Beaumont

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Special Chemistry Reagent Lot to Lot Comparison Procedure

Document Type: Procedure

I. PURPOSE AND OBJECTIVE:

New reagent lots must be tested in parallel with old lots before being placed into service. Comparisons must be done to verify that the new lot of reagent has maintained consistent results for patient specimens. Due to matrix differences, control materials alone are not sufficiently reliable for verifying lot-to-lot consistency of patient results. For qualitative tests, at least one known positive and one known negative sample from the old reagent lot must be tested against the new reagent lot. A weakly positive sample should be used in systems where patient results are reported in that fashion. For quantitative tests, lot to lot comparisons should include samples with results that span the analytical measuring range (AMR), including one or more samples in the lower third, middle third, and upper third of the AMR.

II. DEFINITIONS:

A. **Unassayed Controls** = Quality control (QC) material that is not supplied with pre-determined standard deviation (SD), Mean and ranges for the analytes contained within. Each Lab is expected to assay the material to establish control ranges. Unassayed QC is generally used to routinely monitor precision. Statistics are submitted for peer group comparison. Example: BioRad Liquicheck Immunoassay Plus controls.

B. **Assayed Controls** = QC material that is received with pre-determined SD, Mean and ranges for specific analytes. Some assayed QC are specialty controls used on a daily basis. Others are available for method evaluation, troubleshooting, or for backup in the event of questionable performance of unassayed QC. Example: Siemens BMG controls and DiaSorin Rubella IgG Tri-Level controls.

III. SPECIMEN COLLECTION AND HANDLING:

A. Patient specimens should be used to compare a new lot against the old lot, when possible, since it is patient specimens that are tested. If QC material is used, the material should have a peer group established mean value based on inter-laboratory comparison that is method specific and includes data from at least 10 different laboratories. However, QC materials may be affected by matrix interference between different reagent lots. Thus, even if results show no change following a reagent lot change, a

calibration inconsistency for patient specimens could nonetheless exist, and be masked by matrix interference affecting the QC material. It is for this reason that the use of patient samples is recommended.

B. The use of QC material alone is adequate to check a new shipment of a reagent lot currently in use, as there should be no change in potential matrix interactions between QC material and different shipments of the same lot number of reagent.

C. Patient samples (serum, whole blood, cerebral spinal fluid (CSF), etc.) should be used for the comparisons. Pull specimens from current day's run and/or from recent archive for comparison testing between current and new lots of reagent. Older samples, for difficult to obtain ranges, may be saved and used, but old and new lot comparisons must be run together at the same time for these samples.

NOTE: When selecting samples for quantitative assays, results from the lower third, middle third, and upper third of the AMR should be used for the comparisons. "Less than" and "greater than" values should not be utilized for quantitative assessments.

IV. CALIBRATION:

Check the calibration or adjustment date of the old lot. Recalibrate as applicable to the specific assay before performing the lot to lot evaluation. All new lots must be calibrated. See individual procedures for calibration information as well as reagent, supplies and equipment required to perform the lot to lot.

V. PROCEDURE:

A. **When a new lot of reagent arrives:**

1. Tape a "Last Box, Run New Lot" sheet on the last box of the old lot.
2. Bind all boxes of the new lot together, record the required information for all the fields on the yellow "New Lot" sheet, and affix the completed "New Lot" sheet to the top of the bundle. Place new lot behind the old lot so it is not accidentally put into use before comparison.
3. Evaluate the new reagent lot *as soon as possible after receipt*.

B. **New reagent lot evaluation:**

1. Check the calibration or adjustment, if applicable, of the old lot and recalibrate if needed. Run the appropriate number of patient samples for the comparison (see appendices) on the old lot. For quantitative tests, select a range of patient results that spans the AMR, including representative samples from the lower, middle and upper third of the AMR.
2. Place the old lot to the side (or take off instrument, if necessary).
3. Put the new lot into use, calibrate, and run controls in duplicate. Repeat the same patients that were run using the old lot. For some test systems, controls are matched with a given lot of reagent and have lot-specific ranges; in these cases, the controls should be tested with the appropriate lot.
4. Document QC and patient comparison results on the appropriate worksheet (see appendices). Log the QC results in the laboratory information system (LIS).
5. Evaluate the QC results (must be within current 2 SD QC range) for analyte tested. If QC is unacceptable:
    a. Run assayed QC, if available, on both lots of reagent.

b. Evaluate unassayed QC against peer group established mean.

c. Perform N=5 patient comparisons near range(s) of failed QC level(s).

6. Record the results for both lots on the appropriate lot to lot worksheets (see appendices) and evaluate patient results individually for acceptability. If the new lot is required for immediate use but failure(s) occur(s) within sample patients, accept the new lot based on QC acceptability alone and consult with the Lead Technologist or Technical Director for further direction.
7. Place documentation in the designated mailbox for the Lead Technologist. The Lead Technologist for the technical area may approve the new lot analysis, provided the QC and patient criteria are met. If necessary, consult with the Technical Director for further direction.
8. Place an “OK to Use” sticker on all of the boxes in the new lot. If there is a question regarding the acceptability of the new lot comparison, the “OK to Use” sticker should not be placed on the new lot until the Lead Technologist or Technical Director approves the lot to lot comparison.
9. Put the old reagent lot back into use until it is exhausted.

