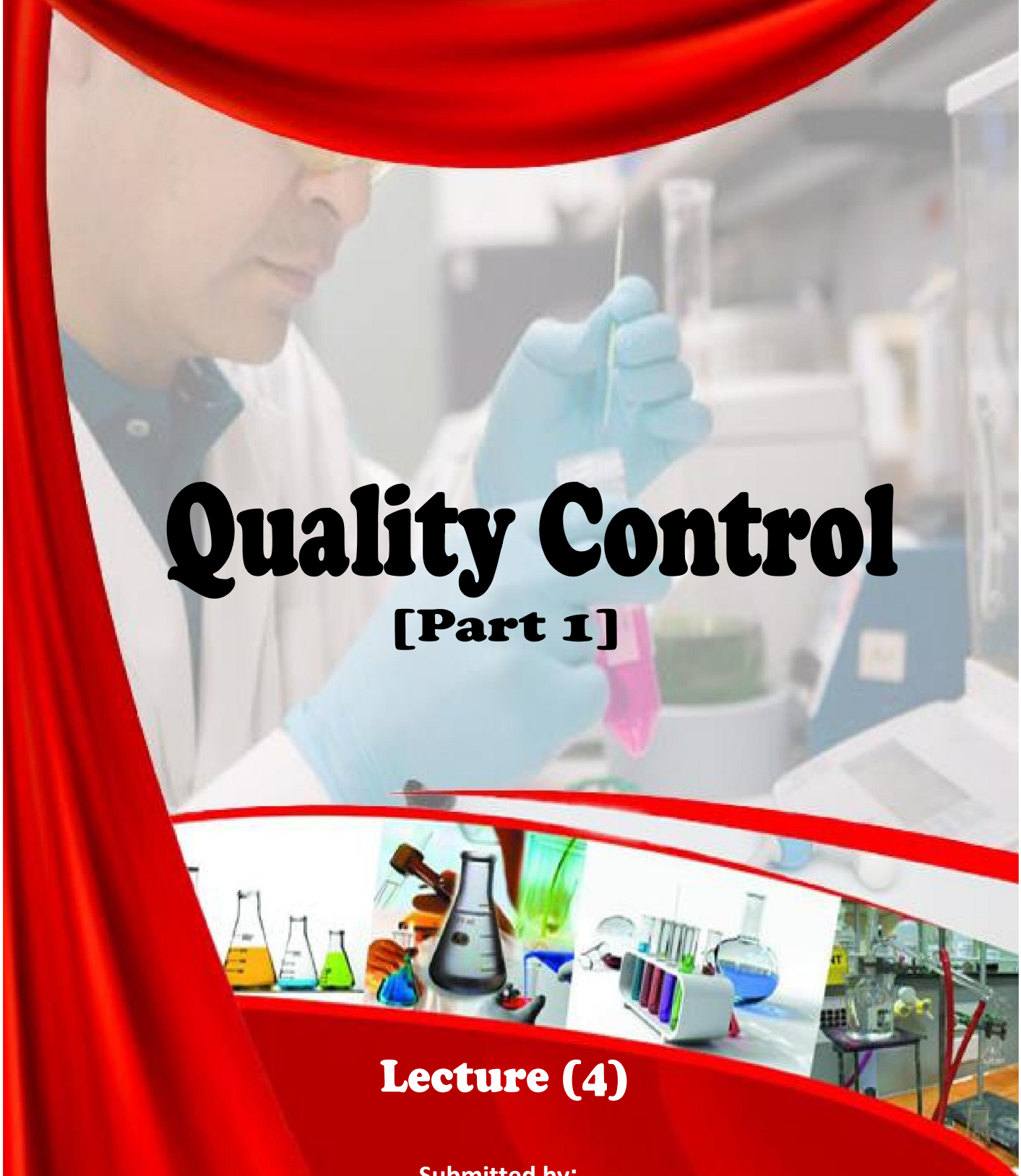
Al-Rasheed University College
Medical Analysis Department
Clinical Chemistry Lab.
Fourth Stage

كليـــــة الرشيد الجامعـــــة
قســـــم التحليلات المرضيــة
مختبر الكيميـــاء السريريـــة
المرحلـــــة الرابعـــــة



Quality Control

[Part 1]

Lecture (4)

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2018

Quality Control

Quality control in the medical laboratory is a statistical process used to monitor and evaluate the analytical process that produces patient results.

