

# QML PATHOLOGY

newsletter April 08

## >>Influenza Epidemic 2007

**Dr Renu Vohra and Dr Paul Bartley**

Influenza is an acute, self-limiting viral infection of the respiratory tract. Most transmission is mediated by airborne infected aerosol droplets produced during coughing and sneezing. Transmission may also occur by direct contact. The health and economic impact of Influenza are a consequence of illness-induced absenteeism, severe disease manifestations and secondary complications.

## >> Influenza Epidemic 2007

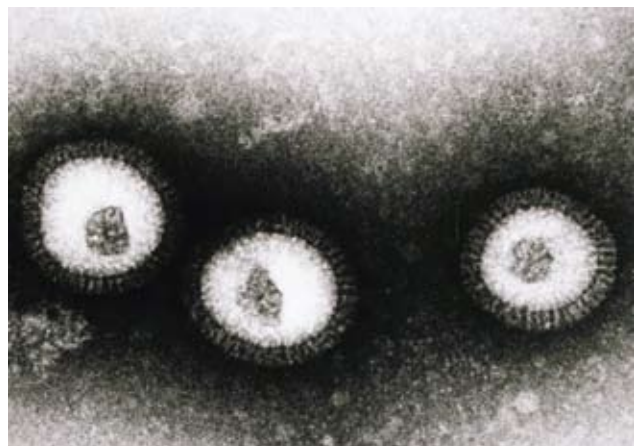
Dr Renu Vohra and Dr Paul Bartley

**Influenza infections are seasonal in temperate climates, more commonly occurring in the colder months (June to September in the Southern Hemisphere and December to April in the Northern Hemisphere). Influenza transmission occurs year-round in tropical regions.**

Three different types of Influenza are recognised: A, B and C. They are classified according to their distinct internal proteins. Type A includes three subtypes (H1N1, H2N2 and H3N2) that are associated with epidemics and pandemics. Type B is associated with regional and widespread epidemics and type C is associated with sporadic cases and minor outbreaks. Influenza A subtypes are classified by two surface proteins: haemagglutinin (H) and neuraminidase (N). Stepwise mutation of the genes encoding the H and N proteins gives rise to antigenic variants that avoid the hosts' immune system, a process that has been termed 'antigenic drift'. This is responsible for the annual outbreaks and influenza epidemics, and the reason for the vaccines to be regularly updated.

Pandemics arise due to emergence of completely new subtypes (antigenic shift) or sometimes by mixing of parts of avian viruses with human or swine Influenza viruses (genetic reassortment). Currently, there is concern that if the avian A (H5N1) virus that has infected and killed millions of poultry in many countries would undergo such changes or naturally mutate and were to gain the capacity to easily spread from person to person, an Influenza pandemic (worldwide outbreak of disease) could begin.

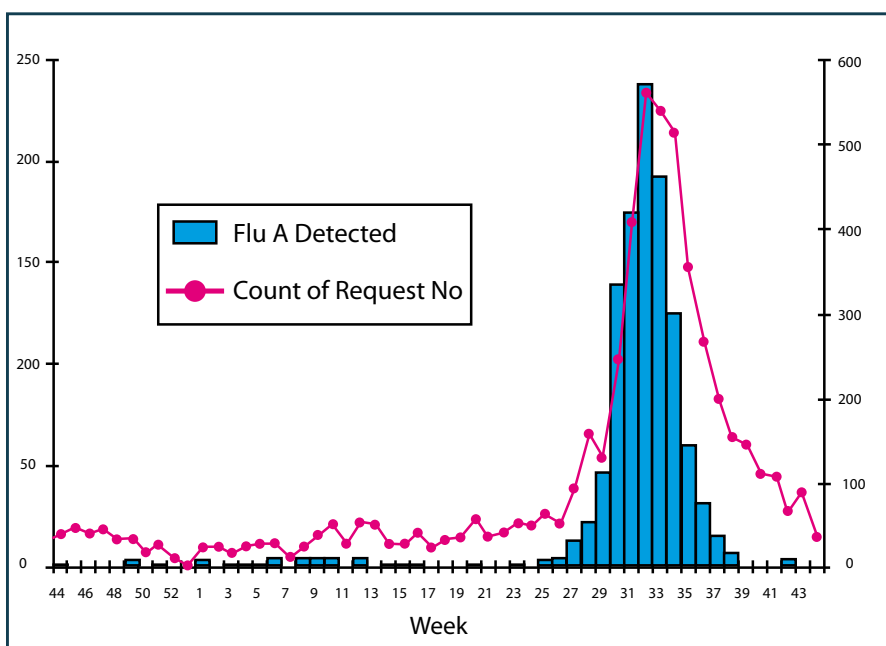
Particularly severe Influenza activity was seen in the winter of 2007 in all states of Australia, especially in Queensland.



