Influenza Updates

The newsletter of the WHO Collaborating Centre for Reference and Research on Influenza in Melbourne

@WHOCCFluMelb

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WHO Recommendations for the Southern Hemisphere 2020 influenza vaccines

The WHO Consultation on the Composition of Influenza Vaccines for the Southern Hemisphere 2019 was held in Geneva, Switzerland, on 23-26 September 2019. Following the Consultation, WHO made the following recommendation:

It is recommended that quadrivalent vaccines for use in the 2020 southern hemisphere influenza season contain the following:

- *an A/Brisbane/02/2018 (H1N1)pdm09-like virus;*
- *an A/South Australia/34/2019 (H3N2)-like virus;*
- *a B/Washington/02/2019-like (B/Victoria lineage) virus; and*
- *a B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage) virus.*

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This differs from the previous vaccine recommendation (for the northern hemisphere 2019-2020), reflecting changing proportions of distinctive genetic and antigenic groups in circulating A(H3N2) and B/Victoria lineage viruses. The new B/Victoria lineage component (B/Washington/2/2019) contains a three amino acid deletion in its HA protein sequence, whereas the previously recommended strain contained a double amino acid deletion in its HA protein. More details about the recommendations can be found at:
https://www.who.int/influenza/vaccines/virus/recommendations/2020_south/en/

Photo courtesy of WHO

Contribution of National Influenza Centres to the WHO vaccine recommendations

Thank you to everyone who sent us influenza samples during the past 2-3 months prior to the Consultation. Your viruses provided essential data on recently circulating strains and helped to inform the choice of recommended vaccine strains. We are especially pleased that the most recently added A(H3N2) virus in the vaccine recommendation, A/South Australia/34/2019, was originally submitted to our Centre by **SA Pathology**.

This is in addition to A/Brisbane/02/2018 (A(H1N1)pdm09, submitted by Queensland Health Forensic and Scientific Services), and B/Phuket/3073/2013 (B/Yamagata lineage, submitted by the Thai National Influenza Center), which were also originally isolated as vaccine candidates at our Centre. In total, three of the viruses recommended for inclusion in the quadrivalent vaccine the 2020 southern hemisphere influenza season were originally isolated as candidate vaccine viruses at the Centre.

We would like to acknowledge the critical role played by WHO National Influenza Centres in providing influenza samples to WHO Collaborating Centres, not only for analysis and surveillance, but also for the provision of potential vaccine candidates. Please continue to send us your samples. The need for constant surveillance remains because the influenza virus continues to circulate and evolve.

Training at the Centre

We have been pleased to welcome Ms Aisha Al Amri (*below left*) and Ms Ahlam Al Amri (*below right*), from the Central Public Health Laboratory, Muscat, Oman, who visited the Centre from 7-18 October and undertook training in virus isolation and serology techniques for the analysis of influenza viruses. Following their training at the Centre, Aisha and Ahlam are now well-equipped to return to their laboratory and share their knowledge and skills with other scientists and National Influenza Centres in the Eastern Mediterranean Region of WHO (EMRO).

Australian Influenza Symposium and Australian Respiratory Virology Meeting

The 13th Australian Influenza Symposium will be held on 28–29 October, followed by the Australian Respiratory Virology Meeting on 30th October. Both meetings will be held at the Queensland University of Technology, Brisbane. The Australian Influenza Symposium will include the following international speakers:

Benjamin Cowling, *The University of Hong Kong*
Janet Englund, *Fred Hutchinson Cancer Research Center*
Belinda Herring*, WHO Regional Office, Brazzaville, Republic of the Congo, Africa*
Jonathan Temte*, University of Wisconsin*
Hui-Ling Yen, *The University of Hong Kong*

Registrations for both meetings are now closed, but you can follow the Australian Influenza Symposium on Twitter: #AIS2019Bris @WHOCCFluMelb

If you would like to be informed of future meetings, please email us at*: symposium@influenzacentre.org*

Grant success: National Institutes of Health funds USD$4.2 million for Centre-led project

Sheena Sullivan

Annette Fox

Adam Kucharski

A/Prof Sheena Sullivan and Dr Annette Fox, both from our Centre, and A/Prof Adam Kucharski (London School of Hygiene & Tropical Medicine) are primary investigators on a 5 year collaborative study on the effects of repeated annual influenza vaccination in health care workers that has been awarded USD$4.2 million by the US National Institutes of Health (NIH).

