Calibration Verification and the i-STAT System

INTRODUCTION

Calibration Verification is a procedure performed to confirm that the calibration of an instrument or test system has remained stable throughout the reportable range. In many countries, this procedure is called a linearity check. Because of the inherent stability of the i-STAT System, Abbott Point of Care Inc. does not make any specific recommendations for the calibration verification procedure. Therefore, it is the responsibility of the laboratory to determine when and how this procedure should be performed. The information presented below is intended to help the laboratory make this determination.

In the United States, laboratory regulations (CLIA) require that for tests categorized as Non-Waived, a calibration verification procedure be performed and documented at least once every six months. The information presented below supports Abbott Point of Care Inc.'s position that it is the cartridges, or more specifically, the sensors, rather than the analyzers that should be subject to the six-month check on the accuracy of the reportable range, and supports Abbott Point of Care Inc.'s claim that all analyzers that pass the Electronic Simulator test are equivalent, which should preclude the testing of three levels, twice a year, on each and every analyzer on site.

In addition to the six-month time frame for a calibration verification procedure for Non-Waived tests, CLIA and laboratory accrediting bodies in the US list the following as possible reasons to perform calibration verification:

- validate the reportable range of a test before the test system is put into use.
- verify that a change in reagent lot numbers does not affect either the reportable range or control values.
- troubleshoot when control values are out-of-range.
- verify that results have not been affected by maintenance or repair procedures.
STABILITY OF CALIBRATION IN THE i-STAT SYSTEM

The i-STAT System is a unit-use testing system. Components that cause shifts and drifts in results in multi-use analyzers: sensors (electrodes), calibration solution, fluid-handling channels and pumps, are housed in a disposable test cartridge. The sensors are exposed to sample only once, so there is no protein build-up which is a major cause for deterioration of sensor slope and the need to calibrate and/or verify calibration on a frequent basis in multi-use analyzers.

The stability and consistency of the manufacturing process allow the slope of the sensors to be programmed into the analyzer's software. A one-point calibration to set the intercept accounts for any day-to-day variation in testing conditions. When stored according to directions, the cartridges are stable up to the expiration date.

The analyzer houses the mechanical and electrical systems necessary to control fluid movement within the cartridge, control the temperature when measurements are performed at 37°C, measure barometric pressure, measure electrical signals generated by the sensors and display and transmit results. The analyzer’s functions are factory calibrated to specifications that are programmed into the analyzer along with acceptability limits, which when exceeded cause the analyzer to display quality check messages or to display *** rather than results.

The accuracy of results and dependability of the internal quality check system depend upon the ability of the analyzer to take accurate and sensitive signal readings from the sensors. To check this function, i-STAT developed an electronic control device. The Electronic Simulator simulates two levels of electronic signals that stress the analyzer's signal detection function both below and above the reportable ranges. Injecting signals directly into the analyzer allows very tight control limits to be set. Control limits for liquid controls are set wide enough to allow for sensor-to-sensor variation. All analyzers that pass the Electronic Simulator test are equivalent and any variations in results are caused by within and between lot variations in the cartridges.

The combination of unit-use cartridges, inherently stable electronics of the analyzer, and reliability of the Electronic Simulator check provides the stability needed for a point-of-care testing system and reduces the need for frequent stability or calibration verification checks.

VALIDATING THE REPORTABLE RANGE

The accuracy of results over the entire reportable range could be assessed by testing the same patient samples on the new system and on a system with known accuracy and comparing results using an acceptable difference criteria. However, it is difficult to find samples that cover the low and high ends of the reportable ranges of many analytes. Ideally, the samples used to validate the ranges should have the same matrix as the patient samples. Tonometered blood can be used to validate the ranges for $PCO_2$ and $PO_2$. But for most analytes, there are no whole blood samples commercially available for this purpose.

Although the i-STAT Calibration Verification Set is aqueous-based, the target values have been determined over many lots of cartridges and results on these solutions when compared to the target values should indicate the performance of a particular lot of cartridges.

ASSESSING LOT-TO-LOT VARIATION

Lot-to-lot variation over the entire reportable range for any reagent system could be assessed by testing calibration verification solutions on old and new lots in parallel. This procedure should be suspended once it has been determined that lot-to-lot variation is acceptable. Quality controls samples with concentrations at decision points should always be used to assess new lots or reagent before results are reported.
Because the manufacturing process for the cartridges produces consistent lots with little lot-to-lot variation, Abbott Point of Care Inc. does not make any recommendations for this procedure. Each new lot of cartridges should be assessed using the i-STAT quality control solutions according to the procedure in the System Manual.

