

After Calibration and Re-Calibration, An Instrument Continues to Perform Nonlinear – all Levels are outside statistical limits and appear visually nonlinear

Initial Results: A laboratory performed routine calibration verification / linearity testing using VALIDATE® TDM1 on a Roche Hitachi. The following was the linearity report for Digoxin (DIGN) generated using MSDRx®, Maine Standards Company's Data Reduction software:

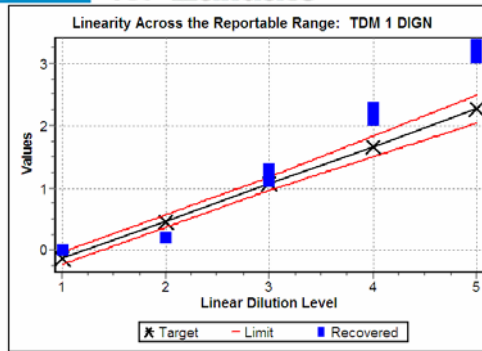
TDM 1 DIGN

published CLIA total allowable error is 0.2 ng/mL or 20%, whichever is greater

L	X	Rep 1	Rep 2	Rep 3	Accept	Comments
B	N/A				<input type="checkbox"/>	
1	1.0	0	0	0	<input type="checkbox"/>	
2	2.0	0.2	0.2	0.2	<input type="checkbox"/>	
3	3.0	1.2	1.1	1.3	<input type="checkbox"/>	
4	4.0	2.2	2.3	2.1	<input type="checkbox"/>	
5	5.0	3.1	3.2	3.3	<input type="checkbox"/>	

Tested 0.00 to 3.20 ng/mL
Validated _____ to _____ ng/mL
Mean versus Target Regression
 $y = 1.400x - 0.133$

X	Target	Mean	+/- Diff	% Diff	+/- Limit	% Limit
1.0	-0.133	0.000	** 0.133	100.0%	0.100	N/A
2.0	0.467	0.200	** 0.267	57.2%	0.100	N/A
3.0	1.067	1.200	0.133	** 12.5%	0.107	10%
4.0	1.667	2.200	0.533	** 32.0%	0.167	10%
5.0	2.267	3.200	0.933	** 41.2%	0.227	10%



Troubleshooting: The results were not consistent with Peers or with typical product performance. The laboratory took the troubleshooting step of recalibrating their DIGN assay. Calibration set points covered the method range of 0.3 – 5.0 ng/mL (calibration set points were 0, 0.5, 1, 2, 3 and 5 ng/mL). After re-calibration, calibration verification / linearity testing was performed and results continued to be nonlinear. The laboratory requested a service call from the instrument manufacturer. During the service call, a probe alignment issue was discovered and corrected. To confirm that the probe alignment issue was causing the nonlinear response, the laboratory re-ran the calibration verification / linearity testing. The updated MSDRx® report shows that all Levels are within the statistical limits.

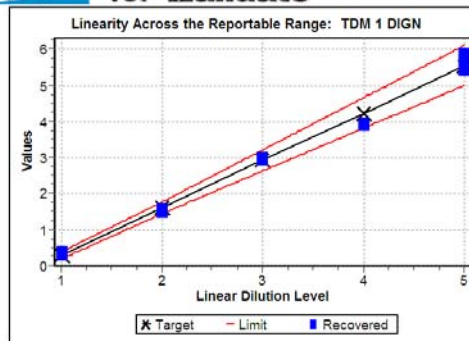
TDM 1 DIGN

published CLIA total allowable error is 0.2 ng/mL or 20%, whichever is greater

L	X	Rep 1	Rep 2	Rep 3	Accept	Comments
B	N/A				<input type="checkbox"/>	
1	1.0	0.38	0.29	0.33	<input type="checkbox"/>	
2	2.0	1.48	1.59	1.54	<input type="checkbox"/>	
3	3.0	2.93	3.0	2.96	<input type="checkbox"/>	
4	4.0	3.96	3.9	3.93	<input type="checkbox"/>	
5	5.0	5.88	5.42	5.65	<input type="checkbox"/>	

Tested 0.33 to 5.65 ng/mL
Validated 0.33 to 5.65 ng/mL
Mean versus Target Regression
 $y = 0.991x - 0.016$

X	Target	Mean	+/- Diff	% Diff	+/- Limit	% Limit
1.0	0.296	0.333	0.037	12.5%	0.100	N/A
2.0	1.611	1.537	0.074	4.6%	0.161	10%
3.0	2.926	2.963	0.037	1.3%	0.293	10%
4.0	4.241	3.930	0.311	7.3%	0.424	10%
5.0	5.556	5.650	0.094	1.7%	0.556	10%



Summary: As calibration is not intended to identify instrument issues, in this case, if the laboratory depended on calibration alone, the laboratory could have reported inaccurate patient results. Calibration verification / linearity testing is the only way to test if a method is giving a nonlinear response.