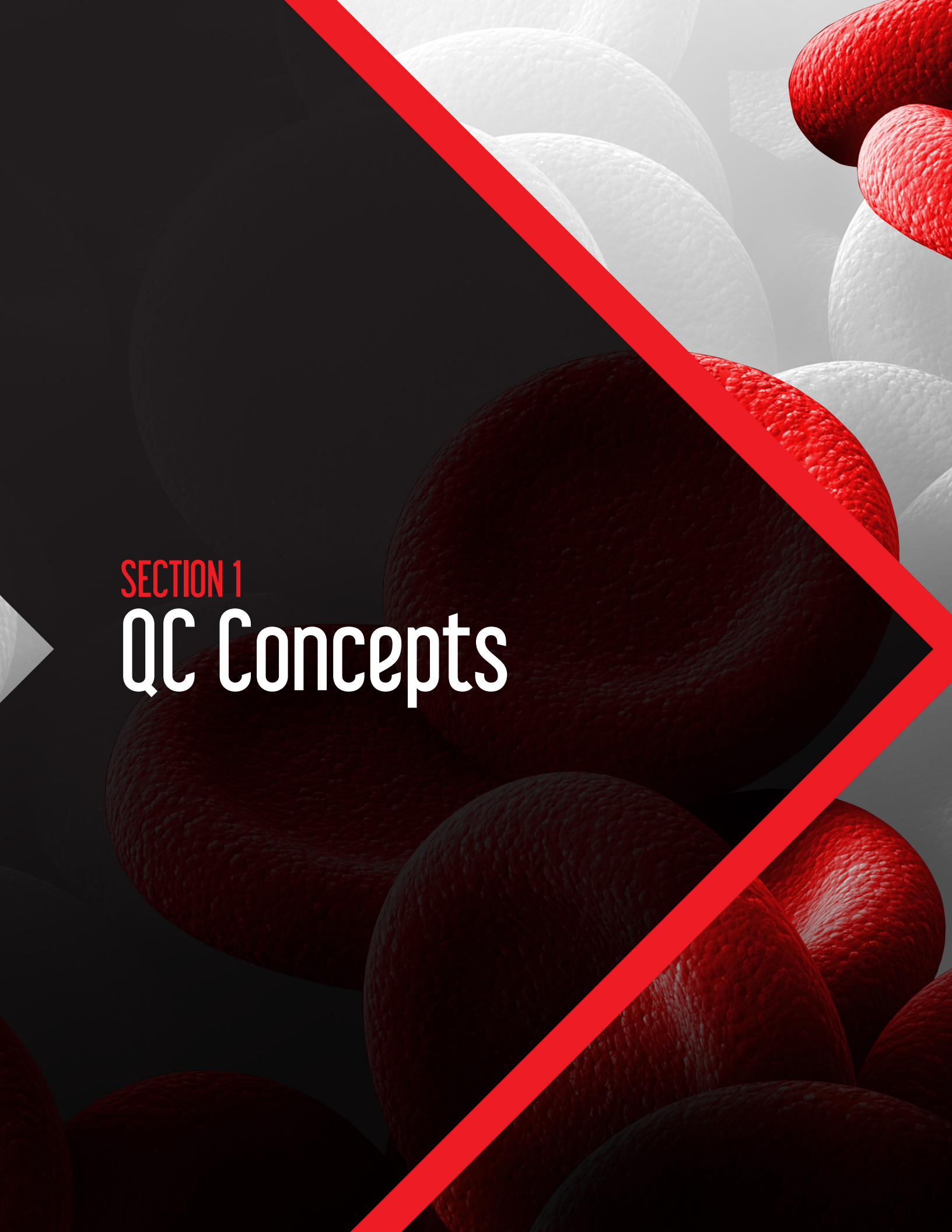
QUALITY CONTROL (QC) INFORMATION AND TROUBLESHOOTING GUIDE

HEMATOLOGY

This document is not intended to replace the information in your Instructions for Use Manuals (IFU).

Information in the Instructions for Use Manual(s) supersedes information in any other manual.

BECKMAN COULTER



SECTION 1

QC Concepts

Quality Control (QC) Overview

QC is performed routinely to ensure that an instrument is consistently reporting reliable sample results. Each laboratory should establish their own QC program, complying with accreditation guidelines.

There are many benefits when a comprehensive QC plan is implemented in the laboratory to ensure the reporting of accurate sample results, verification of instrument functionality and for troubleshooting irregularities. Refer to Section 2, Troubleshooting Checklist.

Beckman Coulter recommends participating in the hematology Inter laboratory Quality Assurance Program (IQAP) as part of the laboratory's quality control plan.

Quality Control Terminology *(Please refer to the Glossary see pg 2-7 for definitions of commonly used quality control terms.)*

Prerequisites of a QC Program

Functionality

The only way to detect if an instrument is malfunctioning is by understanding its functionality.

Need to know all aspects of the:

› principles of operation

› startup or daily checks

› shutdown

› normal sights and sounds of the instrument

Proper Specimen Collection

Analyze only specimens that were properly collected and stored.

› Venipuncture collection - ensure proper amount of blood was drawn into the anticoagulated collection tube and mixed thoroughly; otherwise, cell damage or small clots could occur and the results may be adversely affected.

› Micro collection or finger stick - ensure cleanliness of puncture area, and keep gauze or tissue particle away from the blood sample.

References for whole blood collection:

› Collect whole blood in EDTA according to tube manufacturer's instructions

› CLSI publication H4-A5 (for capillary)

› CLSI publication H3-A6 (for venipuncture)

› CLSI publication H18-A3 - Procedures for the Handling and Processing of Blood Specimen Guidelines

Check Sample Results

Check sample results for flags, codes, messages, normal values, and consistency with the patient's condition. Need to be able to:

recognize printed flags, codes, messages on a sample report

understand the meaning of the flags, codes, messages on the report

Delta Checks

Monitor particular patient sample results by comparing the current results to previous results within laboratory defined limits. Delta check flags are an indication of a significant change if results due to a change in patient condition or possibly instrument operation.

H&H Check

The H&H check uses patient hemoglobin (HGB) and hematocrit (HCT) results as QC method. Typically, HCT = ([HGB x 3] +/- 3). H&H failures may be an indication of change in results due to patient condition or instrument operation.

QC Techniques for the Laboratory

No single QC method can provide all the information for truly effective quality assurance.

A good Quality Control program consists of instrument and control checks, preventive maintenance (if required), good record keeping, and technologist review. In the hematology laboratory, calibration, commercial controls, patient controls, XB, XM, extended QC, participation in IQAP and proficiency testing are all techniques that help assure quality. QC with controls and XB could pick up a trend or shift in the results, and this evaluation of both sources in a combined method could provide very useful information.

Instrument Checks

Even before you run controls to check instrument accuracy and precision, it is important to verify that the entire system is working properly. These routine instrument checks are detailed in the Startup or Daily Checks section of your instrument manuals. If instrument problems are suspected, verify instrument precision and carryover and troubleshoot according to your laboratory protocol.

QC Procedures

Beckman Coulter hematology systems allow the use of multiple quality control techniques. Beckman Coulter recommends that Quality Control checks be performed using patient and/or commercial controls at intervals established by your lab. When using a commercial control, refer to the package insert to determine which method of sample presentation to use.

NOTE: Failure to recover control values within your lab's expected limits or the presence of unexplained shifts or trends in any method of presentation should be investigated. Patient results obtained between the last acceptable control run and an unacceptable control run should be re-evaluated to determine if patient test results have been adversely affected. If necessary, take corrective action.

Setting Up Controls

A control is a substance used in routine practice for monitoring the performance of an analytical process or instrument. Refer to Setup > Quality Control in the respective instrument IFU for information on setting up controls, and for information on automatic configuration, printing, host transmission, Auto Stop and other features.

Commercial Controls

Beckman Coulter controls are manufactured specifically for use with the full range of Beckman Coulter instrument and reagent systems. They are available in levels to monitor a range of clinical values. Be sure to read the control Instructions for Use (IFU) thoroughly. The IFU can be used as a troubleshooting aid. It describes how the product should be used, how to tell if the product has deteriorated, and lists steps to take when investigating a problem.

