HORIBA
Medical

Quality Control Guideline.

Establishing Quality Control Means and Standard Deviations for Hematology Instrumentation

Regulatory agencies require the use of Quality Control (QC) materials to assess the validity of results on patient specimens. Laboratories are required to ensure that the means and standard deviations used in their facilities meet or exceed the regulations put forth by these agencies.

Regulatory bodies require the use of Quality Control

Laboratories must establish their own means and ranges for their instruments. For laboratories subject to CLIA-88, at least two different controls must be assayed and evaluated every 24 hours. For each QC procedure employed, the laboratory must have appropriate QC ranges.

CLIA deems it good laboratory practice for the individual laboratory to establish its own means and ranges.

The CLIA regulation at 493.1256(d)(10) requires a laboratory to establish or verify the criteria for acceptability of all control materials. When control materials providing quantitative results are used, statistical parameters (for example, mean and standard deviation) for each batch or lot number of control materials must be defined and available. The laboratory may use the stated value of a commercially assayed control material provided the stated value is for the methodology and instrumentation employed by the laboratory and is verified by the laboratory."

For the majority of laboratories, establishing their own specific means and ranges would be required.

The published assay range is a range of means. The published assay means and ranges of a commercial hematology control (Difftrol, Minotrol 16 or others) are considered a range of means.

The expected ranges listed represent estimates of variation due to different laboratories, instrument calibration, maintenance, and operator technique. The laboratory's calculated mean should fall within the range listed on the published assay. All QC results for an individual laboratory do not need to fall within the published assay range.

Determination of QC protocols is ultimately the responsibility of the Laboratory Medical Director. JCAHO requirements

The Joint Commission on Accreditation of Health Care Facilities (JCAHO), in a Q&A item on their Web site, stated the following:

The standards require each laboratory to establish its own control ranges through repetitive testing. However, there is an allowance to use manufacturer ranges when the following conditions are met:

   1. the stated values correspond to the method and instrument used by the laboratory, and
   2. the mean obtained by the laboratory reflects the manufacturer's stated mean, and

3. the Laboratory Medical Director assures the range is narrow enough to detect clinically significant error

Manufacturer ranges may also be implemented if a test is used so infrequently that calculation of valid statistics is not possible.

In settings where there is a high reproducibility (precise instrumentation, limited testing personnel), the laboratory's own calculated standard deviation (SD) may be small. When compared with the manufacturer ranges, a laboratory may find that the range spans more than the commonly used +/-2 SD. Using the laboratory's calculated +/-2 SD may produce unnecessarily narrow ranges, causing the testing personnel to frequently repeat QC and investigate when the control performs outside the laboratory's range, but within the manufacturer's range. Alternatively, the full manufacturer range may be too broad to promote the detection of clinically significant error. Selection of the appropriate range is a balance between these two ends of the spectrum.

It is at the determination of the Laboratory Medical Director to approve quality control ranges after giving consideration to the clinically significant variance as compared to the statistically derived SD.

Establishing means and standard deviations

Establishing laboratory-specific means and standard deviations is not a difficult process.

HORIBA Medical supports and suggests CLSI - Document C24-A3, *Internal Quality Control Testing: Principles and Definitions* for establishing each laboratory's individual mean target values and ranges.

CLSI document C24-A3 8.6 Setting Control Limits and 8.6.1 Values for the Mean and Standard Deviation outline these procedures.

8.6.2 Assayed Control Materials also states:

If assayed control materials are used, the values stated on the assay sheet provided by the manufacturer should be used only as guides in setting the initial control limits for testing new control materials. Actual values for the mean and standard deviation must be established by serial testing in the laboratory. The observed mean should fall within the range published by the manufacturer. EQA and peer-comparison programs provide useful measures of the means and SDs observed in other laboratories.

Here is a brief procedure for establishing your own mean and Standard Deviation (SD):

1. Analyze the control a minimum of 20 times.
2. Take the average of these runs.
3. This average should be within the range stated on the assay sheet.
4. If the average is within range, it will be considered as the "new mean."
5. Calculate a two Standard Deviation range from your results.
6. Incorporate this SD range around your new mean and monitor throughout the dating of the product.
7. The mean and SD values should be periodically recalculated during the life of the new lot.

If your instrument is working properly, your SD should not change significantly from lot to lot. Here is a procedure that may be used to set a preliminary mean until you have completed the 20 runs in the previous procedure:

1. Analyze the control ten times.
2. Take the average of these runs.

3. This average should be within the range stated on the assay sheet.

4. If the average is within range, it will be considered as the "temporary mean."

5. Use your established laboratory SD or your SD from your latest **QCP** report (from the same level of control) as your "Temporary SD."

6. When you have run the control 20 times, utilize the above procedure to establish your "new mean" for this lot of control.

Most hematology instruments have quality control files that will calculate these means and ranges automatically.

Other Quality Control situations

Means of parameters that change over time may be handled differently.
Some hematology parameters, such as MCV, will increase slightly over time. CAP gives guidance on how to accommodate this:

Most commercial controls have expected recovery ranges for each parameter, provided by the manufacturer. The mean of such ranges may not be the exact target value in a given laboratory. Each laboratory should assign its own initial target value, based on initial analysis of the material; this target value should fall within the recovery range supplied by the manufacturer, but need not exactly match the package insert mean.

The laboratory should establish specific recovery ranges that accommodate known changes in product attributes, assuming that calibration status has not changed.

If it is known that the MCV rises 2 units over the life of the control, it is acceptable to raise the mean by half this change to accommodate the known rise.

For example, if the initial mean is calculated at 84 and the historical 2 SD is 4, the lab could establish a mean of 85, with a range of 81-89. This will allow the values to start below the mean, rise through the mean and finish above the mean. The cumulative mean calculated at the end of the product life should be 85.

Quality Control for analyzers with two sample modes

Analyzers with multiple sample modes require additional QC.
The following recommendation for quality control of two sample modes is taken from the JCAHO Q&A forum on their Web site.

Since there are two distinct sample pathways, QC is required for each sample mode according to the parameters established in the hematology standards. This would mean (for JCAHO purposes) performance of at least one control every eight hours of patient testing and performance of at least two levels of commercial controls every 24 hours of patient testing.

Summary

Establishing laboratory means and ranges does not need to be a tedious task.
Regulatory agencies require the use of Quality Control (QC) materials to assess the validity of results on patient specimens.

This is achieved by assaying and evaluating at least two levels of control material every 24 hours. Most laboratories are required to establish their own means and standard deviations for the parameters tested and reported on patients. The published assay range for a given control is the range in which a laboratory's mean must fall to be considered acceptable. The determination of mean and range does not have to be a difficult process.