre in 2013 were cultured and isolated in MDCK cells, of which 2611 (73.6%) produced a positive result. The majority of viruses were A(H1N1)pdm09 (37.9%) or B/Yamagata lineage (36.1%), followed by A(H3N2) (21.6%) (Figure 4). The predominance of A(H1N1)pdm09 and B/Yamagata viruses was reflected in the distribution of isolates from all geographic regions (Figure 5).

Figure 4. Influenza sub/types and lineages of samples received in 2013 and analysed by HI assay.

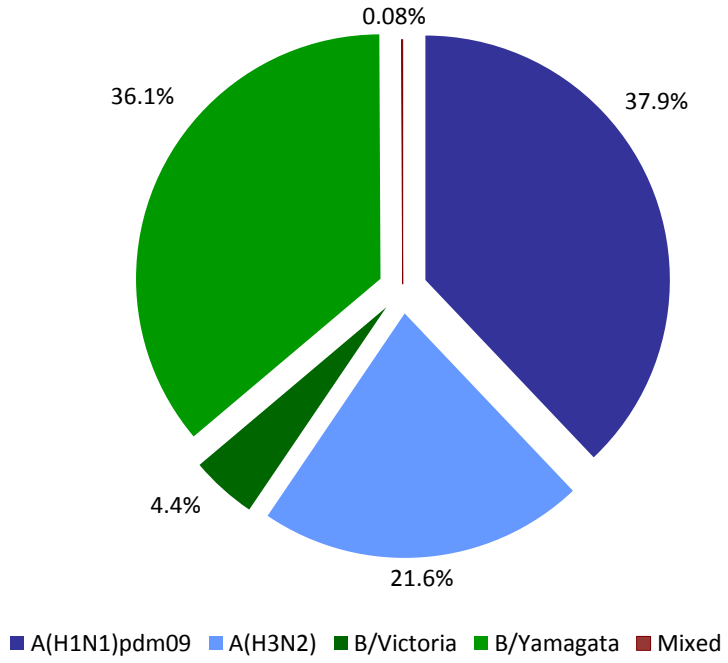
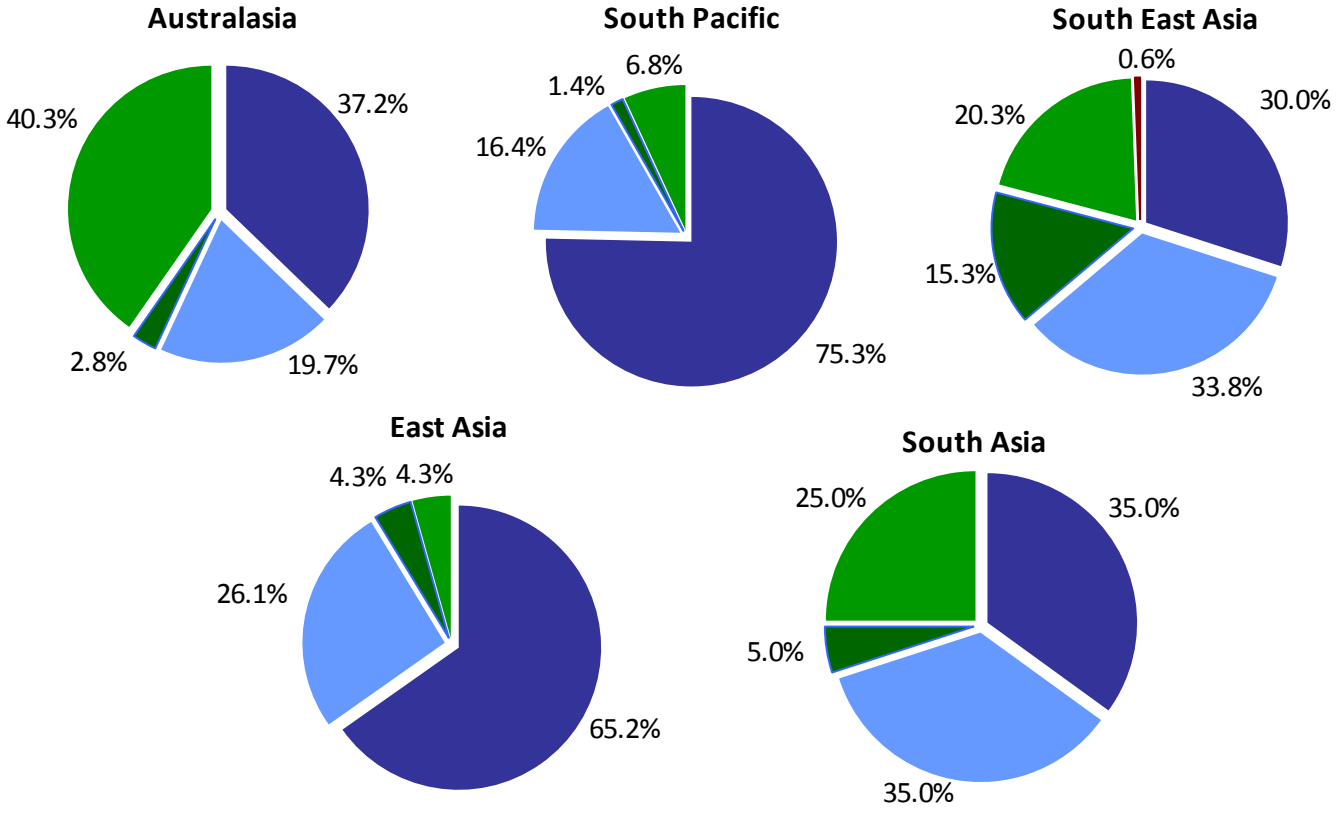


Figure 5. Influenza sub/types and lineages of isolates received from different world regions during 2013 as determined by antigenic analysis.



Genetic Analysis of Influenza Viruses

Background

A subset of all influenza viruses analysed at the Centre undergo genetic analysis by sequencing of viral RNA genes. Determining the amino acid sequence of antigenic regions of the HA and NA proteins provides a sensitive method to examine the extent and direction of change in circulating influenza viruses. Routine sequencing of the matrix protein (MP) and non-structural protein (NS) genes is also performed.

Viruses selected to undergo sequencing include those that exhibit evidence of antigenic drift by HI assay as well as viruses that are generally representative of samples received by the Centre by geography and date of isolation. Sequence data are used to compare viruses from different parts of the world and help to inform the selection of vaccine strains.

Sequencing 2013

In 2013, 419 HA, 393 NA, 271 MP and 185 NS genes of human viruses received at the Centre were sequenced (Figure 6). In addition, 60 viruses were analysed by full genome sequencing (Figure 7) and 27 human influenza A viruses were analysed by pyrosequencing for evidence of reassortment (Figure 8). Viruses were selected for these analyses because they were representative of the viruses received and/or because they displayed unusual properties during antigenic analysis.

Figure 6. Sequence analysis of samples received at the Centre in 2013.

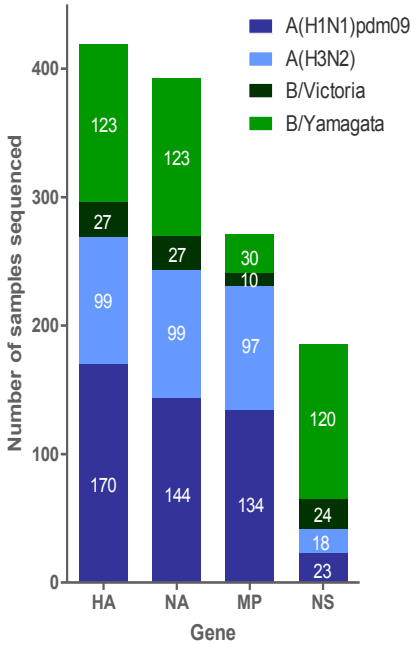


Figure 7. Geographic spread of submitting laboratories and numbers of viruses analysed by full genome sequencing at the Centre in 2013.

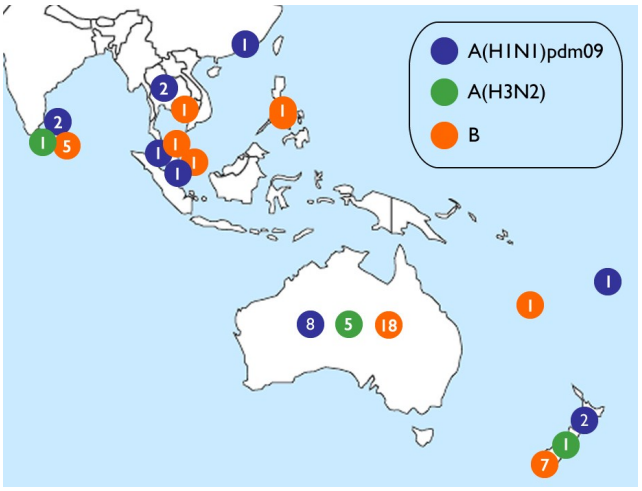
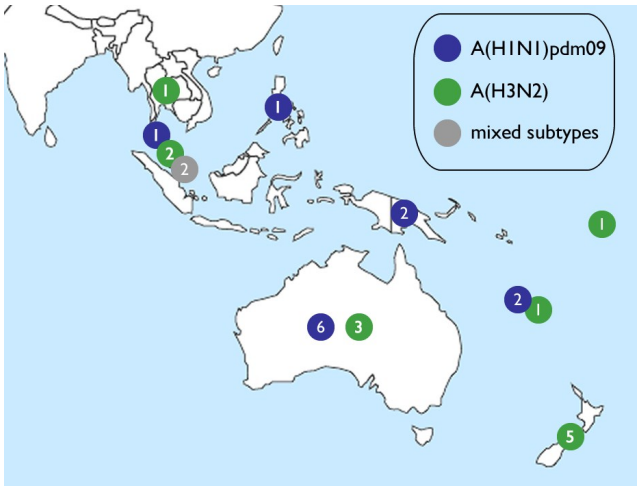


Figure 8. Geographic spread of submitting laboratories and numbers of viruses analysed by pyrosequencing at the Centre in 2013.



Submission of Influenza Sequences to GISAID

Background

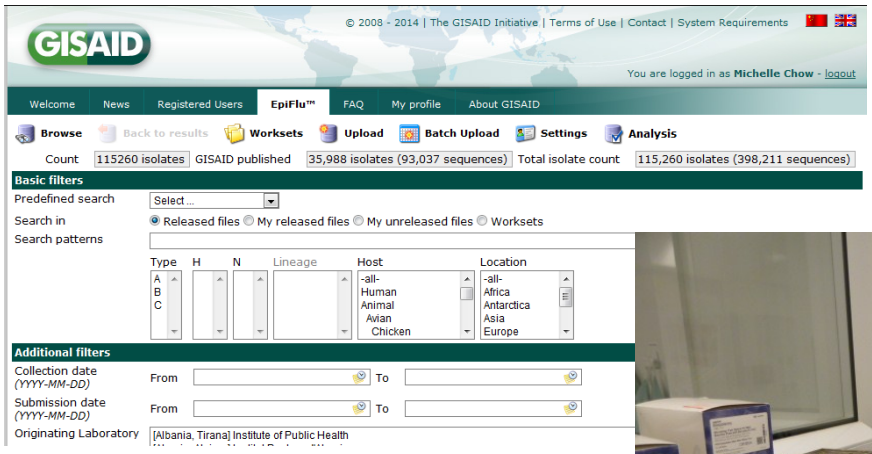
Virus sequences generated at the Centre are shared with the global influenza community through the EpiFlu™ database, a publically accessible international repository of influenza virus sequences developed by the Global Initiative on Sharing All Influenza Data (GISAID) (http://www.gisaid.org).

Sequences submitted in 2013

A total of 1396 gene sequences from 393 viruses were deposited with GISAID in 2013 (Table 2). The largest number of these sequences were of HA and NA genes, followed by MP and NS genes. Full genomes of 55 influenza viruses were also represented in the Centre's submissions (data not shown).

Table 2. Genetic sequences submitted to GISAID of samples received at the Centre in 2013.

Type/ Subtype / Lineage \ Gene	HA	NA	MP	PB2	PB1	PA	NP	NS	Total
A(H1N1)pdm09	105	105	100	12	12	12	12	12	**370**
A(H3N2)	112	97	77	4	4	4	4	4	**306**
B/Victoria	54	54	15	15	15	15	15	43	**226**
B/Yamagata	121	121	28	28	25	27	28	116	**494**
Total	**392**	**377**	**220**	**59**	**56**	**58**	**59**	**175**	**1396**



Natalie Spirason

Surveillance Results by Influenza Subtype

Viruses were analysed by comparison with reference viruses recommended by WHO for the 2013 Southern Hemisphere and 2012-2013 Northern Hemisphere vaccines. Using the HI assay, viruses were identified as low-reactors if their titre with the reference antiserum was at least 8-fold lower than the titre of the reference virus. Results of sequencing analysis of the HA region of the haemagglutinin gene are also described in the following sections.

Influenza A(H1N1)pdm09

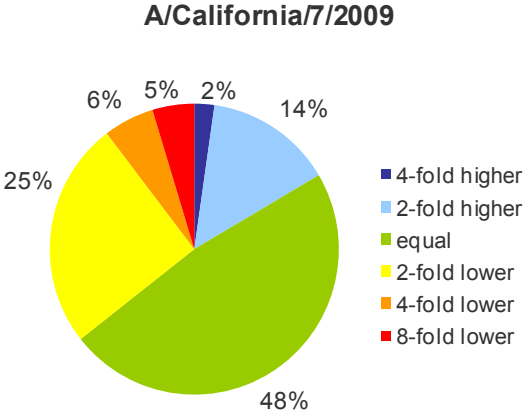
Antigenic analysis

A total of 990 A(H1N1)pdm09 isolates were available for analysis by HI assay in 2013. The majority (95.4%) of these viruses displayed similar antigenic properties to the vaccine reference strain A/California/7/2009 (Table 3, Figure 9).

Table 3. Antigenic characterisation of A(H1N1)pdm09 viruses analysed at the Centre compared to the A/California/7/2009 reference virus.

	A(H1N1)pdm09 reference strain: A/California/7/2009	
Region	**Like**	**Low reactor (%)**
Australasia	755	39 (4.9%)
Pacific	53	2 (3.6%)
South East Asia	98	4 (3.9%)
East Asia	15	0
South Asia	6	1 (14.3%)
Africa	17	0
Total	**944**	**46 (4.6%)**

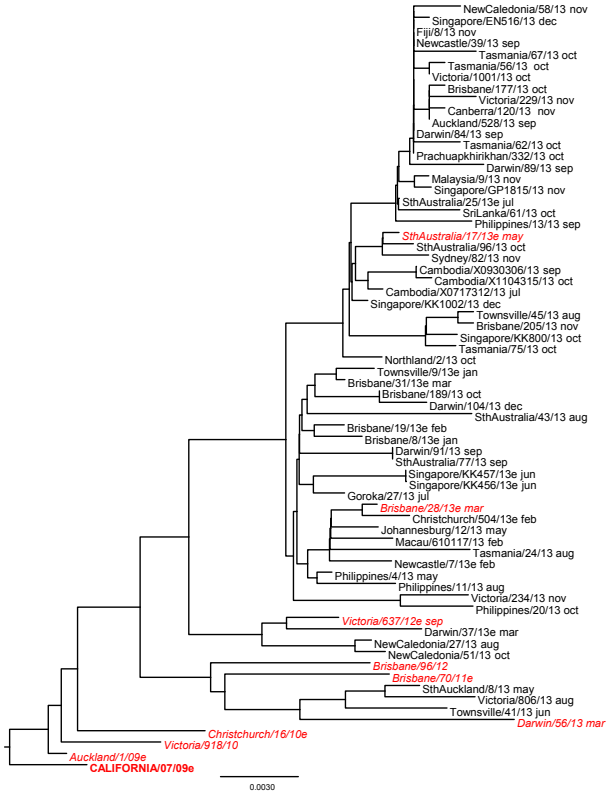
Figure 9. Summary of fold differences in HI titres of A(H1N1)pdm09 viruses analysed at the Centre compared to the A/California/7/2009 reference virus.



Haemagglutinin gene sequencing

Sequencing was performed on HA genes from 170 viruses. Phylogenetic analysis showed that circulating A(H1N1)pdm09 viruses sent to the Centre during 2013 contained some genetic changes compared to the vaccine reference strain A/California/7/2009, however, these changes were non-significant and did not change the antigenic behaviour of the viruses (Figure 10).

Figure 10. Phylogenetic tree of representative HA genes of A(H1N1)pdm09 viruses received by the Centre during 2013.



Legend

2014 SOUTHERN HEMISPHERE VACCINE STRAIN

Reference virus

e: egg isolate

Scale bar represents 0.3% nucleotide sequence difference between viruses

Influenza A(H3N2)

Antigenic analysis

A total of 563 A(H3N2) subtype isolates were available for analysis by HI assay. Amongst all A(H3N2) viruses analysed by HI assay, there were no low reactors to the cell-grown reference strain A/Victoria/361/2011 (Table 4, Figure 11).

Haemagglutinin gene sequencing

Sequencing of HA genes from 99 A(H3N2) viruses indicated that recently circulating viruses showed some variance from the reference strain A/Victoria/361/2011 with the emergence of distinct alternate clades. However, these genetic changes did not change the antigenic behaviour of the viruses (Figure 12).

Table 4. Antigenic characterisation of A(H3N2) viruses analysed at the Centre compared to the A/Victoria/361/2011 reference virus.

	A(H3N2) reference strain: A/Victoria/361/2011	
Region	**Like**	**Low reactor (%)**
Australasia	421	0
Pacific	12	0
South East Asia	115	0
East Asia	6	0
South Asia	7	0
Africa	2	0
Total	**563**	**0**

Figure 11. Summary of fold differences in HI titres of A(H3N2) viruses analysed at the Centre compared to the A/Victoria/361/2011 reference virus.