Monitoring Adjustments

The Clinical and Laboratory Standards Institute (CLSI) recognizes the need for monitoring QC results, and recommends periodically recalculating and adjusting QC statistics. When doing so, it is important to include all valid data collected since the material was put into use. When re-evaluating QC ranges, only omit data points caused by known operator or instrument error. Do not delete data points simply because they lie outside a 2 SD range. These outlying points may be part of the normal distribution, and eliminating them from the data set will not account for true variability.

Introducing a New QC Lot

When evaluating a new lot of the same QC material, it is recommended that data be collected alongside the current QC lot. The existing QC lot SDs, which have been developed over a long period of time, are a good indication of the variation to expect from the new QC lot, assuming that the means do not differ significantly.

Establishing QC Ranges

Each laboratory must establish a test-specific acceptable range of quality control values for each type of analyzer.

If the QC results are out of range, investigate if there is a problem with the control material. Try a new vial or lot number of the commercial product.

Laboratories are required to verify control mean and expected ranges when using commercial controls. Follow guidelines for quality control ranges as established by:

- Clinical and Laboratory Standards Institute (CLSI)
  Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions: Approved Guideline. CLSI document C24-A3 (ISBN 1-56238-613-1). Wayne, Pennsylvania (2006).
- Clinical Laboratory Standards Institute (CLSI)
  Laboratory Quality Control Based on Risk Management Approval Guideline. EP23-A (ISBN 1-56238-767-7) Wayne, Pennsylvania (2011).
- College of American Pathologists (CAP)
  Hematology and Coagulation Checklist. HEM.25870 Commercially Assayed Controls. Northfield, IL (2012).
- International Organization for Standardization (ISO)
  Medical Laboratories - Particular requirements for quality and competence. ISU 15189. Geneva, Switzerland: International Organization for Standardization; 2007.

Levey-Jennings Chart (QC Chart)

The Levey-Jennings QC Chart is the one most commonly used to show the results of a control for a specified period in a graphic form. This chart depicts the position of data points relative to the assigned mean. The results are listed by date and time. The QC Chart is available from either the workstation or data manager.

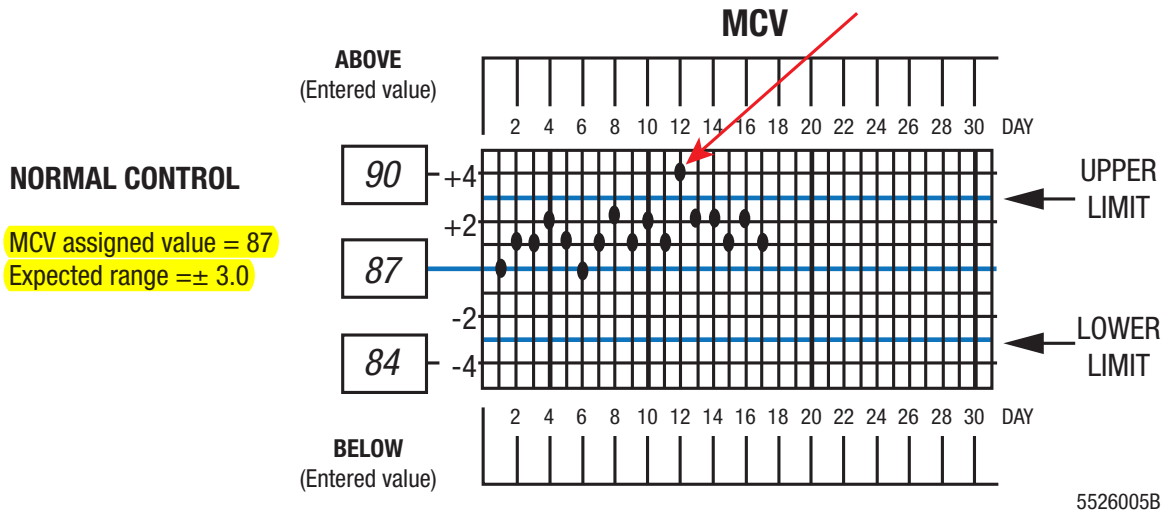
Outliers

Outliers are discrepant values. Values which do not agree with the pattern of the majority of other values. They may be due to mistakes or they may represent a significant finding. Figure 1.1 shows a graph of MCV control results recorded for a 17-day period for a normal control level:

- The MCV assigned value is 87 and is used as the mid-line.
- The expected range is ±3.0 and is used to define the low and high limits.

By using these lines it is easy to quickly identify the outlier on day 12. The reason for the outlier may have been "chance." The probability for this value to be outside the limit is about one time out of every 20 times you run the control. If your run the control one more time, and the result is in, you can presume the original result was out by chance.

Figure 1.1 Outlier on MCV Results



Trends

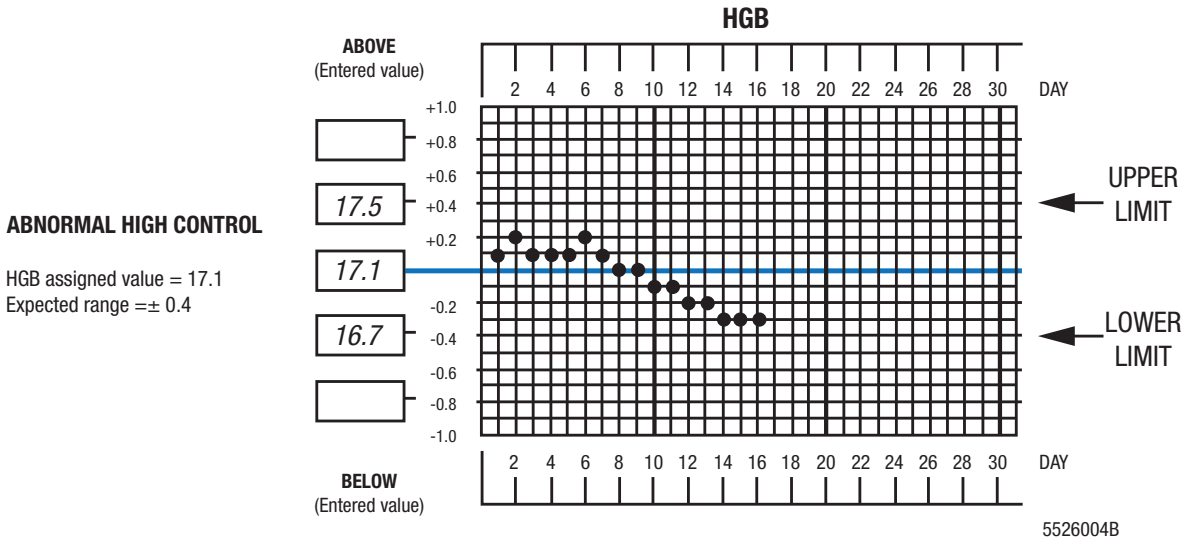
A trend occurs when five or more values show a gradual increase or decrease. Figure 1.2 shows a trend in hemoglobin (HGB) control results for an abnormal control level

› The expected range is ±0.4 and is used to define the low and high limits.

Although none of the results are outside the limits, the graph indicates that a problem exists.

Notice the gradual decline in the hemoglobin control results beginning after the sixth day.

Figure 1.2 Trend of Hgb Control Results



Because hematology controls are cell-based, some trending in sizing parameters can be expected. As stated in the Storage and Stability section of the control product insert, “The MCV, RDW and/or RDW-SD parameters may trend up through the product’s shelf-life. This is inherent to the product and should not be considered an indicator of product instability. Recovered values for these parameters should remain within the Expected Range.”

If an unexpected trend is noticed:

1. Record the information on your corrective action log.
2. Troubleshoot the problem(s) and remedy the situation prior to running patient samples.