The project aims to better understand immunological processes that underlie vaccination responses and the implications for vaccination effectiveness in health care workers who are vaccinated for influenza over multiple years. It is hoped that the findings will provide evidence to inform policy decisions about annual influenza vaccination programs, both among health care workers and the general population.

National Influenza Centres meeting in Ulaanbaatar

Several of our staff members attended the 13th Bi-regional meeting of National Influenza Centres (NICs) and Influenza Surveillance in the Western Pacific and South-East Asia Regions on 21-23 August, in Ulaanbattar, Mongolia. We were pleased to catch up with many of you at the meeting, which was attended by approximately 130 people from 26 countries.

Topics discussed included:

- regional updates and managing the health threat of influenza in an evolving context;
- progress in influenza surveillance systems in the Asia Pacific Region since 2009;
- challenges and future strategies for the prevention and control of influenza;
- advancing influenza vaccination programs, especially in country-specific contexts;
- information needs for pandemic assessment and response;
- pandemic preparedness as a driving force for strengthening influenza surveillance
- fostering regional collaboration
- future developments in technology and data needs and priority setting for influenza management in the Asia Pacific region

A review of the 2018-2019 interseasonal influenza outbreak in Australia

The interseasonal influenza period from October 2018 to April 2019 was very unusual for the high incidence of influenza in Australia. Our Centre recently published a full analysis of viruses that were collected during this period, with consideration of epidemiological, antigenic and genetic factors.

Euro Surveill. 2019 Aug;24(33).
doi: 10.2807/1560-7917.ES.2019.24.33.1900421.

SURVEILLANCE

Intense interseasonal influenza outbreaks, Australia, 2018/19

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Background: Interseasonal influenza outbreaks are not unusual in countries with temperate climates and well-defined influenza seasons. Usually, these are small and diminish before the main influenza season begins. However, the 2018/19 summer-autumn interseasonal influenza period in Australia saw unprecedented large and widespread influenza outbreaks. Aim: Our objective was to determine the extent of the intense 2018/19 interseasonal influenza outbreaks in Australia epidemiologically and examine the genetic, antigenic and structural properties of the viruses responsible for these outbreaks. Methods: This observational study combined the epidemiological and virological data to be fully elucidated but are likely to be a complex mix of climatic, virological and host immunity-related factors. These outbreaks reinforce the need for year-round surveillance of influenza, even in temperate climates with strong seasonality patterns.

Introduction

In 2018, the Australian influenza season was late and progressed with such minimal activity that it barely registered as a season by several surveillance indicators [1]. This was in stark contrast to the 2017 season, when Australia's highest levels of influenza activity were recorded [2]. However, several surveillance

RECENT ACTIVITIES AT THE CENTRE (1 May — 30 September 2019)

The southern hemisphere influenza season in 2019 has been especially busy for us with particularly high levels of influenza in Australia—we have received and processed unprecedented numbers of samples this year.

