COMPLIANCE WITH CLIA CONTROL REQUIREMENTS

The CLIA Regulation, section 493.1256[1] - Control Procedures, states that the laboratory must perform control procedures as specified by the test manufacturer. It goes on to state that at least once each day of patient testing, a positive and negative control must be run for qualitative tests and two controls materials at different levels must be run for quantitative tests.

These requirements have traditionally been met for batch tests by running external controls. For unitized test systems, such as the VerifyNow System, where each patient sample is its own test run, quality control should be run for each sample. External quality controls, such as the VerifyNow Assay WQC (catalog # 85047), are an important element of the entire QC system, but they are not the most important QC element for unitized test systems.

The VerifyNow System provides "equivalent" quality control procedures including daily (or more frequent) system checks with the Electronic Quality Control (EQC) and **two levels of quality control included in each test device**. In addition to these equivalent QC procedures, Wet Quality Control (WQC) is run according to the manufacturer's recommendations. This system provides more comprehensive quality control than can be provided by external quality control testing alone. The quality control features of the VerifyNow System are described in detail below.

Description of the VerifyNow System Control Measures

The VerifyNow System includes a comprehensive system of quality control measures that are designed and manufactured into the VerifyNow System to provide control for the complete analytical process, as defined in the CLIA Regulation. Various QC mechanisms detect errors caused by various factors that can influence test results and potentially lead to erroneous results:

- Instrument system failure
- Reagent system failure
- Adverse environmental conditions
- Variations in operator performance

The VerifyNow quality control measures are described in detail below.

I. VerifyNow Instrument

Startup Checks: The VerifyNow Instrument performs a self-testing procedure each time the instrument is turned on. These startup self–tests include: 1) a system program and data memory check to ensure memory integrity; 2) a system temperature check to ensure the test warming plate reaches and maintains the proper temperature; 3) system check of proper operating voltages; and 4) system intra-communication validation. These self-tests serve as one component of the quality control check of the VerifyNow System.

[1] http://wwwn.cdc.gov/clia/regs/subpart_k.aspx#493.1256

System Security and Access Controls: The VerifyNow Instrument has been designed with features that restrict instrument access and improve patient result traceability:

- The laboratory has the option of assigning a User ID to each user, so that instrument access may be restricted to only trained operators who have demonstrated competency. If this feature is selected, a User ID and a password must be entered before an operator can use the instrument. This can facilitate CLIA compliance and prevent errors due to operator variability.
- If the User ID feature is enabled, it is also possible to assign different authority levels to each user, depending upon the instrument functions delegated to each user (e.g. running patient samples, QC procedures or changing instrument parameters).
- As an additional security feature, various instrument display screens may be set to time out after a default time period set by Accumetrics (2 to 5 minutes), or a time period set by the user (from 0 to 255 minutes). If the instrument is idle for a longer period, it will automatically return to the Main Menu and require re-entry of User ID if applicable.
- The laboratory may decide to assign a Patient ID to each patient sample, to allow traceability of test results. If this option is selected, the laboratory defines the format (number of characters) for the Patient ID number and the VerifyNow Instrument will not accept a patient sample without entry of a Patient ID in the designated format.

Electronic Quality Control: The Electronic Quality Control (EQC) is the primary quality control mechanism for the VerifyNow Instrument. It is a re-usable device that is inserted by the operator into the test port and is used to perform a comprehensive testing routine that confirms performance of the following key VerifyNow Instrument subsystems.

- Verifies proper performance of instrument optics.
- Confirms proper functioning of the pneumatics system that draws the sample into the test device and moves it into the test device for reaction and measurement.
- Monitors reagent mixing parameters and sample data acquisition.
- Confirms correct calibration parameters.
- Simulates testing at two levels of results, to check correct data acquisition and calculations. Specifically, the EQC measures two levels of turbidimetric signal that verify the dynamic range of the instrument. **One of these signals is at the level that would be observed in a patient with a minimal amount of platelet aggregation (Negative or Low Level Control), and the other represents a patient who demonstrates a significant amount of aggregation (Positive or High Level Control).**
- The required EQC testing frequency is specified in the VerifyNow Instrument by the user. Accumetrics recommends that the EQC be run at least on a daily basis, although the institution may select their preferred EQC testing frequency. When the established interval has elapsed, the user is locked out from running a patient test until the EQC test has been successfully completed.
- **When run according to Accumetrics' recommendations, the EQC meets CLIA requirements for daily QC of the instrument system.**

System Controls for Each Sample Tested: Each time a test device is run on the VerifyNow System, the instrument verifies the device expiration date, sample filling, optics performance, correct fluid transfer, and proper mixing. The system controls prevent the operator from running an expired test device. The system also detects certain other operator errors, such as placing the test device or the sample in the instrument at the wrong time, or removing the test device before the test is complete. These controls prevent reporting of an inaccurate test result. These controls exceed the CLIA requirement for daily QC because they are performed for each test device.

