COLLEGE of AMERICAN PATHOLOGISTS

Educational Discussion: Cystatin C Harmonization

2017-A Cystatin C Survey (CYS)

In the 2017 CYS-A mailing, the lower concentration sample (CYS-01) was prepared from off-the-clot fresh frozen pooled serum. It was prepared essentially identically to the 2014 CYS-A mailing wildcard samples. Our main reason for changing from processed human plasma is a concern that processed human plasma might not represent performance on actual clinical samples because of non-commutability problems (1). The higher cystatin C concentration sample (CYS-02) in the 2017 CYS-A mailing was typical processed human plasma, so absolute accuracy assessment might be impacted by non-commutability issues.

Focusing on the CYS-01 off-the-clot fresh frozen pooled serum sample results, it appears that there has been some improvement in calibration traceability leading to better harmonization of the measured concentration of cystatin C across assay platforms compared to the 2014 CYS-A wildcard studies (2). A table showing the results and the percent bias of the method-specific means and method-specific median results is shown below.

	2017 CYS-A CYS-01 Results				
	N	Method-specific mean	% Bias from all-method mean	Method-specific median	% Bias from all-method median
Binding Site SPAplus	5			0.72	104.5%
Diazyme Laboratories	14	0.691	105.5%	0.70	91.0%
Gentian	21	0.610	93.1%	0.61	91.0%
Roche cobas c series	28	0.715	109.2%	0.71	106.0%
Roche Modular	8			0.72	107.5%
Siemens ADVIA Chemistry Systems	5			0.66	98.5%
Siemens Nephelometer Systems	47	0.592	90.4%	0.58	86.6%
Siemens Dimension Vista	5			0.58	86.6%
All Instruments*	166	0.655		0.67	

* All instrument = "all method" mean or median

CAP does not report method-specific means when less than 10 laboratories use a specific method. However, comparing the method specific medians gives some sense of harmonization of the various methods reported results. Note that we did not attempt to assign a ERM DA-471/IFCC traceable target value for 2017 CYS-01 sample as we had in the 2014 CYS-A wildcard samples, so little definitively can be said about the trueness/accuracy of any of the specific instrument platform results.

Generally, it appears that the method specific means and method-specific medians are closer to each other than in the 2014 CYS-A wildcard exercise. With the exception of the Siemens

Nephelometer Systems and Siemens Dimension Vista, the method specific medians are all within ±9% of the all method median and within 16% of each other. The 2014 CYS-A wildcard results showed method-specific medians that varied from -20% to +17% of the target values established with the international certified reference material ERM DA-471/IFCC. Interpretation of Siemens' results is complicated by the fact that Siemens offers two calibration traceabilities in different parts of the world. In most non-US countries, they provide ERM DA-471/IFCC traceable calibration. Because slightly more than half of non-US laboratories enrolled in the 2017 CYS-A CAP Survey used the Siemens' nephelometric platform, the reported results reflect a mixture of two distinct calibration schemes.

Because the 2017 CYS-01 sample is at a low "normal" concentration of cystatin C, we should be cautious about extrapolating these observations to higher concentrations.

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References:

1. Miller WG, Myers GL. Commutability Still Matters. Clin Chem 2013; 59:1291-1293.
2. Eckfeldt JH, Karger AB, Miller WG, Rynders GP, Inker LA. Performance in measurement of serum cystatin C by laboratories participating in the College of American Pathologists 2014 CYS survey. Arch Pathol Lab Med 2015;139:888-893.