FDA LABORATORY LLC
REPUBLIC OF ARMENIA

ISO/IEC 17025:2017

REQUIREMENTS FOR IN-HOUSE METHODS AND SAMPLING ERRORS DURING THE VALIDATION PROCESS BY GC-MS

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1.ISO 17025 REQUIRES THE LABORATORIES TO USE APPROPRIATE METHODS

2.ISO
3.DIN
4.EN
5.GBT
6.GOST
7.AST

If non-standard methods must be used, customer approval is required, and methods must be extensively validated and documented.

Laboratories can develop their own methods, but they must be fully verified to ensure that they are acceptable and fit for purpose.

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- **Stage 1 - Process Design:**

During this stage, the commercial manufacturing process is defined based on knowledge obtained during development and scale-up activities.

- **Stage 2 - Process Qualification:**

The process design is evaluated at this stage to see if the process is capable of reproducible commercial manufacturing.

- **Stage 3 - Continued Process Verification:**

During routine production, constant assurance is gained that the process remains in a state of control.

VALIDATION SHOULD INCLUDE THE FOLLOWING STAGES

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THE FOLLOWING VALIDATION PARAMETERS MUST BE DETERMINED FOR QUANTITATIVE METHODS OF DRUG TESTING

- Specificity | selectivity
- Limit of detection [LOD]
- Limit of quantification [LOQ]
- Precision
- Linearity and working range

- Accuracy
- Uncertainty of measurement
- Stability

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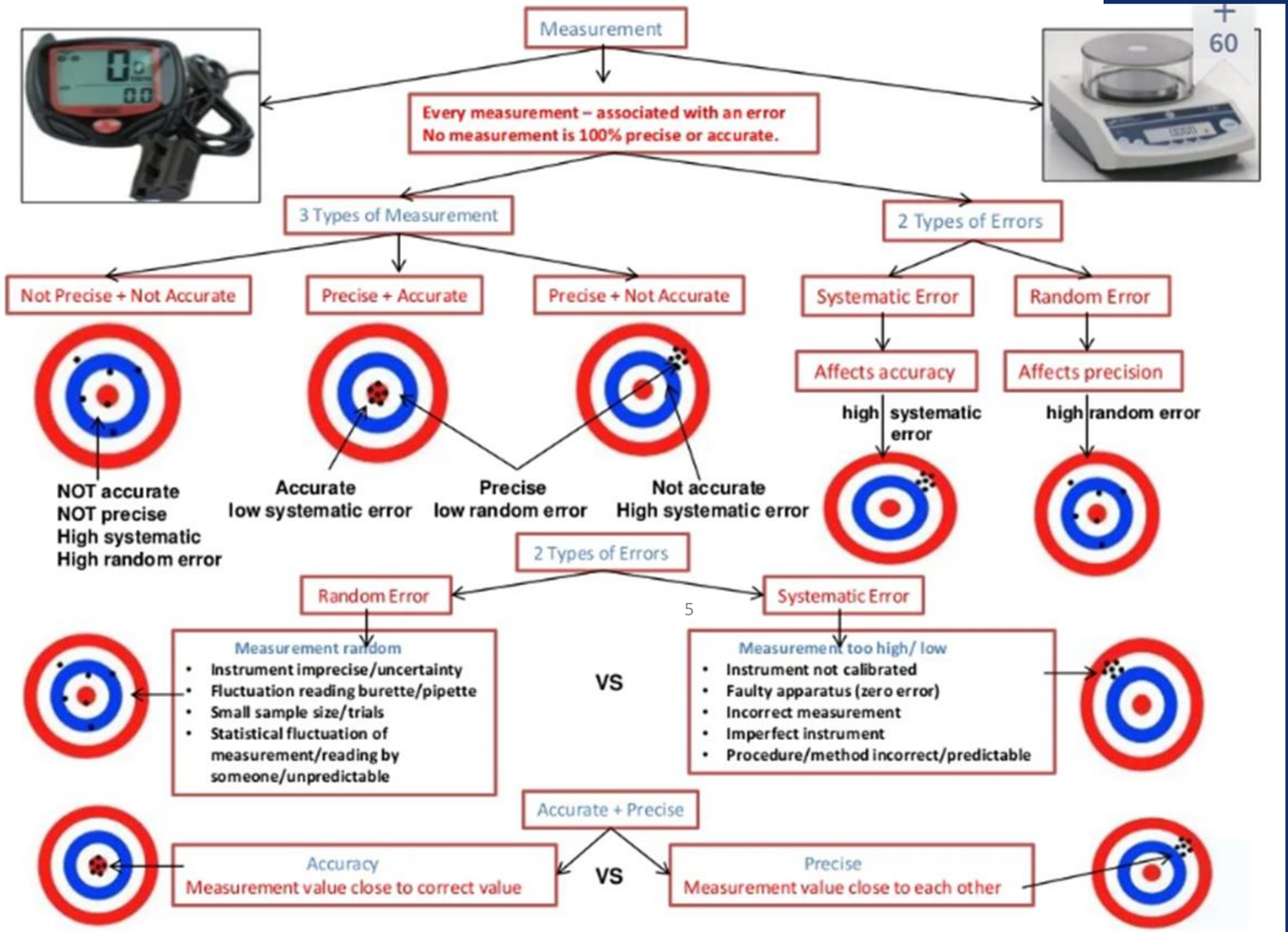
ERRORS IN CHEMICAL ANALYSIS



SAMPLING ERRORS

Sampling errors are statistical errors that occur when a sample does not accurately represent the entire population.