➲ Requirements for the Statistical Process:

a. Regular testing of quality control products along with patient samples.
b. Comparison of quality control results to specific statistical limits (ranges).

When a diagnostic test is performed in the medical laboratory, the outcome of the test is a result. The result may be a patient result or it may be a quality control (QC) result. The result may be quantitative (a number) or qualitative (positive or negative) or semi-quantitative (limited to a few different values).

QC results are used to validate whether the instrument is operating within pre-defined specifications, inferring that patient test results are reliable. Once the test system is validated, patient results can then be used for diagnosis, prognosis, or treatment planning.

Let's assume the measured value of potassium in a patient's serum is 2.8 mmol/L (a unit of measure ,millimoles per liter). This result is abnormally low and indicates an inappropriate loss of potassium. But how does the person performing the test know that this result is truly reliable? It could be possible that the instrument is out of calibration and the patient's true potassium value is 4.2 mmol/L – a normal result. The question of reliability for most testing can be resolved by regular use of quality control materials and statistical process control.

A **quality control product** is a patient-like material ideally made from human serum, urine or spinal fluid and can be a liquid or freeze-dried

(lyophilized) material and is composed of one or more constituents (analytes) of known concentration. Control products should be tested in the same manner as patient samples. A quality control product usually contains many different analytes. For example, a biochemistry control can contain any number of chemistry analytes including Uric acid, glucose, albumin, and calcium.

➲ Comparison of Quality Control Results to Specific Statistical Limits:

In Table 1, there are two ranges reported. The acceptable range for the Level I (Normal Control) is 3.7 – 4.3 mmol/L. The range for Level II (Abnormal Control) is 6.7 – 7.3 mmol/L. When the daily QC result obtained for the normal control is compared to the range calculated for the normal control, it becomes apparent that each result lies somewhere within the expected range. This indicates that the analytical process is "in control" at the normal level on that day of testing. When the daily QC result for the abnormal control (high potassium) is compared to the defined range for the abnormal control, the analytical process is shown to be "in control" for each day of testing except for the last day (11/7). On November 1 through November 6, both controls were "in control" and patient values could be reliably reported. However, the laboratory was "out of control" for abnormal high potassium on November 7 because the value obtained for the QC material (8.0 mmol/L) was outside the acceptable range (6.7 – 7.3 mmol/L).This means that some error occurred which may have made some patient results unreliable. The laboratory should not report any patient samples with an abnormally high potassium result until the error is resolved and the abnormally high sample(s) are re-tested. Perhaps it is now apparent that the range defined for each level of control is fundamental to the quality control system. The next section describes how to calculate the basic statistics required to develop an acceptable control range.

