Case Study #2: Recalibration Does Not Correct Nonlinear Response, Additional Troubleshooting Used

Initial Results: A laboratory performed routine calibration verification / linearity testing using VALIDATE® TDM1. One analyte tested was Digoxin. The following report was generated using MSDRx®, the LGC Maine Standards 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
B	N/A			
1	1.0	0	0	0
2	2.0	0.2	0.2	0.2
3	3.0	1.2	1.1	1.3
4	4.0	2.2	2.3	2.1
5	5.0	3.1	3.2	3.3

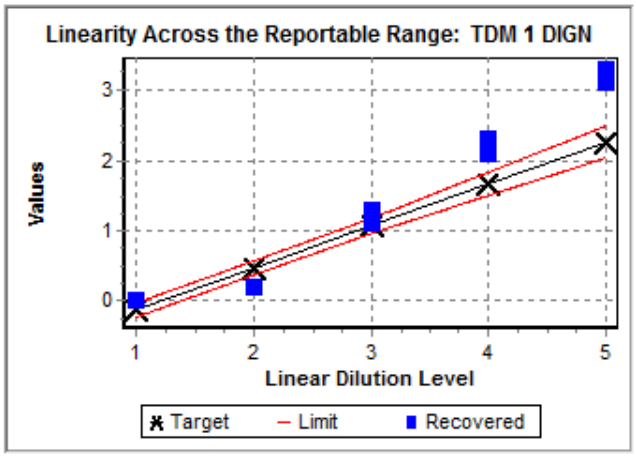
☐ Accept ☐ Comments

Tested 0.000 to 3.20 ng/mL

Validated _____ to _____ ng/mL

Mean versus Target Regression
y = 1.400x - 0.133
r^2=0.9624 SEy,x=0.3

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%



The laboratory contacted LGC Maine Standards Technical Support. Technical Support advised the laboratory that results were not consistent with Peers or with typical product performance. The experiment was showing nonlinearity in the method, and recovery was well below the typical range of the product.

Troubleshooting: The laboratory took the troubleshooting step of recalibrating their DIGN assay. However, the calibration failed. After several unsuccessful attempts to recalibrate the DIGN assay, 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 nonlinear response was corrected, the laboratory re-ran the calibration verification / linearity testing. The updated MSDRx® report shows that all Levels are within the statistical limits. The laboratory accepted the updated results and determined that they had validated the linearity across the reportable range of the method.

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
B	N/A			
1	1.0	0.38	0.29	0.33
2	2.0	1.48	1.59	1.54
3	3.0	2.93	3.0	2.96
4	4.0	3.96	3.9	3.93
5	5.0	5.88	5.42	5.65

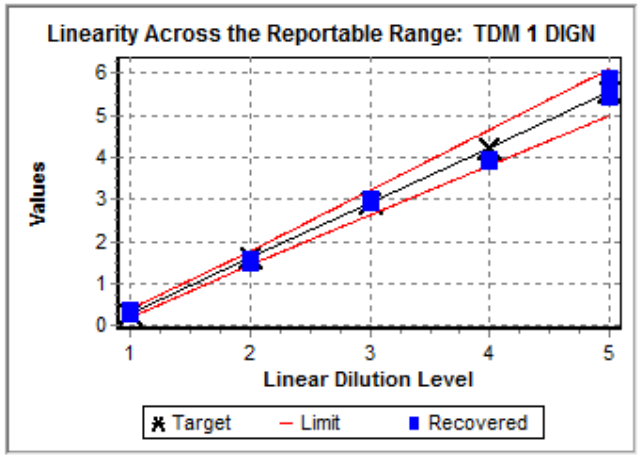
☐ Accept ☐ Comments

Tested 0.333 to 5.65 ng/mL

Validated 0.333 to 5.65 ng/mL

Mean versus Target Regression
y = 0.991x - 0.016
r^2=0.9916 SEy,x=0.2

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: In this case, routine calibration verification / linearity testing demonstrated nonlinear response across the reportable range of the method and LGC Maine Standards Technical Support advised that recovery was not consistent with Peers. Recalibration did not correct the response, and service was called. System maintenance, recalibration, and repeating the calibration verification / linearity testing verified the method's correct response.

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