

RT121 A Structured Approach to New Method Implementation

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Introduction:

Laboratories are implementing new methods and/or instruments on a regular basis. The approach needed may be relatively straightforward, particularly if the vendor is providing technical assistance, but it can be complicated by many factors, including:

1. The availability of specimens for correlation that span the clinical reportable range;
2. Sample integrity/stability;
3. Staff resources to gather and preserve specimens as well as perform the testing (if not performed by the vendor);
4. Laboratory, vendor, and pathologist expectations may or may not be congruent or clearly defined prior to assessing a new method; and
5. Compatibility of data collected with the laboratory's approach to statistical analysis;

The foregoing emphasizes the need for a structured approach that facilitates the process, is sufficiently flexible to accommodate unique aspects of the analyte being assessed, and is reasonably complete, thus reducing the risk of "forgetting something".

Discussion Questions:

1. Having determined a new method/instrument is to be implemented, what are the components of in the evaluation? Is there a defined approach to new method assessment that addresses the following?
 - a. Linearity – clinical reportable range (CRR) analytical measurable range (AMR)
 - b. Calibration (standards of known analyte concentration vis-à-vis signal) and calibration verification
 - c. Assess carryover
 - d. Quality control studies
 - i. Perform sufficient QC challenges to prove system in control before proceeding
 - e. Patient sample correlations
 - i. How many samples are enough to be statistically valid?
 - f. What statistical approach to correlations should be used?
 - i. Quantitative methods – chemistry, hematology
 - ii. Semi-quantitative methods – urinalysis
 - iii. Qualitative methods – immunology
 - iv. Unusual, at least in my experience, situations
 1. Blood culture incubator
 - v. Antimicrobial identification and susceptibility testing
 - g. Establish / validate reference range
 - h. Approve standard operating procedure (SOP)

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- i. Regulatory expectations – CLIA, accreditation
 - i. Observe record retention requirements
- j. Enroll in proficiency testing program
2. Caveats
 - a. Review literature (manufacturer's as well as peer reviewed) to familiarize yourself with the method
 - b. Discuss expectations prior to staff beginning the validation studies
 - c. Ensure study reagents are from the same lot throughout the study

Summary of key learning points:

1. Use a standardized approach to implementing a new method and/or instrument;
2. Apply the same general principles to areas in the laboratory that historically have been subject to this type of approach;
3. Remember to inform clinical staff of changes that may impact practice in a timely manner.

References:

- ⇒ Burtis, CA, et al, Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, Elsevier Saunders, Philadelphia, 4th edition, 2006, page 353;
- ⇒ Westgard, John, Basic Method Validation, Westgard QC, Inc., Madison, WI, 2nd edition, 2003 (<http://www.westgard.com/>);
- ⇒ NCCLS. *Method Comparison and Bias Estimation Using Patient Samples: Approved Guideline – Second Edition*. NCCLS document Ep9-A2 [ISBN 1-56238-472-4]. NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2002

New Method Checklist: Analyte: _____

Provide clinical pathologist/medical director (or designee) an electronic copy of the package insert and other vendor provide information prior to starting new method assessment

Status Date	Item	Comment(s)
<input type="checkbox"/>	Reference Range validation	❖ Age/sex ❖ Source of samples
<input type="checkbox"/>	Patient sample correlation and statistical analysis EP Evaluator Linear regression analysis	❖ Samples to cover AMR ❖ Samples to cover CRR ❖ Address both measured and calculated results ❖ If questions, ask clinical pathologist
<input type="checkbox"/>	Linearity	❖ Define values that are to be reported as > or < ❖ Define dilution expectations – what is medically necessary for quantitative reporting? ❖ List AMR and CRR for each analyte
<input type="checkbox"/>	Carryover	❖
<input type="checkbox"/>	What if tables completed?	❖
<input type="checkbox"/>	QC data and Precision studies	❖ SD and CV ❖ 2 or 3 level ❖ Meets pre-defined criteria? ❖ Available/appropriate at clinical decision levels?
<input type="checkbox"/>	Procedure – written and reviewed?	❖
<input type="checkbox"/>	Proficiency testing (PT) samples Available? / Results	❖
<input type="checkbox"/>	Units of measure	❖ Same as currently reporting? ❖ If not, what information needed for clinicians?
<input type="checkbox"/>	Medical Staff Memo	❖ Inform physicians of change ❖ Unique issues related to new method?
<input type="checkbox"/>	LIS issues addressed?	❖ Test plan developed with specific input from LIS ❖ Test plan implemented with acceptability criteria met per LIS and enduser section manager ❖ Specific signoff sheet indicating approval reviewed/signed by appropriate LIS and end-users a minimum of one week prior to go live
<input type="checkbox"/>	Report format review	<input type="checkbox"/> client <input type="checkbox"/> interim <input type="checkbox"/> cumulative
<input type="checkbox"/>	System issues addressed?	❖ Impact on other markets/consolidated database? If so, list
<input type="checkbox"/>	Staff notification	❖ Training ❖ Departmental communication – all sites
<input type="checkbox"/>	Special issues/concerns	❖

Final Approval: _____ Date: _____

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Carryover Studies

- 1) Reagent vs. sample carryover: these issues need to be conceptually distinguished as the sample paths through the instrument may or may not be common. The manufacture should make a statement as to what carryover studies are needed but the laboratory needs to assure itself that the manufacturer's conclusion is logical and by performing studies to confirm their affirmative statement.
- 2) The following studies are to be performed for each probe in the reagent/patient specimen handling routine, based on the additional information as clarified in the following paragraphs.
- 3) Reagent Studies: Determine if the manufacturer recommends reagent carryover evaluation
 - a) If yes, review type of valve and probe operation to determine if carryover is possible {i.e., is the instrument configured to permit use of the same four way valve for reagents that are known to or could cause crossover contamination?};
 - b) Discuss steps to assess carryover with the manufacturer's representative and the pathologist responsible for the section.
- 4) Patient Sample Studies:
 - a) If the sampling tips are used once ¹, perform the following study using samples that have extremely high values {e.g., use a relatively inexpensive assay with a high biologic dynamic range: bhCG in the 200,000 range [run undiluted] vs. 3 IU/L – the goal is to use a range that compares samples with values as high as reasonably possible vis-à-vis samples just above the low AMR – suitable material may be standards, calibrators, controls or known high or low patient samples}:
 - i) Run sequentially the high specimen once and then two aliquots of the same low specimen;
 - ii) Run sequentially aliquots of the same high specimen twice and then two aliquots of the same low specimen;
 - iii) Run sequentially aliquots of the same high specimen three times and then two aliquots of the same low specimen;
 - b) If the sample tips are washed and reused, perform the following study using samples that have extremely high values, as noted above:
 - i) Over three to five days, run the following combinations
 - (1) Run sequentially the high specimen once and then two aliquots of the same low specimen;
 - (2) Run sequentially aliquots of the same high specimen twice and then two aliquots of the same low specimen;
 - (3) Run sequentially aliquots of the same high specimen three times and then two aliquots of the same low specimen;
- 5) Ongoing assessment of carryover
 - a) Quarterly verification of findings at the time of initiation of the instrument is recommended

¹ The tip is not necessarily the issue – there may be tubing or other common features to the technology that could cause carryover. If there is none and the manufacturer warrants there is no carryover, then the confirmation of this claim is simplified.