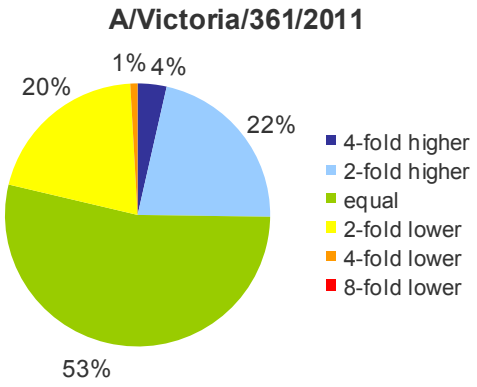
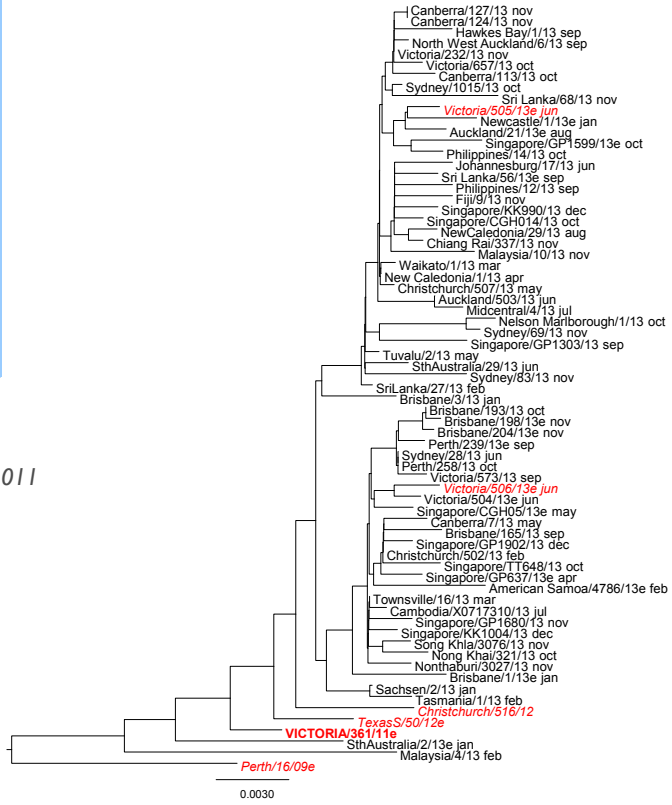


Figure 12. Phylogenetic tree of representative HA genes of A(H3N2) viruses received by the Centre during 2013.



Legend

2014 SOUTHERN HEMISPHERE VACCINE STRAIN

Reference virus

e: egg isolate

Scale bar represents 0.3% nucleotide sequence difference between viruses

Influenza B

Antigenic analysis

There are currently two antigenically and genetically distinct lineages of influenza B virus in circulation, the B/Victoria/2/87 lineage (represented by the 2011 vaccine strain B/Brisbane/60/2008) and the B/Yamagata/16/88 lineage (represented by the 2012-2013 vaccine strain B/Wisconsin/1/2010). Until 2001, B/Victoria lineage viruses had been restricted to Asia where they tended to alternate in predominance with the B/Yamagata lineage. In 2002 the B/Victoria lineage became the predominant influenza B lineage in most parts of the world. This trend was reversed in 2003 and 2004 when the B/Yamagata lineage predominated. Since then both lineages have co-circulated, with alternating cycles of predominance every few years.

During 2013 the B/Yamagata lineage predominated amongst circulating influenza B viruses received at the Centre. A small number (32 viruses) were analysed in comparison to the previous vaccine strain A/Wisconsin/1/2010 (Table 5). However, following a change in the WHO vaccine recommendations in February 2013, the majority (910 viruses) were analysed in comparison to the new vaccine reference strain A/Massachusetts/2/2012 (Table 5, Figure 14), of which the majority were antigenically similar to the reference viruses. Of the 114 B/Victoria viruses received and analysed antigenically at the Centre in 2013, the majority were similar to B/Brisbane/60/2008 (Table 5, Figure 13).

Table 5. Antigenic characterisation of B viruses analysed at the Centre compared to the B/Brisbane/60/2008, B/Wisconsin/1/2010 and B/Massachusetts/2/2012 reference viruses.

	B/Victoria reference strain: B/Brisbane/60/2008		B/Yamagata reference strain: B/Wisconsin/1/2010		B/Yamagata reference strain: B/Massachusetts/2/2012	
Region	**Like**	**Low reactor (%)**	**Like**	**Low reactor (%)**	**Like**	**Low reactor (%)**
Australasia	57	2 (3.4%)	4	5 (55.6%)	838	13 (1.5%)
Pacific	1	0	0	0	5	0
South East Asia	51	1 (1.9%)	17	6 (26.1%)	37	9 (19.6%)
East Asia	1	0	0	0	1	0
South Asia	1	0	0	0	2	3 (60%)
Africa	0	0	0	0	2	0
Total	**111**	**3 (2.6%)**	**21**	**11 (34.4%)**	**885**	**25 (2.7%)**

Figure 13. Summary of fold differences in HI titres of B/Victoria viruses analysed at the Centre compared to the B/Brisbane/60/2008 reference virus.

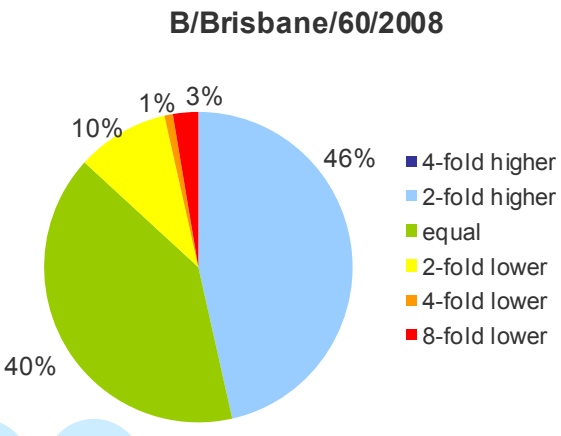
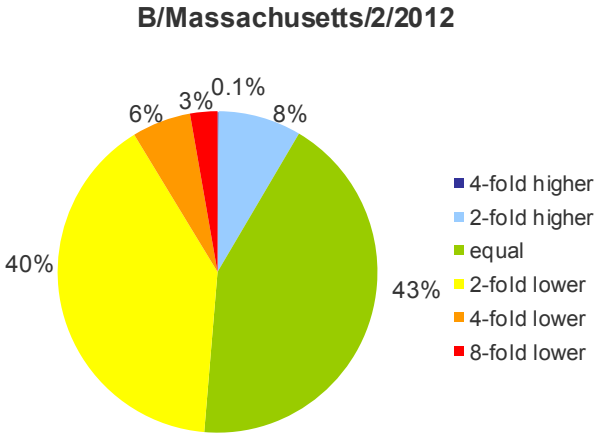


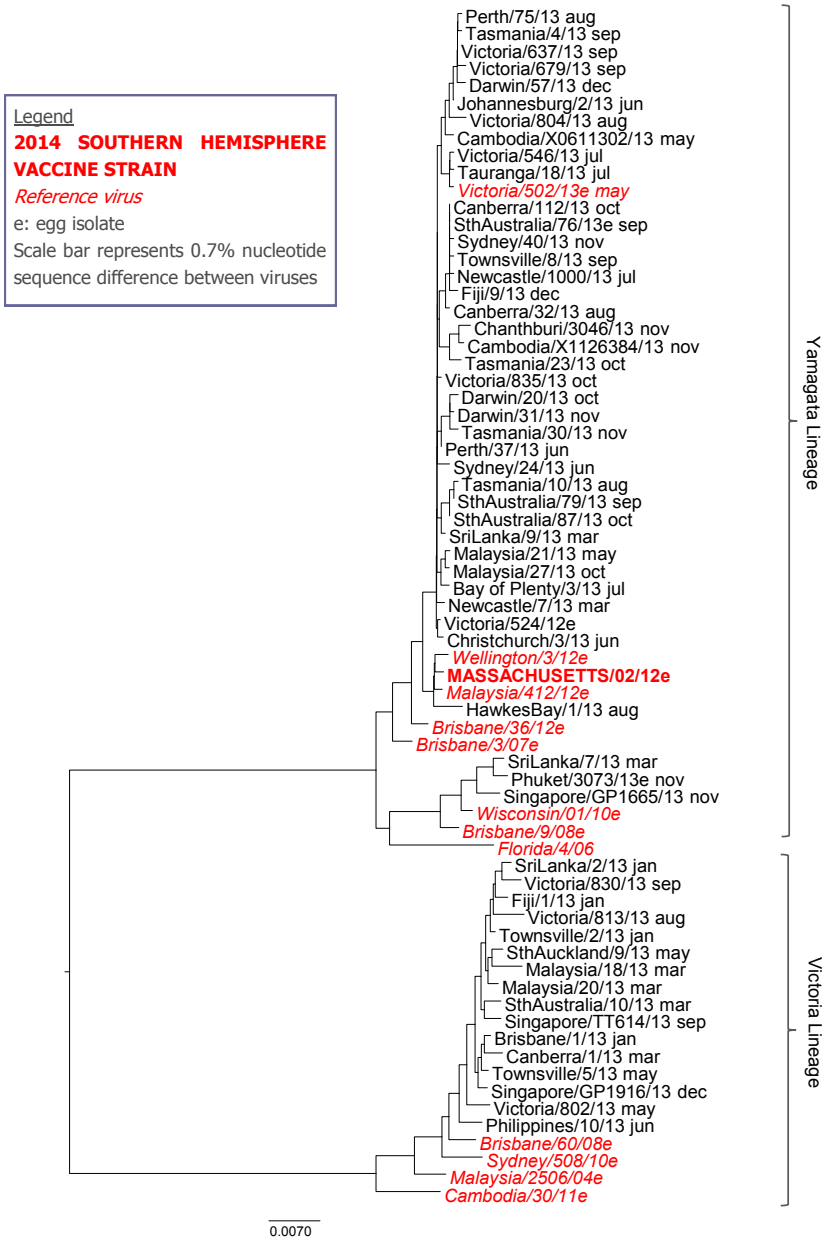
Figure 14. Summary of fold differences in HI titres of B/Yamagata viruses analysed at the Centre compared to the B/Massachusetts/2/2012 reference virus.



Haemagglutinin gene sequencing

A total of 150 HA genes from B viruses were sequenced. They formed two distinct groups corresponding to the B/Victoria and B/Yamagata lineages (Figure 15), with the majority of viruses being B/Yamagata lineage. B/Yamagata lineage viruses fell into two antigenically and genetically closely related clades, one represented by the 2014 vaccine reference strain B/Massachusetts/2/2012 and the other represented by B/Wisconsin/1/2010. All of the viruses of B/Victoria lineage belonged to the same genetic clade as the B/Brisbane/60/2008 reference virus.

Figure 15. Phylogenetic tree of representative HA genes of B viruses received by the Centre during 2013.



Antiviral Drug Resistance Testing

Sensitivity to neuraminidase inhibitors (NAIs)

Background

As influenza viruses continually undergo genetic change, their potential to develop resistance to antiviral drugs is an ongoing concern. To detect the emergence of drug-resistant influenza strains that could present future treatment challenges, viruses are tested for their sensitivity to the currently used neuraminidase inhibitors oseltamivir (Tamiflu), zanamivir (Relenza), laninamivir and peramivir using the neuraminidase inhibition assay. The latter two inhibitors are not currently approved in Australia but are in use in Japan and under clinical trial in many countries around the world. The Centre has routinely tested and reported the sensitivity of viruses to all four NAIs since 2012. The sensitivity of viruses to NAIs is measured according to the concentration of drug required to inhibit 50% of NA activity (IC_{50}) (Table 7).

Antiviral resistance analyses 2013

NAI assays were used to analyse 2629 viruses for reduced inhibition by the NAIs (Tables 6 and 7). Seven virus isolates (1 from Brisbane, 1 from Canberra, 3 from Perth, 1 from New Caledonia and 1 from Singapore) were found to have highly reduced inhibition by oseltamivir and peramivir. These viruses were confirmed to contain an amino acid substitution of histidine to tyrosine at position 275 (H275Y) that reduces inibhition of A(H1N1)pdm09 viruses by oseltamivir. Two B/Victoria viruses from Malaysia were also found to have highly reduced inhibition by peramivir, and were confirmed to contain a H273Y NA mutation (the equivalent NA residue to the H275Y in A(H1N1)pdm09 variant viruses.

Table 6. Viruses received by the Centre and tested by NAI assay in 2013, by country.

Type/subtype / Country	A(H1N1) pdm09	A(H3N2)	A (unsubtyped)	B/ Victoria	B/ Yamagata	Mixed type/ subtype
Australasia						
Australia	717	240	0	40	586	0
New Zealand	97	183	0	19	274	0
South Pacific						
Fiji	1	5	0	1	5	0
New Caledonia	19	7	0	0	0	0
Papua New Guinea	17	0	0	0	0	0
South East Asia						
Cambodia	32	2	0	4	11	0
Malaysia	3	12	1	8	19	2
Philippines	9	15	0	16	2	1
Singapore	55	64	0	24	26	0
Thailand	5	25	0	5	10	0
East Asia						
Macau	17	6	0	1	1	0
South Asia						
Sri Lanka	7	7	0	1	5	0
Africa						
South Africa	18	2	0	0	2	0
TOTAL	**997**	**568**	**1**	**119**	**941**	**3**

Table 7. Neuraminidase inhibitor sensitivity of viruses received by the Centre in 2013.*

Type/Subtype	No. tested	Oseltamivir		Lananamivir		Peramivir		Zanamivir	
		Reduced inhibition	Highly reduced inhibition	Reduced inhibition	Highly reduced inhibition	Reduced inhibition	Highly reduced inhibition	Reduced inhibition	Highly reduced inhibition
A(H1N1)pdm09	997	0	7 (0.7%)	0	0	0	7 (0.7%)	0	0
A(H3N2)	568	0	0	0	0	0	0	0	0
A (unsubtyped)	1	0	0	0	0	0	0	0	0
B/Victoria	119	0	0	0	0	0	2 (1.7%)	0	0
B/Yamagata	941	1 (0.1%)	0	0	0	0	0	1 (0.1%)	0
Mixed type/ subtype	3	0	0	0	0	0	0	0	0
TOTAL	**2629**	**1 (0.04%)**	**7 (0.27%)**	**0**	**0**	**0**	**9 (0.34%)**	**1 (0.04%)**	**0**

**Based on IC_{50}, the NAI sensitivity of each strain is classified as the following:*
Normal inhibition = IC_{50} values which are within or close to the median IC_{50} of type/subtype-matched viruses tested at the Centre in 2012.
Reduced inhibition = IC_{50} values which are 10 to 100 fold above the median value of viruses with normal inhibition (5 to 50 fold for influenza B viruses)
Highly reduced inhibition = IC_{50} values which are greater than 100 fold above the median value of viruses with normal inhibition (above 50 fold for influenza B viruses)

Resistance to Adamantanes

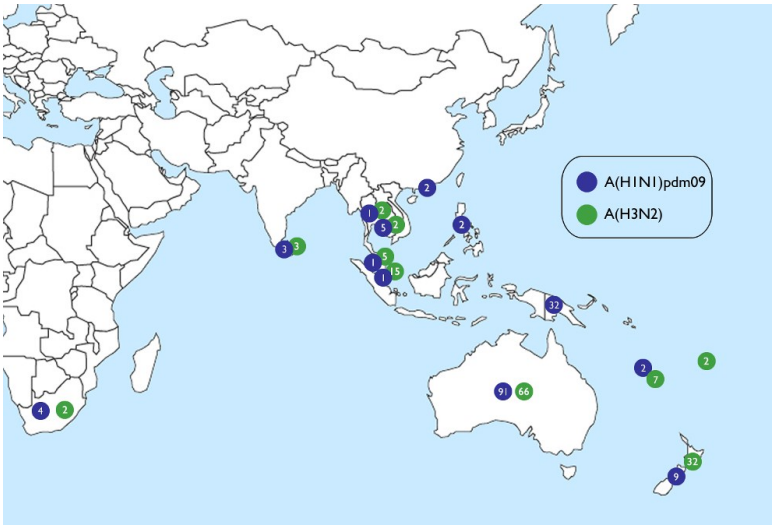
Background

The adamantane class of antiviral drugs (amantadine and rimantadine) were previously used to treat cases of influenza A, but are no longer recommended due to the almost universal adamantane resistance amongst circulating influenza A strains in recent years. All five WHO Collaborating Centres continue to screen submitted viruses for the most common resistance-conferring mutation, serine to alanine at position 31 (S31N), in the influenza A M2 protein.

Screening for adamantane resistance in 2013

Real-time PCR or sequencing was used to analyse 289 influenza A viruses, selected as representative of those submitted to the Centre during 2013 (Figure 16). Based on S31N analysis all tested viruses were resistant to the adamantanes.

Figure 16. Geographic spread of viruses received at the Centre during 2013 and screened for adamantane resistance.



Serological Analyses

Background

Antigenic changes in circulating influenza viruses are also monitored by the extent to which they are inhibited by antibodies produced by subjects who have been immunised with current inactivated seasonal influenza vaccines. Twice a year the WHO Collaborating Centres and Essential Regulatory Laboratories in the WHO surveillance network exchange panels of sera collected from subjects pre- and post-influenza vaccination. These panels are analysed using the HI assay against the current vaccine and representative influenza strains in preparation for the biannual WHO Consultations on the Composition of Influenza Vaccines (Table 8). Serum panels from children, younger adults (20-64 years old) and older adults (≥ 65 years old) are assessed.

Serum panel analyses in 2013

In February the Centre analysed serum panels from recipients of seasonal trivalent influenza vaccines in China, Europe, USA and Japan. The combined data from all WHO Collaborating Centres and ERLs showed that, in general, vaccines containing A/California/7/2009-like antigens stimulated anti-HA antibodies of similar geometric mean titre (GMT) to the vaccine virus and most recent representative A(H1N1)pdm09 viruses respectively. However, vaccines containing A/Victoria/361/2011-like antigens stimulated antibodies with geometric mean HI titres that were lower to the majority of recent cell-grown A(H3N2) viruses in comparison to the egg–grown vaccine virus. In general vaccines containing B/Wisconsin/1/2010-like antigens stimulated antibodies with similar GMT to the vaccine virus and recent representative B/Yamagata/16/88 lineage viruses, excepting one particular clade, for which titres were significantly lower. Titres were also lower to recent A/Victoria/2/87 lineage viruses.

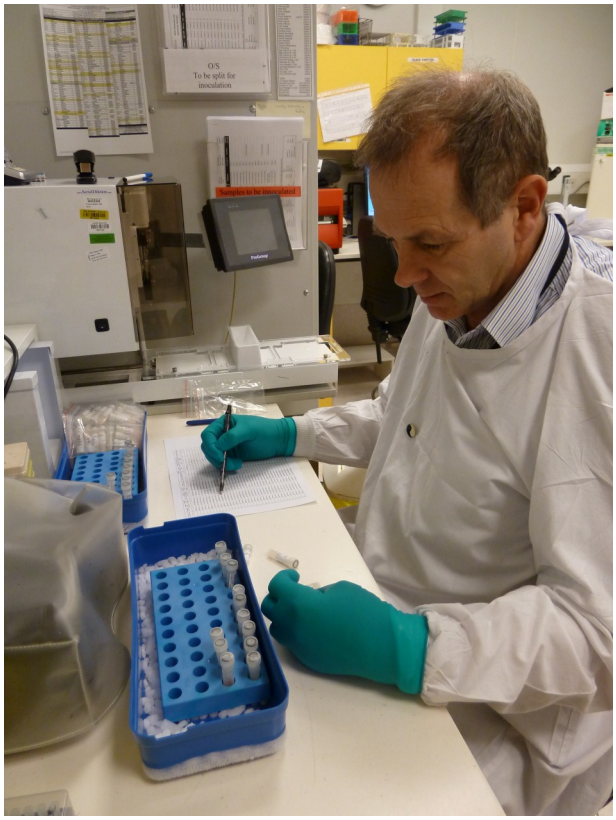
In September, the Centre analysed serum panels from Australia and Europe. The combined data from all ERLs and WHO Collaborating Centres showed that, in general, vaccines containing A/California/7/2009-like, A/Texas/50/2012-like and B/Massachusetts/2/2012-like antigens stimulated anti-HA antibodies of similar GMT to the relevant vaccine virus and most recent representative A(H1N1)pdm09, A(H3N2) and B/Yamagata/16/88 lineage viruses respectively. Titres were lower to recent A/Victoria/2/87 lineage viruses.