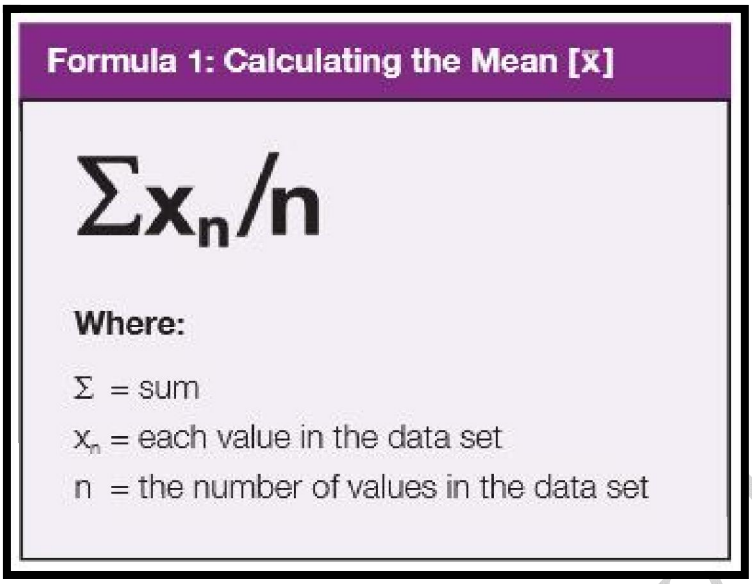
Table 1: example of a QC Log with Patient Results			
Test: Potassium	**Instrument: Instrument No. 1**		**Unit of Measure: mmol/L**
Range	**Level I: Normal Control 3.7-4.3 mmol/L**	**Level II: Abnormal Control 6.7 – 7.3 mmol/L**	**Patient Results**
1 November	4.0	7.0	4.2, 4.0, 3.8, 5.0, 5.8, 4.2
2 November	4.1	7.0	3.8, 4.4, 4.6, 3.9, 4.8, 4.4, 3.9
3 November	4.0	6.9	4.4, 3.9, 3.7, 4.7
4 November	4.2	7.1	4.7, 5.6, 4.2, 3.7, 4.3
5 November	4.1	7.0	4.2, 4.3, 4.1, 4.3
6 November	4.1	7.0	4.6, 4.4, 5.5, 3.8, 3.2
7 November	4.2	8.0	2.8, 4.6, 4.2, 3.2, 3.9, 4.1, 6.0, 4.3

➲ Calculation and Use of QC Statistics:

QC statistics for each test performed in the laboratory are calculated from the QC database collected by regular testing of control products. The data collected is specific for each level of control. Consequently, the statistics and ranges calculated from this data are also specific for each level of control and reflect the behavior of the test at specific concentrations. The most fundamental statistics used by the laboratory are the mean [x] and standard deviation [s].

1) Calculating a Mean [$\bar{x}$]:

The mean (or average) is the laboratory's best estimate of the analyte's true value for a specific level of control. To calculate a mean for a specific level of control, first, add all the values collected for that control. Then divide the sum of these values by the total number of values. For instance, to calculate the mean for the normal control (Level I) in Table 1, find the sum of the data {4.0, 4.1, 4.0, 4.2, 4.1, 4.1, 4.2}. The sum [$\sum$] is 28.7 mmol/L. The number of values is 7 (n = 7). Therefore, the mean for the normal potassium control in Table 1 from November 1–7 is 4.1 mmol/L (or 28.7 mmol/L divided by 7).



2)Calculating a Standard Deviation [s]:

Standard deviation is a statistic that quantifies how close numerical values (i.e., QC values) are in relation to each other. The term precision is often used interchangeably with standard deviation. Another term, imprecision, is used to express how far apart numerical values are from each other. Standard deviation is calculated for control products from the same data used to calculate the mean. It provides the laboratory an estimate of test consistency at specific concentrations. The repeatability of a test may be consistent (low standard deviation, low imprecision) or inconsistent (high standard deviation, high imprecision). Inconsistent repeatability may be due to the chemistry involved or to a malfunction. If it is a malfunction, the laboratory must correct the problem.

It is desirable to get repeated measurements of the same specimen as close as possible. Good precision is especially needed for tests that are repeated regularly on the same patient to track treatment or disease progress. For example, a diabetic patient in a critical care situation may have glucose levels run every 2 to 4 hours. In this case, it is important for the glucose test to be precise because lack of precision can cause loss of test reliability. If there is a lot of variability in the test performance (high imprecision, high standard deviation), the glucose result at different times may not be true.

