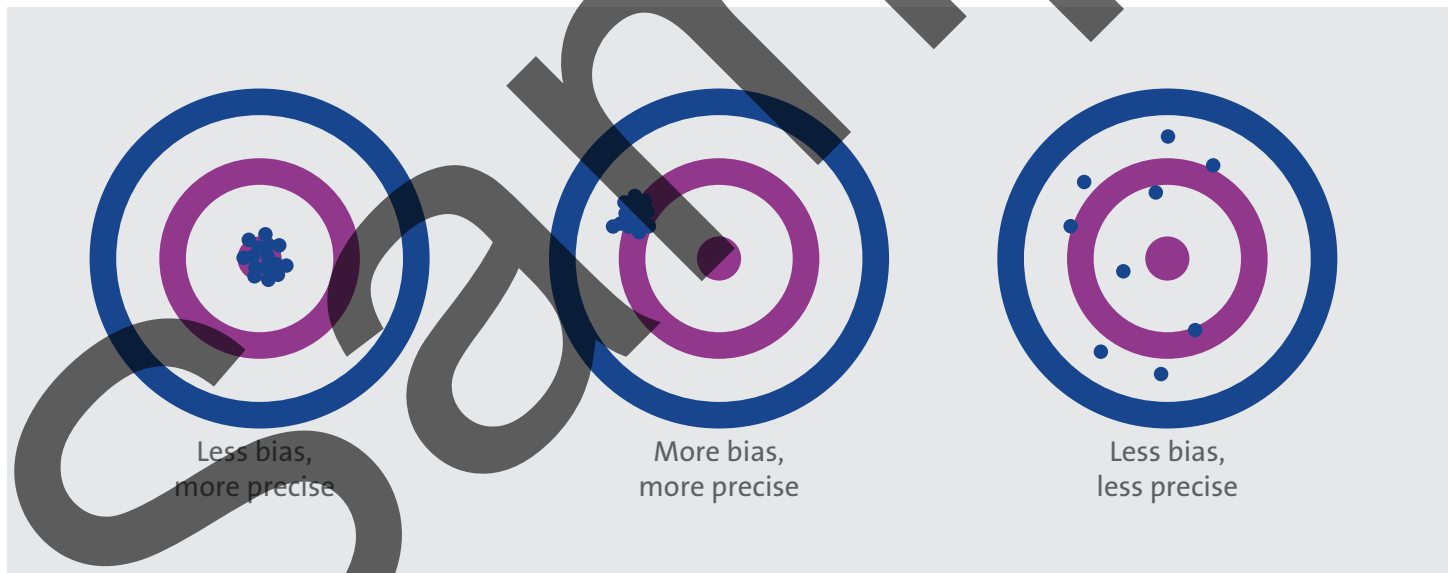CLSI

Implementation Guide
EP15-Ed3-IG1

Introduction

This implementation guide describes the minimum procedures necessary for a medical laboratory to verify a manufacturer's or laboratory-developed test's precision claims. For additional information on verifying precision, see CLSI document EP15.[1]

NOTE: The study described in this implementation guide for verifying precision can also be used to estimate bias (trueness). See CLSI document EP15-Ed3-IG2.[2]

IMPORTANT NOTE: The study described in CLSI document EP15[1] is not intended for use by a test developer to establish precision for a new commercial or laboratory-developed test. Instead, test developers should use CLSI document EP05[3] for guidance on establishing or validating precision. Laboratories and commercial manufacturers are collectively referred to as "developers" in this implementation guide.

Accuracy: A Combination of Precision and Bias

It is important that measurement procedures provide accurate results. In order to do so, they must both be precise and have low bias as shown in the figure below.

Less bias,
more precise

More bias,
more precise

Less bias,
less precise

While CLSI document EP15[1] contains instructions for studying both precision and bias, this implementation guide focuses only on precision. CLSI document EP15-Ed3-IG2[2] focuses on bias.

High precision (low coefficient of variation expressed as a percentage [% CV]) means that when a sample is run repeatedly, the results are very close to each other. Precision can be broken into various components. When the precision of a single run is considered, it is called "within-run precision." "Repeatability" is measured when all components are held essentially the same (single run, operator, lot, calibration, etc.). "Reproducibility" is measured when all components are varied (multiple runs, days, operators, lots, etc.).

Preparing for the Study

The precision goal should be determined by asking, "What is the maximum allowable imprecision (standard deviation [SD] or % CV) at each analyte concentration for which the developer makes precision claims?" The developer's precision claims should be within this goal. Usually, the developer provides claims for repeatability (within-run) and within-laboratory imprecision.

The laboratory should ensure that the operators are trained on the measuring system and that the measuring system has been calibrated according to the developer's instructions and is operating properly, with quality control (QC) results within expected ranges.

Selecting the Samples

The laboratory should select two or more samples to be tested at levels (eg, concentrations) close to those used for the developer's claims. Sample levels higher or lower than the measuring interval should be avoided. If the data will be used for the verification of bias study, as described in CLSI document EP15,[1] the laboratory should choose samples with known values. If the selected samples are not patient samples, they must be commutable with (ie, behave like) patient samples for precision.

Materials Needed

To verify precision, the laboratory needs:

- Selected samples
- Two levels of QC materials

The Study

Designing the Study

The table below shows an example study design for verifying precision.

Samples	Replicates	Runs	Days	QC	Daily Results Review
2	5	1 per day	5	2 levels with each run	Yes

Abbreviation: QC, quality control.

Running the Study

To verify precision, the laboratory should:

1. Test the samples in one run per day, with five replicates for each sample. This testing is repeated for four additional days (or five days total).

   - Different operators should perform the testing each day, if possible.

   - The testing days do not need to be consecutive.

   - If the samples require preprocessing before testing, each replicate should be processed as was done when the developer established the precision claim, ie, each replicate may have been processed separately or each replicate may have been sampled multiple times from a single processed sample.

2. Include QC materials in the run to ensure the test has worked properly.