Linearity Testing
Validation of Analytical Measurement Range (AMR)

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Adopted: 10/14/22 by J. Mills Barbeau, MD JMBarbeau MD

Reviewed	Date	Reviewed	Date
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Revisions:

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Principle and Intended Use

In keeping with CAP Regulations, verification of the analytical measurement range (AMR) is required when a method is initially placed in service and at least every six months. There should be a direct linear relationship between observed and known concentrations of a given analyte. If the calibration values span the AMR and has three levels that include the low, mid and upper range, then the AMR is considered verified. The AMR must also be verified if any of the following occur:

1. At changes of reagent lots unless the laboratory can demonstrate that the use of different lots does not affect the accuracy of patient/client results, and the range used to report patient/client test data
2. If QC shows an unusual trend or shift or is outside acceptable limits, and the system cannot be corrected to bring control values into the acceptable range
3. After major preventive maintenance or change of a critical instrument component i.e. Luminometer
4. When recommended by the manufacturer

Whenever possible, matrix appropriate materials should be run in duplicate at three levels that span the AMR. These three levels are to include an upper and lower limit of the AMR as well as a mid or clinically relevant value. Manufacturer recommended materials with known values and given levels of acceptability will be utilized whenever feasible. Ideally, the materials used should be close to the upper and lower limits of the AMR. If materials are not available to cover the full range of the assay, and/or the observed and known concentrations differ, then the span of the AMR that is tested and proved to be linear must be determined and approved by the Director or his/her designee. In general, the laboratory will utilize commercially available products specifically used to test the AMR. If those meet the upper and lower limit demands of our systems and follow the manufacturer's specifications for acceptability, then no additional testing will be performed.

Verification materials, Non-Commercial products

When choosing samples, an attempt should be made to match the matrix used for linearity to those that are used for clinical assays. If matrix problems occur, NCCLS recommends following manufacturer's guidelines. NCCLS lists the following specimens on which linearity testing may be performed in order of desirability:

Patient Sample Pool
Patient Sample Pool Spiked with Analyte
Pool Diluted with Saline
Commercial Control / Calibrator Material
Under-diluted / Overdiluted Commercial Control Material
Weighed amount of a particular substance diluted to the appropriate concentration

If these products do not include manufacturer's known values and levels of acceptability, then the lab may:

1. Determine a level of acceptability that the Director approves and/or
2. Utilize the CLIA criteria for levels of acceptability for Proficiency Testing as a guide to establishing a target and defined range of acceptability

Final Document and the Data Points

The final document will include a graph of the target values and the mean of the observed values. This document should include target data with acceptable means and ranges, date performed, name of performing technologist, and if applicable, linearity material name, lot and expiration date. The final graph, target and obtained values and statistical challenge will be maintained as a permanent record. This will then be reviewed and accepted by the Director / Manager of the area. If the data is not acceptable, corrective action may be taken to determine the reason why the AMR cannot be validated. (See QA Procedure as detailed in another section of this manual).

Attachment

Appendix L1, Established Limits of Acceptable Performance

Reference

Westgard, J; Westgard QC; www.westgard.com/2019-clia-changes, *Quality Requirements, 2019: CLIA Proposed Changes to PT Acceptable Limits, 2019.*

www.NGSB.org , *NGSP News: Harmonizing Hemoglobin A1c Testing; New certification Criteria beginning 2019.* Update 11/11/19.