Laboratory data from QML Pathology during the last Influenza season of 2007 is presented in this newsletter to show the impact of Influenza in the Queensland community.

### Molecular Testing Data

QML Pathology began using a multiplex PCR in July 2006 to cover 7 common respiratory viruses (Influenza A and B, Parainfluenza 1, 2 and 3, Adenovirus and Respiratory Syncytial Virus). This assay replaced traditional viral culture and offers improved sensitivity and turnaround time in comparison to culture. This procedure tests respiratory samples by first screening with a multiplex assay and then performing a characterization assay to determine the virus identity for any positive samples.



**Graph 1: Influenza A - QML Pathology - All sites - November 2006 through October 2007 (weekly representation)**

The Influenza activity of 2007 started in week 25 and peaked in week 33 as shown in Graph 1 left (weekly representation). QML Pathology performed 2250 Multiplex PCR tests in August 2007 (peak), with 740 (32.8%) of these being positive for influenza A.

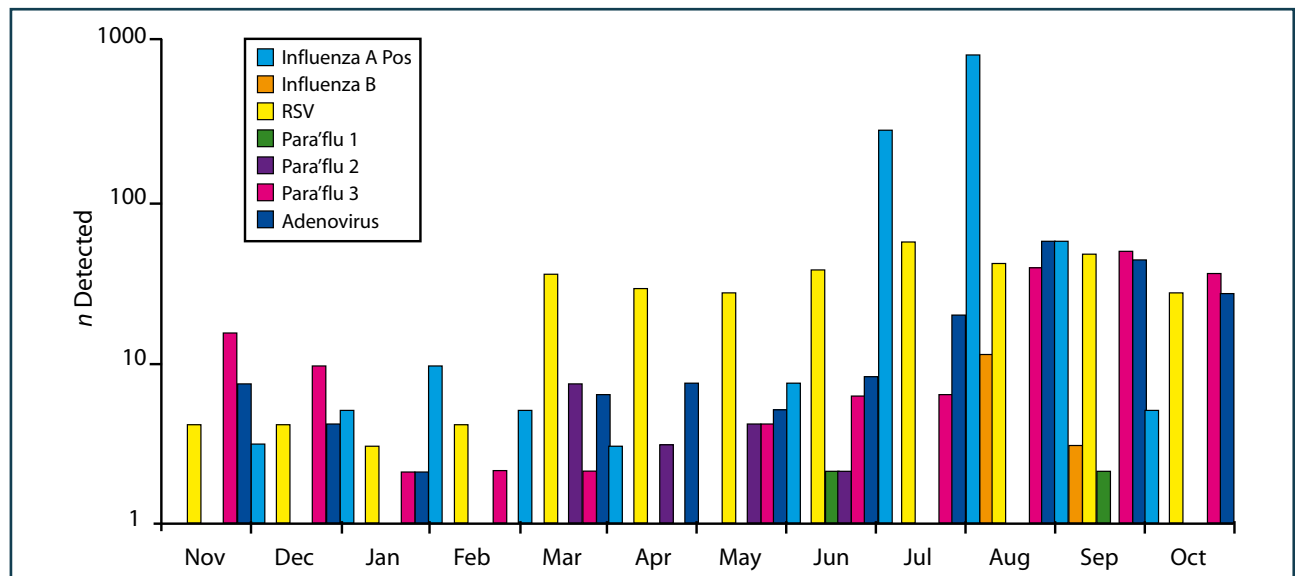
Along with Influenza A, other respiratory viruses like Influenza B, RSV, Para-influenza 3 and Adenovirus were also detected by the multiplex PCR in that time period from June to October 2007 (Graph 2). In comparison to Influenza A, activity for Influenza B was lower. Out of 2250 Multiplex PCR tests performed in August 2007 only 11 (0.5%) specimens were found positive for Influenza B. RSV positivity rate also went up during the period of June-September 2007.

