Quality Control Primer

The ultimate goal of laboratory testing is to provide the physician with as accurate a result as possible on all tests ordered. This is accomplished several ways: adequately trained personnel; following a complete policy and procedure manual; performing scheduled preventative maintenance, calibration, quality control, and quality assurance. This LabFacts focuses on Quality Control (QC) as an essential element of all test systems in your laboratory.

Requirements for good laboratory practice and COLA Laboratory Accreditation programs are underlined.

TEST SYSTEMS

Quality control samples are tested routinely to establish the reliability, accuracy, and precision of a test system. In general, a test system includes the following elements: an instrument, reagents, disposables, specimens, calibrators, and controls. These elements take many forms in the different specialties of clinical laboratory science. A test may be either qualitative or quantitative. Qualitative tests are reported as positive/negative or 1+ to 4+ or few, moderate, many. Quantitative tests report an actual number or amount of a substance being tested. Quality control requirements will vary depending on the test method in use.

Each of the elements of a test system has a role in achieving an accurate result:

- The instrument must be maintained within specifications established by the manufacturer.
- Reagents must be used within their expiration dates and stored according to their label instructions.
- Specimens must be collected, processed, and stored for optimal recovery of the substance being tested.
- Calibration materials (formerly called standards), are solutions of known value for the analyte being tested. They are used to set the instrument to give an accurate result. For example: A 100mg/dL calibrator would be set to read 100mg/dL on the instrument. Most test systems use at least three levels of calibration material. These calibrators set the benchmark figures against which other tests are measured.
- Quality control materials are similar to calibrators. QC material is run in the same manner as a patient specimen to verify that the instrument was set to read properly when it was calibrated. It is also required to be performed each day that patient results are reported to verify the continued good operation of the test system. If the QC material does not give the expected result, it signals an error in the test system that requires further investigation before patient results are reported.

QC material is usually serum- or whole blood-based and contains many substances normally appearing in a patient specimen. Most quantitative quality controls have pre-established, known (assayed) ranges for many analyte/instrument combinations. However, some controls are unassayed and therefore require the laboratory to establish its own control ranges. There is no advantage to purchasing unassayed controls for the POL setting.

Failure in any of the above elements of a test system may compromise patient test results. Test systems are purposely designed to be simple to use in order to eliminate mechanical and human sources of error. Computerization has enhanced this simplicity. However, **no instrument or test system is totally error free** and therefore certain minimum steps to assure quality results are required. CLIA regulations attempt to address all elements of a test system where errors could compromise a result. These regulations established **minimum** standards for assuring that accurate results are reported by a laboratory.

CONTENT OF A QUALITY CONTROL PROGRAM

Quality control is an essential element of all test systems! Therefore, a written quality control program should be in place and routinely followed for all tests performed in your laboratory. (COLA and CLIA do not require QC for waived tests, this additional level of assurance is at the discretion of the laboratory director and staff.)

Your Quality Control Program should specify the:

- Type of controls for each test.
- Number of controls to run and at what frequency.
- Expected range of the control material.
- Corrective actions to take in response to out of control situations.
- Process of proper documentation and periodic review by the laboratory director.

Type

The type of controls to use should be selected based upon the manufacturer's recommendations. Some QC material is supplied as a part of a kit test system, such as rapid Strep tests, mono tests, pregnancy tests, etc. Some manufacturers supply QC material for a specific test system at an additional cost. How-

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ever, it is not always necessary to purchase their QC material. The goal is to find a product that:

- Is relatively inexpensive.
- Can be conveniently stored.
- Has a long shelf-life.
- Is easy to reconstitute.
- Provides reliable and consistent results for the tests it is used to control.

Number and Frequency
The instrument or kit manufacturer determines the stability of the test system and establishes the recommended number and frequency of controls. CLIA regulations set minimum standards for frequency and number of controls. If the manufacturer sets a higher standard than CLIA, then the manufacturer's standard **must** be followed. For example: chemistry tests require a minimum of two levels, normal and abnormal, to be run each day of testing. However, some instrument manufacturers require three levels of controls daily or sometimes more frequently. Review the manufacturer's instructions and the COLA criteria when establishing your quality control program.