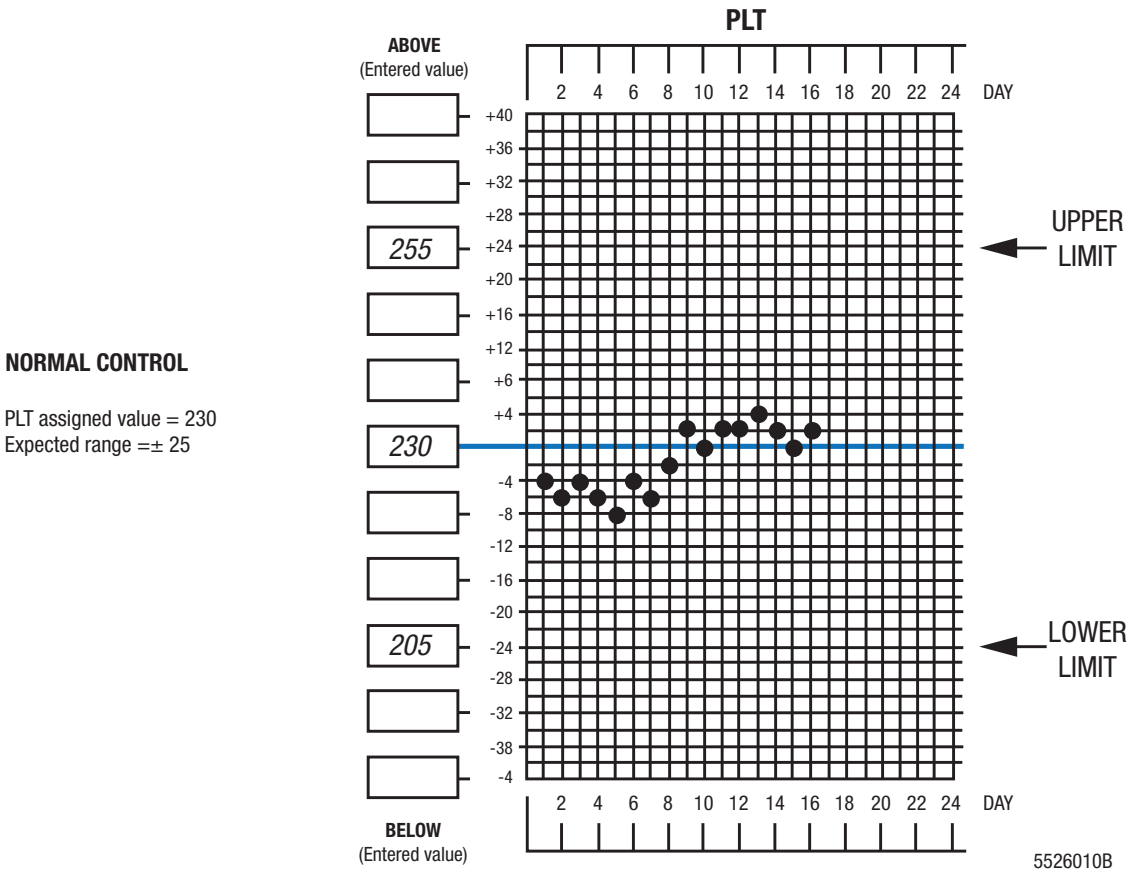
Shifts

A shift occurs when there is a sudden change in control results from one run or day to the next. A shift does not always mean that a problem exists. If the system was calibrated or some troubleshooting was performed before running the control, a shift could occur. Figure 1.3 shows a shift in platelet (PLT) control results for a normal control level:

- The PLT assigned value is 230 and is used as the mid-line.
- The expected range is ±25 and is used to define the low and high limits.

Notice the sudden change in PLT control results between the seventh and ninth days.

Figure 1.3 Shift in PLT Control Results



If a shift is noticed:

1. Record the information on your corrective action log.
2. Troubleshoot the problem(s) and remedy the situation prior to running patient samples.

Determine if the Control is “In” or “Out”

IMPORTANT: Verify the expiration date on the Assay Sheet. Beckman Coulter recommends using the control within its expiration date.

Follow the guidelines on the Instructions for Use and Table of Expected Results (package insert) to determine if the control results are “in” or “out.”

The values for each control level are listed for each specific instrument. An assigned value is an estimate of the true value based on repetitive analysis of the control product on multiple instruments.

Figure 1.4 Example Table of Expected Results for 4C-ES Cell Control - Normal

Coulter 4C-ES Cell Control

Table of Expected Results --Normal (with Sample Values)

35**	Open vial (Days)
78800	LOT
2013-07-15	

AcT 8/10*	AcT diff*	AcT diff 2*	±*	US	AcT 8/10*	AcT diff*	AcT diff 2*	±*	SI1	AcT 8/10*	AcT diff*	AcT diff 2*	±*	SI2	AcT 8/10*	AcT diff*	AcT diff 2*	±*	SI3	AcT 8/10*	AcT diff*	AcT diff 2*	±*	SI4	Parameters
9.3	9.3	9.3	0.7	$x10^3/\mu L$	9.3	9.3	9.3	0.7	$x10^9/L$	9.3	9.3	9.3	0.7	$x10^9/L$	9.3	9.3	9.3	0.7	$x10^3/\mu L$	9.3	9.3	9.3	0.7	$x10^9/L$	WBC
4.21	4.19	4.13	0.25	$x10^6/\mu L$	4.21	4.19	4.13	0.25	$x10^{12}/L$	4.21	4.19	4.13	0.25	$x10^{12}/L$	4.21	4.19	4.13	0.25	$x10^6/\mu L$	4.21	4.19	4.13	0.25	$x10^{12}/L$	RBC
12.4	12.5	12.3	0.9	g/dL	124	125	123	9	g/L	124	125	123	9	g/L	12.4	12.5	12.3	0.9	g/dL	7.7	7.8	7.6	0.6	mmol/L	Hgb
35.7	35.6	35.1	3	%	0.357	0.356	0.351	0.03	L/L	0.357	0.356	0.351	0.03	L/L	0.357	0.356	0.351	0.03	L/L	0.357	0.356	0.351	0.03	L/L	Hct
84.8	85	85	4.5	fL	84.8	85	85	4.5	fL	84.8	85	85	4.5	fL	84.8	85	85	4.5	fL	84.8	85	85	4.5	fL	MCV
29.5	29.8	29.8	3.3	pg	29.5	29.8	29.8	3.3	pg	29.5	29.8	29.8	3.3	pg	29.5	29.8	29.8	3.3	pg	1.83	1.85	1.85	0.2	fmol	MCH
34.7	35.1	35	3.7	g/dL	347	351	350	37	g/L	347	351	350	37	g/L	34.7	35.1	35	3.7	g/dL	21.5	21.8	21.7	2.3	mmol/L	MCHC
	14.5	14.5	1.5	%		14.5	14.5	1.5	%		14.5	14.5	1.5	%		14.5	14.5	1.5	%		14.5	14.5	1.5	%	RDW
212	212	212	40	$x10^3/\mu L$	212	212	212	40	$x10^9/L$	212	212	212	40	$x10^9/L$	212	212	212	40	$x10^3/\mu L$	212	212	212	40	$x10^9/L$	Plt
	10.8	10.4	2	fL		10.8	10.4	2	fL		10.8	10.4	2	fL		10.8	10.4	2	fL		10.8	10.4	2	fL	MPV
	0.229	0.22	0.07	%		0.229	0.22	0.07	%		0.229	0.22	0.07	%		0.229	0.22	0.07	%		0.229	0.22	0.07	%	Plt
	13.3	13.3	2	ratio		13.3	13.3	2	ratio		13.3	13.3	2	ratio		13.3	13.3	2	ratio		13.3	13.3	2	ratio	PDW
32.9	43.6	43.9	5	%	32.9	43.6	43.9	5	%	0.329	0.436	0.439	0.05	ratio	32.9	43.6	43.9	5	%	32.9	43.6	43.9	5	%	LY%
	13.4	13.1	4	%		13.4	13.1	4	%		0.134	0.131	0.04	ratio		13.4	13.1	4	%		13.4	13.1	4	%	MO%
	43	43	6	%		43	43	6	%		0.43	0.43	0.06	ratio		43	43	6	%		43	43	6	%	GR%
3.1	4.1	4.1	0.8	$x10^3/\mu L$	3.1	4.1	4.1	0.8	$x10^9/L$	3.1	4.1	4.1	0.8	$x10^9/L$	3.1	4.1	4.1	0.8	$x10^3/\mu L$	3.1	4.1	4.1	0.8	$x10^9/L$	LY#
	1.2	1.2	0.5	$x10^3/\mu L$		1.2	1.2	0.5	$x10^9/L$		1.2	1.2	0.5	$x10^9/L$		1.2	1.2	0.5	$x10^3/\mu L$		1.2	1.2	0.5	$x10^9/L$	MO#
	4	4	0.9	$x10^3/\mu L$		4	4	0.9	$x10^9/L$		4	4	0.9	$x10^9/L$		4	4	0.9	$x10^3/\mu L$		4	4	0.9	$x10^9/L$	GR#

*Applicable only for parameters measured by the instrument.