SAMPLE ERRORS INCLUDE:

- SAMPLE DEFINITION
- SAMPLE COLLECTION
- SAMPLE HANDLING

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THE FOUR GROUPS OF SAMPLING ERRORS AND THEIR RESPECTIVE SPECIFIC ERRORS ARE AS FOLLOWS

- MATERIAL ERRORS
- PROCESS ERRORS
- SAMPLING ERRORS
- LABORATORY ERRORS

1. The fundamental error relates to the nature or composition of the material. This error is inherent when the material is sampled and is unavoidable. The material we sample varies in its composition or constitution, which generates the fundamental error.

ERROR #1

FUNDAMENTAL ERROR

2. The grouping and segregation error addresses how various particles are distributed both in the lot and at the particular place where we take a sample. Differences between individual particles determine how they are distributed in the lot as well as “locally.” They may segregate during transport or when transferred from one container to another, for instance. Further, the material is never perfectly blended: it always has some degree of settling or segregation.

ERROR #2

GROUPING & SEGREGATION ERROR

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- ERROR #3 NUGGET EFFECT

The nugget effect may occur in sampling pharmaceutical or nutritional materials such as natural products. Nuggets may be individual particles, clumped materials due to moisture or electrostatic charge, or other localized regions of high ingredient concentration in the material to be sampled.

- ERROR #4 NON-PERIODIC PROCESS ERRORS
- ERROR #5 PERIODIC PROCESS ERRORS

Non-periodic process variation is non-random and results from process changes showing data shifts and trends. We might know there was a process upset or that material from a new supplier was non-uniformly introduced into the process - both are examples of non-periodic process variation. Periodic process variation is also non-random and results from cyclic behavior.

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ERROR #6
SAMPLE DEFINITION

- The sample definition determines which subset of the lot material will be included in the sample.

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ERROR #7
SAMPLE COLLECTION

- Sample collection is physically obtaining the material identified to be in the sample. To reduce sample selection errors, the concept of accurate sampling must be followed. Every portion of the lot of equal size must have the same chance of being included in the sample. The integrity of the sample must be preserved both during and after sampling.

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- Sample handling is generally considered to be a subset of sampling. It concerns sample preservation and integrity both during and after sampling. Sample handling refers to physical or chemical changes that alter the sample's material composition and the characteristic of interest, causing our measurement to change.

ERROR #8
SAMPLE HANDLING

- Analytical error also includes errors caused by the analytical instrument. This error may be determined by performing an instrument precision study in which the same sample is injected many times by gas chromatography [GC-MS] and the mean and standard deviation are calculated.

ERROR #9
ANALYTICAL ERROR

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ERROR #10
DATA ERROR

Data errors are categorized as laboratory errors because they are more likely to occur in laboratories.

	SOURCES OF SYSTEMATIC ERROR	SOURCES OF RANDOM ERROR
SAMPLE PREPARATION	The portion of sample to be analyzed [analytical sample] may be incorrectly selected	The analytical sample is in contact and contaminated by other portions of the sample
SAMPLE PROCESSING	Decomposition of analyte during sample processing, cross contamination of the samples	Non homogeneity of the analyte in single units of the analytical sample Non homogeneity of the analyte in the ground/chopped analytical sample Variation of temperature during the homogenization process Texture of plant materials affecting the efficiency of homogenization process

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	SOURCES OF SYSTEMATIC ERROR	SOURCES OF RANDOM ERROR
EXTRACTION | CLEAN UP	Incomplete recovery of analyte Interference of co-extracted materials [load of the adsorbent]	Variation in the composition [e.g. water, fat, and sugar content] of sample materials Temperature and composition of sample/solvent matrix
QUANTITATIVE DETERMINATION	Interference of co-extracted compounds	Variation of nominal volume of devices within the permitted tolerance intervals
	Incorrect purity of analytical standard	Precision and linearity of balances
	Operator bias in reading analogue instruments, equipment	Changing of laboratory-environmental conditions during analysis
	Determination of substance differing from the residue definition	Operator effects [lack of attention]
	Determination of substance which do not originate from the sample [e.g. contamination from the packing material]	Varying injection, chromatographic and detection conditions [matrix effect, system inertness, detector response, signal to noise variation etc.]

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KEY TAKEAWAYS

- A sampling error occurs when the study's sample is not representative of the whole population.
- Sampling is an analysis performed by selecting a number of observations from a larger population.
- Even randomized samples will have some degree of sampling error because a sample is only an approximation of the population from which it is drawn.
- The prevalence of sampling errors can be reduced by increasing the sample size.
- Random sampling is an additional way to minimize the occurrence of sampling errors.
- In general, sampling errors can be placed into three categories: population-specific error, selection error, sample frame error.

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THANK YOU!

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