Case Study #1: Level 4 and 5 Results Outside Statistical Limits and Appear Visually Nonlinear

Initial Results: A laboratory performed routine calibration verification / linearity testing using VALIDATE® TDM1. One analyte tested was Carbamazepine. The following report was generated using MSDRx®, the LGC Maine Standards Data Reduction software:

TDM 1 CARB

suggested total allowable error is 0.5 µg/mL or 25%, whichever is greater

L	X	Rep 1	Rep 2	Rep 3
B	N/A			
1	1.0	0.5	0.5	0.5
2	2.0	4.2	4.2	4.2
3	3.0	8.0	7.9	7.7
4	4.0	14.3	13.5	13.2
5	5.0	29.8	27.8	28.7

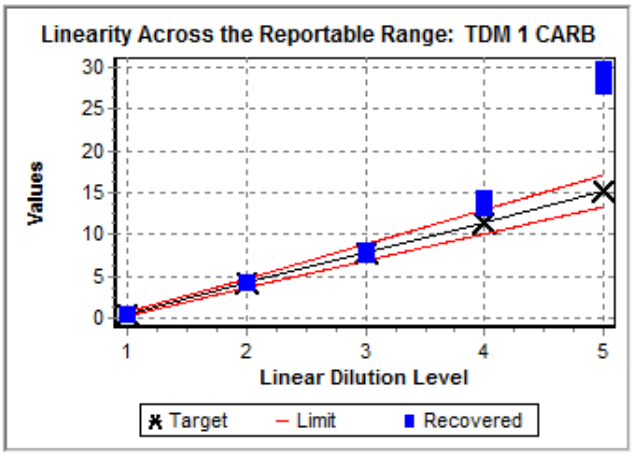
☐ Accept ☐ Comments

Tested 0.50 to 28.8 µg/mL

Validated _____ to _____ µg/mL

Mean versus Target Regression
y = 1.792x - 3.106
r^2=0.8890 SEy,x=3.5

X	Target	Mean	+/- Diff	% Diff	+/- Limit	% Limit
1.0	0.51	0.50	0.01	2.0%	0.25	N/A
2.0	4.19	4.20	0.01	0.2%	0.52	12.5%
3.0	7.87	7.87	0.00	0.0%	0.98	12.5%
4.0	11.56	13.67	2.11	** 18.3%	1.44	12.5%
5.0	15.24	28.77	13.53	** 88.8%	1.90	12.5%



The laboratory contacted LGC Maine Standards Technical Support. Technical Support advised the laboratory that their results were not consistent with Peers or with typical product performance and that the laboratory needed to determine if the linearity flags were clinically significant. If they believe the nonlinearity was clinically significant, they would want to perform troubleshooting.

Troubleshooting: The laboratory determined that the statistical nonlinearity was clinically significant. They took the troubleshooting step of recalibrating their CARB assay. To confirm that the recalibration corrected 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. The laboratory accepted the updated results and determined that they had validated the linearity across the reportable range of the method.

TDM 1 CARB

suggested total allowable error is 0.5 µg/mL or 25%, whichever is greater

L	X	Rep 1	Rep 2	Rep 3
B	N/A			
1	1.0	0.5	0.5	0.5
2	2.0	4.7	4.7	4.6
3	3.0	9.8	9.7	9.7
4	4.0	14.6	14.8	14.8
5	5.0	19.73	19.97	19.88

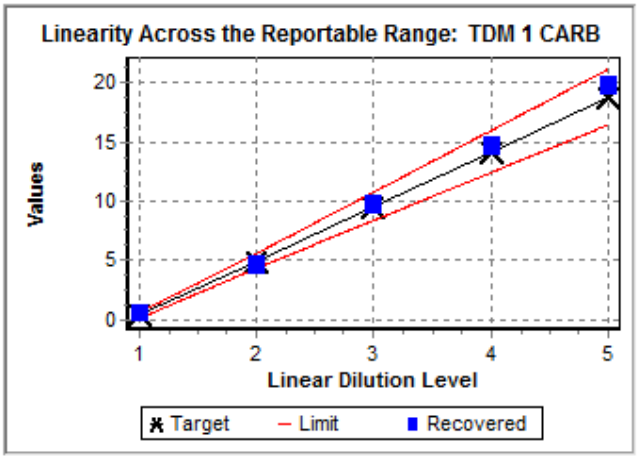
☐ Accept ☐ Comments

Tested 0.50 to 19.9 µg/mL

Validated 0.50 to 19.9 µg/mL

Mean versus Target Regression
y = 1.057x - 0.229
r^2=0.9985 SEy,x=0.3

X	Target	Mean	+/- Diff	% Diff	+/- Limit	% Limit
1.0	0.35	0.50	0.15	42.9%	0.25	N/A
2.0	4.97	4.67	0.30	6.0%	0.62	12.5%
3.0	9.58	9.73	0.15	1.6%	1.20	12.5%
4.0	14.20	14.73	0.53	3.7%	1.78	12.5%
5.0	18.82	19.86	1.04	5.5%	2.35	12.5%



Summary: In this case, calibration verification / linearity testing demonstrated that the method was giving a nonlinear response at the upper end and LGC Maine Standards Technical Support advised that recovery was not consistent with Peers. Recalibration and repeating the calibration verification / linearity testing verified the method's correct response.

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