**Assumes that the Instruction Section of the package insert is performed a maximum of 20 times within 35 days.

Control "In" or "Out"

Use Figure 1.4 to practice determining if the results printed by your instrument are within the control value parameters for the control level that you analyzed on your instrument.

Assuming you ran the Normal control on your instrument:

1. Find the WBC assigned value for the Normal control.
   (Answer: 9.3)
2. Find the WBC expected range.
   (Answer: The expected range is 8.6 to 10.0 whereby 8.6 is seven-tenths (0.7) less than the assigned value of 9.3, and 10.0 is seven-tenths (0.7) greater than the assigned value of 8.7.)
3. If your instrument printed WBC results of:
   - 9.2, is the control "in" or "out"?
     (Answer: The control is "in" because 9.2 falls within the range of 8.6 to 10.0.)
   - 10.7, is the control "in" or "out"?
     (Answer: The control is "out" because 10.7 falls outside the range of 8.6 to 10.0.)

What to Do if the Control is "In"

If the control is "in", run the remaining levels of control before starting patient samples. After running all control levels and determining that the instrument is performing as expected, then the patient samples can be analyzed.

What to Do if the Control is "Out"

If the control is "out", DO NOT run any patient samples until determining what caused the control to be out, and solve the irregularity. Beckman Coulter recommends following your laboratory's protocol. After troubleshooting, record the corrective action in the comments section of your control files, or in a correction action log sheet.

To record a Corrective Action, enter:

1. The date of the occurrence.
2. The condition (such as: WBC low on 4C PLUS Normal).
3. The lot number and expiration date.
5. The action performed, such as "repeated-back in range."
6. The initials of the person who performed the corrective action.

Troubleshoot the control out condition according to your laboratory's protocol and to the Table of Expected Results for the specific control, the instrument's IFU and the control IFU.

Calibration

Calibration is the process used to adjust the accuracy of the instrument being used. It requires the use of a calibrator, such as COULTER S-CAL. Calibration is an essential part of the hematology laboratory's quality assurance program. Before performing a calibration, know what to expect as an outcome.

A calibrator is a substance traceable to a reference preparation or material, used to verify or adjust a measurement. The College of American Pathologists checklist states that acceptable calibration techniques include: "The use of multiple analyzed whole blood specimens, and the use of a manufactured, certified, stabilized preparation of red cells, white cells (or white cell surrogates) and platelets (platelet surrogates)."

The checklist continues: "All calibration techniques should include periodic verifications of analyzer hemoglobin measurements against a certified hemoglobin preparation (ICSH/WHO International haemoglobin cyanide standard) or material that has been certified by its manufacturer as being derived from the certified international hemoglobin cyanide standard using reference procedures."

Consider changes that are appropriate, although not "mandatory." There are times when minor calibration changes may improve control recovery and XB batch mean recovery. Do not accept changes to cal factors that are not logical. For example, if:

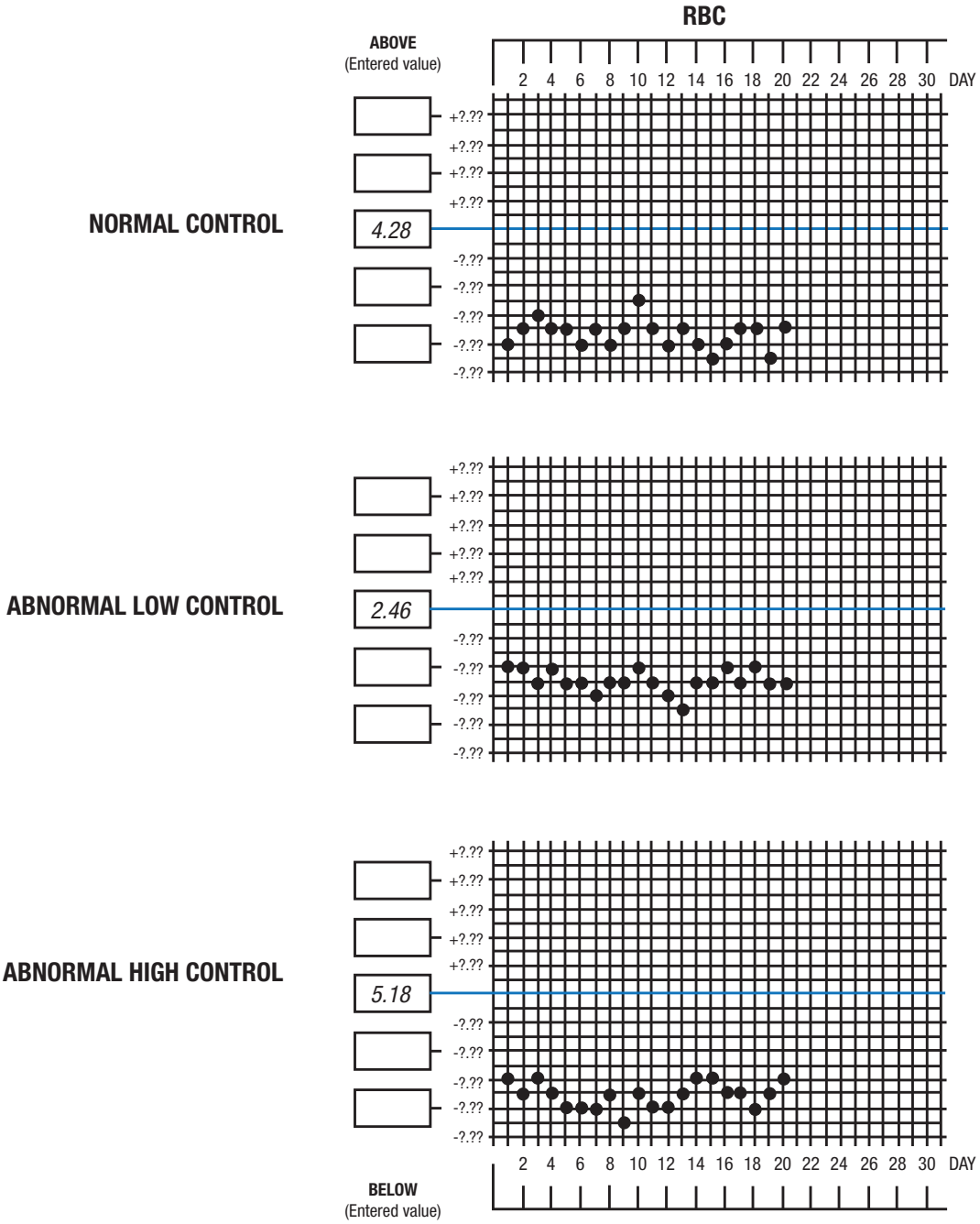
- Control recovery values are already low but the calibration data indicates an adjustment to lower levels
- Control recovery values are high but the calibration data indicates an adjustment to higher levels
- The product was compromised during shipping

For optimal performance, Beckman Coulter recommends assessing and verifying calibration periodically. The calibration values on the kit Table of Expected Results are traceable to reference methods detailed on the product insert.

Determining if Calibration is Required

Control graphs can help determine if calibration is required. Figure 1.5 shows the graphs of all three levels of control for the RBC parameter.