Figure 1: Example of Good Precision & Accuracy

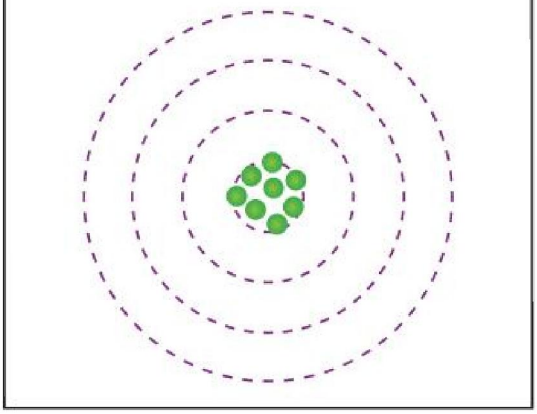
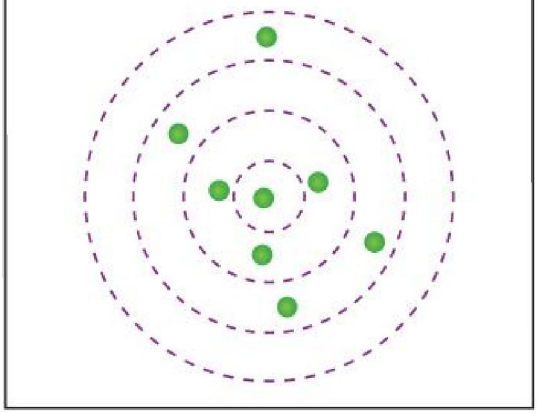


Figure 2: Example of Poor Precision (High Imprecision)



Standard deviation may also be used to monitor on-going day-to-day performance. For instance, if during the next week of testing, the standard deviation calculated in the example for the normal potassium control increases from (0.08 to 0.16 mmol/L), this indicates a serious loss of precision. This instability may be due to a malfunction of the analytical process. Investigation of the test system is necessary and the following questions should be asked:

- Has the reagent or reagent lot changed recently?
- Has maintenance been performed routinely and on schedule?
- Does the potassium electrode require cleaning or replacement?
- Are the reagent and sample pipettes operating correctly?
- Has the test operator changed recently?

Formula 2: Calculating a Standard Deviation [s] For a Set of QC Values

$$s = \sqrt{\frac{\Sigma(x_n - \bar{x})^2}{n - 1}}$$

Where:

- s = standard deviation
- $\bar{x}$ = mean (average) of the QC values
- $\Sigma(x_n - \bar{x})^2$ = the sum of the squares of differences between individual QC values and the mean
- n = the number of values in the data set

Although most calculators and spreadsheet programs automatically calculate standard deviation, it is important to understand the underlying mathematics.

To calculate the standard deviation for the normal level of control (Level I) in Table 1,

begin by calculating the mean [$\bar{x}$]:

$\bar{x}$ = 4.0 + 4.1 + 4.0 + 4.2 + 4.1 + 4.1 + 4.2 mmol/L ÷ 7

$\bar{x}$ = 28.7 mmol/L ÷ 7

$\bar{x}$ = 4.1 mmol/L

Calculate the standard deviation [s] as follows:

$$s = \sqrt{\frac{\sum(x_n - \bar{x})^2}{n-1}}$$

$$= \sqrt{\frac{(4-4.1)^2 + (4.1-4.1)^2 + (4-4.1)^2 + (4.2-4.1)^2 + (4.1-4.1)^2 + (4.1-4.1)^2 + (4.2-4.1)^2}{6}}$$

$$= \sqrt{\frac{(-0.1)^2 + (0.0)^2 + (-0.1)^2 + (+0.1)^2 + (0.0)^2 + (0.0)^2 + (+0.1)^2}{6}}$$

$$= \sqrt{\frac{0.01 + 0.0 + 0.01 + 0.01 + 0.0 + 0.0 + 0.01}{6}}$$

$$= \sqrt{\frac{0.04}{6}}$$

s = 0.082 OR 0.1 (Rounded)

The standard deviation for one week of testing of the normal potassium control level is 0.082 mmol/L. Now that the amount of precision is known, some assumptions can be made about how well this test is performing.