Table 8. Representative and vaccine candidate strains used for serological analyses during 2013.

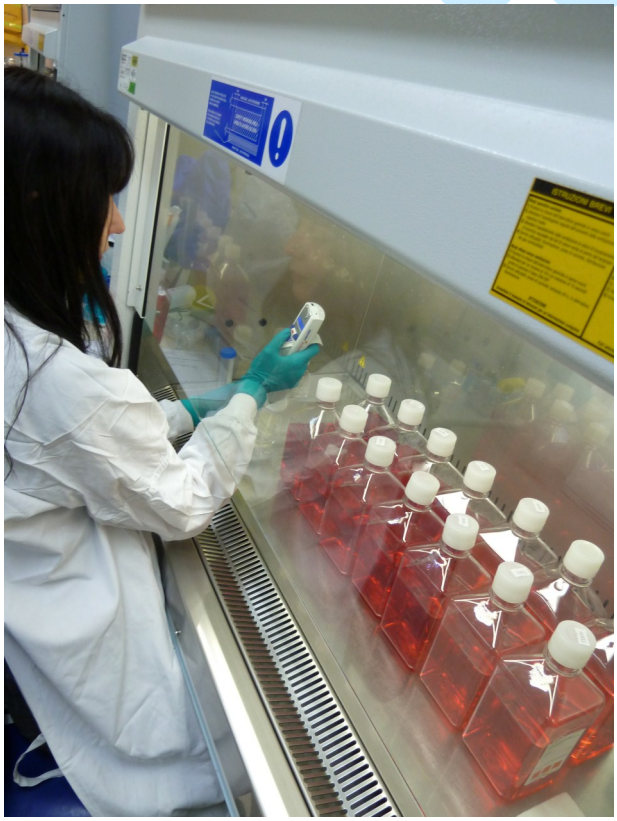
A(H1N1)pdm09	
February	**September**
A/California/7/2009*	A/California/07/2009 * (E)
A/Bangladesh/2021/2012	A/Fukuoka-C/8/2013 (C)
	A/Dominican Republic/7293/2013 (C)
	A/Bolivia/559/2013 (E)
	A/Brisbane/28/2013 (E)
	A/Bolivia/559/2013 (C)
	A/South Australia/17/2013 (E)
A(H3N2)	
February	**September**
A/Victoria/361/2011*	A/Texas/50/2012 * (E)
A/Hawaii/22/2012	A/Texas/50/2013 (C)
A/Singapore/22/2012	A/Victoria/505/2013 (E)
A/Yamaguchi/30/2012	A/Victoria/504/2013 (E)
A/Texas/50/2012 (E)	A/Jianxi-Yushi/1220/2013 (C)
A/Texas/50/2012 (C)	A/New York/39/2012 (E)
	A/Brisbane/1/2013 (E)
	A/New York/39/2012 (C)
B/Victoria	
February	**September**
B/South Australia/36/2012	B/Brisbane/60/2008 (E)
	B/Texas/02/2013 (E)
	B/Texas/02/2013 (C)
	B/South Australia/36/2012 (E)
	B/South Australia/81/2012 (E)
B/Yamagata	
February	**September**
B/Wisconsin/1/2010*	B/Massachusetts/2/2012* (E)
B/Massachusetts/2/2012 (E)	B/Massachusetts/2/2012 (C)
B/Massachusetts/2/2012 (C)	B/Hawaii/1/2013 (C)
B/Brisbane/36/2012	B Wisconsin/1/2010 (E)
B/England/580/2012	B/Victoria/502/2013 (E)

** Vaccine strain (E): Egg-grown virus (C): Cell-grown virus*

Surveillance



Chris Durrant



Iwona Buettner

Ian Barr

Malet Aban

Candidate Vaccine Strains

Background

The Centre collaborates closely with the other WHO Collaborating Centres and vaccine manufacturers to ensure the suitability of candidate strains for inclusion in seasonal vaccines. Regulatory requirements stipulate that viruses used to produce human vaccines are isolated and passaged only in embryonated hen's eggs or primary egg-derived cell cultures. Accordingly, the Centre undertakes primary isolation of selected viruses from clinical samples directly into eggs. These isolates are then analysed by HI assay and genetic sequencing.

Since 2009, the number of viruses isolated in eggs at the Centre has increased as a result of additional support received under a Letter of Agreement with the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA).

Isolation of viruses in eggs in 2013

In 2013, 37 viruses were successfully isolated in eggs at the Centre, representing an overall isolation rate of 32% (Tables 9 and 10).

Table 9. Virus isolation in eggs at the Centre in 2013.

Type/subtype	Isolates attempted	Isolates obtained	Success rate (%)
A(H1N1)pdm09	55	18	33%
A(H3N2)	34	14	41%
B/Victoria	9	1	44%
B/Yamagata	9	4	11%
Total	**107**	**37**	**32%**

Table 10. Potential candidate vaccine strains isolated in eggs at the Centre in 2013.

A(H1N1)pdm09	A(H3N2)	B/Victoria
A/Singapore/48/2012	A/South Australia/2/2013	B/Brisbane/18/2013
A/Brisbane/5/2013	A/Newcastle/1/2013	
A/Darwin/37/2013	A/Brisbane/1/2013	**B/Yamagata**
A/Brisbane/8/2013	A/Victoria/700/2013	B/Victoria/502/2013
A/Townsville/1/2013	A/Victoria/710/2013	B/Victoria/504/2013
A/Christchurch/504/2013	A/Brisbane/21/2013	B/South Australia/16/2013
A/Brisbane/19/2013	A/Victoria/504/2013	B/South Australia/76/2013
A/Townsville/9/2013	A/Victoria/505/2013	
A/Townsville/12/2013	A/Victoria/506/2013	
A/Newcastle/7/2013	A/Singapore/GP637/2013	
A/Brisbane/28/2013	A/Singapore/CGH05/2013	
A/Brisbane/31/2013	A/Perth/98/2013	
A/South Australia/17/2013	A/Auckland/21/2013	
A/South Australia/20/2013	A/Perth/239/2013	
A/South Australia/25/2013		
A/South Australia/26/2013		
A/Singapore/KK456/2013		
A/Singapore/KK457/2013		

Preparation and Analysis of Vaccine Seed Viruses

The Centre exchanges candidate vaccine viruses that have been isolated in eggs, as well as post-infection ferret antisera raised against these and other reference viruses, with the other WHO Collaborating Centres to enable direct comparison of strains isolated in the five centres. During 2013, 23 candidate vaccine viruses were received from other WHO Collaborating Centres and laboratories and then passaged in eggs at the Centre (Table 11).

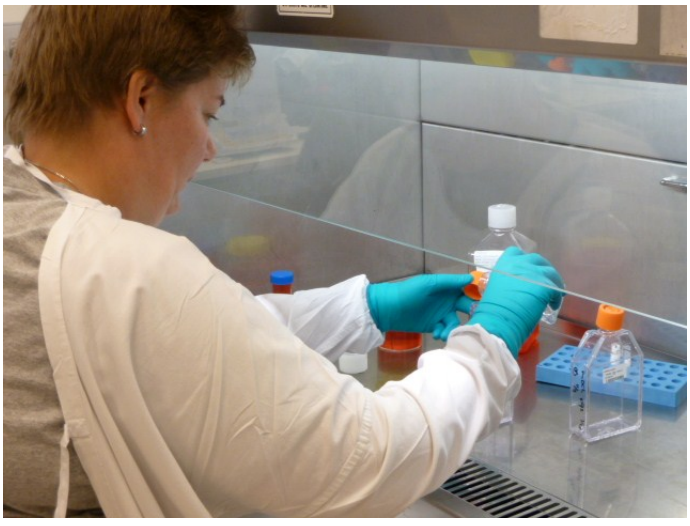
Selected egg-isolated candidate vaccine strains are made available to the three laboratories that undertake virus reassortment for WHO — BioCSL (Australia), the National Institute for Biological Standards and Control (NIBSC, UK) and New York Medical College (NYMC, USA) — where they are reassorted with established egg-adapted strains to produce potential vaccine seed strains. The reassortant vaccine seed viruses are returned to the Centre, where they are analysed by HI assay and genetic sequencing to ensure that key antigenic and genetic properties of the vaccine virus have been retained.

The vaccine seed viruses are distributed to other WHO Collaborating Centres and vaccine manufacturers worldwide through Essential Regulatory Laboratories at the Therapeutic Goods Administration (Australia), NIBSC and the Centre for Biologics Evaluation and Research, Food and Drug Administration (USA).

Table 11. Potential candidate vaccine viruses received from other WHO Collaborating Centres during 2013.

Type/Subtype	Strain
A(H1N1)pdm09	A/Gansu-Ganzhou/SWL33/2012
	A/Bangladesh/2021/2012
	A/Guangdong-Yuexiu/SWL1651/2013
	A/Shanghai-Putuo/1203/2013
	A/Bolivia/559/2013
A(H3N2)	NYMC X-223 (HY A/Texas/50/2012)
	NYMC X-223A (HY A/Texas/50/2012)
	NYMC X-225 (HY A/Hawaii/22/2012)
	NYMC X-225A (HY A/Hawaii/22/2012)
	IVR-165 (A/Victoria/361/2011)
	A/American Samoa/4786/2013
	A/New York/39/2012
B	B/Jiangsu-Tianning/1666/2012
	B/Norway/2290/2012
	NYMC BX-51B (B/Massachusetts/02/2012)
	NYMC BX-51C (B/Massachusetts/02/2012)
	B/Norway/2290/2012
	B/Texas/02/2013
	B/Jiangsu-Qingpu/1256/2013
	B/Jiangsu-Chongchuan/11052/2013
A(H7N9)	A/Anhui/1/2013
	NIBRG-268 LOT 35630 (A/Anhui/1/2013)
	NIBRG-267 LOT 35610 (A/Shanghai/2/2013)

Kit for antigenic typing of influenza viruses



Chantal Baas

Preparation and Distribution of Diagnostic Reagents

Reagents for Antigenic Typing of Influenza Viruses

Each year the Centre prepares and distributes kits to regional and reference laboratories to enable influenza preliminary analysis and characterisation of influenza specimens prior to submission of samples to the Centre. The kits contain polyclonal sera and viral antigens for reference influenza strains. During 2013, 48 kits were sent to 23 laboratories in 15 countries. Each kit contained 10 mL each of the reference antigens A/Perth/16/2009, A/California/7/2009, B/Wisconsin/1/2010 and B/Brisbane/60/2008, and homologous antisera.

Recipients of the 2013 Kit

Australia	Institute of Medical and Veterinary Science, Adelaide, South Australia Queensland Health Scientific Services, Brisbane, Queensland Westmead Hospital, Sydney, New South Wales The University of Queensland, Brisbane, Queensland Vaxxas Ptd Ltd, Brisbane, Queensland	Malaysia	University of Malaya, Kuala Lumpur
		New Zealand	Institute of Environmental Science and Research, Wellington Auckland City Hospital, Auckland
		Philippines	Research Institute for Tropical Medicine, Mutinlupa City
		Romania	Cantacuzino National Institute, Bucharest
Cambodia	Institut Pasteur du Cambodge, Phnom Penh	Singapore	Singapore General Hospital DSO National Laboratories Duke-NUS Graduate Medical School
Fiji	Fiji Centre for Communicable Disease Control, Suva		
India	Manipal University, Karnataka Haffkine Institute, Mumbai	South Africa	National Institute for Communicable Diseases, Johannesburg
Kenya	Center for Virus Research, Kenya Medical Research Institute, Nairobi	Sri Lanka	Medical Research Institute, Colombo
		Taiwan	National Cheng Kung University, Tainan
Macau, China	Public Health Laboratory	Thailand	National Institute of Health, Bangkok

Primer Sequences for Full Genome Sequencing

The Centre has developed primer sequences and protocols for full genome sequencing of both Type A and Type B viruses, as well as avian influenza A(H7N9) viruses and makes these available other influenza laboratories on request. Primer sequences and protocols were sent to the following institutions during 2013:

- Hangzhou Center for Disease Control and Prevention, Hangzhou, China (Types A and B)
- National Public Health Laboratory, Singapore (Types A and B)
- Army Medical and Veterinary Research Center, Rome, Italy (Types A and B)
- Military Veterinary Research Institute, Changchun, China (Types A, B, and A(H7N9))
- Department of Microbiology and Molecular Genetics, Michigan State University, East Lansing, MI, USA (Types A, B, and A(H7N9))
- Department of Microbiology and Hygiene, Bangladesh Agricultural University, Mymensingh, Bangladesh (A(H7N9))
- DSO National Laboratories, Singapore (Type A and A(H7N9))
- University of Colorado, Aurora, CO, USA (Types A and B)

Virus Panels for Analysis of Resistance to Antiviral Drugs

The Centre produces and distributes a panel of reference viruses on request to laboratories conducting NAI assays on behalf of the International Society for Influenza and other Respiratory Virus Diseases (isirv) Antiviral Group. In 2013 panel kits were composed of 2 vials (250 µL) of each of the reference viruses listed in the table below.

Contents of the NAI assay panel in 2013

Reference virus ***Amino acid residues of interest in NA protein***	**Sensitivity to antiviral drugs**			
	Oseltamivir	**Laninamivir**	**Peramivir**	**Zanamivir**
A/Mississippi/3/01 (H1N1) wild-type (A/New Caledonia/20/99-like) *Histidine at position 275 (275H)*	Susceptible	Susceptible	Susceptible	Susceptible
A/Mississippi/3/01 (H1N1) variant (A/New Caledonia/20/99-like) *Tyrosine at position 275 (275Y)*	Reduced susceptibility	Susceptible	Reduced susceptibility	Susceptible
A/Fukui/20/04 (H3N2) wild-type (A/Fujian/411/2002-like) *Glutamic acid at position 119 (119E)*	Susceptible	Susceptible	Susceptible	Susceptible
A/Fukui/45/04 (H3N2) variant (A/Fujian/411/2002-like) *Valine acid at position 119 (119V)*	Reduced susceptibility	Susceptible	Susceptible	Susceptible
B/Perth/211/2009 wild-type (B/Sichuan/379/1999-like) *Aspartic acid at position 197 (197D)*	Susceptible	Susceptible	Susceptible	Susceptible
B/Perth/211/2009 variant (B/Sichuan/379/1999-like) *Glutamic acid at position 197 (197E)*	Reduced susceptibility	Susceptible	Reduced susceptibility	Susceptible
A/Perth/265/2009 (H1N1)pdm09 wild-type (A/California/7/2009)-like *Histidine at position 275 (275H)*	Susceptible	Susceptible	Susceptible	Susceptible
A/Perth/261/2009 (H1N1)pdm09 variant (A/California/7/2009)-like *Tyrosine at position 275 (275Y)*	Reduced susceptibility	Susceptible	Reduced susceptibility	Susceptible

Recipients of the NAI assay panel

Health Canada, Ottawa, Canada
Duke-NUS Medical School, Singapore
Department of Public Health Laboratories, Montevideo, Uruguay
Institut Pasteur Hellénique, Athens, Greece
University of Münster, Münster, Germany
Eberhard Karls Universität, Tubingen, Germany
Viroclinics Biosciences BV, Rotterdam, The Netherlands
Redx Oncology, Liverpool, UK
Osaka Prefectural Institute of Public Health, Osaka, Japan
Centro Nacional de Microbiología Instituto de Salud Carlos III, Madrid, Spain
Integrated BioTherapeutics Inc, Gaithersburg MD, USA
Fukushima Medical University, Fukushima, Japan
Meiji Seika Pharma Co, Tokyo, Japan
Central Public Health Laboratory, Colindale, UK
Institute of Virology, Slovak Academy of Sciences, Bratislava, Slovak Republic

Recommendations on Influenza Vaccines

WHO Consultations on the Composition of Seasonal Influenza Vaccines

The antigenic, genetic, antiviral resistance and serological data generated from the Centre's surveillance activities are incorporated into detailed dossiers for use at the WHO Consultations on the Composition of Influenza Vaccines in February (for the northern hemisphere) and September (for the southern hemisphere).

The Centre Director and Deputy Director participate in preparatory teleconferences and then meet at the face-to-face Consultation with WHO, representatives from the other WHO Collaborating Centres and the four Essential Regulatory Laboratories (Center for Biologics Evaluation and Research, US Food and Drug Administration; National Institute for Biological Standards and Control, UK; National Institute of Infectious Diseases, Japan; Therapeutic Goods Administration, Australia). Consultations are also attended by observers from OFFLU, the University of Cambridge, several WHO National Influenza Centres and other relevant organisations from time to time. In 2013, WHO made the recommendations reported here.

WHO Consultation on the Composition of Influenza Vaccines for the Northern Hemisphere 2013–2014, Geneva, Switzerland, 18–20 February 2013

It is recommended that vaccines for use in the 2013–2014 influenza season (northern hemisphere winter) contain the following:

- an A/California/7/2009 (H1N1)pdm09-like virus;
- an A(H3N2) virus antigenically like the cell-propagated prototype virus A/Victoria/361/2011*
- a B/Wisconsin/1/2010-like virus.

It is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Brisbane/60/2008-like virus*.

WHO Consultation on the Composition of Influenza Vaccines for the Southern Hemisphere 2014, Geneva, Switzerland, 23-26 September 2013

It is recommended that vaccines for use in the 2014 influenza season (southern hemisphere winter) contain the following:

- an A/California/7/2009 (H1N1)pdm09-like virus;
- an A/Texas/50/2012 (H3N2)-like virus;
- a B/Massachusetts/2/2012-like virus.

It is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Brisbane/60/2008-like virus*.

* *These viruses were originally isolated at the WHO Collaborating Centre in Melbourne.*

Australian Seasonal Influenza Vaccine Recommendation

Whereas WHO makes recommendations on suitable viruses for inclusion in seasonal influenza vaccines, in individual countries the decision on the composition of vaccines is made by national or regional authorities. In Australia, the relevant authority is the Therapeutic Goods Administration which makes the decision on the advice of the Australian Influenza Vaccine Committee (AIVC). The Centre Director and Deputy Director both serve on AIVC.