Figure 1.5 Three control levels for RBC



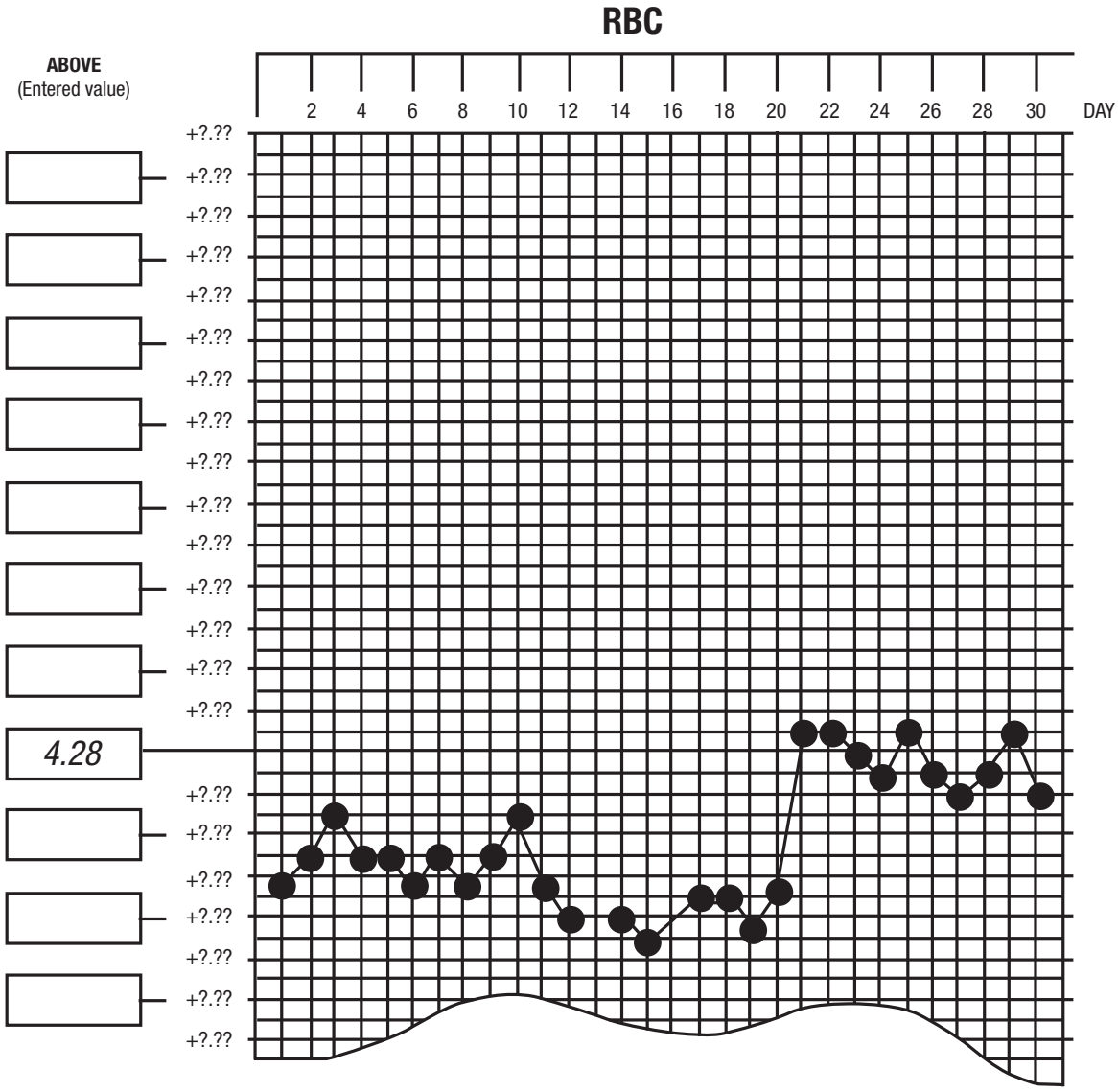
All three graphs show the same issue. The instrument is providing precise (reproducible) results; however, the results are not as accurate as they could be. The results for each control are on the low side of the assigned values–a shift away from assigned mean. If there are no instrument problems, and a pattern is detected in the graphs, as shown above, it may be necessary to calibrate (adjust the accuracy) of the instrument.

Calibration Procedure

Refer to the calibrator's product insert, instruments IFU or Special Procedures and Troubleshooting manual for detailed procedures.

After calibrating the instrument, you may see a shift in the control results. Calibration is a normal cause for a shift. Figure 1.6 shows how the normal control graph for the RBC parameter, as previously illustrated in Figure 1.5. Three control levels for RBC, might look if you calibrated the instrument on day 20. Notice the shift in results as they moved closer to the assigned value of 4.28.

Figure 1.6 Calibration on Day 20 for RBC Normal Control



XB Analysis

XB Analysis is a cost effective quality control method that allows for continuous monitoring of system performance using patient samples in conjunction with commercial controls.

› X = Mean

› B = Bull (for Brian S. Bull, M.D.)

XB evaluates RBC indices which are typically stable for an individual patient, from day to day, and stable for patient population over time. The lab's assayed commercial control is the final indicator to determine if the analyzer is in or out of control.

The use of XB check should be considered as added support to a lab's QC program, and can be very effective if a lab has a volume of >100 samples/day. Once established, the target values for XB will be as static unless the actual patient population changes. Changes to XB with no supporting change to QC might indicate a need to update targets.

As a **Weighted Moving Average,** XB uses small batches of 20 samples to calculate each mean. The mean of each batch is used to compare to the target values. Each laboratory establishes their target values for each MCV, MCH and MCHC. The target default values according to Dr. Bull's targets, are based on general population across the nation: MCV = 89.5, MCH = 30.5, and MCHC = 34.0.

XB Value is Out of Range

If the XB value is out of range, check:

› which directly measured parameters are most affected

› if the change is sudden or ongoing

› batch contained samples from particular population (renal, oncology)

Refer to Using XB for Troubleshooting Specific Cases.

XM Analysis

XM Analysis is available on the DxH 800/DxH 600 and LH 780 instruments. This is a quality-control method that uses an Exponentially Weighted Moving Average (EWMA) of CBC, Diff, NRBC and Reticulocyte parameters and compares them with known target values, to monitor instrument performance. For more information, refer to the specific instrument's IFU manual. For the DxH 800/DxH 600, refer to the chapter titled Set Up XM Control, and for the LH 780, refer to the chapter titled XM Analysis.

Inter-laboratory Quality Assurance Program (IQAP)

A program administered by Beckman Coulter, Inc. for users of its hematology instruments and controls. It allows a laboratory to compare its performance to all other laboratories in the program that use the same or similar instrument category and control products.

Recording Control Results

Beckman Coulter strongly recommends that if your laboratory is not benefiting from automatic storage of control results, then use the Daily Data application found in the Electronic Interlaboratory Quality Assurance Program (eIQAP).

Control Summary Data

Control Summary Data should be submitted to IQAP as soon as possible. This allows the IQAP Department to issue an updated report more frequently, and be able to troubleshoot any response time irregularity, in case there is an instrument issue.

- It is necessary to submit the minimum number of ten (10) runs; 16 runs provide statistical validity when submitting data to IQAP. If the report reflects less than 10 data points, it will not be included in the peer comparison pool, and will not receive SDI and CVI comparisons.

  If there is a limited number of participating laboratories (less than 10 participants), laboratories should evaluate peer group performance.
- If submitting data via the Reagent Management Card (RMC) or external media, ensure that any data which has already been submitted, even if it is the same lot number, has been deleted and is not included.
- If submitting data via the RMC, ensure that only current lots of control data are stored on the card. The IQAP Department cannot separate the old data stored in the card from the new data.
- IQAP reports are cumulative for the same lot of controls.

NOTE

- DxH 800/DxH 600 - the QC files can be submitted as data accumulates. Data can also be submitted daily until the control expires.
- AcT Diff - DO NOT enter data manually twice. This will generate a flag for the report and the results will not be accurate.

Other Controls for the Hematology Laboratory

The College of American Pathologists states that quality control procedures for hematology processes may include:

- The use of preserved or stabilized whole-blood controls
- Retained patient specimens
- Moving average monitoring of red cell indices
- Some combination of the above

There are two main ways that labs use patient blood as controls:

- Replicate testing of pooled or designated patient blood at specified times during the day
- Continual moving average calculations on routine patient samples XB or XM. XB is automated in Beckman Coulter instruments with data management and workstations.

Studies (Bull 1974, Koepke 1981) indicate that the red cell indices (MCV, MCH, and MCHC) of patient populations are stable over time. This stability characteristic of the indices is the basis for XB analysis. XB is helpful to compare performance of patients across instrument systems.