Expected Range
Included with your quality control material will be an assay sheet or package insert. The product has been tested and a range of expected values was determined by the manufacturer. Review this enclosed assay sheet to find your instrument or method and the expected range established. This is the range of values that your QC results will fall within if your test system is functioning properly.

Corrective Action
Most quantitative quality control ranges are set by the manufacturer at plus or minus (+/-) two standard deviations (2 SD). This is a statistical range calculated to include 95 percent of all values achieved by repetitive testing when a test system is functioning normally. This also means that, statistically, one value out of 20 can be expected to fall outside this range. These are called statistical outliers and are not due to error in the test system. You will never be able to eliminate these statistical outliers.

The purpose of quality control is to identify and eliminate, through corrective action, sources of error. Put simply, corrective action should be taken when controls for a test system give values outside the expected range or when other out of control situations are identified. The specific corrective action will vary with the test system and the problem.

QA Review and Director Review
Essential elements of a QC program are:

- Periodic lab director or supervisor reviews of QC results for all specialties of testing.
- Periodic reviews of corrective actions taken and their effectiveness in identifying and solving errors.
- Periodic reviews to ensure that all QC policies are being followed.

These activities are easily accomplished, but are often overlooked in some laboratories. Refer to COLA LabFacts 3 *Responsibilities of the Laboratory Director* for further information.

So far, a test system with quality control as an essential element has been defined, and the essential elements of a quality control program have been outlined. This is the basic structure of a Quality Control Program that will serve as an early warning system for problems developing in your test system.

DOCUMENTATION

Evaluation of QC results is easy if you know what questions to ask. The key is proper documentation at every stage of the process. QC logs/charts should contain the following information for each test and level of control:

- Lot number.
- Expiration date.
- Appropriate expected QC range.
- Dates performed.
- The initials of the person performing the test.
- Results obtained from daily QC performance.

These details are necessary to allow for proper evaluation of the QC results. Most laboratories establish a protocol to record QC results on a log and/or chart that contains this information. Any results that fall outside the expected range are identified and followed-up with corrective action. QC records should be retained for two years, or in the case of immunohematology, five years.

QUANTITATIVE QUALITY CONTROL

Some tests are more critical than others or have a narrower range of tolerance for error. Your laboratory director or clinical consultant can help determine which tests in your laboratory require closer scrutiny. Hospital and reference laboratories routinely evaluate QC results using basic statistical tools. One such tool is the Levey-Jennings (L-J) chart or graph. Some QC material or instrument manufacturers encourage the use of these charts by providing forms for that purpose. Most charts provide a means of "plotting your dots" on a graph where the horizontal axis corresponds to the days of the month and the vertical axis is incremented by the expected range of values for the QC material. Some form of graphical representation of quantitative QC data is required.

Figure 1 is an example of a modified and simplified version of this type of chart. (Also attached are two blank forms that can be adapted for use in your laboratory.) This chart allows the user to "plot" the QC result at the same time that the result is logged. This is a big time saver over the standard method, which had been one of the roadblocks to its use. The same information can be gleaned using this chart in lieu of the standard one. It provides information that is invaluable when evaluating the reliability of a test system.

Some quality control manufacturers offer a monthly statistical analysis service to laboratories that use their products. This analysis calculates the expected range and graphs the results submitted by the laboratory. There are also many instruments that automatically plot and store the values in its computer memory for periodic retrieval or printout. The major drawback of these systems are their lack of timeliness. The value of using QC charts is their ability to visually represent systemic errors as they develop, allowing corrective action to be taken often before the controls fall outside the expected range. Corrective action performed at this point would cause little or no downtime, while patient test results can still be reported. Reviewing the charts at monthly intervals or more, negates the early warning system and is, therefore, not as effective. The review, in many cases, would not be timely enough to anticipate a major breakdown.

For example, suppose a laboratory does not evaluate its controls routinely using charts but relies solely on a monthly analysis program.

- A problem requiring corrective action occurs in Week One.
- Proficiency testing specimens are tested and reported in Week Two along with numerous patient specimens.
- The problem is not recognized until over a month later when the monthly analysis is returned to the lab. Corrective action is taken, but the laboratory's proficiency testing and patient test results may have been inaccurate.

Timeliness is key when evaluating the need for corrective action in response to out-of-control situations identified using these charts. Evaluation of QC data should be a routine part of performing daily quality control.