Established Limits of Acceptable Performance

Biochemistry	NEW Criteria for AP 2019	Immunology	NEW Criteria for AP 2019
Alanine aminotransferase (ALT/SGPT)	TV ± 15%	Alpha-fetoprotein (tumor marker)	TV ± 20% or positive or negative
Albumin	TV ± 8%	Anti-TG	MCM used with manufacturer's ranges
Alkaline Phosphatase	TV ± 20%	ATPO	MCM used with manufacturer's ranges
Ammonia	TV ± 20%	Br	MCM used with manufacturer's ranges
Amylase	TV ± 10%	CA-19-9	MCM used with manufacturer's ranges
AST	TV ± 20%	C-reactive protein (HS)	TV ± 1 mg/dL or ± 30% (greater)
Bile Acid	TV ± 15%	Cancer antigen (CA) 125	TV ± 20%
Bilirubin Direct	TV ± 0.4 mg/dl or 20%	Carcinoembryonic antigen (CEA)	TV ± 15%
Bilirubin, total	TV ±20%	Cortisol	TV ± 20%
Blood gas pCO2	TV ± 5mm Hg or ± 8% (greater)	Estradiol	TV ± 30%
Blood gas pO2	TV ± 15 mm Hg or ± 15% (greater)	Ferritin	MCM used with manufacturer's ranges
Blood gas pH	TV ± 0.04	Folate, serum	TV ± 1 ng/mL or ± 30% (greater)
B-natriuretic peptide (BNP) & (proBNP)	TV ± 30%	Follicle stimulating hormone	TV ± 2 IU/L or ± 18% (greater)
Calcium, total	TV ± 1.0 mg/dL	Free thyroxine	TV ± 0.3 ng/dL or ± 15% (greater)
Carbon dioxide	TV ± 20%	Free T3	MCM used with manufacturer's ranges
Chloride	TV ± 5%	Free T4	MCM used with manufacturer's ranges
Cholesterol, total	TV ± 10%	Homocysteine	MCM used with manufacturer's ranges
Cholesterol, HDL	TV ± 20%	Insulin	MCM used with manufacturer's ranges
Cholesterol, LDLm	TV ± 20%	Human chorionic gonadotropin	TV ± 18% or positive or negative
Creatine kinase (CK)	TV ± 20%	Luteinizing hormone	TV ± 20%
Creatinine	TV ± 0.2 mg/dL or ± 10% (greater)	Parathyroid hormone	TV ± 30%
Ferritin	TV ± 20%	Progesterone	TV ± 25%
Gamma glutamyl transferase	TV ± 5 U/L or ±15% (greater)	Prolactin	TV ± 20%
Glucose (excluding FDA home use)	TV ± 8%	SHBG	MCM used with manufacturer's ranges
Hemoglobin A1c	TV ± 10% CAP ± 5%	Testosterone	TV ± 20 ng/dL or ±30% (greater)
Iron, total	TV ± 15%	T3 uptake	TV ± 18%
Lactate dehydrogenase (LDH)	TV ± 15%	T3	TV ± 30%
Lactic Acid	TV ± 0.4 mmol/L or 3 SD	TSH	TV ± 20% or ± 2 mIU/L (greater)
Lipase	TV ± 30%	T4	TV ± 20% or ± 1.0 mcg/dL (greater)
Magnesium	TV ± 15%	Vitamin B12	TV ± 25%
MTP/CSF	TV ± 20% or 2 SD (whichever is greater)	Vitamin D	MCM used with manufacturer's ranges
Osmo (Plasma/Urine)	Use Maine Standard data reduction (MSDR3) ± 3%	**Toxicology**	**NEW Criteria for AP 2019**
Phosphorus	TV ± 0.3 mg/dL or 10% (greater)	Acetaminophen	TV ± 15%
Potassium	TV ± 0.3 mmol/L	Alcohol, blood	TV ± 20%
Prostate Specific Antigen, total	TV ± 0.2 ng/dL or 20% (greater)	Blood lead	TV ± 10% or 2mcg/dL (greater)
Sodium	TV ± 4 mmol/L	Carbamazepine	TV ± 20%
Total Iron Binding Capacity (direct)	TV ± 20%	Digoxin	TV ± 15% or ± 2 ng/mL (greater)
Total Protein	TV ± 8%	Gentamicin	TV ± 25%
Triglycerides	TV ± 15%	Lithium	TV ± 15%
Troponin I	TV ± 0.9 ng/mL or 30% (greater)	Phenobarbital	TV ± 15%
Troponin T	TV ± 0.2 ng/ML or 30% (greater)	Phenytoin	TV ± 15% or ± 2 mcg/dL (greater)
Urea Nitrogen	TV ± 2 mg/dL or ± 9% (greater)	Salicylate	TV ± 15%
Uric Acid	TV ± 10%	Theophylline	TV ± 20%
Urine		Tobramycin	TV ± 20%
Sodium	Verichem 9000 use data reduction	Valproic acid	TV ±20%
Potassium	Verichem 9000 use data reduction	Vancomycin	TV ± 15% or ± 2 mcg/dL (greater)
Chloride	Verichem 9000 use data reduction	Total Bile Acids	Diazyme Linearity used with manufacturer's ranges
UN	Verichem 9000 use data reduction		* The red indicates Dr Latif's ranges
Creat	Verichem 9000 use data reduction		added on 12/2/2019 AU on 12/5/2019 Centaur.
Phosphorus	Verichem 9000 use data reduction		RFP. (draft)
Calcium	Verichem 9000 use data reduction		* + or - % of PEER (TARGET)
Uric	Verichem 9020 use data reduction		* + or - SD of PEER (TARGET)