## >> Influenza Epidemic 2007

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**Graph 2:**

**Positive Respiratory Virus Specimens - QML Pathology November 2006 through October 2007**



### Rapid Antigen Test Data

At QML Pathology Directigen kits are used for rapid antigen testing which detects Influenza A, B and RSV. Peer reviewed publications and our own data indicate that the direct antigen rapid test methods currently available are only about – 50-60% sensitive in comparison to molecular testing. At QML Pathology sensitivity, specificity, positive predictive value and negative predictive value of Directigen test when compared to PCR for Influenza A in samples analyzed from November 2006 through October 2007 was found to be 52.7%, 98.7%, 93.2% and 85.7% respectively as shown in table 1 below.

Rapid antigen testing is insensitive and should not be relied upon to make a diagnosis of Influenza without confirmatory testing by a reference method (e.g. PCR). Occasionally, we see some non-specific reactions using these test methods. The reasons for these false positive tests are unknown.

**Table 1:**

**QML Pathology Data: Antigen testing vs PCR: November 2006 - October 2007 (n=1408)**

Influenza A		EIA	
		POS	NEG
PCR	POS	192	172
	NEG	14	1030

Sensitivity 52.7%

Positive predictive value 93.2%

Specificity 98.7%

Negative predictive value 85.7%

### Sample Type Data

A number of studies have reported that nasopharyngeal swabs have higher detection rate for Influenza compared to nasopharyngeal aspirates. In our analyses, the positivity rate of Influenza A from nasopharyngeal swabs were found to be higher 23.7% when compared to nasopharyngeal aspirates 20.1% (statistically significant) thus supporting the findings in the literature. Therefore, QML Pathology recommends collection of nasopharyngeal swabs rather than aspirates as a preferred method for the detection of Influenza virus by PCR.

**Table 2:**

**Swabs vs. NPAs for detection of Influenza A by PCR**

2007	POS	NEG	Total
NP Swabs	186 (23.7%)	599 (76.3%)	785
NP Aspirates	569 (20.1%)	2259 (79.9%)	2828
Total	755	2858	3613

Fisher's Exact test: p = 0.033 (two-tailed)

### Antigenic Characteristics

All samples positive for Influenza A and B from QML Pathology were referred to Queensland Health Scientific Services for typing and some strains were forwarded to the WHO Typing Centre in Melbourne.

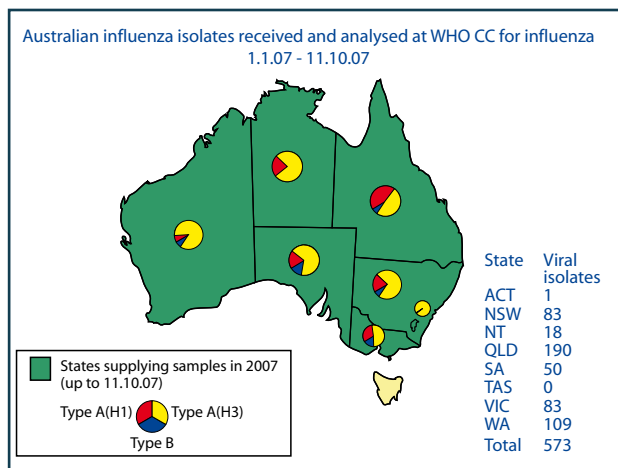
Data obtained from Australian Influenza isolates typed by the WHO Influenza Centre, showed that the predominant strain circulating in Australia in 2007 was A (H3). Although, in Queensland there was an equal mix of A (H3) and A (H1)



