



Method Validation and Accreditation

Dr Hamide Z Şenyuva
Senior Research Scientist
TÜBİTAK-ATAL, TURKEY
hamide.senyuva@tubitak.gov.tr

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Why it is needed?

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■ **Laboratory accreditation**

Why it is needed?

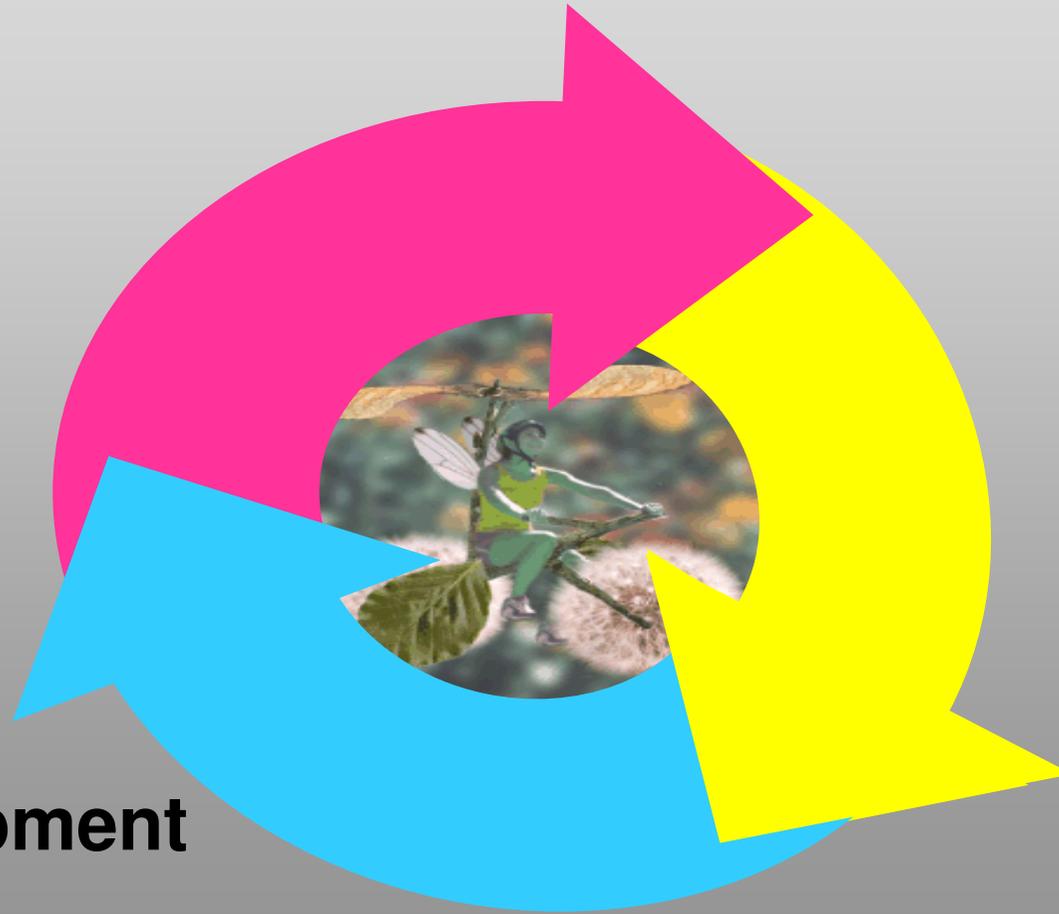
The fundamental components of a quality system

■ **Validation and accreditation**



Method Life Tour

Validation



Development

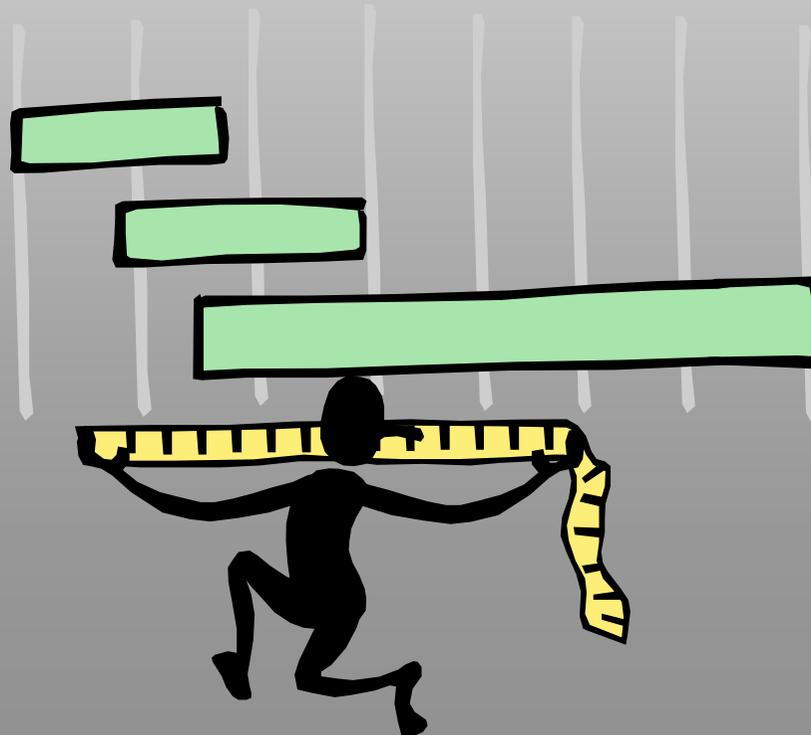
Optimization

Why it is needed?

