Introduction of a Body Fluids External Quality Assurance Program

Bernadette James[1,2], Graham Jones[2], John Calleja[2], Fernando San Gil[2], Kay Weng Choy[2], Peter Graham[1,2]

[1]The Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP), St Leonards 2066 NSW, Australia;
[2]Members of the AACB RCPAQAP Body Fluids Working Party, St Leonards 2066 NSW, Australia.

Introduction

The Royal College of Pathologists Australasia Quality Assurance Programs (RCPAQAP) introduced a Body Fluids External Quality Assurance (EQA) program in March 2018 with input from the Australasian Association of Clinical Biochemists (AACB)/RCPAQAP Body Fluids Working Party (BFWP).

This was largely in response to requests from RCPAQAP participants to assist with the validation of their body fluid testing, given most in-vitro diagnostic device (IVDD) providers have no validation claims for these matrices.

Methods

The material is liquid with diluted human plasma as a base and supplemented to mimic a range of body fluids. The samples included in the pilot program had analyte levels consistent with a malignant ascites, a non-infectious pleural effusion and a parapneumonic effusion. Participants were asked to report values for the following chemistry analytes: albumin, amylase, cholesterol, creatinine, glucose, lactate, lactate dehydrogenase, lipase*, osmolality*, pH*, protein, sodium*, and triglycerides. They were also asked to report results for the following tumour markers: AFP*, CA 125*, CA 15-3*, CA 19-9, CEA, and hCG*. Results from 70 participating laboratories were assessed.

**These analytes were not listed in the original manufacturer specifications, but were requested to be included "as found".*

Results and Discussion

The first survey report in the Body Fluids program was issued in May 2018. The BFWP elected to empirically widen the Analytical Performance Specifications (APS's) by at least twice those of the equivalent analytes in serum-based RCPAQAP Programs, namely General Chemistry, Tumour Markers, and Blood Gases. With further assessment of participant performance, the BFWP may choose to revise the APS's for some analytes.

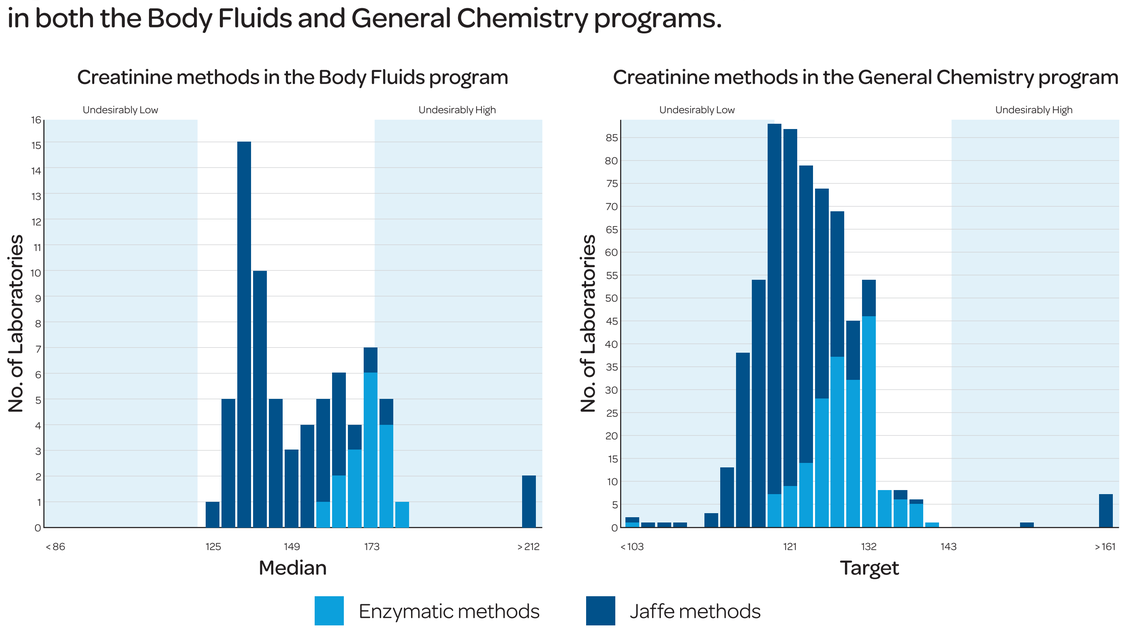
The returned results for the surveyed analytes typically fell within the APS. Similar patterns and performance between several analytes in the Body Fluids and other RCPAQAP programs were evident; however, there were some analytes/methods where differences were noted.

Creatinine

Method differences were observed between enzymatic and Jaffe (alkaline picrate) methods for creatinine measurement, with participants using Jaffe methods generally returning lower concentrations of creatinine compared to those using enzymatic methods. As shown in Figure 1, this pattern is similar to the General Chemistry program for samples at equivalent creatinine concentrations. The median difference between the two method types (median of Jaffe creatinine participants subtracted from the median of enzymatic creatinine participants) in the General Chemistry program is 8 mmol/L; however, the median difference between the same groups in the Body Fluids program was greater at 35 mmol/L. The sample with lower protein concentration (median 16 mmol/L) also had fewer returned results for creatinine, which may be due to these methods producing negative values in this setting.

The correction factor used in rate-blanked compensated Jaffe methods to allow for non-creatinine chromogens may explain the lower relative values in the Body Fluids matrix, compared to enzymatic methods. The effect of protein may be particularly important as this is often at a lower concentration in the body fluid samples. However, these differences are not clinically significant for body fluid analysis at these concentrations, as creatinine is mainly used to assess urine leakage post-surgery/trauma.