At its meeting on 10 October AIVC accepted the September WHO recommendation and decided that the Australian influenza vaccine for 2014 should contain the following:

A (H1N1): an A/California/7/2009 (H1N1) - like virus, 15 µg HA per dose
A (H3N2): an A/Texas/50/2012 (H3N2) - like virus, 15 µg HA per dose
B: a B/Massachusetts/02/2012 - like virus, 15 µg HA per dose

Response to Viruses with Pandemic Potential

In April 2013, with the emergence of human infections by a novel avian influenza A(H7N9) virus in eastern China, the Centre joined in the international efforts with WHO and GISRS to monitor and respond to the outbreak.

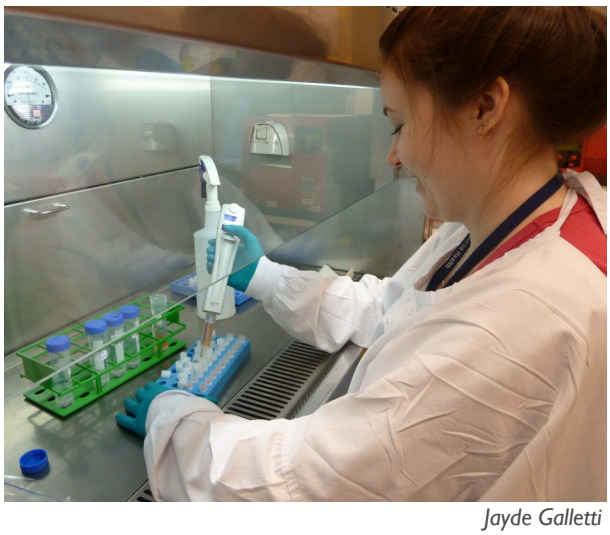
The Centre participated in frequent teleconferences with WHO Headquarters, the other WHO Collaborating Centres and Essential Regulatory Laboratories to exchange information on virological analyses and to recommend candidate vaccine viruses. The Centre received the reference virus A/Anhui/1/2013 from the WHO Collaborating Centre at the Chinese Center for Disease Control and Prevention and reverse-genetics provisional candidate vaccine viruses from NIBSC. The Centre also made available RNA, primer sequences and protocols for sequencing of avian influenza A(H7N9) viruses to other influenza laboratories on request.

Anne Kelso participated as one of three international experts in a Joint China-WHO Mission to provide guidance on China's response to the outbreak. She also provided ongoing advice to the Australian Government on the avian influenza A(H7N9) virus outbreak, both informally and through several meetings:

- Teleconference with the Commonwealth Chief Medical Officer, Department of Health and Ageing, 5 April
- Teleconference with the Australian Health Protection Principal Committee (AHPPC), 8 April
- Teleconference with National Health and Medical Research Council, 29 April
- Teleconference with Australian Government Pandemic Response Implementation Advisory Committee (PRIAC), 7 May
- Briefing with The Hon. Tanya Plibersek MP, Minister for Health, at VIDRL, 8 May

Recipients of A(H7N9) RNA

Institute of Medical and Veterinary Science, Adelaide, South Australia
PathWest Laboratory Medicine, Perth, Western Australia
Westmead Hospital, Sydney, NSW
Queensland Health Scientific Services, Brisbane, Queensland
Institute of Environmental Science and Research, Wellington, New Zealand
Prince of Wales Hospital, Sydney, NSW
BioCSL, Melbourne, Victoria
National Institute of Health Research and Development, Jakarta, Indonesia
Sullivan Nicolaides Pathology, Brisbane, Queensland
Institute for Medical Research, Kuala Lumpur, Malaysia
ACT Pathology, Canberra, ACT
Princess Margaret Hospital, Perth, Western Australia
Hunter Area Pathology Service, NSW



Jayde Galletti

Heidi Peck

Training

Training and Support of National Influenza Centres and Regional Laboratories

The Centre provides support to the GISRS surveillance network by offering training and advice to WHO National Influenza Centres (NICs) and other diagnostic laboratories, especially in the Asia-Pacific region. Strengthening technical capabilities and infrastructure for surveillance work in regional laboratories increases their capacity to detect and characterise circulating influenza viruses and to identify viruses with pandemic potential.

Sequencing and Phylogenetic Analysis Workshop

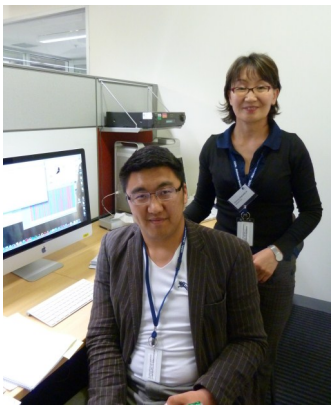
The Centre hosted a Regional Workshop on Sequencing and Phylogenetic Analysis of Influenza Viruses from 29 April to 3 May. A total of 16 participants from National Influenza Laboratories in Cambodia, Fiji, Laos, Malaysia, Mongolia, New Caledonia, New Zealand, Singapore and Vietnam attended the workshop. Staff members from the Centre were joined by other experts from Duke University in Singapore, the WHO Collaborating Centre for Reference and Research on Influenza in Japan, The University of Sydney and Monash University to provide instruction and lead sessions in practical laboratory activities, lectures and computer tutorials. Dr Frank Konings from the WHO Western Pacific Regional Office (WPRO) also attended the workshop.

Feedback from participants was very positive, indicating that they found the workshop — and especially the practical sessions — to be very informative, and that the knowledge gained would be useful on returning to their own laboratories. We are grateful to WPRO, US Centers for Disease Control and Prevention (CDC) and the Australian Government Department of Health for their support which made the workshop possible.

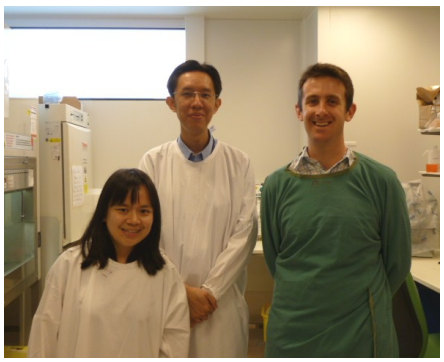
Workshop participants and faculty
***(From back to front, left to right)*:**
1. Dr Bayasgalan NAMUUTSETSEG, Patrick Reading, Aeron Hurt
2. Ian Barr, Seiichiro Fujisaki, Natalie Spirason, Anne Kelso
3. Dr NGO Thanh Long, Hilda Lau, Frank Konings, Yi-Mo Deng
4. Naomi Komadina, Dr Darmaa BADARCH, Mr Vimatha XAYSITTHIDETH
5. Ms Judy BOCACAO, Dr Ann-Claire GOURINAT, Mr CHIN Savuth
6. Mr RITH Sareth (left of stairs), Ms PHUAH Shiau Pheng, Ms Shalini Pravin SINGH, Dr Phouvong PHOMMACHANH
7. Ms Jeyanthi SUPPIAH, Ms NGUYEN Thu Ngoc, Ms TRAN Thi Thu Huong, Simon Ho, Gavin JD Smith, Dr TO Long Thanh

In-house Training

Dr Darmaa Badarch (*standing, right*) and Dr Bayasgalan Namuutsetseg, from the National Influenza Center of Mongolia in Ulaanbaatar, Mongolia, visited the Centre 6–10 May. They undertook training in RT-PCR techniques for H275Y and other drug resistance markers, phenotypic NAI resistance assays, sequencing techniques and phylogenetic analysis, and also improved their knowledge of quality assurance and quality control.



Dr Kian Sing Chan (pictured centre, below, with Leah Leang (*left*) and Jeffrey Butler (*right*)), from Singapore General Hospital, visited the Centre on 12–16 March for training in molecular genetics techniques and to obtain a general overview of techniques in serology and NAI assays.



Other Training

Dr Patrick Reading, the Centre's educator, visited regional National Influenza Centres (NICs) throughout the year to assist and facilitate the development of laboratory programs, infrastructure and staff training.

National Institute of Health Research and Development, Jakarta, Indonesia, 18 February–1 March and 20–31 May
Further development of laboratory procedures in virus isolation and serology, molecular genetic techniques and NAI assays.

Institute of Medical Research, Goroka, Papua New Guinea, 4–13 March
Establishment of reagents and equipment to implement cell culture and virus isolation procedures.

Fiji Centre for Communicable Disease Control, Suva, Fiji, 26–29 August
Training of scientists in real-time PCR to detect influenza viruses in clinical specimens, including the generation of new positive control material, reconstitution of primers and probes, validation of typing and subtyping assays, review and update of SOPs, development of competency assessment forms and establishment of internal quality assessment panels.

WHO Regional Office for South-East Asia Region: Training on Influenza Data Management and Epidemiological Analysis workshop, Bangkok, Thailand, 11–15 February
Dr Sheena Sullivan participated as a lecturer and facilitator at this workshop, which was attended by participants from Bhutan, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand and Timor Leste.

5th LabNet Meeting 'Strengthening Pacific Laboratory Quality Management Systems (LQMS) towards accreditation', Noumea, New Caledonia, 17–20 September 2013 *(pictured at right)*
This meeting, which was attended by scientists and laboratory managers from over 20 Pacific Island Countries and Territories, aimed to develop strategies to strengthen and sustain laboratory quality management systems throughout laboratories in the Pacific region. Dr Patrick Reading delivered an oral presentation and facilitated working groups relevant to strengthening laboratory quality management.

Influenza Data Management and Epidemiological Analysis Workshop, Phnom Penh, Cambodia, 27 July–2 August
Dr Sheena Sullivan participated as a facilitator in this workshop, which was attended by representatives from Cambodia, Fiji, Laos, Mongolia, Papua New Guinea, Philippines, Solomon Islands, Vanuatu and Vietnam and two observers from the Secretariat of the Pacific Community.

Research

Research interests at the Centre encompass a broad range of in-house and collaborative projects. During 2013, Centre staff were involved in the project areas described below.

Immune response and influenza

Assessment of cytokine responses in ferrets

Centre staff: Karen Laurie, Louise Carolan, Aeron Hurt, Jeffrey Butler, Patrick Reading, Ian Butler, Anne Kelso
Collaborators: Steve Rockman (bioCSL)

Project overview
Understanding the immune response following influenza virus infection can lead to improvements in treatment or prevention of virus infection. This study aims to assess cytokine responses in ferrets as markers of the early and late immune response.

Highlights and developments 2013
The cytokine and chemokine real time PCR assays were used to characterise the *in vitro* response of ferret leukocytes to mitogens and influenza virus. Cytokine and chemokine mRNA induction profiles are similar to those described for human and mouse leukocytes. Measurement of cytokines and chemokines mRNA expression after influenza virus infection of ferrets is underway. Results were presented at two conferences and a manuscript is in preparation.

Related publications 2013
Quantitation of mRNA cytokine levels in ferrets following influenza infection. Carolan LA, Butler J, Guarnaccia T, Rockman S, Hurt AC, Reading PC, Kelso A, Barr I and Laurie KL. (poster, presented at the 15th International Congress of Immunology, Milan, Italy, 22–27 August)

Quantitation of cytokine mRNA levels in ferrets following influenza virus infection. Carolan LA, Butler J, Guarnaccia T, Rockman S, Hurt AC, Reading PC, Kelso A, Barr I and Laurie KL. (Poster, presented at the 43rd Annual Scientific Meeting of the Australasian Society for Immunology, Wellington, New Zealand, 2–5 December)

Seroprevalence surveys to assess human population immunity to the 2013 avian influenza A(H7N9) outbreak

Centre staff: Karen Laurie, Louise Carolan, Ian Barr, Anne Kelso
Collaborators: Jodie McVernon (The University of Melbourne); Stephen Lambert (Queensland Children's Medical Research Institute, The University of Queensland, and Queensland Children's Health Services, Queensland Health Immunisation Program, Queensland); Helen Faddy, Catherine Hyland and Hugh Capper (Australian Red Cross Blood Service, Queensland); Brenda White and Amanda di Carlo (The Royal Children's Hospital)

Project overview
The level of antibodies to the novel avian influenza A(H7N9) virus detected in China during 2013 was assessed in sera and plasma collected from Australian children and adults in late December 2011. This is the only serosurvey against this novel virus that has been performed in Australia.

Highlights and developments 2013
Antibodies that cross-reacted with the newly emerging A(H7N9) virus were not detected in Australian adults.

Influenza epidemiology and immunity in the first year of life

Centre staff: Karen Laurie, Louise Carolan, Malet Aban, Ian Barr
Collaborators: Cameron Simmons (Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam and the Department of Microbiology and Immunology, The University of Melbourne); Katie Anders (Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam)

Project overview
Little is known about seroconversion following infection and vaccination with influenza virus in infants under the age of 1 year and the protective effect and persistence of maternal antibodies to influenza virus. This prospective birth cohort study followed mothers and infants from birth for the first year of life in Vietnam, with the aim to determine the sero- and case-epidemiology of influenza in infants and characterise the immune response following primary infection and influenza vaccination.

Highlights and developments 2013
All commonly circulating subtypes of influenza A (A(H1N1), A(H3N2) and A(H1N1)pdm09) and influenza B lineages (B/Yamagata and B/Victoria) were detected in Vietnam over the period of collection of samples. Assays to detect antibodies to different strains of circulating influenza viruses in plasma samples have been performed.

Immune response and influenza (continued)

Investigating the hypothesis of temporary immunity in the ferret model

Centre staff and student: Karen Laurie, Louise Carolan, Teagan Guarnaccia, Patrick Reading, Ian Barr, Anne Kelso
Collaborators: Jenny Mosse (Monash University); James McCaw, Stephen Price and Ada Yan (The University of Melbourne)

Project overview
Epidemiological and modelling evidence suggests that, following infection with an influenza virus, there is a short period of time during which the host experiences lower susceptibility to infection with any strain of influenza or other respiratory virus. This phenomenon is independent of antigenic similarity, and has been termed temporary non-specific immunity. The ferret is an ideal model of human influenza as human influenza viruses can directly infect ferrets without the need for adaptation. This project has investigated the concept of temporary immunity between unrelated influenza virus types.

Highlights and developments 2013
Temporary immunity has been demonstrated in the ferret model. Prior infection with influenza A(H1N1pdm09) virus could protect ferrets from infection with influenza B virus, when infections occurred less than a week apart. However, if the infections were reversed and influenza B virus was infected before influenza A(H1N1)pdm09, no protection was seen, indicating the effect may be influenza virus-specific. Further work to understand the mechanism/s behind this is underway.

Related publications 2013
Teagan Guarnaccia commenced writing her PhD thesis during 2013, and these data were included. A manuscript is in preparation.

Comparison of serology microneutralisation assay protocols

Centre staff: Karen Laurie, Louise Carolan

Collaborators: Ralf Wagner (Paul-Ehrlich-Institut, Germany); Malik Peiris (University of Hong Kong); Katja Hoschler (Health Protection Agency (HPA), London); Tian Bai (WHO CC for Influenza (CNIC), China); Jackie Katz, Xiuhua Lu and Vic Veguilla (CDC, Atlanta, GA, USA); Emanuele Montomoli (University of Sienna, Italy); Maria Rita Castrucci (Istituto Superiore di Sanità, Italy); Noriko Kishida (National Institute of Infectious Diseases (NIID), Japan); John Wood, Diane Major and Othmar Engelhardt (National Institute for Biological Standards and Control (NIBSC), UK); Olav Hungnes (Norwegian Institute of Public Health, Norway); Thedi Ziegler (National Institute for Health and Welfare, Finland); Nicholas Martin (Naval Medical Research Center, Silver Spring, MD, USA); Gary Brice (Naval Health Research Center, San Diego, CA, USA); Maria van Kerkhove (Imperial College, UK)

Project overview
This project is being carried out as part of the Consortium for the Standardization of Influenza Seroepidemiology (CONSISE). The Consortium has been divided into two streams to consider a) Epidemiology and b) Laboratory Issues. The Centre is part of the Laboratory Issues group, which is comparing different methods for microneutralisation assays. Two main protocols, which take either 2 days or 3 days to perform, are used for microneutralisation assays in influenza seroepidemiology laboratories worldwide. This study is focused on comparing the 2-day and 3-day protocols. A protocol comparison of the haemagglutination inhibition (HI) assays is also underway, as well as a comparison of assays to test anti-neuraminidase antibodies.

Highlights and developments 2013
Building on the comparison of microneutralisation assay methods to detect antibodies to A(H1N1)pdm09 in 2012, a further study was performed in 2013 to compare microneutralisation assay methods to detect antibodies to A(H3N2) and A(H5N1). Eight international laboratories participated in this comparison. The Centre co-ordinated and participated in the studies. These data were presented in talks at two international meetings – CONSISE Regional Influenza Seroepidemiology Expert Meeting in Hong Kong SAR, China on 22–23 January, and the 4th International Meeting of CONSISE in Cape Town, South Africa, held 3– 4 September. A manuscript is in preparation.

Related publications 2013
An international laboratory comparative examination of influenza 2 day ELISA and 3 day hemagglutination consensus microneutralization assays conducted by the Consortium for the Standardization of Influenza Seroepidemiology (CONSISE). Laurie KL, Katz K, Peiris M, Heath A, Engelhardt OG, Wood J, Van Kerkhove MD, Nicoll A, on behalf of members of CONSISE Laboratory Working Group. (Poster, presented at Options for the Control of Influenza VIII, Cape Town, South Africa, 5–9 September)

Antivirals and viral fitness

Viral fitness in ferret models

Centre staff: Aeron Hurt, Jeffrey Butler, Ian Barr
Collaborators: James McCaw and Jodie McVernon (The University of Melbourne)

Project overview
This project uses a competitive mixtures model in ferrets to investigate the relative fitness and transmissibility of different influenza viruses. Groups of ferrets are infected with a mixture of two influenza strains and the relative proportions of those viruses are monitored over time and over multiple cycles of transmission. The data are analysed by mathematical modelling to determine the relative fitness of one virus compared with another. The model has been applied to determining the fitness of neuraminidase inhibitor-resistant viruses and new antigenic variants. This project is supported by funding from the University of Melbourne Faculty Research Grant Support Scheme.

Highlights and developments 2013
Results from this project were presented in talks by Jeffrey Butler and Aeron Hurt at various conference and meetings.