Samples received - the Centre received 5512 influenza samples from:

AUSTRALIA: SA Pathology, Queensland Health Forensic and Scientific Services, Canberra Hospital, Royal Darwin Hospital, Hobart Pathology, Royal Hobart Hospital, Dorevitch Pathology, Healthscope Pathology, Alfred Hospital, Austin Health, Australian Clinical Labs, Cabrini Pathology, Monash Medical Centre, Royal Children's Hospital, VIDRL, John Hunter Hospital, Pathwest QEII Medical Centre, The Children's Hospital at Westmead, Douglass Hanly Moir Pathology, Prince of Wales Hospital, Westmead Hospital

BRUNEI: RIPAS Hospital

CAMBODIA: Institut Pasteur du Cambodge

FIJI: Fiji Centre for Communicable Disease Control

FRENCH POLYNESIA: Institut Louis-Malardé

INDONESIA: National Institute of Health Research and Development

MACAU: Public Health Laboratory

MALAYSIA: Institute for Medical Research

NEW CALEDONIA: Institut Pasteur

NEW ZEALAND: Canterbury Health Services, Institute of Environmental Science and Research

SINGAPORE: National Public Health Laboratory

SOUTH AFRICA: National Institute for Communicable Disease

SRI LANKA: Medical Research Institute

THAILAND: Thai National Influenza Center

TIMOR-LESTE: Laboratorio Nacional da Saude

Isolation of viruses in eggs

The Centre undertakes primary isolation of selected viruses in eggs to obtain potential vaccine strains.

From 1 May to 30 September:
- 5 A(H1N1)pdm09
- 17 A(H3N2)
- 3 B/Victoria and
- 4 B/Yamagata viruses

were successfully isolated in eggs at the Centre.

RECENT ACTIVITIES AT THE CENTRE (continued)
(1 May — 30 September 2019)

Antigenic analysis
2096 viruses analysed by haemagglutination inhibition (HI) assay

Sequencing
1095 viruses analysed
1095 HA genes
955 NA genes
702 MP genes
258 NS genes

Antiviral drug susceptibility
2564 viruses analysed by neurminidase inhibition (NAI) assay

Country of submitting laboratory	Number of viruses analysed by HI assay					Number of viruses analysed by sequencing				
	A(H1N1)pdm09	A(H3N2)	A (mixed subtype)	B/Victoria	B/Yamagata	A(H1N1)pdm09	A(H3N2)	A (mixed subtype)	B/Victoria	B/Yamagata
Australia	351	742	5	180	26	188	491	4	98	7
Brunei	17	4	0	0	8	11	3	0	0	1
Cambodia	5	12	0	14	5	11	4	0	3	4
Fiji	34	16	2	75	0	11	12	0	3	0
Indonesia	5	5	0	7	6	5	4	0	0	0
Macau SAR, China	1	0	0	13	1	5	1	0	3	1
Malaysia	26	73	1	26	2	14	13	0	3	5
New Caledonia	67	15	1	15	0	30	21	0	7	1
New Zealand	13	79	0	53	1	13	40	0	21	0
Philippines	0	0	0	0	2	1	0	0	0	0
Singapore	14	18	0	20	9	0	0	0	0	0
South Africa	4	15	0	0	0	3	6	0	0	0
Sri Lanka	6	5	0	4	0	4	8	0	2	0
Thailand	13	10	0	18	1	8	2	0	0	1
Timor-Leste	31	16	0	4	0	9	9	0	4	0
TOTAL	587	1010	9	429	61	313	614	4	144	20