II. VerifyNow Test Device

Test Device Internal Controls: Each test device incorporates two levels of quality control to identify invalid test runs caused by random errors, reagent degradation or inappropriate blood samples. Before platelet activation and fibrinogen binding begin, the Negative (Aspirin) or Low-Level (PRUTest and IIb/IIIa) Internal Control performs a test for non-specific aggregation. During the active phase of the test, the Positive (Aspirin) or High-Level Internal Control channel monitors the reaction and calculates Clinical Control Units, which must fall within specified limits. A failure of either internal control results in an error message by the VerifyNow Instrument, which prevents the reporting of an inaccurate result. The test device internal controls can detect failures of the reagent system due to improper storage or handling conditions. The internal controls will also flag an improperly collected or mishandled blood sample, or a blood sample with certain types of interfering substances. The Test Device Internal Controls detect errors from the reagent system, adverse environmental conditions, and additional types of operator errors. **The Test Device Internal Controls exceed the CLIA requirement of daily controls because two levels of control are run with each test.**

Test Device Kit Temperature Indicator: Each VerifyNow Aspirin and IIb/IIIaTest kit has a temperature indicator on the outside of the packaging. The user is instructed to inspect the indicator upon receipt of the kit. If the indicator has changed color, the kit has been exposed to elevated temperatures, and a WQC Level 2 must be run to ensure that the reagents are performing properly. The Temperature Indicator detects errors due to adverse environmental conditions.

III. VerifyNow Test Wet Quality Controls (WQC)

WQC Levels 1 and 2 are available from the manufacturer for verifying the integrity of the VerifyNow System and for evaluating operator proficiency. WQC Level 1 and Level 2 are formulated at clinically relevant levels. In the VerifyNow Tests, Level 1 is representative of a sample with platelet inhibition, and Level 2 is representative of a sample with no platelet inhibition.

Laboratories may elect to run these controls on a regular basis for QC of the VerifyNow Tests. The manufacturer recommends that Level 2 WQC be run under the following conditions:

- Whenever a new shipment or lot number of VerifyNow Test sevices is received.
- When a temperature indicator changes color, indicating that a VerifyNow Aspirin or IIb/IIIa Test kit has been exposed to elevated temperatures.

- In the case of repeated failures of the test device internal control, to rule out degradation of test device reagents as the cause of the failure.
- VerifyNow Asaay WQC may be used as a tool for other types of activities required by the CLIA Regulation, other than the daily quality control requirements. These activities include the following:
- Proficiency testing
- Laboratory personnel competency evaluation
- Establishment and verification of system performance specifications (493.1253)[2]
- Analytical system quality assessment (493.1289)[3]

Accumetrics Customer Support can advise on the use of WQC as tools in meeting these CLIA requirements.

> **NOTE**: The recommendation for the VerifyNow IIb/IIIa Test and the VerifyNow PRUTest is to run Level 2 WQC with each lot or shipment, or every 30 days.

IV. Manufacturer's Quality Control Procedures

To ensure that VerifyNow System components are of the highest quality, the manufacturer subjects its products to rigorous quality control procedures before they are shipped to customers.

- Each VerifyNow Instrument is tested mechanically, optically and electrically throughout the manufacturing process. The instrument's performance is validated by comparing it to Accumetrics' internal reference standards. The validation process consists of the following:
- Test results are correlated to results from a qualified reference VerifyNow Instrument
- Each instrument is extensively tested with previously qualified lots of VerifyNow Test devices.
- Testing includes multiple replicates of previously qualified lots of WQC control materials.
- Each lot of VerifyNow Test devices is tested against a previously qualified lot of test devices. Testing includes multiple replicates of WQC and blood from several normal donors.

In summary, the VerifyNow System includes a comprehensive set of quality control features, which have been designed and incorporated into the system. The VerifyNow quality control features control all aspects of the analytical process, as defined in the CLIA Regulation:

- Test system – instrument and reagent system
- Operator
- Environmental factors

Running the VerifyNow System according to Accumetrics' recommended procedures meets all the CLIA quality control requirements.

[2] http://wwwn.cdc.gov/clia/regs/subpart_k.aspx#493.1253
[3] http://wwwn.cdc.gov/clia/regs/subpart_k.aspx#493.1289