Investigation of results obtained for an external QC sample used for monitoring Infectious Disease Screening at the Australian Red Cross Blood Service

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Australian Red Cross Blood Service
Introduction

• Australian Red Cross Blood Service Infectious Disease Screening (IDS) testing
• IDS Quality Control (QC) Monitoring
• Observed decrease in QC reactivity with HBsAg on Primary Screening assay
• Investigation
• Outcomes
Infectious Disease Screening

The Australian Red Cross Blood Service Infectious Disease Screening (IDS) Laboratories screen Blood donors for Transfusion Transmitted Infection (TTI) serological markers.

- IDS Laboratories in Perth, Brisbane, Sydney & Melbourne
  - Adelaide laboratory closed mid 2012
- Abbott PRISM (ChLIA)
  - HBsAg
  - anti-HCV
  - anti-HIV -1/2 (HIV Ag/ Ab Combo assay implemented from mid July 2013)
  - anti-HTLV-I/II
  - 6 channels with 2 sub-channels per channel
  - Independent hardware and test kit reagents on each channel
  - Tests each sample for each marker concurrently
Abbott PRISM (ChLIA)
IDS QC Monitoring

- eQC sample – PeliSpy Type 36 (T36) multi-marker control
  - AcroMetrix by Life Technologies, supplied by the NRL
  - Data entered into EDCNet
  - Shewart charts generated & reviewed
  - Batch report generated & reviewed
  - Control Limits are calculated by reviewing cumulative EDCNet data collected from multiple labs over multiple reagent lot numbers, and are then set approx 4 – 6 weeks post implementation
  - Control Ranges reviewed regularly – adjustments made if necessary
T36: 035717: exp 31Mar2013

- Blood Service implemented use of T36: 035717 in mid 2011
- Control Limits calculated and set ~ 5 weeks post implementation
- Example: PRISM HBsAg
  - Mean: S/CO = 1.86
  - SD: 0.18
  - Upper Control Limit: S/CO = 2.40
  - Lower Control Limit: S/CO = 1.32

- Based on data from:
  - 10 Laboratories
  - n = 1168
  - 7 Reagent batches
T36: 035717 HBsAg - QLD Prism B 1/08/2011 – 30/08/2012
T36: 035717 QLD PRISM's A, B & C 1/08/2011 to 30/08/2012

The graph shows a scatter plot of data points with a trend line. The equation of the trend line is $y = -0.0004x + 1.8484$. The x-axis represents the Reagent values, and the y-axis represents the %CD values. The data appears to follow a linear trend with a slight decrease as the Reagent values increase.
T36: 035717  SA PRISM A 1/08/2011 to 30/08/2012
T36: 035717 PRISM HBsAg – All Users (adhoc reporter)

Negative result: S/CO<1.00
QC sample, T36:S2381:035717, was tested in the Abbott PRISM HBsAg ChLIA in reagent batches designated. The number of observations, mean and variations around the mean over the period 01/06/2011 to 31/08/2012 are shown.
QC sample, T36:S2381:035717, was tested in the Abbott PRISM HBsAg ChLIA in reagent batches designated. The number of observations, mean and variations around the mean over the period 01/06/2011 to 31/08/2012 are shown.

<table>
<thead>
<tr>
<th>Batch ID</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>x-2SD</th>
<th>x+2SD</th>
<th>Min</th>
<th>Max</th>
<th>CV(%)</th>
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N/A: Statistical calculations based on standard deviation not performed when n < 10
What’s causing this???