Related publications 2013 (see page 38): Reference no. 28

Recent A(H1N1)pdm09 influenza viruses encode permissive NA mutations which improve the fitness of oseltamivir-resistant H275Y variants. Butler J, Hooper K, Bloom J, Lee R, Maurer-Stroh S, Petrie S, McCaw J, Reh L, Guarnaccia T, Baas C, Xue L, Kelso A, Barr I and Hurt AC. (Poster and short talk, presented at Options for the Control of Influenza VIII, Cape Town, South Africa, 5–9 September)

Effectiveness of anti-viral treatments in a ferret model

Centre staff: Aeron Hurt, Karen Laurie, Ian Barr, Anne Kelso
Collaborators: Deborah Middleton and Sue Lowther (Australian Animal Health Laboratory); James McCaw and Jodie McVernon (The University of Melbourne)

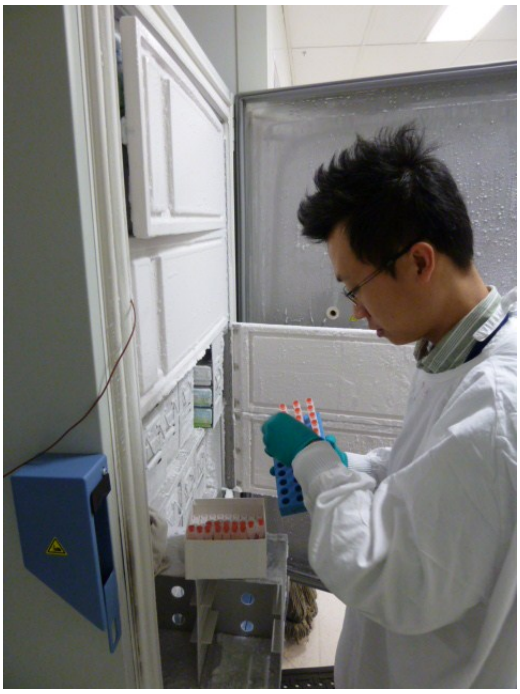
Project overview
This project investigates the effectiveness of oseltamivir as a treatment or prophylactic agent in reducing infectivity, transmissibility and growth of different viruses. To investigate the impact of different treatment strategies, ferrets are dosed with different concentrations of the drug at various time intervals either pre- or post-exposure to the virus. Virological, symptomatic and immunological variables are then measured over the course of infection and treatment.

Sensitivity to antiviral treatments and clinical effectiveness in ferret models

Centre staff: Aeron Hurt, Ding Yuan Thomas Oh
Collaborators: Sebastian Maurer-Stroh (A*STAR, Singapore); Veronika Von Messling and Gary Lau (Duke-NUS, Singapore; Carl Kirkpatrick (Monash University)

Project overview
The relationship between *in vitro* NAI sensitivity data and the clinical effectiveness of a neuraminidase inhibitor against a given virus is not well understood. The project aims to explore this relationship in the ferret model. This involves optimising NAI dosing, virus infectivity and immune status in ferrets for use in treatment effectiveness studies. Viruses with differing levels of reduced drug sensitivity will then be assessed in the ferret model to determine if drug treatment is having any effect on morbidity, viral load or inflammatory processes. The project is jointly funded by a grant from the NHMRC, Australia, and A*STAR, Singapore.

Highlights and developments 2013
This project commenced during 2013. Results from this project were presented in talks by Aeron Hurt at various conference and meetings.



Ding Yuan Oh

Epidemiology

Vaccine effectiveness

Centre staff: Sheena Sullivan
Collaborators: Heath Kelly and Kristina Grant (Epidemiology Unit, VIDRL); James Fielding and Ee Laine Tay (VIDRL; National Centre for Epidemiology & Population Health, Australian National University, ACT); Avram Levy, David Smith (PathWest Laboratory Medicine, Western Australia); Paul Effler, Annette Regan (Department of Health, Western Australia); Nigel Stocks, Monique Chilver (Australian Sentinel Practices Research Network, South Australia); Ben Cowling (University of Hong Kong, Hong Kong)

Project overview
The WHO recommendations on the composition of influenza vaccines are issued 5-6 months prior to the release of the vaccine, leaving insufficient time to test vaccine efficacy and safety. There are three influenza sentinel surveillance systems operating in Australia, namely the Australian Sentinel Practices Research Network (ASPREN), the sentinel practices network of WA (SPN(WA)) and the Victorian General Practice Sentinel Surveillance (GPSS) network. In each of these systems, vaccination and influenza status is collected for patients recruited through the surveillance system to estimate influenza vaccine effectiveness in the community. This project has used data from each of these networks to make vaccine effectiveness estimates, to understand how modifications of the study design can affect the validity of the study design used, and to pool data to understand how effectiveness may vary across sub-populations.

Highlights and developments 2013
In 2013 all influenza-positive samples from the Victorian sentinel system as well as a selection of specimens and isolates from ASPREN and SPN(WA) were forwarded to the Centre for antigenic analysis to aid interpretation of the vaccine effectiveness estimates. The Centre also began working with ASPREN and SPNWA to develop manuscripts for publication of their data. Four papers were published with VIDRL exploring the validity of the study design used to estimate vaccine effectiveness.

Understanding the representativeness of influenza virus samples sent to the Centre

Centre staff: Sheena Sullivan

Project overview
It is important to understand whether the influenza viruses evaluated by the Centre are representative of the viruses circulating during a season. While it is infeasible to ensure equal representation of each virus strain, it is possible to estimate the proportion of samples received among laboratory-confirmed cases. This study attempts to understand whether viruses received by the Centre are representative of those reported to National Notifiable Diseases Surveillance System (NNDSS) in terms of type/subtype and the demographic, geographic and temporal distribution of infections.

Highlights and developments 2013
An application was lodged with the Communicable Diseases Network of Australia to access NNDSS data for the study.

Evolution and modelling of influenza viruses

Antigenic cartography and molecular evolution of the influenza virus

Centre staff: Ian Barr, Aeron Hurt, Malet Aban
Collaborators: Derek Smith and Colin Russell (University of Cambridge, UK); Yoshihiro Kawaoka (University of Wisconsin-Madison, WI, USA; University of Tokyo, Japan)

Project overview
This project involves analysis of influenza viruses by antigenic cartography in combination with known amino acid changes in HA. The cartography system uses sophisticated computer algorithims to spatially plot each influenza virus in terms of its reactivity in an HI assay — analogous to a road map that interconnects towns and cities. Over the course of each year the virus strains form clusters that map differently over time, reflecting the changing nature of the influenza virus. Integration of these data with sequence data provides insight into the reasons for antigenic drift, with the ultimate goal of predicting the direction of antigenic drift before it occurs. This work has been partially funded by a grant from the HFSP (Human Frontier Science Program).

Highlights and developments 2013
With the established large "base-map" that covered influenza A(H3) viruses from 1968 to 2003 and ferret antisera generated to these viruses, it was determined that the major antigenic changes that occurred were mainly caused by single amino acid substitutions, which happened at only seven positions in HA immediately adjacent to the receptor binding site. Most of these substitutions were involved in antigenic change more than once. Equivalent positions were responsible for the recent antigenic changes of influenza B and A(H1N1) viruses. Substitution of a single amino acid at one of these positions substantially changed the virus-specific antibody response in infected ferrets. These findings may help us to determine which changes are likely to result in a variant virus which may not be well covered by the existing influenza vaccine and may ultimately allow us to predict the evolution of human influenza viruses more accurately . These findings resulted in the publication of a major paper during 2013.

Related publications 2013
Reference no. 23

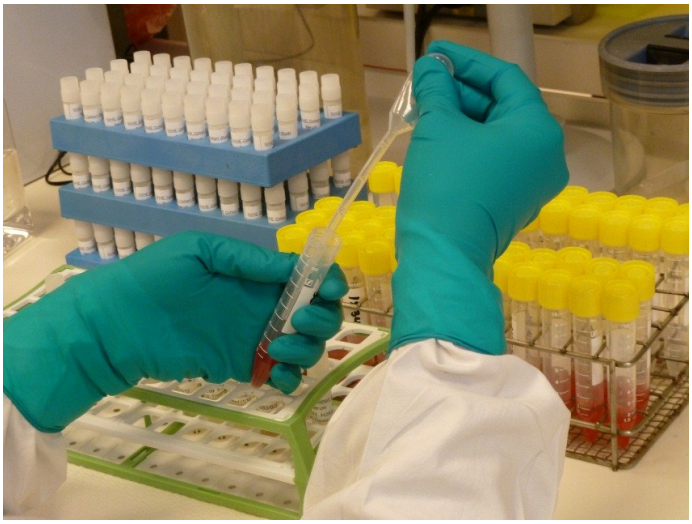
Spatial and temporal dynamics of human seasonal influenza B in Australia and New Zealand

Centre staff: Ian Barr, Yi-Mo Deng, Natalie Spirason, Aeron Hurt
Collaborators: Rebecca Halpin and David Wentworth (J. Craig Venter Institute, Rockville, MD, USA)**;** Vijaykrishna Dhanasekaran and Gavin Smith (Duke-NUS Graduate Medical School, Singapore)

Project overview
Whilst the evolutionary dynamics of seasonal A(H1N1) and A(H3N2) viruses have been extensively studied, the evolutionary dynamics of influenza B viruses are not well known and to date a large-scale population dynamic study has not been undertaken. Furthermore, the extent and consequences of reassortment between viruses of the B/Victoria and B/Yamagata lineages that have been co-circulating since the mid-1980s have not been well characterised.

This project aimed to perform full genome sequencing on over 900 influenza B viruses collected in Australia and New Zealand from 2002 to 2011 and isolated at the Centre. Genomic data from this repository will be crucial to understanding the fundamental processes of molecular evolution of each gene segment including reassortment events and also to determine the processes of importation, regional distribution and diversity of influenza B viruses over the 10 years since 2002 when the B/Victoria lineage became re-established in Australia and New Zealand. The full genome characterisation of these viruses will also play an important role in global efforts to better understand the molecular epidemiology, evolution and adaptive potential of these viruses.

Highlights and developments 2013
This project has completed the full genome sequencing on 908 influenza B viruses collected in Australia and New Zealand from 2002 to 2013. The full genome characterisation of these viruses has been summarised in a manuscript that has been submitted for publication.



Evolution and modelling of influenza viruses (continued)

Molecular analysis and structural modelling of influenza proteins

Centre staff: Ian Barr, Yi-Mo Deng, Aeron Hurt, Naomi Komadina
Collaborators: Sebastian Maurer-Stroh (Bioinformatics Institute (BII), A*STAR, National University of Singapore, Singapore); Michael Parker (St Vincent's Institute of Medical Research)

Project overview
The Centre has several collaborations with external groups to use computer modelling to explore the structures of proteins of interest such as HA and NA. This analysis allows a better understanding of the molecular basis for changes that affect the efficacy of influenza vaccines and antiviral drugs.

Highlights and developments 2013
Work has continued with collaborators at the Bioinformatics Institute (A*STAR) in several areas during 2013 including structural analysis of amino acid changes in the HA and NA proteins. The work with the Bioinformatics Institute is partly funded by a grant from the NHMRC, Australia, and A*STAR, Singapore.

Related publications 2013
Reference no. 12

Early recognition and response to influenza

Centre staff: Patrick Reading
Collaborators: Alberto Mantovani (Instituto Clinico Humanitas, IRCCS & State University of Milan, Italy); Erika Crouch (Washington University School of Medicine, St. Louis, MO, USA); Stuart Turville (Westmead Millennium Institute, New South Wales); Nigel McMillan (Griffith University, Queensland); Andrew Brooks, Stephen Kent, Lorena Brown, Carol Hartley and Joanne Devlin (The University of Melbourne)

Project overview
This research project characterises how influenza virus is first recognised and destroyed by immune cells and soluble factors of the innate immune system. The innate immune response comprises pre-existing or rapidly induced defences that limit the spread of pathogens in the body during the first few days of infection prior to the emergence of more targeted adaptive immune responses. Many innate defences have been highly conserved throughout evolution and, as such, animal models of infection are widely used to investigate the role of innate defences and to gain insight as to how they might limit human disease.

Current studies in Dr Reading's laboratory at the University of Melbourne are focused on (i) understanding the role of soluble innate immune proteins of the collectin and pentraxin superfamilies in early host defence against influenza virus, (ii) understanding the role of membrane -associated C-type lectins expressed by macrophages and dendritic cells as receptors for influenza virus entry and destruction, (iii) showing how short interfering (si)RNA can be used to induce innate immunity and prevent influenza disease, and (iv) understanding influenza virus-bacterial synergism in the development of otitis media and pneumonia. The research involves both *in vitro* studies using human proteins and cells and *in vivo* studies using mouse and ferret models of infection.

Highlights and developments 2013
This research contributed to 10 peer-reviewed publications during 2013. Dr Reading presented several research talks at conferences and institutes during the year, including the 7th Australasian Virology Meeting in Queenstown, New Zealand 8–12 December, and the Institute of Medical Research in Goroka, Papua New Guinea. Additionally, Dr Reading is a chief investigator on an Australian Research Council (ARC) Discovery Project Grant and a NHMRC Project Grant, with funding to commence in 2014. Dr Reading's PhD student Emma Job also submitted her thesis and was awarded her PhD in 2013.

Related publications 2013: Reference nos. 19, 20, 32-36

NHMRC Program Grant: Understanding and controlling influenza (2010 - 2014)

The Centre is a participant in a National Health and Medical Research Council Program Grant which commenced on 1 January 2010.

Centre staff	Anne Kelso, Patrick Reading, Karen Laurie
Chief Investigators	Peter Doherty (The University of Melbourne)
	David Jackson (The University of Melbourne)
	Anne Kelso (WHO Collaborating Centre for Reference and Research on Influenza)
	Weisan Chen (La Trobe University)
	Stephen Turner (The University of Melbourne)
	Lorena Brown (The University of Melbourne)

Program overview

The Program has two broad goals:

- to understand fundamental mechanisms that establish maximum effective cellular immunity to influenza A viruses
- to build the foundations for clinical application of strategies to induce cellular immunity to these viruses.

These goals are being addressed through a range of collaborative projects between the chief investigators and team members at the Department of Microbiology and Immunology at the University of Melbourne (UM), the WHO Collaborating Centre, La Trobe University, the School of Population and Global Health (UM) and the CSIRO Australian Animal Health Laboratory.

Highlights and developments 2013

Dr Bridie Day (until February 2013) and Kim Charlton, working in the Department of Microbiology and Immunology under the supervision of Anne Kelso, have continued investigating the regulation of CD8 co-receptor expression in T lymphocytes and found that the IL-4-induced loss of CD8 expression and induction of a type 2 cytokine profile in peripheral $CD8^+$ T cells was associated with heritable epigenetic silencing of the CD8a locus both *in vitro* and *in vivo*.

A Program retreat held on 15 –16 October was attended by 66 people representing all of the research groups in the Program. Anne Kelso chaired a session and Karen Laurie gave a presentation. Aeron Hurt also attended.

After 18 months of preparation, an application for a renewal of the Program Grant was submitted in June with the title "Limiting the impact of influenza". The application was short-listed and the Chief Investigators were interviewed in October.

Related Publications 2013

Reference no. 43

Epigenetic and cytokine control of $CD8^+$ T cell plasticity. Charlton, K, Day, EB, Russ, BE, Apte, SH, Turner, SJ, and Kelso, A. (Oral presentation and poster presented at the International Congress of Immunology, Milan, 22–27 August 2013)

Additional research collaborations

Assessment of a novel assay to detect ADCC antibodies to A(H1N1)pdm09 virus

Centre staff: Karen Laurie, Louise Carolan, Ian Barr, Patrick Reading, Aeron Hurt
Collaborators: Stephen Kent and Sinthujan Jegaskanda (The University of Melbourne)

Project overview
Engagement of antibody-dependent cellular cytotoxicity (ADCC) antibodies by natural killer cells leads to killing of virus-infected cells and secretion of antiviral cytokines and chemokines. ADCC antibodies may target more conserved influenza virus antigens compared to neutralising antibodies. Novel assays have been developed to assess the specificity and function of influenza-specific ADCC antibodies. ADCC antibodies were found in healthy influenza seropositive young adults without detectable neutralising antibodies.

Related publications 2013: Reference nos. 17, 18

Assessment of trivalent live attenuated influenza-SIV vaccines in macaques

Centre staff: Karen Laurie, Louise Carolan, Aeron Hurt
Collaborators: Stephen Kent and Sinthujan Jegaskanda (The University of Melbourne)
Related publications 2013: Reference nos. 16, 29

Monoclonal antibodies targeting the influenza neuraminidase

Centre staff: Aeron Hurt
Collaborators: Tracey Doyle, Xuguang (Sean) Li (Centre for Vaccine Evaluation, Health Canada, Ottawa, Canada)
Related publications 2013: Reference nos. 7, 8

Surveillance of penguins in Antarctica for avian influenza

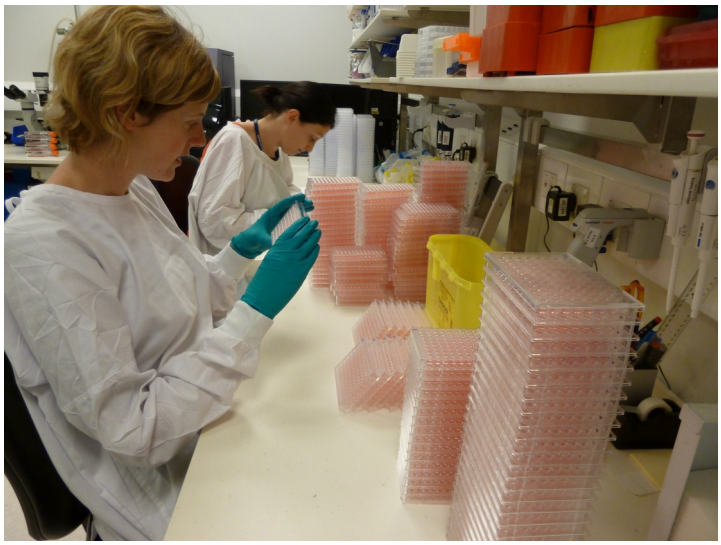
Centre staff: Aeron Hurt
Collaborators: Daniel Gonzalez-Acuna (University of Concepcion, Chile); Bjorn Olsen (Uppsala University, Sweden)

Project overview
Avian influenza viruses have not previously been detected in birds in Antarctica. Swabs and serum were taken from Adelie penguins on the Antarctic Peninsula and analysed at the Centre. The project was the first to successfully detect, sequence and isolate an avian influenza virus from Antarctica. The virus was of subtype H11N2 and was found to be highly diverged from all other known avian influenza viruses in either the Southern or Northern Hemisphere, suggesting the maintenance and evolution of the virus in Antarctica over many years.

Highlights and developments 2013
The field trip for this project was undertaken in January 2013 and the viruses were analysed in subsequent months. Results were presented by Aeron Hurt in talks at two conferences and a manuscript was submitted for publication.

Wild bird avian influenza sequencing

Centre staff: Aeron Hurt
Collaborators: Simone Warner (Victorian Government Department of Environment and Primary Industries); Edla Arzey (NSW Government Departments of Primary Industries)
Related publications 2013: Reference no. 44



Karen Laurie (front) and Louise Carolan (back)

Research Funding and Awards

Centre staff are chief or associate investigators in four grants awarded by Australian research funding bodies in 2013:

A*STAR/NHMRC Joint Grant for Research on Utilising Integrative Technologies to Combat Emerging Infectious Disease: *Determining the clinical effectiveness of antiviral drugs against oseltamivir and laninamivir-resistant influenza viruses in animal models.* AUD $374,673 + SGD $406,620 for the period 1 January 2013 – 31 December 2015. Chief Investigators **Aeron Hurt**, **Ian Barr** and Sebastian Maurer-Ströh (Bioinformatics Institute, Singapore). **Anne Kelso** is an Associate Investigator. The Australian component of the grant will be administered by Melbourne Health, with the work being undertaken at the Centre. The Singaporean component will be administered and undertaken at the Bioinformatics Institute.