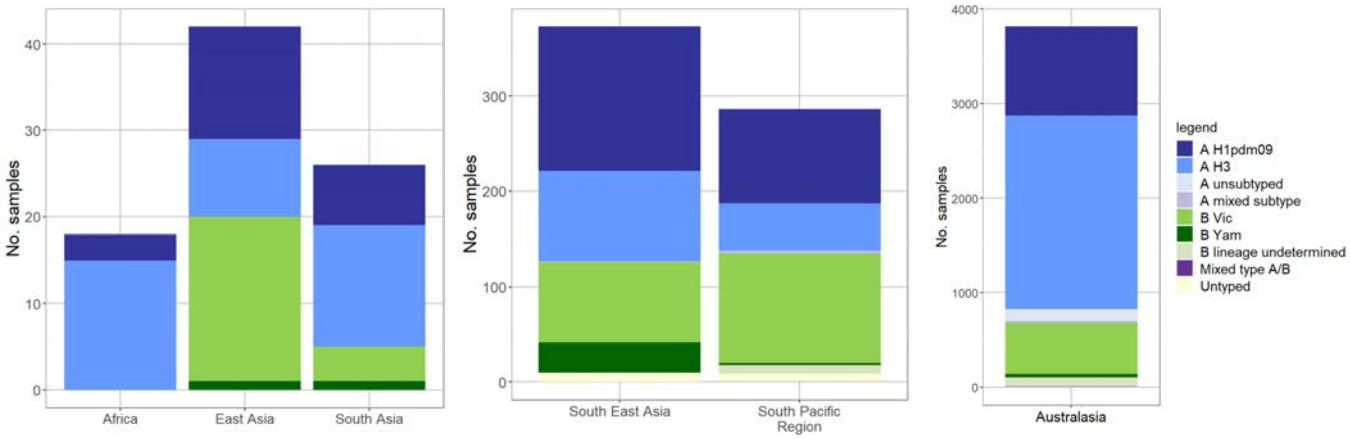
Country of submitting laboratory	Number of viruses analysed by NAI assay						
	A(H1N1)pdm09	A(H3N2)	A (mixed subtype)	B/Victoria	B/Yamagata	Mixed type (A/B)	B (lineage undetermined)
Australia	403	1098	8	192	16	3	0
Brunei	17	8	0	0	4	0	0
Cambodia	5	6	0	17	5	0	0
Fiji	34	16	2	96	0	1	1
Indonesia	5	5	0	6	6	0	0
Macau SAR, China	0	0	0	19	1	0	0
Malaysia	26	74	1	24	2	0	0
New Caledonia	69	23	1	24	0	0	0
New Zealand	26	89	0	94	1	0	0
Singapore	14	0	0	20	9	0	0
South Africa	3	0	0	0	0	0	0
Sri Lanka	6	11	0	5	0	0	0
Thailand	12	8	0	18	1	0	0
Timor-Leste	9	16	0	4	0	0	0
TOTAL	629	1354	12	519	45	4	1

SURVEILLANCE UPDATE
Virus activity 1 January — 30 September 2019 (as of 3 October 2019)

Virus types/subtypes*
Type and subtype/lineage determined for **4562** viruses

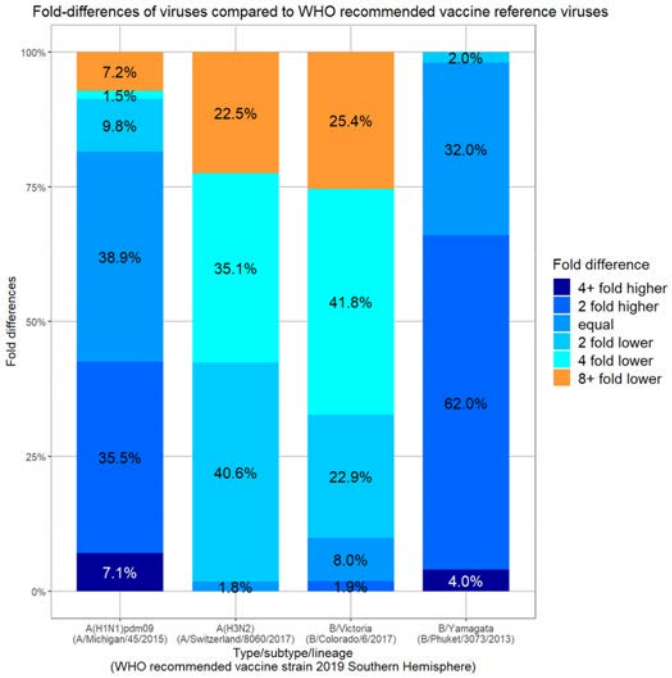
49.7% A(H3N2)
26.9% A(H1N1)pdm09
16.8% B/Victoria
1.5% B/Yamagata

Subtypes of viruses analysed, by region of submitting laboratory^



Antigenic analysis*:
2129 viruses tested by haemagglutination inhibition (HI) assay

Viruses were identified as low reactors if their titre with reference antiserum was at least 8-fold lower than the titre against the reference virus. The majority of viruses were antigenically similar to their respective 2019 Southern Hemisphere vaccine reference strains, however, a larger proportion of A(H3N2) and B/Victoria viruses were low reactors to the A/Switzerland/8060/2017 and B/Colorado/6/2017 reference strains, respectively.