QUANTITATIVE QC CHART INTERPRETATION / CORRECTIVE ACTION

The remainder of this LabFacts outlines the easy interpretation of the QC charts shown in *Figure 1*, and when appropriate corrective actions are necessary. Two basic situations are identified by the QC chart — shifts and trends. These can only be identified by using some form of graphic representation of quality control results.

Trends: Trends consist of five consecutive values in a row (higher or lower), that start anywhere and end anywhere on the chart (*Figure 1*). Trends reflect gradual changes in control values due to changes in instruments, reagents, or controls. Some causes include:

- Gradual deterioration of reagents or controls.
- Increasing contamination of reagents or controls.
- Reagents or controls approaching expiration dates.
- Protein build-up or occlusion of tubing or apertures.
- Lamp bulbs fading.

A key to identifying the source of a trend can be found by asking:

- Is the trend appearing only on one or all levels of control?
- Is the trend appearing on other tests the control material is used to control?
- Is the trend appearing on one test performed by that instrument or many?

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Corrective action depends on the problem. Deteriorated reagents or controls should be replaced with fresh ones; new vials or lot numbers of controls should be tested; or preventive maintenance and cleaning should be performed. If the problem is not corrected by these measures, consult your instrument manual troubleshooting guide or call the manufacturer for assistance.

Shifts

Shifts consists of five consecutive values randomly scattered on one side of the mid-range value (mean) or the other (*Figure 1*). If the average was calculated using the values for the previous five days, a new mean value would result. Therefore, it is said that there was a "shift" in the mean value away from what was expected. It is not necessary to calculate the mean because it is visually obvious from the chart.

A shift is observed when:

- New lot numbers of reagents are put in use.
- Major instrument preventive maintenance work-up is performed.
- New lot numbers of controls are put in use.
- Major instrument malfunction occurs.

The first two situations are easy to identify and correct by recalibrating. When new lot numbers or brand names of controls are put into use, the QC chart and computer interface (if present) must be adjusted for the appropriate QC ranges for proper interpretation.

The value in reviewing these charts is to identify an instrument malfunction before patient results are affected. Recalibration may solve the problem, however, sometimes more detective work is needed to find the source of the shift. Your instrument manual may provide clues to help in this process. A step-up in the frequency at which preventive maintenance is performed may be a possible solution. A service call is sometimes necessary.

All corrective action should be documented either on the QC chart or in a corrective action log. *Figure 2* is a combination Quality Control/Quality Assurance Log. It incorporates all of the information useful to include (using our example in *Figure 1*). This log can be photocopied on the reverse side of the QC chart for easy reference by all laboratory staff.

It is the laboratory director's responsibility to assure the accuracy of all test results. Laboratory staff usually require training in the performance of quality control according to established protocol and in the evaluation of the results. The laboratory director must review the quality control values periodically and document this review.

These notations will provide clues when evaluating future QC problems. It is also necessary to maintain these records for review during an on-site survey. The survey goes more quickly when the QC documentation is complete. A quality assurance review should be conducted periodically to evaluate the effectiveness of the corrective action taken. From this, measures can be identified that will prevent future QC problems.

Examples of these include:

- Limiting the time controls are left at room temperature
- Using a more accurate pipette to reconstitute controls
- Increasing the frequency of preventive maintenance
- Increasing the frequency of recalibration or calibration verification

CONCLUSION

Performing tests without quality control is like playing darts without a dart board, the results are meaningless! Quality control will tell you when you hit the bullseye with patient test results. Carrying the analogy of the dart board a bit farther:

- The dart board is the expected range the QC values should fall within, usually +/- 2 standard deviations.
- The bullseye is the mean or mid-range value of the expected range.
- The darts are the QC results obtained.

The more values that fall close to mean, then the more accurate the test is considered to be. The distribution of the darts on the dart board is an indication of the precision of the test. The frequency of total values that land on the board is a measure of a test system's reliability.

Some laboratories with more sophisticated testing or more specially trained laboratory staff will elect more involved quality control procedures. However, the process outlined here will satisfy the quality control needs for most quantitative physician office laboratory testing.