NHMRC Project Grant: *Understanding the parameters of innate immune activation that govern protection during influenza virus and secondary bacterial infection: development of a TLR2-based antimicrobial agent.* $447,111 awarded for the period 1 January 2014 – 31 December 2016. Chief Investigators David Jackson, Amabel Tan and **Patrick Reading**. The grant will be administered by The University of Melbourne and the work will be undertaken at the University.

Australian Research Council (ARC) Discovery Project Grant: *Linking immunomodulation and latency in alphaherpesvirus infection.* $370,000 awarded for the period 1 January 2014 – 31 December 2016. Chief Investigators Carol Hartley, Joanne Devlin, James R Gilkerson and **Patrick Reading**. The grant will be administered by The University of Melbourne and the work will be undertaken at the University.

Women's and Children's Hospital Foundation Research Project Grant: *Does obesity in pregnancy impact on immune response to influenza vaccines?* $69,290 awarded for the period 1 January 2014 – 31 December 2015. Chief Investigator Helen Marshall. **Ian Barr** is an Associate Investigator. The grant will be administered by the Women's and Children's Hospital. While most of the work will be undertaken at the hospital, antigenic characterisation of collected samples will take place at the Centre.

Collaborative Agreements

The Centre is party to two ongoing collaborative research and development agreements with industry bodies. As with all potential collaborations with the commercial sector, these agreements have undergone review by the Australian Government Advisory Committee to ensure that they support the Centre's objective of advancing global public health, have scientific merit and adhere to the principles of neutrality, transparency, independence and accountability.

Agreement with the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) (2012-2013)

Centre staff: Chantal Baas, Jayde Galletti, Robert Shaw, Anne Kelso, Ian Barr

Project overview
This project aims to enhance the number and geographic range of influenza viruses isolated in eggs as candidates for commercial influenza vaccine manufacture.

Highlights and developments 2013
A total of 37 egg isolates were obtained from 107 inoculations with original clinical specimens from various geographical locations. Isolation rates varied from 11% to 44% according to virus type/subtype and lineage. Suitable isolates were made available to other laboratories and industry for reassortment and assessment as vaccine candidates.

Cooperative Research and Development Agreement (CRADA) with Novartis Vaccines & Diagnostics (Marburg, Germany): Development and provision of influenza virus strains isolated on MDCK 33016PF cells for vaccine production (2012–2013)

Centre staff: Heidi Peck, Joelle Dharmakumara, Robert Shaw, Anne Kelso, Ian Barr

Project overview
The suitability of a proprietary Novartis cell line for isolating and growing influenza viruses as a basis for cell-based vaccine manufacture is being evaluated. A number of original clinical specimens are used to isolate viruses directly into the MDCK33016PF cell line in parallel with egg isolation. The resultant isolates undergo analysis of their growth, antigenic and other properties.

Highlights and developments 2013
During 2013, 128 clinical specimens were cultured in MDCK 33016PF cells, of which 102 (79.7%) produced isolates. As in previous years, this was much higher than the rate of isolation in eggs. The isolates, which comprised A(H1N1)pdm09, A(H3N2) and B viruses, were sent to Novartis in Marburg, Germany, and Holly Springs NC, USA, for further evaluation as potential vaccine candidates produced by cell culture. Heidi Peck gave an oral presentation based on this work at the Options for the Control of Influenza VIII, Cape Town, South Africa, 5–9 September.

Research Students

PhD Candidate

Ms Teagan Guarnaccia, who commenced her PhD candidature at the Centre in 2010, has continued her project entitled "Analysis of the contribution of immune pressure on antigenic drift of influenza A viruses", under the supervision of Dr Karen Laurie and Ms Jenny Mosse (Monash University, Gippsland). Teagan gave an oral presentation at the 9th Australian Influenza Symposium (Sydney, October 3–4).

MSc Candidate

Ms Chantal Baas, who commenced her MSc candidature part-time at the Centre in 2012, has continued her project entitled" "Investigating the risk of non-human influenza viruses for public health by using a ferret model", under the supervision of Dr Aeron Hurt, Dr Ian Barr and Ms Jenny Mosse (Monash University, Gippsland).

Honours Student

Ms Rubaiyea Farrukee, a BSc (Biotechnology) student from Monash University, Gippsland, completed her Honours research project at the Centre during 2012. She was supervised by Dr Aeron Hurt and achieved First Class Honours. Her project, titled "Investigating the effect of key mutations in influenza B neuraminidase by reverse genetics", used reverse genetics to investigate the effect of key NA mutations on neuraminidase inhibitor resistance in B/Yamagata-like and B/Victoria-like influenza B neuraminidases. It was found that some mutations have a considerably greater effect on resistance in the NA of one lineage than when the same mutation is introduced into a virus of the other lineage.

Masters Student

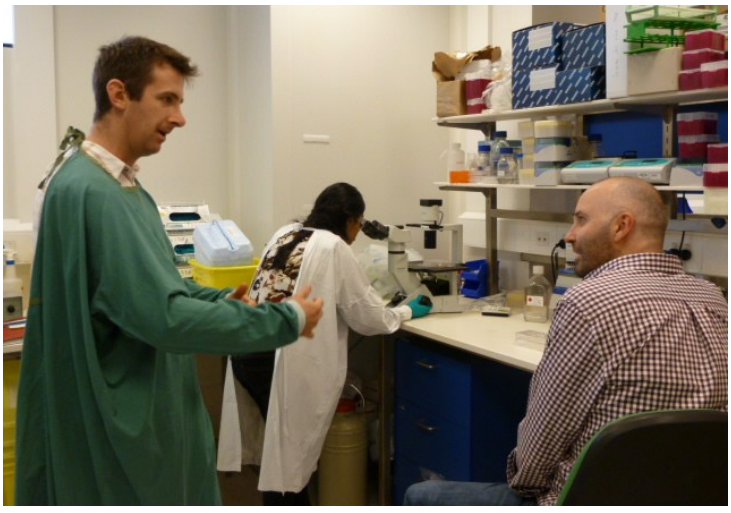
Ms Kerry Wong, Masters of Biostatistics student from the University of Melbourne, undertook a research project, titled "Estimation of influenza vaccine effectiveness in Western Australia from routine surveillance data using a test-negative method, 2010 and 2011", under the supervision of Dr Sheena Sullivan from December 2012 to June 2013.

Undergraduate Student

Ms Mary Cousinery, a Bachelor of Biomedical Science student from Deakin University, completed a work placement at the Centre 24 June–5 July.

Staff Development

Ding Yuan Thomas Oh completed a course on performing aseptic surgery on rodents for scientific purposes (AAS01) at Box Hill Institute of TAFE, Melbourne, 5–6 December.



Jeffrey Butler (left) and Aeron Hurt (right)

Communications and Advisory Activities

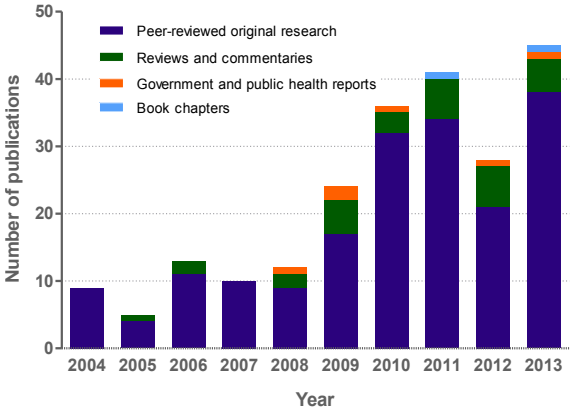
The Centre actively contributes to the knowledge and understanding of influenza in scientific and public health domains through many different forums. Centre staff members participate in WHO meetings and workshops to support the ongoing work and growth of WHO GISRS, as well as providing advice on influenza to the Australian Government. Centre staff members also co-organise the Australian Influenza Symposium, publish peer-reviewed journal papers and present numerous talks and posters.

Publications and Reports

Publication Highlights

The Centre continued to build its research profile in 2013 with the publication of 45 original research papers, reviews, reports and book chapters (Figure 17).

Figure 17. Centre publications 2004-2013.



Centre Publications 2013

1. **Baas C**, **Barr I**, Fouchier R, **Kelso A**, and **Hurt A**. A comparison of rapid point-of-care tests for the detection of avian influenza A(H7N9) virus, 2013. *Euro Surveill*, 2013. 18(21). pii: 20487
2. **Barr IG** and **Hurt AC**. Double dose oseltamivir for severe influenza--does it help? *BMJ*, 2013. 346: f3449. doi: 10.1136/bmj.f3449
3. Bodle J, Verity EE, Ong C, Vandenberg K, **Shaw R**, **Barr IG**, and Rockman S. Development of an enzyme-linked immunoassay for the quantitation of influenza haemagglutinin: an alternative method to single radial immunodiffusion. *Influenza Other Respi Viruses*, 2013. 7(2): 191-200. doi:10.1111/j.1750-2659.2012.00375.x
4. Chen MI, Cook AR, Lim WY, Lin R, Cui L, **Barr IG**, **Kelso A**, Chow VT, Leo YS, Hsu JP, **Shaw R**, Chew S, Yap JK, Phoon MC, Koh HW, Zheng H, Tan L, and Lee VJ. Factors influencing infection by pandemic influenza A(H1N1)pdm09 over three epidemic waves in Singapore. *Influenza Other Respir Viruses*, 2013. 7(6): 1380-9. doi:10.1111/irv.12129
5. Chin R, Earnest-Silviera L, Gordon CL, Olsen K, **Barr I**, Brown LE, Jackson DC, and Torresi J. Impaired dendritic cell maturation in response to pandemic H1N109 influenza virus. *J Clin Virol*, 2013. 56(3): 310-5. doi:10.1016/j.jcv.2012.11.009
6. **Deng YM**, **Iannello P**, **Caldwell N**, **Jelley L**, **Komadina N**, **Baas C**, **Kelso A**, and **Barr IG**. The use of pyrosequencer-generated sequence-signatures to identify the influenza B-lineage and the subclade of the B/Yamataga-lineage viruses from currently circulating human influenza B viruses. *J Clin Virol*, 2013. 58(1): 94-9. doi:10.1016/j.jcv.2013.04.018
7. Doyle TM, Hashem AM, Li C, Van Domselaar G, Larocque L, Wang J, Smith D, Cyr T, Farnsworth A, He R, **Hurt AC**, Brown EG, and Li X. Universal anti-neuraminidase antibody inhibiting all influenza A subtypes. *Antiviral Res*, 2013. 100(2): 567-74. doi:10.1016/j.antiviral.2013.09.018
8. Doyle TM, Li C, Bucher DJ, Hashem AM, Van Domselaar G, Wang J, Farnsworth A, She YM, Cyr T, He R, Brown EG, **Hurt AC**, and Li X. A monoclonal antibody targeting a highly conserved epitope in influenza B neuraminidase provides protection against drug resistant strains. *Biochem Biophys Res Commun*, 2013. 441(1): 226-9. doi:10.1016/j.bbrc.2013.10.041

Centre Publications (continued)

9. Dwyer D, **Barr I**, **Hurt A**, **Kelso A**, **Reading P**, **Sullivan S**, Buchy P, Yu H, Zheng J, Shu Y, Wang D, Lam, Aguon A, Oliva RQ, Odagiri T, Tashiro M, Verasahib K, Yusof MA, Nymadawa P, Alexander B, Gourinat AC, Grangeon JP, Jennings L, Huang S, Horwood P, Lucero M, Roque V Jr., Lee Suy L, Cardon P, Tandoc A 3rd, Olveda RM, Kang C, Young-Joon P, Cutter J, Lin R, Low C, Mai le TQ, Balish A, Kile J, Mei S, McFarland J, Moen A, Olsen S, Samaan G, Xiyan X, Chea N, Diorditsa S, Feldon K, Fox K, Jamsran M, Konings F, Lewis HC, McPherson M, Nilles E, Olowokure B, and Partridge J. Seasonal influenza vaccine policies, recommendations and use in the World Health Organization's Western Pacific Region. *Western Pac Surveill Response J*, 2013. 4(3): 51-9. doi:10.5365/WPSAR.2013.4.1.009
10. **Farrukee R**, Mosse J, and **Hurt AC**. Review of the clinical effectiveness of the neuraminidase inhibitors against influenza B viruses. *Expert Rev Anti Infect Ther*, 2013. 11(11): 1135-45. doi:10.1586/14787210.2013.842466
11. Fielding J, Grant K, Franklin L, **Sullivan S**, Papadakis G, Kelly H, and Cheng A. Epidemiology of the 2012 influenza season in Victoria, Australia. *WPSAR*, 2013. 4(3, Jul-Sep 2013): 42-50. doi:10.5365/wpsar.2013.4.2.007
12. **Guarnaccia T**, **Carolan LA**, Maurer-Stroh S, Lee RT, Job E, **Reading PC**, Petrie S, McCaw JM, McVernon J, **Hurt AC**, **Kelso A**, Mosse J, **Barr IG**, and **Laurie KL**. Antigenic drift of the pandemic 2009 A(H1N1) influenza virus in a ferret model. *PLoS Pathog*, 2013. 9(5): e1003354. doi:10.1371/journal.ppat.1003354
13. **Hurt AC**, Ison MG, Hayden FG, and Hay AJ. Second isirv antiviral group conference: overview. *Influenza Other Respir Viruses*, 2013. 7 Suppl 3: 1-7. doi:10.1111/irv.12207
14. **Hurt AC**, **Leang SK**, Tiedemann K, **Butler J**, Mechinaud F, **Kelso A**, Downie P, and **Barr IG**. Progressive emergence of an oseltamivir-resistant A(H3N2) virus over two courses of oseltamivir treatment in an immunocompromised paediatric patient. *Influenza Other Respi Viruses*, 2013. doi:10.1111/irv.12108
15. Inforzato A, **Reading PC**, Barbati E, Bottazzi B, Garlanda C, and Mantovani A. The "sweet" side of a long pentraxin: how glycosylation affects PTX3 functions in innate immunity and inflammation. *Front Immunol*, 2013. 3: 407. doi:10.3389/fimmu.2012.00407
16. Jegaskanda S, Amarasena TH, **Laurie KL**, Tan HX, **Butler J**, Parsons MS, Alcantara S, Petravic J, Davenport MP, **Hurt AC**, **Reading PC**, and Kent SJ. Standard trivalent influenza virus protein vaccination does not prime antibody-dependent cellular cytotoxicity in macaques. *J Virol*, 2013. 87(24): 13706-18. doi:10.1128/jvi.01666-13
17. Jegaskanda S, Job ER, Kramski M, **Laurie K**, Isitman G, de Rose R, Winnall WR, Stratov I, Brooks AG, **Reading PC**, and Kent SJ. Cross-reactive influenza-specific antibody-dependent cellular cytotoxicity antibodies in the absence of neutralizing antibodies. *J Immunol*, 2013. 190(4): 1837-48. doi:10.4049/jimmunol.1201574
18. Jegaskanda S, **Laurie KL**, Amarasena TH, Winnall WR, Kramski M, De Rose R, **Barr IG**, Brooks AG, **Reading PC**, and Kent SJ. Age-associated cross-reactive antibody-dependent cellular cytotoxicity toward 2009 pandemic influenza A virus subtype H1N1. *J Infect Dis*, 2013. 208(7): 1051-61. doi:10.1093/infdis/jit294
19. Job ER, Bottazzi B, Gilbertson B, Edenborough KM, Brown LE, Mantovani A, Brooks AG, and **Reading PC**. Serum amyloid P is a sialylated glycoprotein inhibitor of influenza A viruses. *PLoS One*, 2013. 8(3): e59623. doi:10.1371/journal.pone.0059623
20. Job ER, **Deng YM**, Barfod KK, Tate MD, **Caldwell N**, Reddiex S, Maurer-Stroh S, Brooks AG, and **Reading PC**. Addition of glycosylation to influenza A virus hemagglutinin modulates antibody-mediated recognition of H1N1 2009 pandemic viruses. *J Immunol*, 2013. 190(5): 2169-77. doi:10.4049/jimmunol.1202433
21. Kelly HA, Grant KA, Tay EL, Franklin L, and **Hurt AC**. The significance of increased influenza notifications during spring and summer of 2010-11 in Australia. *Influenza Other Respir Viruses*, 2013. 7(6): 1136-41. doi:10.1111/irv.12057
22. Kelly HA, **Sullivan SG**, Grant KA, and Fielding JE. Moderate influenza vaccine effectiveness with variable effectiveness by match between circulating and vaccine strains in Australian adults aged 20-64 years, 2007-2011. *Influenza Other Respir Viruses*, 2013. 7(5): 729-37. doi:10.1111/irv.12018
23. Koel BF, Burke DF, Bestebroer TM, van der Vliet S, Zondag GC, Vervaet G, Skepner E, Lewis NS, Spronken MI, Russell CA, Eropkin MY, **Hurt AC**, **Barr IG**, de Jong JC, Rimmelzwaan GF, Osterhaus AD, Fouchier RA, and Smith DJ. Substitutions near the receptor binding site determine major antigenic change during influenza virus evolution. *Science*, 2013. 342(6161): 976-9. doi:10.1126/science.1244730

Centre Publications (continued)

24. **Laurie KL**, Huston P, Riley S, Katz JM, Willison DJ, Tam JS, Mounts AW, Hoschler K, Miller E, Vandemaele K, Broberg E, Van Kerkhove MD, and Nicoll A. Influenza serological studies to inform public health action: best practices to optimise timing, quality and reporting. *Influenza Other Respi Viruses*, 2013. 7(2): 211-224. doi:10.1111/j.1750-2659.2012.0370a.x

25. **Leang SK**, **Deng YM**, **Shaw R**, **Caldwell N**, **Iannello P**, **Komadina N**, Buchy P, Chittaganpitch M, Dwyer DE, Fagan P, Gourinat AC, Hammill F, Horwood PF, Huang QS, Ip PK, Jennings L, Kesson A, Kok T, Kool JL, Levy A, Lin C, Lindsay K, Osman O, Papadakis G, Rahnamal F, Rawlinson W, Redden C, Ridgway J, Sam IC, Svobodova S, Tandoc A, Wickramasinghe G, Williamson J, Wilson N, Yusof MA, **Kelso A**, **Barr IG**, and **Hurt AC**. Influenza antiviral resistance in the Asia-Pacific region during 2011. *Antiviral Res*, 2013. 97(2): 206-10. doi:10.1016/j.antiviral.2012.12.016