## >> Influenza Epidemic 2007

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**Figure 1: Shows the breakdown of Australian Influenza A H1, Influenza A H3 and Influenza B received by WHO Typing Centre in Melbourne<sup>1</sup>**



viruses (figure 1). In contrast, there were low levels of Influenza B activity reported<sup>1</sup>.

As per the thirteenth and final report on Influenza activity for 2007 published by the Department of Health and Ageing the following results were obtained till the period leading to 12/10/07<sup>2</sup>.

1. The WHO Collaborating Centre for Reference and Research on Influenza in Melbourne analysed 567 Influenza isolates supplied by laboratories in Australia 2007. Of these, 529 (93%) were type A, of which 165 (31%) were A (H1) strains, and 364 (69%) were A (H3) strains. 38 (7.2%) isolates were type B. Of the B isolates 24 (63%) were Shanghai-like and 14 (37%) were Malaysia-like.
2. Of the 9,988 laboratory-confirmed cases reported to NNDSS year-to-date, 8,458 (84.7%) were type A, 692 (6.9%) were type B, 41 cases (0.4%) were typed as A and B and for 797 cases (8.0%) type was not reported.
3. Queensland had the highest number of notifications followed by NSW, Victoria and WA.
4. Age specific notification indicated that highest rate of Influenza notification occurred in 0-4 years followed by 5-9 years group and the 80-84 years age group for males.

### Vaccine

Vaccination is the principal measure for preventing Influenza and reducing the impact of epidemics

The composition of vaccines for use in Australia is determined annually by the Australian Influenza Vaccine Committee. Vaccines usually contain three strains of virus as being the most appropriate to protect against the recent variants in the three families of human Influenza viruses - Type A (H1N1), Type A (H3N2) and Type B.

In healthy persons <65 years of age the vaccine is 70-90% effective when the antigenic match between the vaccine and the circulating virus is close. Among the elderly the vaccine is 30-70% effective in preventing all hospitalisations for pneumonia and Influenza for those living outside nursing homes and similar chronic care facilities.

Influenza vaccine is recommended for (as per the 9th Immunisation Handbook):

1. People at increased risk of complications from Influenza infection:

- All individuals  $\geq 65$  years of age
- Individuals  $\geq 6$  months old with conditions predisposing them to severe Influenza like cardiac diseases, chronic respiratory conditions, chronic neurological conditions, people with impaired immunity
- All Aboriginal and Torres Strait Islander people  $\geq 15$  years of age
- Pregnant women
- Residents of nursing homes and long term facilities
- Homeless people and those providing care to them.

2. People working with essential services

3. People who may potentially transmit Influenza to those at high risk of complications from Influenza:

- Staff of nursing homes
- Health care providers
- Staff of long term care facilities
- Household contacts of individuals in high risk groups.

4. Workers in other industries

5. People involved in the commercial poultry industry or in culling poultry during confirmed avian Influenza activity

6. Travellers.

### The 2008 Influenza vaccine composition is shown below and is now available:

A/Solomon Islands/3/2006 (IVR-145)  
(A/Solomon Islands/3/2006 (H1N1) – like)

A/Brisbane/10/2007 (IVR-147)  
(A/Brisbane/10/2007 (H3N2) – like)

B/Brisbane/3/2007 (B/Florida/4/2006 – like)

The full report detailing these recommendations can be accessed at: <http://www.who.int/csr/disease/influenza/recommendationlong2.pdf>.<sup>3</sup>