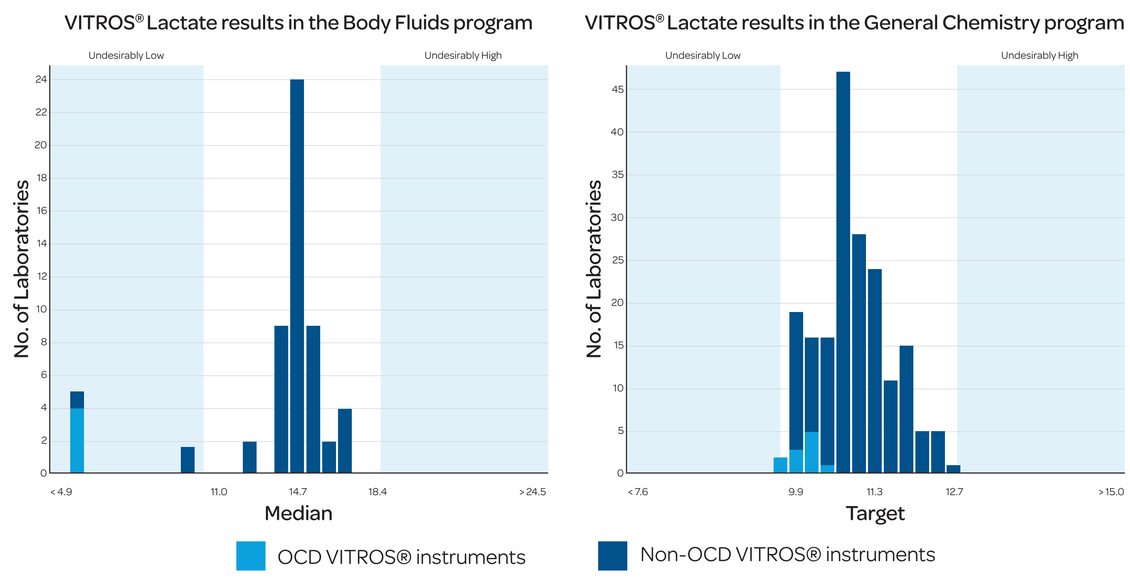
Figure 1: Enzymatic creatinine method measurements compared to Jaffe methods in both the Body Fluids and General Chemistry programs.



Lactate

Participants reporting in the Body Fluids program using the Ortho Clinical Diagnostics VITROS® 4600/5600 analyser recovered significantly lower concentrations of Lactate compared to participants using other instruments. In the General Chemistry program, VITROS® instruments also have a low bias, although it is not as pronounced as in the Body Fluids program. At a concentration of 10.9 mmol/L for Lactate in the General Chemistry program, the median value of VITROS® instruments is 10.1 mmol/L (bias: -0.7%). In the Body Fluids program, the median of Lactate is 14.7 mmol/L; however, the median value of the VITROS® instruments is only 5.3 mmol/L (bias -64%). As per Figure 2, the VITROS® performance in the General Chemistry program still falls within the APS; however, that in the Body Fluids program falls out of the APS despite the APS being twice as wide in the Body Fluids program than in the General Chemistry program. This may be the result of a commutability issue between the material and the dry slide technology of VITROS® instruments, in addition to a lower total protein concentration in the Body Fluids material.

Figure 2: The Ortho Clinical Diagnostics VITROS® 4600/5600 Lactate measurements compared to other platforms in the Body Fluids and General Chemistry programs.



pH

43 participants reported pH values of 6.6–8.0 for a Body Fluid sample with a median of 7.35 (min–max difference 1.4). This spread of results is wider than is seen for this analyte in other programs. For example, for a median value of pH 7.13 in the RCPAQAP Blood Gases program, participants reported a range of 7.10 to 7.15 (min–max difference only 0.05).

The Body Fluids program includes some methods not used in the Blood Gases program, e.g. pH strips and certain pH meter brands; however, most laboratories (40 out of 43) quoted a blood gas instrument as their measuring device. Because the overall spread of results was so large, it was not possible to determine if there were any significant instrument/method-specific differences. The stability of the material may have been a factor, however further investigation is warranted, as body fluid pH is used to guide clinical decisions in some situations[1].

Conclusions

Method differences were not immediately evident for most analytes in the Body Fluids program, except in the cases of creatinine and lactate. However, more may be revealed as more survey results are received with different analyte compositions. Further tightening of some APS's may highlight method differences in the future. Finally, it is important that the variable performance of pH is reviewed on an ongoing basis.

While recognising that a Body Fluids EQA program will not be able to simulate all scenarios in a laboratory setting, the initial results indicate that it should be a useful tool to assist laboratories in validating their methods for analysing various body fluids and ensuring ongoing acceptable performance. It is encouraging that most laboratories and platforms show concordance in analyte recoveries across the program.

Reference

[1] Saguil A, Wyrick K, Hallgren J. Diagnostic approach to pleural effusion. Am Fam Physician. 2014 15; 90 (2): 99-104.

Acknowledgements

Wilson Punyalack (RCPAQAP) who facilitated the initial contact with Aalto Scientific and assisted with the setup and pre-testing.
Samantha Shepherd (RCPAQAP) and Rizzi de Leon (RCPAQAP) for their assistance with the program initiation.
NSW Pathology at Royal North Shore Hospital for their pre-testing evaluation.