26. Ng WC, Liong S, Tate MD, Irimura T, Denda-Nagai K, Brooks AG, Londrigan SL, and **Reading PC**. The macrophage galactose-type lectin can function as an attachment and entry receptor for influenza virus. *J Virol*, 2013. doi:10.1128/jvi.02014-13

27. Olver S, Apte SH, Baz A, **Kelso A**, and Kienzle N. Interleukin-4-induced loss of CD8 expression and cytolytic function in effector CD8 T cells persists long term *in vivo*. *Immunology*, 2013. 139(2): 187-96. doi:10.1111/imm.12068

28. Petrie SM, **Guarnaccia T**, **Laurie KL**, **Hurt AC**, McVernon J, and McCaw JM. Reducing uncertainty in within-host parameter estimates of influenza infection by measuring both infectious and total viral load. *PLoS One*, 2013. 8(5): e64098. doi:10.1371/journal.pone.0064098

29. Reece JC, Alcantara S, Gooneratne S, Jegaskanda S, Amaresena T, Fernandez CS, **Laurie K**, **Hurt A**, O'Connor SL, Harris M, Petravic J, Martyushev A, Grimm A, Davenport MP, Stambas J, De Rose R, and Kent SJ. Trivalent live attenuated influenza-simian immunodeficiency virus vaccines: efficacy and evolution of cytotoxic T lymphocyte escape in macaques. *J Virol*, 2013. 87(8): 4146-60. doi:10.1128/JVI.02645-12

30. Rockman S, Brown LE, **Barr IG**, Gilbertson B, Lowther S, Kachurin A, Kachurina O, Klippel J, Bodle J, Pearse M, and Middleton D. Neuraminidase-inhibiting antibody is a correlate of cross-protection against lethal H5N1 influenza virus in ferrets immunized with seasonal influenza vaccine. *J Virol*, 2013. 87(6): 3053-61. doi:10.1128/JVI.02434-12

31. Sam IC, **Shaw R**, Chan YF, Hooi PS, **Hurt AC**, and **Barr IG**. Seroprevalence of seasonal and pandemic influenza A in Kuala Lumpur, Malaysia in 2008-2010. *J Med Virol*, 2013. 85(8): 1420-5. doi:10.1002/jmv.23622

32. Short KR, Grant EJ, Vissers M, **Reading PC**, Diavatopoulos DA, and Kedzierska K. A novel method linking antigen presentation by human monocyte-derived macrophages to $CD8^+$ T cell polyfunctionality. *Front Immunol*, 2013. 4: 389. doi:10.3389/fimmu.2013.00389

33. Short KR, Habets MN, Payne J, **Reading PC**, Diavatopoulos DA, and Wijburg OL. Influenza A virus induced bacterial otitis media is independent of virus tropism for α2,6-linked sialic acid. *Virol J*, 2013. 10: 128. doi:10.1186/1743-422X-10-128

34. Short KR, **Reading PC**, Brown LE, Pedersen J, Gilbertson B, Job ER, Edenborough KM, Habets MN, Zomer A, Hermans PW, Diavatopoulos DA, and Wijburg OL. Influenza-induced inflammation drives pneumococcal otitis media. *Infect Immun*, 2013. 81(3): 645-52. doi:10.1128/IAI.01278-12

35. Short KR, Vissers M, de Kleijn S, Zomer AL, Kedzierska K, Grant E, **Reading PC**, Hermans PW, Ferwerda G, and Diavatopoulos DA. Bacterial lipopolysaccharide inhibits influenza virus infection of human macrophages and the consequent induction of $CD8^+$ T cell immunity. *J Innate Immun*, 2013. doi:10.1159/000353905

36. Short KR, von Kockritz-Blickwede M, Langereis JD, Chew KY, Job ER, Armitage CW, Hatcher B, Fujihashi K, **Reading PC**, Hermans PW, Wijburg OL, and Diavatopoulos DA. Antibodies mediate the formation of neutrophil extracellular traps (NETs) in the middle ear and facilitate secondary pneumococcal otitis media. *Infect Immun*, 2013. doi:10.1128/iai.01104-13

37. **Sullivan SG** and Greenland S. Bayesian regression in SAS software. *Int J Epidemiol*, 2013. 42(1): 308-17. doi:10.1093/ije/dys213

38. **Sullivan SG** and Kelly H. Late season interim estimates of influenza vaccine effectiveness reliably predict end of season estimates in Victoria, Australia, 2007 to 2012. *Euro Surveill*, 2013. 18(41): 20605.

39. **Sullivan SG** and Kelly H. Stratified estimates of influenza vaccine effectiveness by prior vaccination: caution required. *Clin Infect Dis*, 2013. 57(3): 474-6. doi:10.1093/cid/cit255

Centre Publications (continued)

40. **Sullivan SG**, Tay EL, and Kelly H. Variable definitions of the influenza season and their impact on vaccine effectiveness estimates. *Vaccine*, 2013. 31(40): 4280-3. doi:10.1016/j.vaccine.2013.06.103

41. Trauer JM, Bandaranayake D, Booy R, Chen MI, Cretikos M, Dowse GK, Dwyer DE, Greenberg ME, Huang QS, Khandaker G, Kok J, **Laurie KL**, Lee VJ, McVernon J, Walter S, and Markey PG. Seroepidemiologic effects of influenza A(H1N1) pdm09 in Australia, New Zealand, and Singapore. *Emerg Infect Dis*, 2013. 19(1): 92-101. doi:10.3201/eid1901.111643

42. Turner SJ, Doherty PC, and **Kelso A**, *Cell-mediated immunity*, in *Textbook of Influenza*, R.G. Webster, A.S. Monto, T.J. Braciale, and R.A. Lamb, Editors. 2013, Wiley-Blackwell. p. 298-310.

43. Valkenburg SA, Quinones-Parra S, Gras S, **Komadina N**, McVernon J, Wang Z, Halim H, **Iannello P**, Cole C, **Laurie K**, **Kelso A**, Rossjohn J, Doherty PC, Turner SJ, and Kedzierska K. Acute emergence and reversion of influenza A virus quasispecies within $CD8^+$ T cell antigenic peptides. *Nat Commun*, 2013. 4: 2663. doi:10.1038/ncomms3663

44. Vijaykrishna D, **Deng YM**, Su YC, Fourment M, **Iannello P**, Arzey GG, Hansbro PM, Arzey KE, Kirkland PD, Warner S, O'Riley K, **Barr IG**, Smith GJ, and **Hurt AC**. The recent establishment of North American H10 lineage influenza viruses in Australian wild waterfowl and the evolution of Australian avian influenza viruses. *J Virol*, 2013. 87(18): 10182-9. doi:10.1128/jvi.03437-12

45. WHO, *China—WHO joint mission on human infection with avian influenza A(H7N9) virus 18 – 24 April 2013*, Mission Report. 2013, WHO.

Oral Presentations

Centre staff members gave oral presentations at numerous events during 2013, including national and international conferences, WHO meetings, government advisory meetings, educational lectures and research seminars.

Event **Location, date**	**Speaker, Title**
Shanghai Municipal Center for Disease Control and Prevention Shanghai, China, 6 January	Yi-Mo Deng: *Influenza in the post pandemic era - challenges and actions*
CONSISE: Consortium for the Standardization of Influenza Seroepidemiology Regional Meeting Hong Kong SAR, China, 22–23 January	Karen Laurie: *A comparative examination of influenza 2 day and 3 day HA consensus microneutralization assays.*
WHO Regional Office for South-East Asia Region: Training on Influenza Data Management and Epidemiological Analysis Bangkok, Thailand, 11–15 February	Sheena Sullivan: *Routine data analysis procedures/minimum analyses for reporting.* *Introduction to baselines & significance for interpretation.* *Introduction to risk factor analysis.*
Research field trip Base General Bernardo O'Higgins Riquelme, Antarctic Peninsula, 16 February	Aeron Hurt: *¿Qué pingüinos tienen que ver con la influenza? (What do penguins have to do with influenza?)*
Communicable Disease Control Conference 2013 Canberra, 19–20 March	Aeron Hurt: *Antiviral resistance in influenza: the current situation and future risks.*
Institute of Medical Research Goroka, Papua New Guinea, 6 March	Patrick Reading: *Innate immunity to influenza virus infection.*
9th Indo-Australian Biotechnology Conference Melbourne, 4–9 April	Anne Kelso: *The continuing challenge of influenza.*

Oral Presentations (continued)

Event **Location, date**	**Speaker, *Title***
Presentation to animal house staff, Department of Microbiology and Immunology, The University of Melbourne Melbourne, 12 April	Karen Laurie: *The ferret model of human influenza virus infection.*
Presentation to infectious disease registrars at the Royal Melbourne Hospital Melbourne, 22 April	Aeron Hurt: *Avian influenza A(H7N9) in China.*
Viruses in May Katoomba, New South Wales, 9–11 May	Anne Kelso: *The A(H7N9) influenza outbreak in China.*
Lecture to 3rd year students, University of Melbourne Breadth Subject "Global health, security and sustainability" Melbourne, 15 May	Anne Kelso: *Influenza.*
Seminar presentation at the Australian Animal Health Laboratory (AAHL) Geelong, Victoria, 16 May	Ian Barr: *The influenza A(H7N9) outbreak in China.*
Melbourne Health Research Week Symposium Melbourne, 23–30 May	Sheena Sullivan: *Evidence not shown for waning of influenza vaccine effectiveness during the 2012 influenza season in Victoria, Australia.*
National Institute of Health Research and Development Jakarta, Indonesia, 31 May	Patrick Reading: *Reference laboratories for characterisation of influenza virus.* *Assays to characterise cell-grown isolates of influenza virus.*
WHO PCR Working Group Meeting Geneva, Switzerland, 2–3 July	Yi-Mo Deng: *Molecular surveillance updates at the WHO CC Melbourne, Australia.* *Applications of sequencing in influenza surveillance.*
WHO Antivirals Working Group Meeting Geneva, Switzerland, 4–5 July	Aeron Hurt: *Update on antiviral susceptibility lab activities - Asia Pacific.* *Update on uptake of antivirals.* *Update of amino acid substitutions associated with reduced susceptibility to antivirals.*
The Australian Society for Microbiology Annual Scientific Meeting Adelaide, 7–10 July	Aeron Hurt: *Antiviral resistance in influenza: the past, present and the future...*
The Walter and Eliza Hall Student Association Seminar Series Melbourne, 1 August	Anne Kelso: *Drift and shift.*
International Congress of Pediatrics Melbourne, 24–29 August	Anne Kelso: *Influenza in the 21st century.*

Oral Presentations (continued)

Event Location, date	Speaker, *Title*
Avian Influenza in Wild Birds Group Meeting Melbourne, 27–28 August	Aeron Hurt: *Penguins and avian influenza.*
CONSISE: Consortium for the Standardization of Influenza Seroepidemiology Regional Meeting Cape Town, South Africa, 3–4 September	Karen Laurie: *A comparative examination of influenza 2 day ELISA and 3 day HA consensus microneutralization assays using A(H3N2) and A(H5N1) influenza viruses.*
Options for the Control of Influenza VIII Cape Town, South Africa, 5–9 September	Aeron Hurt: *The first detection and isolation of avian influenza viruses in Antarctica.* *Recent A(H1N1)pdm09 influenza viruses encode permissive NA mutations which improve the fitness of oseltamivir-resistant H275Y variants. [poster + short talk]* Yi-Mo Deng: *Applications of pyrosequencing in the molecular surveillance of influenza.* Heidi Peck: *Evaluation of influenza A and B viruses isolated and passaged in the qualified MDCK suspension cell line (MDCK33016PF) and embryonated chicken eggs.*
GISAID/isirv-AVG Training Workshop: Sequence Analysis and Detection of Antiviral Resistance Cape Town, South Africa, 7 September	Aeron Hurt: *Influenza antivirals, emergence of resistance and surveillance.* *Control virus panels.* *Assessing frequency and significance of mutations using FluSurver. [demonstration]* Naomi Komadina: *Analysis and interpretation of sequence data on the GISAID platform.* *GISAID's EpiFlu database for sequence comparisons. [demonstration]*
5th LabNet Meeting, Strengthening Pacific Laboratory Quality Management Systems (LQMS) towards accreditation Noumea, New Caledonia, 17–20 September	Patrick Reading: *Laboratory-based surveillance of influenza virus in the Asia-Pacific Region.*
Laboratory research meeting, Department of Microbiology and Immunology, The University of Melbourne Melbourne, 2 October	Karen Laurie: *Development and characterisation of a TaqMan real time RT-PCR assay to quantify cytokine and chemokine mRNA levels in ferrets.*

Oral Presentations (continued)

Event Location, date	Speaker, Title
9th Australian Influenza Symposium Sydney, 3–4 October	Aeron Hurt: *The first detection of avian influenza in Antarctica reveals highly diverged viruses.* Sheena Sullivan: *Unresolved methodological questions in VE studies.* Teagan Guarnaccia: *Antigenic drift of the pandemic 2009 A(H1N1) influenza virus in a ferret model.*
Victorian Leadership Seminar, Medical Student Council of Victoria Melbourne, 12 October	Anne Kelso: *From laboratory bench to global health – leadership opportunities in medical science.*
National Health and Medical Research Council Program on Understanding and Controlling Influenza Annual Retreat Melbourne, 15–16 October	Karen Laurie: *Development and characterisation of a TaqMan real time RT-PCR assay to quantify cytokine and chemokine mRNA levels in ferrets.*
School of Public Health & Preventative Medicine, Alfred Centre, Monash University Melbourne, 15 October	Naomi Komadina: *Understanding the likely population impact of new and improved influenza vaccines.*
Australasian Epidemiological Association Brisbane, 21–22 October	Sheena Sullivan: *Repeated exposure to influenza vaccine may attenuate effectiveness: implications across the lifespan.*
J. Craig Venter Institute Rockville, MD, USA, 21 October	Yi-Mo Deng: *Influenza surveillance at the WHO CC Melbourne.*
University of Hong Kong Hong Kong, 7 November	Sheena Sullivan: *Studies to estimate influenza vaccine effectiveness.*
7th Meeting of National Influenza Centres and Influenza Surveillance in the Western Pacific and South-East Asia Regions Beijing, China, 12–15 November	Ian Barr: *Influenza activity in the Southern Hemisphere.*
9th Annual Nossal Institute for Global Health Forum: From Cell to Globe: Collaborations in communicable disease Melbourne, 29 November	Anne Kelso: *The A(H7N9) outbreak in China – a test case for human influenza surveillance and responsiveness in the molecular age.*
The 7th Australasian Virology Society Meeting Queenstown, New Zealand, 8–12 December	Sook Kwan (Leah) Leang: *Susceptibility of circulating influenza viruses to three new antiviral drugs: Peramivir, Laninamivir & T-705.* Patrick Reading: *Cells, sialic acids and C-type lectins in innate immunity to influenza virus.*

Poster Presentations

Centre staff contributed to the authorship and presentation of several posters and talks that were presented at conferences and meetings during 2013 as listed below.

Event **Location, date**	**Title and authors** (presentations are posters unless otherwise indicated, Centre authors are marked in bold, presenting author is underlined)
Communicable Disease Control Conference 2013 Canberra, 19–20 March	Cross-sectional serosurvey of cross-reactive antibody to emerging swine influenza A(H3N2)v in australian blood donors and children. McVernon J, **Laurie K**, Lambert SB, Faddy H, Irving D, **Barr I** and **Kelso A.**
15th International Congress of Immunology Milan, Italy, 22–27 August	Quantitation of mRNA cytokine levels in ferrets following influenza infection. **Carolan LA**, **Butler J**, **Guarnaccia T**, Rockman S, **Hurt AC**, **Reading PC**, **Kelso A**, **Barr I** and **Laurie KL**. Epigenetic and cytokine control of $CD8^+$ T cell plasticity. Charlton KL, Day EB, Russ BE, Apte SH, Turner SJ and **Kelso A**. (oral presentation and poster)
Options for the Control of Influenza VIII Cape Town, South Africa, 5–9 September	Recent A(H1N1)pdm09 influenza viruses encode permissive NA mutations which improve the fitness of oseltamivir-resistant H275Y variants. **Butler J**, Hooper K, Bloom J, Lee R, Maurer-Stroh S, Petrie S, McCaw J, **Reh L**, **Guarnaccia T**, **Baas C**, **Xue L**, **Kelso A**, **Barr I** and **Hurt AC**. (poster + short talk) A comparison of rapid point-of-care tests for the detection of avian influenza A (H7N9) virus. **Baas C**, **Barr I**, Fouchier R, **Kelso A** and **Hurt AC**. An international laboratory comparative examination of influenza 2 day ELISA and 3 day hemagglutination consensus microneutralization assays conducted by the Consortium for the Standardization of Influenza Seroepidemiology (CONSISE). **Laurie KL**, Katz K, Peiris M, Heath A, Engelhardt OG, Wood J, Van Kerkhove MD, Nicoll A, on behalf of members of CONSISE Laboratory Working Group. Antigenic drift of the pandemic 2009 A(H1N1) influenza virus in a ferret model. **Guarnaccia T, Carolan LA**, Maurer-Stroh S, Lee RTC, Job E, **Reading PC**, Petrie S, McCaw JM, McVernon J, **Hurt AC**, **Kelso A**, Mosse J, **Barr IG** and **Laurie KL**. A comparison of human influenza A H1N2 nucleoprotein T cell epitopes with circulating influenza A viruses from 1918-2003. **Komadina N**, Quinones-Para S, Kedzierska K, McCaw J, Hall R, Leder K and McVernon J. Playing hide and seek – understanding the role of collectins and pentraxins in limiting novel and seasonal influenza viruses. Job ER, Bottazzi B, Tate MD, **Deng YM**, Mantovani A, Brooks AG and **Reading PC**. Solving the complexities of influenza A virus infection of macrophages: macrophage galactose-type lectin (MGL) can mediate virus attachment and entry. Londrigan SL, Ng WC, Liong S, Tate MD, Brooks AG and **Reading PC**.

Poster Presentations (continued)

Event Location, date	Title and authors (presentations are posters unless otherwise indicated, Centre authors are marked in bold, presenting author is underlined)
43rd Annual Scientific Meeting Australasian Society for Immunology Wellington, New Zealand, 2–5 December	Quantitation of cytokine mRNA levels in ferrets following influenza virus infection. **Carolan LA**, **Butler J**, **Guarnaccia T**, Rockman S, **Hurt AC**, **Reading PC**, **Kelso A**, **Barr I** and **Laurie KL**.
The 7th Australasian Virology Society Meeting Queenstown, New Zealand, 8–12 December	Determining the risk of swine influenza viruses for human health: Pathogenesis and transmissibility experiments using a ferret model. **Baas C**, **Barr IG**, Mosse J, **Kelso A** and **Hurt AC**. Estimates of vaccine effectiveness within the 2012 Victorian influenza season. **Sullivan S**, **Komadina N**, Grant K, **Jelley L**, Papadakis G and Kelly H. Identification of multiple respiratory viruses in paediatric patients from Papua New Guinea with influenza-like-illness, in 2012-2013. **Spirason N**, Horwood P, **Barr IG** and **Deng YM**. A role for sialylated pentraxins of the innate immune system in the evolution of novel and seasonal influenza viruses in the human population. Job E, Bottazzi B, **Deng Y**, Mantovani A, Brooks A and **Reading P**.