Mean values established from a large portion of the patient population are used as reference. Subsequent moving averages from the indices of smaller batches of patient samples are compared with these target values. Significant changes (more than 3%) can indicate a change in system performance.

Delta Checks

Delta checking can also be used as a quality control method. It is a means of checking to see if certain parameters are within a user-defined range when the parameter results of two samples from the same patient are compared. Some Beckman Coulter instruments perform delta checks automatically.

Preventive Maintenance

Refer to your instrument manual to determine which, if any, preventive maintenance procedures are required for your instrument. Most Beckman Coulter instruments do not require routine preventive maintenance, but there are cleaning and replacement procedures available for troubleshooting purposes.

Maintaining a Log

It is essential that you maintain a log documenting your instrument's use. This will assist you both in the laboratory routine and when you need service. Use your log book and your instrument certification documents to keep your system's history current.

Technologist Review

An experienced medical technologist who reviews the data from an instrument can detect possible malfunctions or irregularities. Technologist review includes assessing the reasonableness of results, investigating questionable cases, knowing when to repeat an analysis, knowing how to interpret QC results, knowing how to interpret calibration recommendations, and when there is a problem, knowing how to define and solve it. These are important skills necessary for any QC program.

SECTION 2

Troubleshooting

Troubleshooting Overview

This section provides information on how to troubleshoot common quality control issues, as well as specific issues related to XB. Irregularities could be detected by means of observation, history/event log entries, calibration or control failures, unexpected patient results, or system error messages.

If unable to solve the irregularity, contact your lab administrator or your Beckman Coulter representative.

Troubleshooting Guidelines

Always look at the whole picture and obtain as much information as possible prior to determining the most suitable method for the investigation. Use the following checklist to assist tracking your investigation.

Table 2.1 Troubleshooting Checklist

Investigation	Yes	No	Comments
What is unique to the case?			
› new reagent			
› new control			
› new calibrator			
› recent part replacement			
› maintenance recently performed			
› having failures on controls or patient samples and controls			
What is common to the situation?			
› more than one parameter affected			
› affected parameter is directly measured			
› WBC			
› RBC			
› Hgb			
› MCV			
› PLT			
› MPV			
› Diff%			
› Retic%			
› related parameters			
› analysis method for each parameter			
› multiple levels of control material affected			
› problem occurring on multiple instruments			
› change of laboratory environment within range			

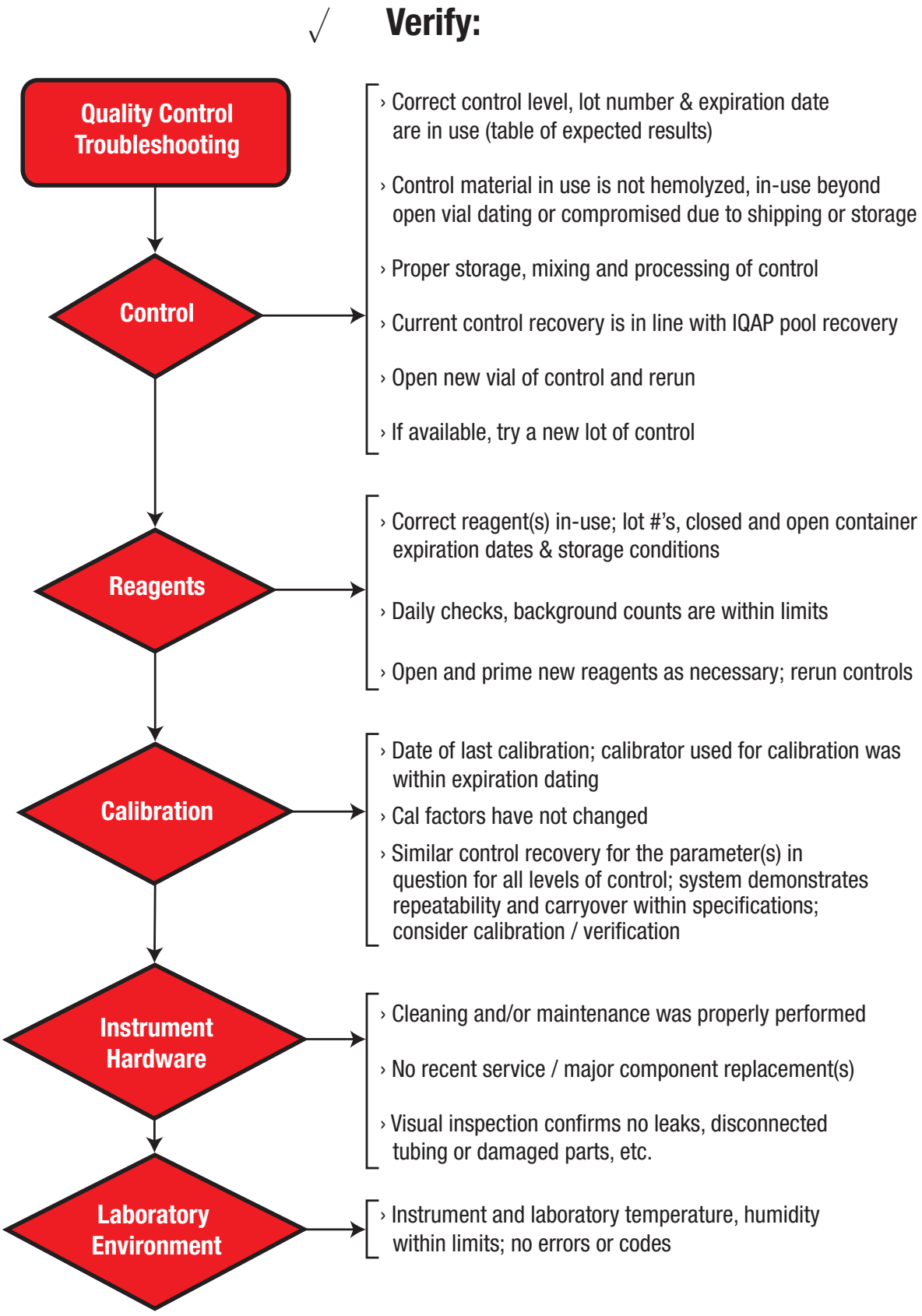
Investigation	Yes	No	Comments
› laboratory temperature			
› humidity			
› storage conditions			
› other			
› reagent shipment			
› irregularities in packaging			
› reagents stored according to package insert			
› calibrators stored according to package insert			
› controls stored according to package insert			
› receiving error messages (refer to the IFU)			
› flags			
› codes			
› QC target ranges (appropriate/correct)			
› package insert (appropriate/correct)			
› table of expected results (appropriate/correct)			
› any recent manufacturer's notification(s)			
Have the control samples been checked?			
› new lot(s) of control			
› proper analysis of correct samples			
› controls exceed			
› open/closed vial expiration dates			
› claims			
› controls stored properly			
› controls mixed properly			
› control properly presented			
› control failures become apparent after recent calibration			
› control failures after service			
Has the reagent(s) been checked?			
› correct reagent(s)			
› reagent(s) loaded and connected correctly			
› new reagent(s) lot number			
› reagent(s) stored properly			
› reagent(s) properly prepared			
› reagent(s) expired			
› reagent(s) exceed the open/closed container stability			

Investigation	Yes	No	Comments
Has the calibration been checked?			
› date of last calibration			
› lot number and expiration date of calibrator			
› correct calibration information been entered			
› calibrator stored, prepared and properly analyzed			
› any parameter adjustment			
› WBC			
› RBC			
› Hgb			
› MCV			
› PLT			
› MPV			
› calibrator expired			
› calibrator used past open vial stability claims			
› control failures post-calibration			
› agreement between the control recovery post-calibration and the change(s) made during calibration			
› waited for the next lot of controls to determine need for adjustment			
IQAP Checks			
Evaluate IQAP statistical data by parameter for each level of control including:			
› Mean(s), SD, SE diff			
› Current and historic CVs			
› SDI (accuracy vs. pool)			
› CVI (precision vs. pool)			
› IPI (overall accuracy and precision vs. pool)			
› any indication of similar recovery from the peer group in IQAP for the same lot			
› any indication of similar recovery from the peer group in IQAP for the same parameters			

Investigation	Yes	No	Comments
Has the instrument hardware been checked?			
› date and reason for last service			
› maintenance performed correctly and up-to-date			
› Carryover within specs			
› Precision (repeatability) within specs			
› cleaning reagents freshly prepared and installed			
› maintenance reagents freshly prepared and installed			
› visual inspection of hardware, check for:			
› leaks			
› build up			
› disconnected tubing			
› bent probes			
› worn-out components			
How does the control recovery for this system compare with:			
› XB			
› XM			
› extended QC			
› survey material results			

To assist in determining corrective actions based on your conclusions, refer to Figure 2.1.