## >> Influenza Epidemic 2007 (Cntd.)

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### QML Pathology recommendations for specimen collection and testing

With Influenza season approaching we would recommend the following specimens to be collected for the detection of Influenza and other respiratory viruses:

Test request name	Influenza PCR/Respiratory virus PCR
<b>Preferred sample types</b>	Samples are best collected early in the illness (preferably within four days of onset)  <b>Children and adults:</b> <ul style="list-style-type: none"> <li>Nasopharyngeal swab: send it dry in either a <b>blue top Nasopharyngeal swab</b> (no media), <b>orange top flocced swab*</b> (no media) or a <b>green top viral swab</b> (if none of these swabs are available). <i>As mentioned previously the detection rate of Influenza from swabs was found to be superior to nasopharyngeal aspirates.</i></li> <li>*Flocked swabs are considered to be superior to rayon nasopharyngeal swabs for recovery of viruses</li> <li>Throat swab: one throat swab collected dry and sent in a blue top container</li> <li>Nasopharyngeal aspirates: sent in the mucus trap. (Note: generates aerosol).</li> </ul> <b>Infants &lt;2 years:</b> <ul style="list-style-type: none"> <li>Nasopharyngeal aspirate, or</li> <li>Nose/throat swab.</li> </ul> Also request RSV antigen testing if appropriate.
<b>Assay frequency</b>	Daily on week days
<b>Results</b>	Available within 24 hours
<b>Interpretation note</b>	Detection of Influenza nucleic acids by PCR is approximately 100 times more sensitive than either viral IF or culture. Other respiratory viruses RSV, Adenovirus, Parainfluenza 1, 2 and 3 can be detected in the assay.
Test request name	Directigen assay for detection of Influenza A and B
<b>Preferred sample types</b>	Samples are best collected early in the illness (preferably within four days of onset). <ul style="list-style-type: none"> <li>Nasopharyngeal aspirates (preferred specimen): sensitivity is highest for aspirates than for any other respiratory samples</li> <li>Nasopharyngeal swabs</li> <li>Throat swabs</li> </ul>
<b>Assay frequency</b>	Daily. Only for after hours and urgent test requests. All results will be confirmed by PCR
<b>Results</b>	Available same day
<b>Interpretation note</b>	Should not be relied upon to make a diagnosis of Influenza without confirmatory testing by a reference method (e.g. PCR).
Test request name	Serology for Influenza A and B
<b>Preferred sample types</b>	Acute and convalescent samples required
<b>Assay frequency</b>	Daily on week days
<b>Results</b>	Available next day
<b>Interpretation note</b>	Serological testing results for human Influenza on a single serum specimen is not interpretable and is not recommended.

### Treatment of Influenza

The Australian Antibiotic Guidelines (13th edition) recommend that treatment with neuraminidase inhibitors can be beneficial if commenced within 48 hours of symptomatic onset. Either 75mg BD of oseltamivir for 5 days orally or 10mg BD of zanamivir for 5 days by inhalation are recommended.<sup>4</sup> Not surprisingly, reports of de novo antiviral resistance are emerging from overseas. It is too early to comment on the epidemiology of resistance to the neuraminidase inhibitors at this stage. Reports of neuropsychiatric disturbances after neuraminidase inhibitor therapy have emerged - predominantly from Japan. The implications for local prescribing practices are uncertain at present.

### References

1. WHO collaborating centre for reference and research in Influenza, Australia website: [www.influenzacentre.org](http://www.influenzacentre.org)
2. The Commonwealth health website: [www.health.gov.au](http://www.health.gov.au)
3. Australian Influenza Report. Report No. 13 October 2007
4. WHO website: [www.who.int](http://www.who.int)
4. Therapeutic guidelines Version 13, 2006.