QUALITY CONTROL CHART

TEST/INSTRUMENT_____**TESTING PERIOD**_____

LEVEL 1 LOT#_____**EXP.**_____ **LEVEL 2 LOT#**_____**EXP.**_____

DATE	O	Low	Mean	High	O	O	Low	Mean	High	O	I

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EXAMPLE

QUALITY CONTROL CHART

TEST/INSTRUMENT *Glucose* **TESTING PERIOD** *January 1 - February 8, 1995*

LEVEL 1 LOT# *123456* **EXP.** *3/95* **LEVEL 2 LOT#** *78910* **EXP.** *3/95*

RANGE *90 ? 100 ? 110* *180 ? 200 ? 220*

DATE	O	Low	Mean	High	O	O	Low	Mean	High	O	I
1/2/95			100					204			BS
1/3/95			102				195				BS
1/4/95		97						210			PJ
1/5/95			105					201			BS
1/6/95			102				185				PJ
1/7/95		96					190				BS
1/9/95			100					205			BS
1/10/95		95					199				BS
1/11/95		97						203			PJ
1/12/95			101					210			BS
1/13/95			105					214			PJ
1/14/95				110			(see note Figure 2)		221		PJ
1/17/95		(see note Figure 2)			112		199		225		PJ
1/18/95		97						205			PJ
1/19/95			100					201			BS
1/20/95			102				190				BS
1/21/95		97					185				BS
1/23/95		96					191				PJ
1/24/95			105					215			PJ
1/25/95			104					220			BS
1/26/95				110				210			BS
1/27/95			106				200				PJ
1/28/95			107					215			BS
1/30/95			101					208			BS
1/31/95		(see note Figure 2)	105					220			BS
2/1/95				110				204			BS
2/2/95					112			210			BS
2/3/95		(see note Figure 2)	104				197				PJ
2/4/95		99					190				PJ
2/6/95			100					208			PJ
2/7/95		95						210			BS
2/8/95		90					183				BS

Figure 1

QUALITY CONTROL CHART

TEST NAME_____ **INSTRUMENT**_____ **TESTING PERIOD**_____

	LEVEL 1 LOT#			EXP.		LEVEL 2 LOT#			EXP.		LEVEL 3	LOT#		EXP.	
	RANGE					RANGE					RANGE				
DATE	O	Low	Mean	High	O	O	Low	Mean	High	O	O	Low	Mean	High	O	Init

QUALITY CONTROL / QUALITY ASSURANCE LOG

DATE	PROBLEM IDENTIFIED	CORRECTIVE ACTION	INITIAL
	QA REVIEW	LAB DIRECTOR REVIEW	

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	QA REVIEW	LAB DIRECTOR REVIEW	

QUALITY CONTROL / QUALITY ASSURANCE LOG

DATE	PROBLEM IDENTIFIED	CORRECTIVE ACTION	INITIAL
1/14/95	*High control--outlier*	*Watch for trend--could be statistical--*	*PJ*
		accept run	
	QA REVIEW	**LAB DIRECTOR REVIEW**	*JD*
	None needed		

DATE	PROBLEM IDENTIFIED	CORRECTIVE ACTION	INITIAL
1/17/95	*Definite trend--both levels of control.*	*Opened new vials of controls--reran--*	*PJ*
		both OK--no further action.	
	QA REVIEW *--Recommend review*	**LAB DIRECTOR REVIEW** *John Doe, MD*	
	of time controls at room temperature.		

DATE	PROBLEM IDENTIFIED	CORRECTIVE ACTION	INITIAL
1/31/95	*Shift on both levels of controls--new lot*	*Recalibrated.*	*BS*
	number of reagents used as of 1/26/95--		
	not recalibrated.		
	QA REVIEW	**LAB DIRECTOR REVIEW**	

DATE	PROBLEM IDENTIFIED	CORRECTIVE ACTION	INITIAL
2/2/95	*Trend possible--level one only--or*	*No action taken--watch closely.*	*BS*
	possible shift uncorrected by recalibration		
	on 1/31/95.		
	QA REVIEW	**LAB DIRECTOR REVIEW**	

DATE	PROBLEM IDENTIFIED	CORRECTIVE ACTION	INITIAL
2/3/95	*Trend on level one only.*	*Made up new level one control--reran it--*	*PJ*
		it is in range.	
	QA REVIEW*--Look into new brand*	**LAB DIRECTOR REVIEW** *John Doe, MD*	
	of controls with longer shelf life or aliguot them.		

Figure 2