- Problem with eQC Materiel (PeliSpy T36)???
- Problem with PRISM HBsAg Reagent??? Manufacture???
- Equipment???
- Internal processes???
Blood Service Investigations

• Comprehensive review of:
  ▪ All PRISM maintenance / service in each IDS Laboratory
  ▪ Breakdown and repair
  ▪ Manufacturer control data
  ▪ Assay Calibration data
  ▪ No adverse findings

• Contact and discuss with:
  ▪ NRL (liaise with AcroMetrix / Life Technologies)
  ▪ Abbott Diagnostics
Implement new T36 Lot 201305

- While investigations continued…
  - Decided to implement new lot of T36: 201305 into Blood Service Laboratories – August 2012

- Pre-Acceptance Testing (PAT) performed on PRISM HBsAg reagent batch 09105LI00
  - Mean: S/CO = 1.76
  - SD = 0.08
  - CV = 4.48%
Comparison of T36 Lots

- Comparison of PRISM HBsAg Reactivity of T36 Lot 035717 and 201305 using PRISM HBsAg reagent Lot 09105LI00

<table>
<thead>
<tr>
<th>PeliSpy T36 lot</th>
<th>T36: 035717</th>
<th>T36: 201305</th>
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<tr>
<td>SD</td>
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Negative results: S/CO<1.00
T36: 201305 – QLD PRISM HBsAg - PRISM B
31/08/2012 – 31/01/2013

Negative results: S/CO<1.00
QC sample, T36:S2381:201305, was tested in the Abbott PRISM HBsAg ChLIA in reagent batches designated. The number of observations, mean and variations around the mean over the period 01/08/2012 to 31/01/2013 are shown.
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<td><strong>8.73</strong></td>
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Blood Service Investigations

- Comprehensive review of:
  - All PRISM maintenance / service in each IDS Laboratory
  - Breakdown and repair
  - Manufacturer control data
  - Assay Calibration data
  - Again - No adverse findings

- Continue to discuss with:
  - NRL (liaise with AcroMetrix / Life Technologies
  - Abbott Diagnostic
Notification to TGA

- Negative T36: 201305 results delaying release of test results
- Significant impact on workflow
- Significant impact on time for blood component release into inventory for issue to AHP’s
- Blood Service notified TGA via a “Sponsors/Manufacturers Medical Device Incident Report
Abbott Diagnostics Investigations

- Product review for PRISM HBsAg reagent lots released in 2012 for use by the Blood Service
- Comprehensive investigation / review performed for:
  - Key rare biological component changes
  - Release criteria changes and performance against release criteria
  - Analytical sensitivity lots
  - Sensitivity panels used for analytical evaluation
  - On-board stability test evaluation
  - Statistical Process Control (SPC) for release criteria
  - Complaint review for lots released in 2012
- Conclusion – The PRISM HBsAg product review showed no indication that the shift down of the PeliSpy Control values of control lot T36: 201305 is caused by the reagent.
Outcomes - TGA Report

- Report received by the Blood Service in February 2013
- Investigation summary stated ……
  “The root cause investigation has determined that the presence of varying amounts of HBs antibodies in the diluents matrix resulted in decreased reactivity of the HBs antigen.”

- Life Technologies conducted a recall of
  - PeliSpy T36 lot 035717
  - PeliSpy T36 lot 201305
  - PeliSpy T38 lot 035716
  - PeliSpy T38 lot 220905

These lots were manufactured using the implicated diluents matrix.
Outcomes - Implementation of new T36 lots

- The Blood Service implemented use of an interim T36 lot (234203) from 21/01/2013 – 10/04/2013 while a new T36 lot was being manufactured.
- Implemented use of T36: 303601 on 11/04/2013
  - PAT Mean: S/CO = 2.49
  - PAT SD = 0.07
  - Performing without incident
Conclusion

- This incident highlights the importance of good communication and information sharing:
  - Within a QC peer group
  - And between……..
  - Participant organisation
  - QC Material provider / manufacturer
  - Assay manufacturers
  - Regulatory bodies
Acknowledgements

- Australian governments fully fund the Australian Red Cross Blood Service for the provision of blood products and services to the Australian community

- IDS staff (Blood Service)
- Margaret Arthur & Philip May (Abbott Diagnostics)
- Kathy Smeh (NRL)
Questions?

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