VI. CALCULATIONS:

(New Lot Result (B) - Old Lot Result (A)) / Old Lot Result (A) X 100 = % Difference

VII. INTERPRETATION:

The Lead Technologist will compare the results from the two lots. Specific acceptability criteria are noted on each lot to lot worksheet and in the following chart. If the results do not meet the stated tolerances, the Lead Technologist will remove the “OK to Use” sticker(s) and initiate appropriate action. The Lead Technologist will maintain records of each comparison.

Acceptability Criteria Options for Patient Specimens

A. Within absolute or percent limits, defined by analyte and analyzer, that are currently applied for semi-annual instrument-to-instrument comparisons.

B. Within evaluation limits (percent, absolute, SD) by analyte that are utilized by College of American Pathologists (CAP for proficiency testing.

C. Medical significance criteria.

Lot to Lot Criteria				
Assay	**Number of Samples**	**Qualitative**	**Quantitative**	**Tolerance**
AFT/Image Navigator				
ANA	3 (1 Neg, 2 Pos)	X		w/in 2 fold dilution
AtheNA				
SSA	2 (1 Neg, 1 Pos)	X		
SSB	2 (1 Neg, 1 Pos)	X		
Sm	2 (1 Neg, 1 Pos)	X		
RNP	2 (1 Neg, 1 Pos)	X		
Scl-70	2 (1 Neg, 1 Pos)	X		
Jo-1	2 (1 Neg, 1 Pos)	X		

Centromere B	2 (1 Neg, 1 Pos)	X		
Histone	2 (1 Neg, 1 Pos)	X		
dsDNA	2 (1 Neg, 1 Pos)	X		
DSX				
ACL IgA	3 (Neg,Low,High)	X		
ACL IgG	3 (Neg,Low,High)	X		
ACL IgM	3 (Neg,Low,High)	X		
B2GP IgG	3 (1 Neg, 2 Pos)	X		
B2GP IgM	3 (1 Neg, 2 Pos)	X		
CCP	3 (1 Neg, 2 Pos)	X		
Calprotectin	3 (Neg, Borderline, High)		X	15%
Gliadin IgG	3 (1 Neg, 2 Pos)	X		
Gliadin IgA	3 (1 Neg, 2 Pos)	X		
Myco IgG	3 (1 Neg, 2 Pos)	X		
Myco IgM	3 (1 Neg, 2 Pos)	X		
Parvo IgG	3 (1 Neg, 2 Pos)	X		
Parvo IgM	3 (2 Neg, Pos Pool)	X		
tTG	3 (1 Neg, 2 Pos)	X		
QuantiFERON	3 (1 Neg, 2 Pos)	X		
DxI				
AFP	20 (Spanning the AMR)		X	5.5%
Inhibin	20 (Spanning the AMR)		X	8.3%
PAPP-A	20 (Spanning the AMR)		X	10.0%
hCG	20 (Spanning the AMR)		X	8.3%
uE3	20 (Spanning the AMR)		X	10.0%
EPO	5 (Spanning the AMR)		X	15%
BAP	5 (Spanning the AMR)		X	15%
sTfR	5 (Spanning the AMR)		X	15%
EUROLab Workstation				
COVID-19 IgA	5 (2 Neg, 3 Pos)	X		
COVID-19 IgG	5 (2 Neg, 3 Pos)	X		
Immulite				
ACT	5 (Spanning the AMR)		X	15%
ATA	5 (Spanning the AMR)		X	15%
ATG	5 (Spanning the AMR)		X	15%

BP3	5 (Spanning the AMR)		X	15%
GH	5 (Spanning the AMR)		X	15%
IGF	5 (Spanning the AMR)		X	15%
TG	5 (Spanning the AMR)		X	15%
TSI	5 (Spanning the AMR)		X	15%
TIE	5 (Spanning the AMR)		X	15%
Liaison				
Measles	3 (1 Neg, 2 Pos)	X		
Mumps	3 (1 Neg, 2 Pos)	X		
Rubella	3 (1 Neg, 2 Pos)	X		
VZV	3 (1 Neg, 2 Pos)	X		
Toxoplasma IgG	3 (1 Neg, 2 Pos)	X		
Toxoplasma IgM	3 (1 Neg, 2 Pos)	X		
Lyme	3 (1 Neg, 2 Pos)	X		
CMV IgG	3 (1 Neg, 2 Pos)	X		
CMV IgM	3 (1 Neg, 2 Pos)	X		
EA	3 (1 Neg, 2 Pos)	X		
EBNA	3 (1 Neg, 2 Pos)	X		
VCA	3 (1 Neg, 2 Pos)	X		
VCM	3 (1 Neg, 2 Pos)	X		
HSV-1 IgG	3 (1 Neg, 2 Pos)	X		
HSV-2 IgG	3 (1 Neg, 2 Pos)	X		
Manual Tests				
VDRL	3 (1 NR, 2 R)	X		w/in 1 titer value
RPR	3 (1 NR, 2 R)	X		w/in 1 titer value
TP-PA	3 (1 NR, 2 R)	X		
HPF4	3 (1 Neg, 2 Pos)	X		
Endomysial IgA	3 (1 Neg, 2 Pos)	X		w/in 1 titer value
Mono	2 (1 Neg, 1 Pos)	X		
ANCA	3 (1 Neg, 2 Pos)	X		w/in 2 fold dilution
APCA	3 (1 Neg, 2 Pos)	X		w/in 2 fold dilution
APA	3 (1 Neg, 2 Pos)	X		w/in 2 fold dilution
AMA	3 (1 Neg, 2 Pos)	X		w/in 2 fold dilution
ASMA	3 (1 Neg, 2 Pos)	X		w/in 2 fold dilution
DNA Crithidia	3 (1 Neg, 2 Pos)	X		w/in 2 fold dilution