Figure 2.1 Corrective Action Flowchart



Using XB for Troubleshooting Specific Cases

XB(bar above X) analysis is an automated quality control technique comparing the RBC indices obtained from patient samples to established target values. This analysis provides valuable data on the RBC parameters. When XB batch means exceed the target values it is necessary to determine if there was a change in the patient population or an instrument problem. Using the information in this section identification of the causes for the change in batch mean values can be determined. Determining which directly measured parameter(s) are associated with the RBC indice in question will aid in troubleshooting an instrument problem.

It is necessary to determine any population changes:

› which parameter is out of range

› how is the parameter or indices are derived

MCV - derived from RBC histogram

MCH = Hgb x 10/RBC

MCHC = Hgb x 100 /Hct

HCT = RBC x MCV/10 (HCT=RBC X MCV/10)

› RBC indices tell us about the three (3) directly measured parameters:

RBC

HGB

MCV

Table 2.2 identifies the directly measured parameter (X axis) and the change to the RBC indice (Y axis)

	MCV Low	MCV High	MCH Low	MCH High	MCHC Low	MCHC High
MCV	Decrease	Increase	----	----	Increase	Decrease
RBC	----	----	Increase	Decrease	Increase	Decrease
HGB	----	----	Decrease	Increase	Decrease	Increase
Hct	Decrease	Increase	----	----	Increase	Decrease

Table 2.3 Using XB for Troubleshooting Specific Cases

Cases	Action
Batch mean is skewed by the inclusion of diluted samples, or the results are repeats of same abnormal patient.	Turn off XB for repeated abnormals or dilutions. If possible, exclude the samples. If unable to delete or turn off XB, reestablish a more meaningful XB target.
Change in patient population because one or more types of patients are added or removed from the mix of patient population (neonatal group was added, or dialysis samples).	XB targets should be re-established to reflect current population or the XB should be turned off when these patients are processed.
Calibration drift (except MCV and MPV) exhibited by XB and controls.	Instrument may need cleaning or maintenance service. Ensure service status is OK before attempting calibration.
Sudden change in: › component failure › the cal factor during routine recalibration	Instrument may need cleaning or maintenance service. Ensure service status is OK before attempting calibration.

Glossary

This glossary is a collection of specialized terms and their meanings that are either used in this document or related to the information in it. If a term has more than one meaning, all meanings relevant to this manual are included.

Accuracy

The ability of the instrument to agree with a predetermined reference (true) value; closeness of agreement between a measured quantity value and a true quantity value of a measurement; closeness of agreement between a measurement result and the accepted reference value.

The closeness of a result to the true (accepted) value ("hitting the bull's eye"). In IQAP, the peer group (pool) represents truth. Refer to SDI.

Assay

A procedure of repeat testing to determine the assigned value for a given control lot.

Bias

Control values demonstrate a consistent recovery above or below the assigned value.

Calibration

The procedure used to set an instrument at a specific value or values using a reference method.

Calibrator

A substance traceable to a reference method, preparation, or material used to calibrate or adjust a measurement. COULTER S-CAL calibrator is an example.

Carryover

The amount, in percent, of sample remaining in the system and picked up by the next sample cycled. Low-to-high carryover is the amount of sample with low cell concentrations carried over to samples with high cell concentration, such as diluent to blood. High-to-low carryover is the amount of samples with high cell concentrations carried over to samples with low cell concentrations, such as blood to diluent.

Carryover is performed to determine if one sample interferes with the analysis of the next sample. Ideally, carryover is negligible.

Coefficient of Variation (CV)

The reproducibility of your results expressed as a percentage. It describes variation around a mean and is calculated as a ratio between standard deviation and the mean.

$$CV\% = \frac{SD}{Mean} \times 100$$

Coefficient of Variation Index (CVI)

Indicates how your precision compares to that of your peers. It is expressed in units as a ratio of your CV divided by the pool CV. Plotted on the Instrument Performance Matrix, the CVI is a visual indicator of overall precision for the data set.

$$\text{CVI} = \frac{\text{Your Lab CV}}{\text{Pool CV}}$$

Control

A substance used in routine practice for monitoring the performance of an analytical process or instrument.

By comparing your instrument control results against the assigned value (assay value), you can monitor your instrument's accuracy and precision. The assigned value is determined by repeatedly testing the control material on many instruments, and then determine a close estimate of the true value. This process is known as assaying. When assaying is complete, we can obtain an average of all the results using the prepared sample (control). The determined value is called an assigned value.

Beckman Coulter's cell controls are designed specifically for each type of instrument.

Delta check

A check on sample results that is made by clinical laboratories to determine if the current result on a particular patient is within certain limits when compared to the last result obtained on that same patient.

Electronic IQAP (eIQAP)

The web based version of IQAP providing the fastest turn-around-time for reports, simplified data submission and administrator and user controls and corporate reports. To access Electronic IQAP, go to **www.beckmancoulter.com/qap/index.jsp.** eIQAP is available to registered IQAP participants using your existing IQAP participant number.

Inter-laboratory Quality Assurance Program (IQAP)

A program administered by Beckman Coulter, Inc. for users of its hematology instruments and controls. It allows a laboratory to compare its performance to all other laboratories in the program that use the same or similar instrument category and control products.

Instructions for Use (IFU, package inserts)

IFU and package inserts are included with any Beckman Coulter hematology or flow cytometry products. The package insert contains specific information pertaining to the batch or lot of controls from which your control product was manufactured. The assigned values are listed on a Table of Expected Results that is included within the cell control kit. The Table of Expected Results is specific to the batch or lot of controls.

Instrument Performance Index (IPI)

IPI is a single point that represents both the precision and accuracy of your system as compared to that of your peers. This point is plotted on the Instrument Performance Matrix for each parameter and level. Refer to Standard Deviation Index (SDI) and Coefficient of Variation Index (CVI) for further details.

Levey-Jennings Graph

A tool for graphing daily control results to visually detect shifts or trends. Refer to Shift and Trend for further details.

Mean

Mathematical average for a group of data points.

$$X = \frac{\sum x_1}{N}$$

Outliers

Outliers are results that fall outside the low/high limits for any parameter.

A value usually so far separated from the other values that it suggests that it may be from a different population, or the result of an error in measurement.

Pool

The heart of peer review. It is the average of all participant means excluding your laboratory data that use the same control lot and similar instrument systems. The pool is the standard against which individual laboratory results are compared.

Pool Variance

The squared standard deviation of the means of all the other labs.

Precision (Reproducibility or Repeatability)

Precision of a given measurement procedure is subdivided according to the specified precision conditions. Repeatability relates to essentially unchanged conditions and is often termed “within-series precision” or “within-run precision”. Reproducibility relates to change in conditions, i.e.: different laboratories, operators, and measuring systems (including different calibrations and reagent batches) and is often termed “interlaboratory precision”.

The closeness of successive test results on the same sample. Refer to Accuracy for further details.

Quality Control (QC)

In laboratory testing, quality control is the assurance that results are reported correctly (accuractely) and that subsequent results do not change significantly unless the patient’s condition changes (precision).

Repeatability

The closeness of agreement between the results of successive measurements of the same substance carried out under the same conditions of measurement. Also known as reproducibility, precision, within-run precision, within-assay, within-run, intra-assay, and intra-run precision.

Shift

On a Levey-Jennings graph, a shift is indicated by an abrupt change in the pattern of data points to a higher or lower level, or a sudden change in results from one day to the next.