TROUBLESHOOTING

Should quality control sample results fall outside of the acceptable ranges, calibration verification samples with very low or very high concentrations could be helpful in characterizing a reagent problem.

The i-STAT System was designed so that the intended users, who are not familiar with laboratory procedures, cannot make any adjustments that would affect results. The characteristics of the sensors are well known and results of control solutions would be sufficient for Technical Support specialists to help users resolve control out-of-range problems.

VERIFYING THAT RESULTS HAVE NOT BEEN AFFECTED BY MAINTENANCE OR REPAIR PROCEDURES

In multi-use systems, reagents and samples are run through the analyzer and, therefore, there should be a method of checking that all components are performing together according to specifications after any one component is affected. Calibration verification solutions can be used to verify that the calibration or slope of the measuring system has not been affected by the maintenance or repair procedure.

The user cannot perform any maintenance procedures on the i-STAT System. However, the software in the analyzer is updated periodically – a procedure that potentially could cause a change in results. In fact, software updates are released to ensure that results do not change over time. Calibration verification solutions could be tested to verify that results have not been affected. This procedure should be suspended or replaced with controls once it has been determined that software updates do not affect results. Since i-STAT has been effectively updating software for over 10 years, this procedure is not part of Abbott Point of Care Inc's. recommended quality program.

Repaired and newly purchased analyzers are received with factory calibration. Again, the Electronic Simulator can better assure that the analyzer's most important function is within factory specifications than calibration verification or control solutions.

Testing calibration verification samples or comparing patient sample results on a new or repaired analyzer with an older analyzer will assess cartridge performance only. Any variations in analyzer performance will not be statistically discernable above the performance of the cartridges. When multiple analyzers are to be used at a facility, Abbott Point of Care Inc. recommends including at least two analyzers in any performance verification studies so that statistics reflect the “system.”
<table>
<thead>
<tr>
<th>Product Title</th>
<th>Applicable Cartridges</th>
<th>Analytes</th>
<th>Available Levels</th>
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<tbody>
<tr>
<td>i-STAT Calibration Verification Set</td>
<td>G, Crea, E3+, EC4+, 6+, EC8+, G3+, EG6+, EG7+, CG4+, CG8+ and CHEM8+</td>
<td>Sodium, Potassium, Chloride, Ionized Calcium, pH, $P_{CO_2}$, $P_{O_2}$, $TCO_2$, Glucose, Lactate, BUN/Urea, Creatinine</td>
<td>1, 2, 3, 4, and 5</td>
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<tr>
<td>i-STAT TriControls Calibration Verification Set</td>
<td>G, Crea, E3+, EC4+, 6+, EC8+, G3+, EG6+, EG7+, CG4+, CG8+ and CHEM8+</td>
<td>Sodium, Potassium, Chloride, Ionized Calcium, pH, $P_{CO_2}$, $P_{O_2}$, $TCO_2$, Glucose, Lactate, BUN/Urea, Creatinine</td>
<td>1, 2, 3, 4, and 5</td>
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<tr>
<td>i-STAT CHEM8+ Calibration Verification Level 1B</td>
<td>CHEM8+</td>
<td>$TCO_2$</td>
<td>i-STAT CHEM8+ Level 1B material is available for purchase for customers who want to test lower levels of $TCO_2$.</td>
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<tr>
<td>i-STAT cTnI Calibration Verification Control Set</td>
<td>cTnI</td>
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<td>i-STAT BNP Calibration Verification Control Set</td>
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<tr>
<td>i-STAT CK-MB Calibration Verification Control Set</td>
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<td>i-STAT β-hCG Calibration Verification Kit</td>
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When performing the calibration verification procedure to meet a six-month calibration verification requirement, include each sensor and a representative selection of analyzers.
NOTES:

Calibration Verification or a linearity check for hematocrit can also be performed by a manual method using blood collected in lithium heparin tubes and manipulated to create three levels of hematocrit. Target values for Hematocrit for this manual method can be obtained from the bench top lab analyzer.

The upper limit of the reportable range for $P_O_2$ is 800 mmHg. The highest $P_O_2$ level in the i-STAT Calibration Verification set is just over 450 mmHg. Oxygen levels above 450 mmHg are so unstable in aqueous solutions that it would be impossible to make reliable measurements above 450 mmHg. Whole blood samples can be tonometered with 100% oxygen to create a sample around 700 mmHg at sea level.

REFERENCE