Phadia				
Various	10 (2 of each class 0-5)		X	15%
SPA				
CH50	5 (Spanning the AMR)		X	30%
Free Kappa	5 (Spanning the AMR)		X	20% or 0.3 mg/dL
Free Lambda	5 (Spanning the AMR)		X	20% or 0.3 mg/dL
IgG1	5 (Spanning the AMR)		X	15% or 40 mg/dL
IgG2	5 (Spanning the AMR)		X	15% or 15 mg/dL
IgG3	5 (Spanning the AMR)		X	15% or 10 mg/dL
IgG4	5 (Spanning the AMR)		X	15% or 10 mg/dL
Spectrophotometer				
G6PD	5 (Spanning the AMR)		X	20% or 3.0 U/g Hb
Citrate	5 (Spanning the AMR)		X	20% or 5 mg/L
Oxalate	5 (Spanning the AMR)		X	20% or 5 mg/L
Variant/D100				
A1c	5 (Spanning the AMR)		X	6% or 0.5 (% units)
A2/F	5 (Spanning the AMR)		X	8% or 0.4 (% units)
S	5 (Spanning the AMR)		X	6% or 0.3 (% units)

NOTE: Titering positive VDRL QC demonstrates various degrees of reactivity including reactive and weakly reactive results. This confirms that the reagents are able to detect specimens with low-grade reactivity, satisfying CAP checklist item IMM.41400.

The following assays/systems do not require a lot to lot evaluation as described above. However, follow the directions as indicated below:

A. Breath Hydrogen: Quantitative. Each new tank of calibrator gases is tested in duplicate against the previous calibrator tank. The tolerance is $\pm$4ppm H_2 and $\pm$1% CO_2.

B. Cold Agglutinin: Quantitative. No reagents to evaluate.

C. Cryofibrinogen: Qualitative. No reagents to evaluate.

D. Cryoglobulin: Qualitative. No reagents to evaluate.

E. Electrophoresis (Gel Techniques and Automated Electrophoresis): Controls and patient samples have a similar matrix. Therefore, the procedural controls are adequate to evaluate the performance of new lots.

F. Sweat Chloride: Quantitative.

1. Collection Reagents are evaluated for lot to lot performance concurrent with use. New lots of pilocarpine and K_2SO_4 electrolyte solution are acceptable when sufficient sweat is collected. New lots of sodium-free gauze are acceptable when the Level 2 control is acceptable in the quantitation procedure.
2. Quantitation Reagents are evaluated for lot to lot performance concurrent with use. New lots of the acid reagent are checked using blank, standards, and controls. New lots of gelatin reagent are also

validated by the blank, standards, and controls tested during each run. Tolerance for blanks and standards are given in the procedure, and quality control ranges are posted for the two levels of control materials.

G. Viscosity: No reagents to evaluate.

VIII. QUALITY CONTROL:

A. All levels of routine controls and assayed controls should be run with both old and new lots. The QC should be run on the new reagent in duplicate. See individual procedures. QC results must meet established acceptability criteria in order to approve a lot to lot comparison.

B. If the new lot is required for immediate use, but failure(s) occur within patient samples, accept the new lot based on QC criteria and consult with a Lead Technologist, Supervisor or Technical Director for further direction.

NOTE: For some test systems, controls are matched with a given lot of reagent and have lot-specific ranges; in these cases, the controls should be tested with the appropriate lot. For example, kit QC from the old lot for DSX assays should not be run with the new lot of reagent.

Attachments

Lot to Lot Forms

Approval Signatures

Step Description	Approver	Date
	Peter Millward: Chief, Clinical Pathology	9/28/2020
Policy and Forms Steering Committee Approval (if needed)	Jillian Trueman: Medical Technologist Lead	9/28/2020
	Timothy Kennedy: Pathologist	9/22/2020
	Leah Fontana: Mgr Laboratory	9/16/2020
	Jillian Trueman: Medical Technologist Lead	9/16/2020

Applicability

Royal Oak