Standard Deviation (SD)

Variation around the mean expressed in units being measured. A ±2SD is an accepted laboratory standard; 95% of all results in a normal population should fall within two standard deviations of the mean.

$$SD = \sqrt{\frac{\Sigma(\bar{x} - x)^2}{N - 1}}$$

Standard Deviation Index (SDI)

Indicates how well your mean compares with the peer group mean for a given parameter and level of control. It is expressed in units as a ratio of the difference in means to the standard error of the differences (SE diff). Plotted on the Instrument Performance Matrix, the SDI is a visual indicator of overall accuracy for the data set.

$$SDI = \frac{\text{Your Lab Mean} - \text{Pool Mean}}{\text{SE diff}}$$

Standard Error of the Differences (SE diff)

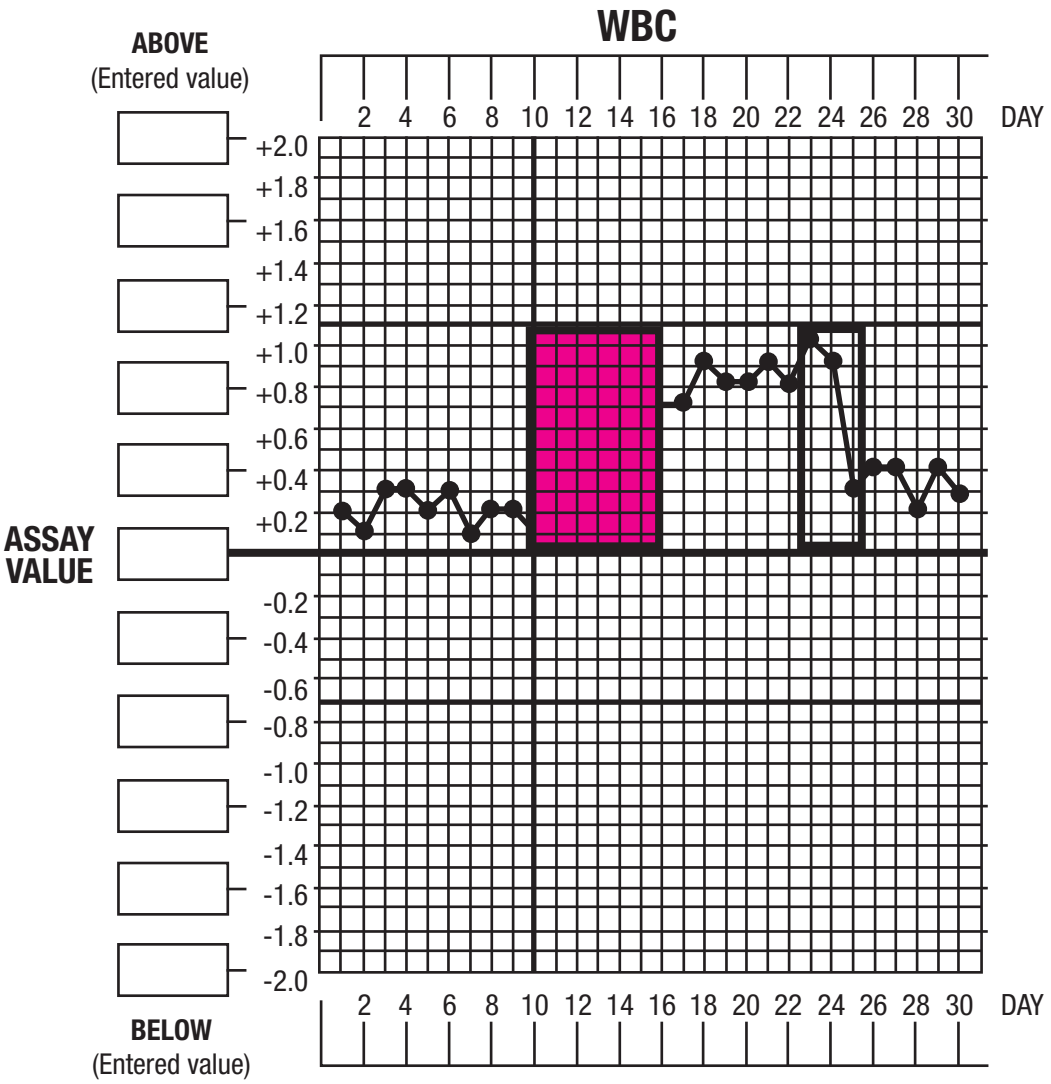
The denominator in the SDI formula calculated as the square root of your lab variance plus the pool variance.

$$\text{SE DIFF} = \sqrt{(\text{Pool SD})^2 + (\text{Lab SD})^2}$$

Trend

A trend is a gradual change in direction of the data points. A trend is identified when, on repeated analysis, results form an increasing or decreasing pattern away from the established mean.

A trend occurs when five or more control values show a gradual increase or decrease.



XB Method

A hematology quality control technique using routine patient blood analyses in a weighted moving average algorithm. XB analyses are performed automatically by many Beckman Coulter instruments.

Your Lab Variance

The squared standard deviation of your individual data points.

References

A Method for the Independent Assessment of the Accuracy of Hematology Whole-Blood Calibrators, 1992, B. Bull, A. Richardson-Jones, M. Gibson and D. Twedt, Am. J. Clin. Pathol., 98, 623-629.

Advances in Hematological Methods: 1982. O.W. van Assendelft and J.M. England, eds. CRC Press: Boca Raton, FL.

Barnett R.N.: 1979. Clinical Laboratory Statistics. Little, Brown and Co.: Boston.

Basic Concepts of QC: 1986. Coulter Electronics, Inc., Hialeah, Florida (Coulter PN 4235526).

Biometry: 1995. Robert R. Sokel and F. James Rohlf, eds. W.H. Freeman and Company: New York.

Bull B.S. and Korpman R.E.: 1982. Intralaboratory Quality Control Using Patient Data. In Methods in Hematology Quality Control, I. Cavill (ed). Churchill Livingston: New York.

College of American Pathologists: 2012 CAP Checklist. Skokie, IL.

Concepts of XB Analysis - A Programmed text: 1985. Coulter Electronics, Inc: Hialeah, Florida (Coulter PN 4235294).

First International Conference on Advances in Clinical Haematology: Current Practice and Future Directions for Quality Assessment in Laboratory Haematology, 1990. J.A. Koepke and J.M. England eds. Clinical and Laboratory Haematology, Vol 12, Suppl.1, 1990.

Gilmer P.R. and Williams L.J.: 1980. Status of Methods of Calibration in hematology. Am J Clin Path 74(4):600.

Interlaboratory Quality Assurance Program, F.C. Anderson, Clin. Lab. Haemat. 1190, 12, Suppl.1, 111-116.

Introductory Statistics: 1999. Neil A. Weiss - Arizona State University, eds. Addison-Wesley, Inc.: Massachusetts.

Koepke J.A.: 1984. Laboratory Hematology. London: Churchill Livingston.

Koepke J.A. and Protextor T.J.: 1981. Quality Assurance for Multichannel Hematology Instruments. Four years experience with patient mean erythrocyte indices. Am J Clin Path 75(1):28.

Laboratory Quality Assurance: 1987. P.J. Howanitz and J.H. Howanitz, eds. McGraw-Hill: New York.

Levey S. and Jennings E.R.: 1950. The use of control charts in the clinical laboratory. Am J Clin Path 20:1059.

Oxford BS: 1985. Statistical Methods in Quality Assurance Software. J Med Tech 2:629.

Performance Goals for the Internal Quality Control of Multichannel Hematology Analyzers, Proposed Standard NCCLS H26-P, Vol 9, No. 9, 1989.

Quality Assurance in Haematology, 1988. S.M. Lewis and R.L. Reference-2 A62451AA

Quality Control in Haematology, Symposium of the International Committee for Standardization in Haematology, 1975. S.M. Lewis and J. Coster eds. AP Press, ISBN 0-12-446850-0, LONDON.

Quality Control of Automated Cellular Analyses - The Fallibility of Embalmed Blood, 1985, J.M. Gibson, Blood Cells, 11, 301-307.

S-CAL Calibrator: 1985. Hematology Analyzer Vol. 4 No.3. Coulter Electronics, Inc.: Hialeah, FL.

Stewart C.E.: 1985. The Choice of Control Material: Important factors. J Med Tech 2:634. Verwilghen eds. Bailliere Tindall Press, ISBN. 0-7020-1322-6, LONDON.

BECKMAN COULTER