** Subtypes and lineages are based on analysis of the HA and in some cases confirmed by genetic analysis of NA.*
^ The Pacific region comprises countries in Polynesia, Melanesia and Micronesia.

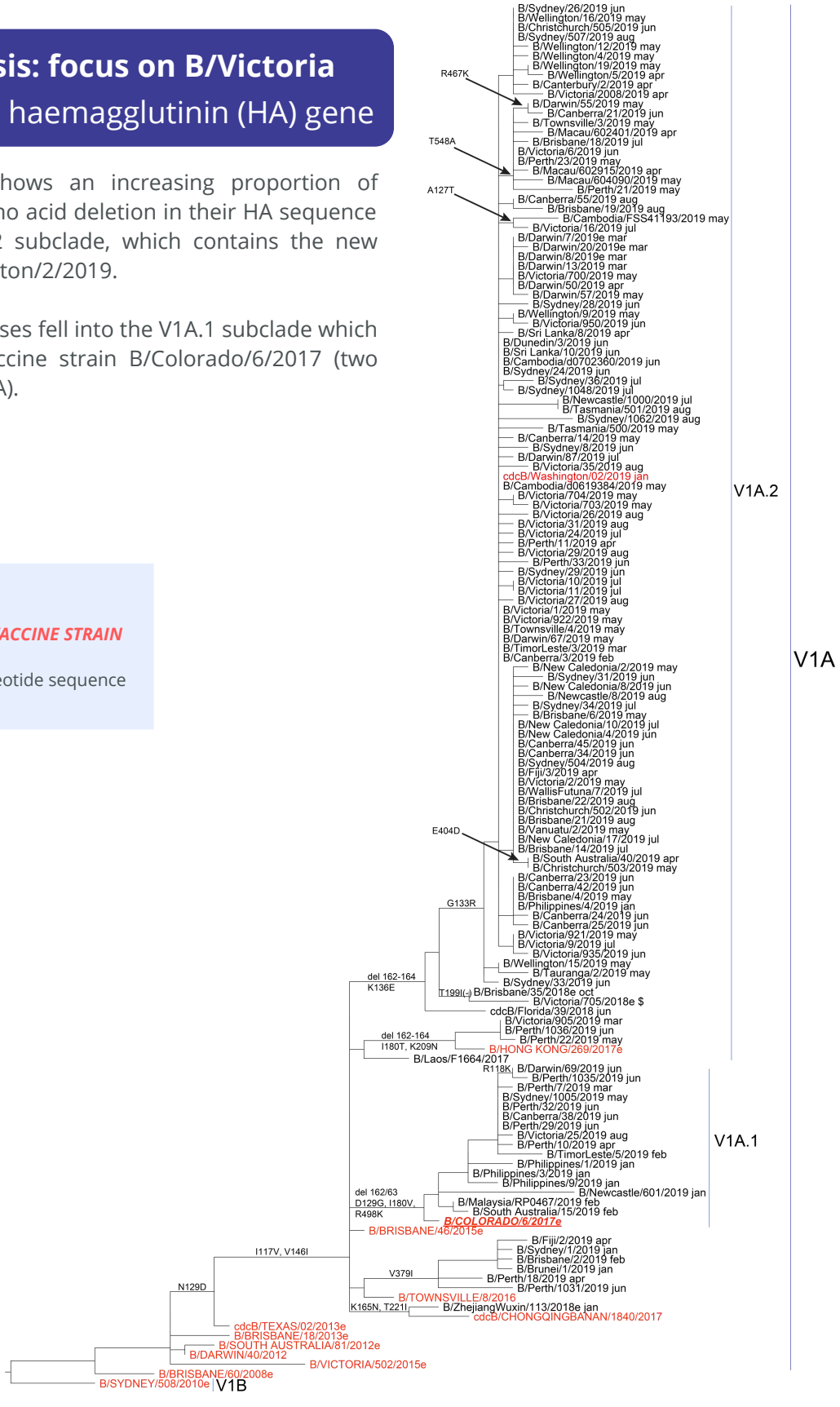
SURVEILLANCE UPDATE (continued)
Virus activity 1 January — 30 September 2019