Other Conference Participation and Professional Engagement

Centre staff members also participated in the following events as attendees and/or in other roles.

Event; Location, date	Centre staff involvement
International Conference on Human Infection with Novel Influenza Viruses Beijing, China, 15–17 August	Anne Kelso attended.
External review of the Diabetes Program, St Vincent's Institute of Medical Research Melbourne, 22 August	Anne Kelso chaired the review.
CONSISE: Consortium for the Standardization of Influenza Seroepidemiology Regional Meeting Cape Town, South Africa, 3–4 September	Karen Laurie was a member of the steering group and organising committee.
Options for the Control of Influenza VIII Cape Town, South Africa, 5–9 September	Anne Kelso was a member of the scientific organising committee and chaired a session. Ian Barr attended.
National Press Club address by Dr John Pournoor on pandemic planning Canberra, 19 November	Anne Kelso attended.
43rd Annual Scientific Meeting Australasian Society for Immunology Wellington, NZ, 2–5 December	Anne Kelso chaired a plenary session and a workshop.
13th Congress of the Immunology of Diabetes Society Melbourne, 7 December	Anne Kelso chaired a plenary session.

Engagement in WHO Activities

Event; Location, Date	Centre staff involved
WHO integrated meeting on development and clinical trials of influenza vaccines Hong Kong, 24–25 January	Anne Kelso attended.
WHO Regional Office for South-East Asia Region: Training on influenza data management and epidemiological analysis Bangkok, Thailand, 11–15 February	Sheena Sullivan was a lecturer and facilitator.
WHO Consultation on the Composition of Influenza Vaccines for the Northern Hemisphere 2013-2014 Geneva, Switzerland, 18–20 February	Ian Barr and Anne Kelso attended.
Periodic teleconferences of the WHO Global Influenza Programme on the avian influenza A(H7N9) outbreak, April–May.	Ian Barr and Anne Kelso participated.
Joint China-WHO Mission on avian influenza A(H7N9) Beijing and Shanghai, China, 18–24 April	Anne Kelso participated.
WHO PCR Working Group Meeting Geneva, Switzerland, 2–3 July	Yi-Mo Deng presented two talks.
WHO Antivirals Working Group Meeting Geneva, Switzerland, 4–5 July	Aeron Hurt was a session facilitator and presented three talks.
WHO Consultation on Global Influenza Surveillance Geneva, Switzerland, 10–12 July	Anne Kelso chaired the meeting.
WHO Consultation on the Composition of Influenza Vaccines for the Southern Hemisphere 2014 Geneva, Switzerland, 23–26 September	Ian Barr and Anne Kelso attended.
7th Meeting of the National Influenza Centres and Influenza Surveillance in the Western Pacific and South-East Asia Regions Beijing, China, 12–15 November	Ian Barr presented a talk. Anne Kelso chaired a panel/floor discussion. Iwona Buettner, Patrick Reading, Robert Shaw and Sheena Sullivan also attended.

WHO Consultation on the Composition of Influenza Vaccines for the Northern Hemisphere 2013-2014, meeting with industry groups, 21 February 2013.

Australian Influenza Symposium

The 9th Australian Influenza Symposium, co-hosted by the Centre and the Therapeutic Goods Administration (TGA), was held at the University of Sydney on 3–4 October 2013. The organising committee was Ian Barr, Anne Kelso, Katie Milne, Jayde Simpson and Gary Grohmann (TGA).

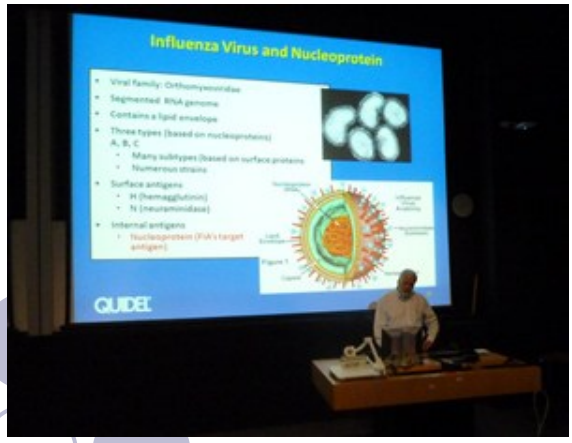
The symposium was attended by over 200 delegates from Australia, China, Indonesia, New Zealand, Singapore, United Kingdom and USA. As usual a wide variety of talks was presented, encompassing surveillance, pandemic response, epidemiology, clinical research, zoonotic influenza, influenza biology, viral evolution and emerging treatments.

Six invited international speakers attended and gave presentations:

Dr Peter Horby, Oxford University Clinical Research Unit, Hanoi, Vietnam
Dr Richard Pebody, Public Health England, Colindale, London, UK
Dr Colin Russell, Cambridge University, UK
Dr Fan Wu, Shanghai Municipal Center for Disease Control and Prevention, Shanghai, PR China
Dr Jean-Francois Rossignol, Romark Laboratories, Tampa FL, USA
Dr John Tamerius, Quidel Corporation, San Diego CA, USA

Highlights included a roundtable discussion on the needs of the Australian influenza surveillance system, and a recount of the outbreak of avian influenza A(H7N9) and response by Chinese health authorities by Dr Fan Wu of the Shanghai Municipal Center for Disease Control.

The majority of staff members from the Centre attended the Symposium. Ian Barr and Anne Kelso chaired sessions. Aeron Hurt, Teagan Guarnaccia and Sheena Sullivan presented talks.

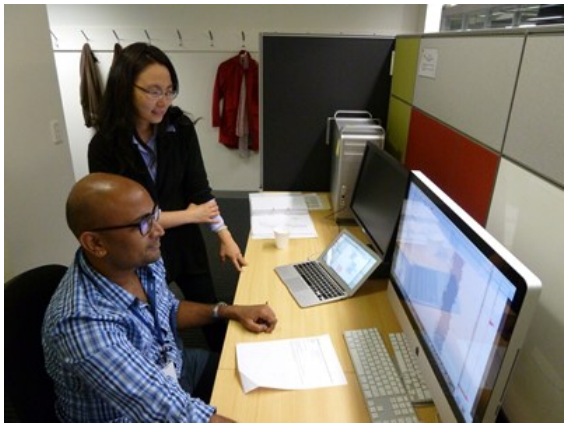


Visitors to the Centre

The Centre was pleased to host the following visitors during 2013:

Date	Visitor and affiliation
21 April	Dr Cameron Simmons and Ms Katie Anders, Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam. *Research collaborators*
8 May	The Hon. Tanya Plibersek MP, Australian Government Minister for Health *Briefing on avian influenza A(H7N9)*
12 July	Dr Paul Horwood, Head, Emerging Infectious Diseases Unit, Institute of Medical Research, Goroka, Papua New Guinea
28 August – 5 September	Dr Vijay Dhanasekaran, Program of Emerging Infectious Diseases, Duke-NUS Graduate Medical School in Singapore, Singapore *Research collaborator*
23 October	Miss Monique Chilvers, Australian Sentinel Practices Research Network (ASPREN), The University of Adelaide *Research collaborator*
30 September	Dr Richard Pebody, Public Health England, Colindale, London, UK.
1 October	Dr Colin Russell, Cambridge University, UK *Research collaborator*
25 November	Delegation from the Ministry of Agriculture, China: Mr Diao Xinyu (Delegation Head) — Ms Yang Lin (Secretary) Mr Ma Chong — Mr Liu Xiaodong Mr Yu Chunming — Mr Sun Wei Mr Xie Hua — Mr Yan Ruaqian Ms Wang Jinxiang — Mr Gao Qingchao *Discussion of animal disease surveillance and early warning technology in Australia*

The Hon. Tanya Plibersek MP (centre) with (from L to R) Louise Carolan, Heidi Peck, Anne Kelso and Dr Mike Catton (Director of VIDRL)



Dr Vijay Dhanasekaran (seated) with Yi-Mo Deng

Committees and Advisory Groups

Centre staff members served on the following governing boards, committees and advisory groups during 2013.

Chantal Baas
Peter Doherty Institute for Infection and Immunity, *Shared PC3 Laboratory Advisory Committee*

Ian Barr
Australian Influenza Vaccine Committee (Therapeutic Goods Administration)
Australian Vaccine and Immunotherapeutics Development (AVID) Group, *Organising Committee*
Influenza Research and Treatment, *Editorial Board*
Influenza and Other Respiratory Viruses, *Editorial Board*
Peter Doherty Institute for Infection and Immunity, *Shared PC3 Laboratory Advisory Committee*
Public Health Laboratory Network (Department of Health)
16th International Congress of Immunology, Melbourne 2016, *Organising Committee*

Michelle Chow
Peter Doherty Institute for Infection and Immunity: *Operational Management Committee Communications Working Group*

Yi-Mo Deng
WHO Working Group for GISRS PCR detection for influenza surveillance

Aeron Hurt
Antiviral Research, *Editorial Board*
International Society for Influenza and other Respiratory Virus Diseases, Antiviral Special Interest Group, *Committee member*
Influenza Specialist Group, *Scientific Committee*
Avian Influenza in Wild Birds, Australian Wildlife Health Network, *Steering Committee*
WHO Expert Group for GISRS Surveillance on Antiviral Susceptibility, *Chair*
Virology Journal, *Associate Editor*

Anne Kelso
Australian Influenza Vaccine Committee (Therapeutic Goods Administration)
BioMed Central Immunology, *Editorial Board*
Burnet Institute, *Research Advisory Committee*
Else Kröner-Fresenius-Stiftung Award, *Selection Committee*
Florey Institute of Neuroscience and Mental Health, *Board*, *Council of Governors* and *Nomination Committee*
Influenza and Other Respiratory Viruses, *Associate Editor*
Influenza Surveillance Strategy Working Group (Department of Health)
International Immunology, *Associate Editor*
International Society for Influenza and other Respiratory Virus Diseases, *Board of Trustees*
National Health and Medical Research Council, *Assigners Academy*
National Health and Medical Research Council, *Council*
Nossal Institute for Global Health (The University of Melbourne), *Advisory Council* and *Selection Committee for the Director*
Options for the Control of Influenza VIII, Cape Town, 2013, *Scientific Committee*
Peter Doherty Institute for Infection and Immunity: *Project Control Group, Collocation Group, Operational Management Committee (Chair), Research Strategy Advisory Group (Chair)*
Telethon Institute for Child Health Research, *Board*
WHO/OIE/FAO H5N1 Evolution Working Group

Naomi Komadina
GISAID Database Technical Committee, Global Initiative on Sharing All Influenza Data (GISAID) Database, *Chair*

Karen Laurie
Consortium for the Standardization of Influenza Seroepidemiology (CONSISE), *Steering Committee*
Global Influenza Seroepidemiology Standardisation Working Group
Peter Doherty Institute for Infection and Immunity: *Research Strategy Advisory Group, Bioresources Working Group*
Victorian Infectious Diseases Reference Laboratory, *Safety Committee*

Committees and Advisory Groups (continued)

Patrick Reading
Influenza and Other Respiratory Viruses, *Editorial Board*
Peter Doherty Institute for Infection and Immunity: *Education Strategy Advisory Group* (*Deputy Chair)*

Sheena Sullivan
Influenza Surveillance Strategy Working Group (Department of Health and Ageing)*, Observer*
Peter Doherty Institute for Infection and Immunity: *Public Health Strategy Advisory Group*

Community Engagement

The Director, Deputy Director and other staff members participated in requests from media representatives for interviews and comments throughout the year.

Anne Kelso
Interview with MyMP 1377 radio, Melbourne, 16 January
Talking Health with Dr Feelgood, 3AW Radio, 20 January
"Deadly, however it moves" The Economist, 4 April
"China hit by deadly new strain of bird flu", The World Today, ABC Radio, 5 April
Interview with Australian Financial Review, 16 April
Press briefing on Joint China-WHO Mission on H7N9, Beijing, comments widely reported in international press, 24 April
Interview with Channel 7 television, 2 May
"Bird flu eases as China shuts poultry markets", Bloomberg.com, 3 May
"Urgent restock of flu vaccines", Medical Observer, 7 May
"Aligning immunology and virology", Australian Life Scientist, 12 June

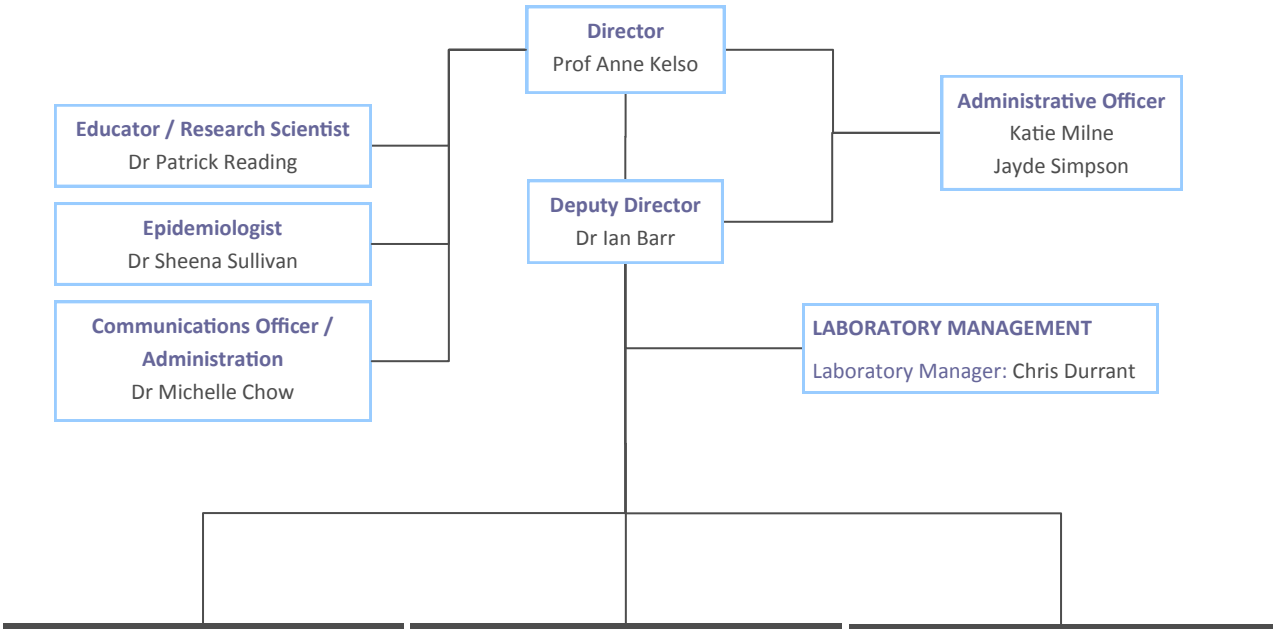
Ian Barr
"Influenza, mutating viruses, bears - oh my!", Community radio station 2SER 107.3
"New fears over bird flu", The Age, 26 April
"Australian scientists working on vaccine for new strain of bird flu", ABC Radio Australia, 30 April
"Tune your engine - avian influenza", Radio New Zealand, 13 May
"Brace yourselves: winter flu is coming!", Lifehacker website, 31 May
"You rotten swine: nastier flu bugs already hard at work", The Sydney Morning Herald, 1 June
Influenza vaccine for 2013: who, what, why and when?, The Conversation, 4 June
Rear Vision, ABC Radio, 16 June
"Scientists zero in on flu virus defences", ABC Science, 22 November

Aeron Hurt
Interviews with various print, radio and television media outlets, 19 March
"Drug resistant flu is spreading", ABC Radio News, The World Today
"Swine flu virus now resistant to Tamiflu", The Australian
"Drug-resistant pandemic swine flu 'community risk'", BBC News Health
"Swine flu cases resistant to Tamiflu are becoming more common, say scientists", The Guardian
"Swine flu 'growing in resistance' to Tamiflu", The Telegraph
"Virus responsible for swine flu pandemic becoming increasingly resistant to Tamiflu", The Independent
"Flu findings spark vaccinations call", The Canberra Times
"Swine flu becoming more resistant to 'Tamiflu,' Scientists Say", Nature World News
"Tamiflu resistance may be rising", MedPage Today
"Preparing for new strain of Influenza", SBS World News

Centre Website

The Centre website was maintained and updated throughout the year. During 2013, the website was viewed by 7,969 unique visitors from 138 different countries. The majority of visits to the website came from Australia, followed by the United States. Most of the traffic to the website came from search engines.

Management and Staff



SURVEILLANCE

ANTIGENIC ANALYSIS

Head: Robert Shaw
Medical Scientist: Helen Sjogren
Medical Scientist: Tasoula Mastorakos
Medical Scientist: Lauren Jelley
Medical Scientist: Jayde Galletti
Medical Scientist: Hilda Lau
Laboratory Technician: Iwona Buettner

GENETIC ANALYSIS

Head: Naomi Komadina
Senior Medical Scientist: Dr Yi-Mo Deng
Medical Scientist: Pina Iannello
Medical Scientist: Natalie Spirason
Medical Scientist: Lauren Jelley
Medical Scientist: Hilda Lau

ANTIVIRAL DRUG SENSITIVITY

Head: Dr Aeron Hurt
Medical Scientist: Leah Sook-Kwan Leang

CONTRACTS

INTERNATIONAL FEDERATION OF PHARMACEUTICAL MANUFACTUERS AND ASSOCIATIONS

Medical Scientist: Chantal Baas
Medical Scientist: Jayde Galletti
Medical Scientist: Hilda Lau

NOVARTIS VACCINES AND DIAGNOSTICS

Medical Scientist: Heidi Peck
Medical Scientist: Joelle Dharmakumara

RESEARCH

RESEARCH I

Senior Virologist: Dr Karen Laurie
Research Assistant: Louise Carolan

RESEARCH II

Research Scientist: Dr Aeron Hurt
Medical Scientist: Dr Ding Yuan Thomas Oh
Medical Scientist: Jeffrey Butler
Medical Scientist: Malet Aban

PhD Candidate: Teagan Guarnaccia
MSc Candidate: Chantal Baas (P/T)

Staff Changes 2013

Mrs Malet Aban was appointed in February to replace Dr Lumin Xue who left at the end of 2012.

Ms Hilda Lau joined the Centre in April in the Antigenic Analysis and Genetic Analysis groups to replace Ms Lauren Jelley while she was on maternity leave.

Dr Ding Yuan Thomas Oh, who completed his BSc (Hons) project at the Centre in 2006, joined the Centre in July to replace Mr Jeffrey Butler, who left in August.

Ms Jayde Galletti left the Centre in November to pursue further studies.