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# clinical data Apr 08

## Infectious Diseases Report - Geographic Distribution - March 2008

ORGANISM	Regions (as per key below)															Total			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Mar	Feb	Jan	Dec
Adenovirus (not typed)	2	2					1				1					6	9	15	12
Adenovirus (typing pending)		4					2		2	1		1				10	6	8	3
Barmah Forest virus	10	5	2	1			7		8	12	10	11	3	5	6	80	69	49	29
Bordetella pertussis	1	1	1				10	1	3	1	3	3	1	1		26	31	41	27
Brucella species									1		1					2	5	4	0
Campylobacter jejuni																0	0	0	0
Chlamydia pneumoniae																0	0	0	0
Chlamydia trachomatis, not typed	31	36	11	15	1		51		26	9	71	33	7	8	12	311	475	464	426
Coxiella burnetii			1									1				2	19	18	8
Cryptococcus species											1					1	3	4	1
Cytomegalovirus (CMV)		7	2				6		3	1	9	5	2		1	36	44	64	56
Entamoeba histolytica																0	0	0	0
Enterovirus - not typed																0	7	5	4
Epstein-Barr virus (EBV)	2	6	2				11		9	3	13	4	4	1	3	58	79	96	88
Flavivirus unspecified	3			1						2		1		2		9	15	6	5
Hepatitis A virus		1									1					2	0	6	3
Hepatitis B virus	4	2	2				10		2		21	2	2	3	1	49	63	56	46
Hepatitis C virus	9	23	17	5	1		21		11	4	48	15	4	5	3	166	189	249	160
Hepatitis D virus																0	0	0	0
Hepatitis E virus																0	0	0	0
Herpes simplex Type 1	3	17	8	2		1	14		14	6	25	25	1	5	8	129	163	209	226
Herpes simplex Type 2	7	12	2	6	1		15		5	2	19	10	3	1		83	130	157	131
Herpes simplex virus - not typed	1	2	1	3			2		3	1	1	3		1	1	19	29	47	40
HIV-1	1								1		1	1				4	11	7	5
HTLV-1																0	0	0	0
Influenza A virus								2		2	5	1				10	10	10	11
Influenza B virus											1	1				2	0	1	2
Legionella species																0	0	0	0
Leptospira species	11											1		1		13	3	6	3
Measles																0	1		1
Mumps virus																0	0	4	1
Mycoplasma pneumoniae		1	2				3	2	2	1	6	1		2	1	21	23	20	23
Neisseria gonorrhoeae	7	4	1		1		11				4			1		29	29	34	16
Parainfluenza virus Type 1		2					1		1		1					5	4	1	1
Parainfluenza virus Type 2											2					2	1	2	1
Parainfluenza virus Type 3														1		1	0	0	7
Parvovirus		1	2						3		1	1	3			11	14	23	38
Pneumocystis carinii																0	1	1	1
Respiratory Syncytial virus		1	2				6		3	3	6	3		2		26	38	21	22
Ross River virus	21	12	7	8			26	1	19	20	18	24	4	18	17	195	246	116	81
Rubella virus																0	2	1	1
Salmonella paratyphi A																0		0	0
Salmonella paratyphi B																0		0	0
Salmonella typhi							1									1		0	0
Shigella dysenteriae																0		0	0
Shigella flexneri																0		0	0
Streptococcus Group A	7	9	3	1			8	4	6	1	2	5	2	2	2	52	56	79	84
Toxoplasma gondii																0	0	0	1
Treponema pallidum	11	3	4		2		5	3	8	3	14	3	1	5	2	64	104	99	94
Trichomonas vaginalis	4															4	13	11	3
Varicella Zoster virus	6	12	9	1		2	15		7	3	18	7	2	7		89	120	153	158
Yersinia enterocolitica																0	1	0	0
<b>TOTAL</b>	<b>141</b>	<b>163</b>	<b>79</b>	<b>43</b>	<b>6</b>	<b>3</b>	<b>226</b>	<b>13</b>	<b>137</b>	<b>75</b>	<b>303</b>	<b>162</b>	<b>39</b>	<b>71</b>	<b>57</b>	<b>1518</b>	<b>2013</b>	<b>2087</b>	<b>1819</b>