Genetic analysis: focus on B/Victoria

Sequencing of the haemagglutinin (HA) gene

Phylogenetic analysis shows an increasing proportion of viruses with a three amino acid deletion in their HA sequence and falling in the V1A.2 subclade, which contains the new vaccine strain B/Washington/2/2019.

A smaller number of viruses fell into the V1A.1 subclade which contains the former vaccine strain B/Colorado/6/2017 (two amino acid deletion in HA).



LEGEND

Reference strains

2019 SOUTHERN HEMISPHERE VACCINE STRAIN

| Vertical bars indicate clades

Scale bar represents 0.3% nucleotide sequence difference between viruses

SURVEILLANCE UPDATE (continued)
Virus activity 1 January — 30 September 2019

Antiviral drug susceptibility testing:
2903 viruses tested by neuraminidase inhibition (NAI) assay

Testing for susceptibility to the antiviral drugs oseltamivir (Tamiflu), zanamivir (Relenza), peramivir and laninamivir showed that two A(H1N1)pdm09 and four B/Victoria lineage viruses had highly reduced inhibition by one or more neuraminidase inhibitors (NAI).

Viruses tested by NAI assay

Type/subtype/lineage	Oseltamivir			Peramivir			Laninamivir			Zanamivir		
	Normal Inhibition	Reduced Inhibition	Highly Reduced Inhibition	Normal Inhibition	Reduced Inhibition	Highly Reduced Inhibition	Normal Inhibition	Reduced Inhibition	Highly Reduced Inhibition	Normal Inhibition	Reduced Inhibition	Highly Reduced Inhibition
A(H1N1)pdm09	853		1 (0.12%)	851	2 (0.23%)	1 (0.12%)	853	1 (0.12%)		852	1 (0.12%)	1 (0.12%)
A(H3N2)	1466			1466			1466			1466		
A (mixed subtype)	14			14			14			14		
B/Victoria	503	7 (1.4%)		502	4 (0.78%)	4 (0.78%)	507	3 (0.59%)		506	3 (0.59%)	1 (0.20%)
B/Yamagata	54			53	1 (1.85%)		54			54		
B (lineage undetermined)	1			1			1			1		
Mixed type A/B	4			4			4			4		
Total	2895	7 (0.24%)	1 (0.03%)	2891	7 (0.24%)	5 (0.17%)	2899	4 (0.14%)	-	2897	4 (0.14%)	2 (0.07%)

Viruses with reduced inhibition by antiviral drugs in the NAI assay undergo genetic analysis of the neuraminidase gene to detect mutations associated with the functional change. The relationship between reduced inhibition and the clinical effectiveness of a neuraminidase inhibitor is not well understood. Further studies would be required to determine whether a virus with reduced inhibition in the NAI assay is clinically resistant.

Viruses with highly reduced inhibition to one or more NAI

Type/subtype/ lineage	Country of submitting laboratory	NAI(s) with highly reduced inhibition (marked with *)				Mutation(s) detected
		Oseltamivir	Peramivir	Laninamivir	Zanamivir	
A(H1N1)pdm09	Australia	*	*			H275Y
	Australia				*	E119G
B Victoria	Australia		*			G140R
	Malaysia		*		*	E105K
	Malaysia		*			E105K
	Malaysia		*			E105K

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