### REGIONS

1 Cairns	4 Mackay	8 Northern Territory	12 Sunshine Coast
2 Gold Coast/Northern Rivers	5 Mount Isa	9 Redcliffe	13 Toowoomba
3 Ipswich	6 New England	10 Rockhampton	14 Townsville
	7 North Brisbane Suburbs	11 South Brisbane Suburbs	15 Wide Bay/Burnett

February 2008 and further historical clinical data can be obtained by contacting your local Medical Liaison Officer

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# QML Pathology updates Apr 08

## >> Implementation of Universal Pre-Storage Leucodepletion of Red Cells

Dr Stewart Bryant, Transfusion Medicine Specialist, ARCBS Queensland

The Australian Health Ministers' Conference (AHMC) recently announced moving toward 100% leucodepletion of red blood cells and platelets over the next four years with completion by 2010-2011. The exact timelines for implementation of universal leucodepletion in each state is still subject to funding approval by jurisdictional governments and AHMC. ARCBS has been advised that some jurisdictions may choose to move to 100% leucodepletion in 2008/09. Further information will be provided when available.

ARCBS has introduced blood packs that will enable the pre-storage manufacture of leucodepleted red cells and platelets (WCC <1x10<sup>6</sup> per unit) that will not require bedside leucocyte filtration. These components will still require

administration via a standard blood giving set containing a 170-200\_μm filter to remove clots and aggregates.

Please note that, during the move towards 100% pre-storage leucodepletion, there will be a 42 day period following implementation when laboratories may have a dual inventory, comprising both leucodepleted and non-leucodepleted red cells. All leucodepleted red cell components will be labelled as such, but during this period, bedside leucodepletion may need to continue for non-leucodepleted red cell components if indicated.

Please direct any enquiries to Dr Stewart Bryant, Transfusion Medicine Specialist on (07) 3838 9238.

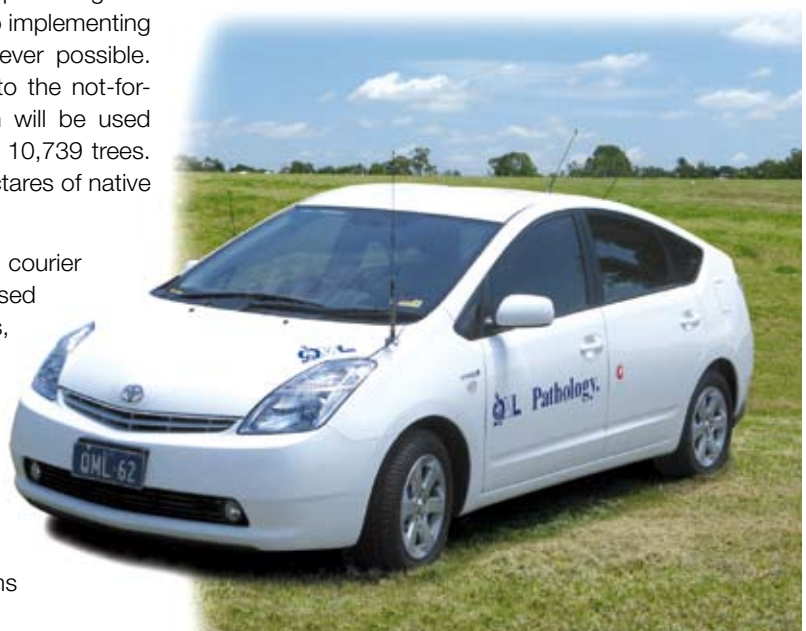
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## QML Pathology Goes Green

QML Pathology has for many years supported green initiatives in its operations and is committed to implementing environmentally responsible processes wherever possible. Recently QML Pathology donated \$27,760 to the not-for-profit organisation Greenfleet. This donation will be used to offset carbon emissions by the planting of 10,739 trees. This is the equivalent of approximately 27 hectares of native forest and 2752 tonnes of carbon per annum.

Our green commitment also extends to our courier vehicles with over 90% of the fleet being comprised of Toyota Yaris or Toyota Corolla vehicles, which are favourably rated for greenhouse gas emissions and air pollution in the Australian Government's Green Vehicle Guide. Add to this the Prius, which is ideal for congested city traffic conditions using battery power at low speeds. The recent introduction of the Toyota Hybrid to the Brisbane metropolitan fleet only confirms our commitment to the environment.

If you would like more information about Greenfleet please visit the Greenfleet website [www.greenfleet.com.au](http://www.greenfleet.com.au).



The new Prius

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## New Request Form with Blood Product Information

It is now an accreditation and Australian Red Cross Blood Service requirement that requests for transfusion have a relevant clinical summation to ensure the appropriate usage of blood and blood products. In response we have developed a B5 request form that includes a section for this

information. While the size and format of this form is different, the information required remains the same with the exception of the blood product information. To obtain copies of this request form please contact our Liaison Department on (07) 3121 4943 or your local branch Medical Liaison Officer.



# QML Pathology updates Apr 08

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## >> QML Pathology Olympic Hopeful

Did you know that the fastest man in Australia works at QML Pathology? On Friday, 29 February Otis Gowa won the 100-metre sprint at the National Championships, surging ahead of fellow sprinters Matt Shirvington and Patrick Johnson to win the race in 10.63 seconds.

As a member of Athletics Australia's government backed indigenous development programme called 'Jump Start to the 2012', Otis has been training hard to make the 2012 Olympics in London. However, Otis may be achieving his dream a little earlier with a surprise debut at the Beijing Olympics.

After his performance at the National Championships Otis was invited to participate in one of the world's most famous and prestigious foot races - The Stawell Gift.



Over the next few months Otis will train hard to improve his times and hopefully make the 4x100m relay team. We will continue to monitor Otis's progress and will let you know how his Olympic campaign goes.

## Travel Health Service Fax Number

Due to the relocation of our Central Laboratory in April 2006 the travel health fax number '3840 4478' is no longer in operation. Please discard any old travel health pads. If you require a new travel health pad, please contact Liaison Department on (07) 3121 4943 or your local Medical Liaison Officer.

## Change to Test

### D-DIMER

Please note that the sample for a D-Dimer test is no longer collected in an EDTA tube. All samples should now be collected in a SODIUM CITRATE tube.

## Doctor's Noticeboard

- Dr Steven Stylian wishes to announce the opening of his second office complex at:  
AHC House, Suite 6, Level 1  
14 Carrara Street, Benowa.  
Services include Haematology, Oncology, Stem Cell Transplantation and Palliative Care.  
Appointments can be made by phoning  
(07) 5598 0562 or (07) 5597 1305.
- Dr Warren de Ambrosis has been away from his practice for six months due to medical reasons. He has returned, limiting his practice to the field of infertility only.
- Dr Daniel Kleinig wishes to announce the opening of his new surgery:  
Queensland Specialised Health Services  
7/102 Burnett Street, Buderim QLD 4556  
Phone: (07) 5476 7777  
Fax: (07) 5476 7277.

## New Collection Centres

### Springfield Lakes

76/31 Springfield Lakes Boulevard  
Spring Lake Village  
Springfield Lakes QLD 4300

Phone: (07) 3288 3617  
Fax: (07) 3288 2637

Hours:  
8.00am - 12.00pm and 1.00pm - 4.30pm (Mon-Fri)  
8.30am - 11.30am (Saturday)

### Zilzie

The Rec Club - Seaspray  
28 Cocoanut Point Drive  
Zilzie QLD 4740

Phone: (07) 4938 8179  
Fax: (07) 4938 7821

Hours:  
9.00am - 12.00pm and 1.00pm - 3.00pm (Mon-Fri)