The purpose of analytical measurement is to get **consistent, reliable and accurate** data.

Incorrect measurement results can lead to tremendous costs.

Equal importance for those working in a **regulated** and in a **accredited** environment.



Analytical Method Selection

❖ 'Fitness for Purpose'

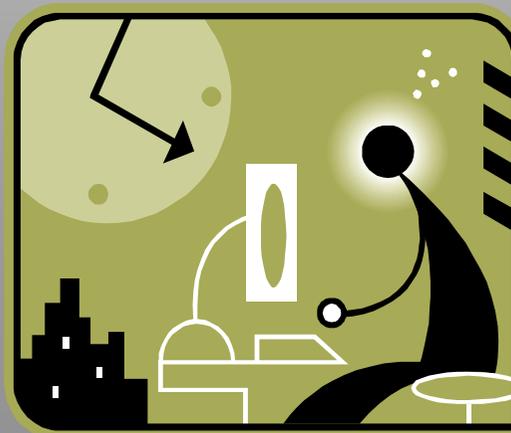
Provide evidence that the method does what it is intended to do, with the required accuracy and precision

❖ 'Criteria-based Approach'

Methods should have recovery in range

Minimum RSD_r depending on LOD

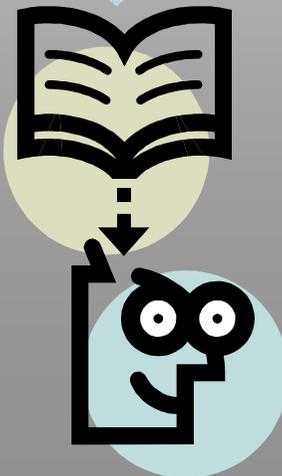
Minimum RSD_R depending on LOD



Method Validation

Method validation is the process of establishing a number of method characteristics which can be used to confirm that the analytical procedure employed for a specific test is suitable for its intended use.

Goal for a validated method is to provide confidence in the results produced with this method



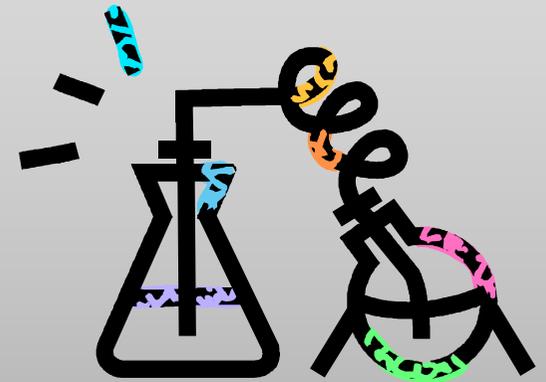
When should methods be validated /revalidated ?

Validated

- Before their introduction into routine use
- For accreditation to ISO17025
- Customer request

Revalidated

- Whenever the conditions, for which the method has been validated, change, like change of instrument characteristics, sample matrix, change in analyte concentration, change of analyst
- Whenever the original method is changed, and the change is outside the original scope of the method



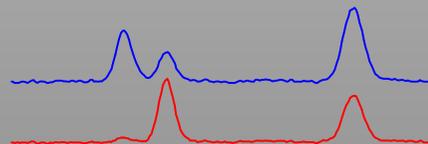
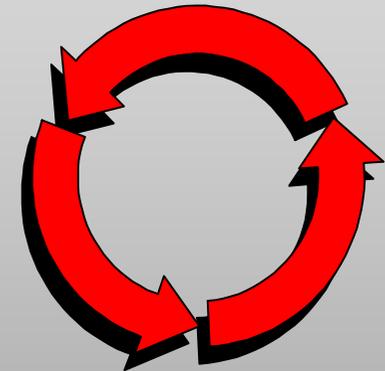
Method Re-validation (*Summarize*)

When

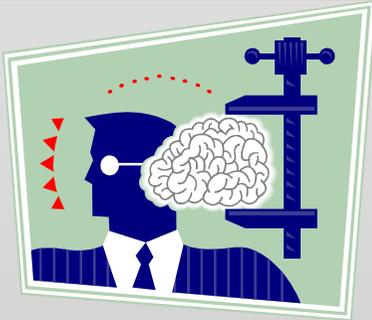
- Method parameters have been changed
- The scope of the method has been changed (for example from one specific type of GC instrument to general Gas Chromatograph)

What

Preferably everything. Exceptions should be scientifically justified



Types of Method Vaidation



❖ 'In-house laboratory method validation'

❖ 'Peer-verified laboratory method validation'

❖ 'Inter-laboratory method validation'



In-house Laboratory Validation

First stage in establishing how well a method performs is carry out in-house validation

- 'Single Analyst'
- 'Single Laboratory'
- 'Same equipment and instrumentation'

LOD and LOQ values should not differ much whether determined in one laboratory or established in several laboratories.

- ✓ LOD & LOQ
- ✓ Linearity
- ✓ Accuracy (Recovery)
- ✓ Repeatability (r)



Peer-verified laboratory method validation

Testing of a method in a second or third laboratory is known as 'peer verification'.



Peer verification is “half-way house” to the full method validation

- ✓ LOD & LOQ
- ✓ Linearity
- ✓ Accuracy (Recovery)
- ✓ Repeatability (r)
- ✓ Limited Reproducibility (R)

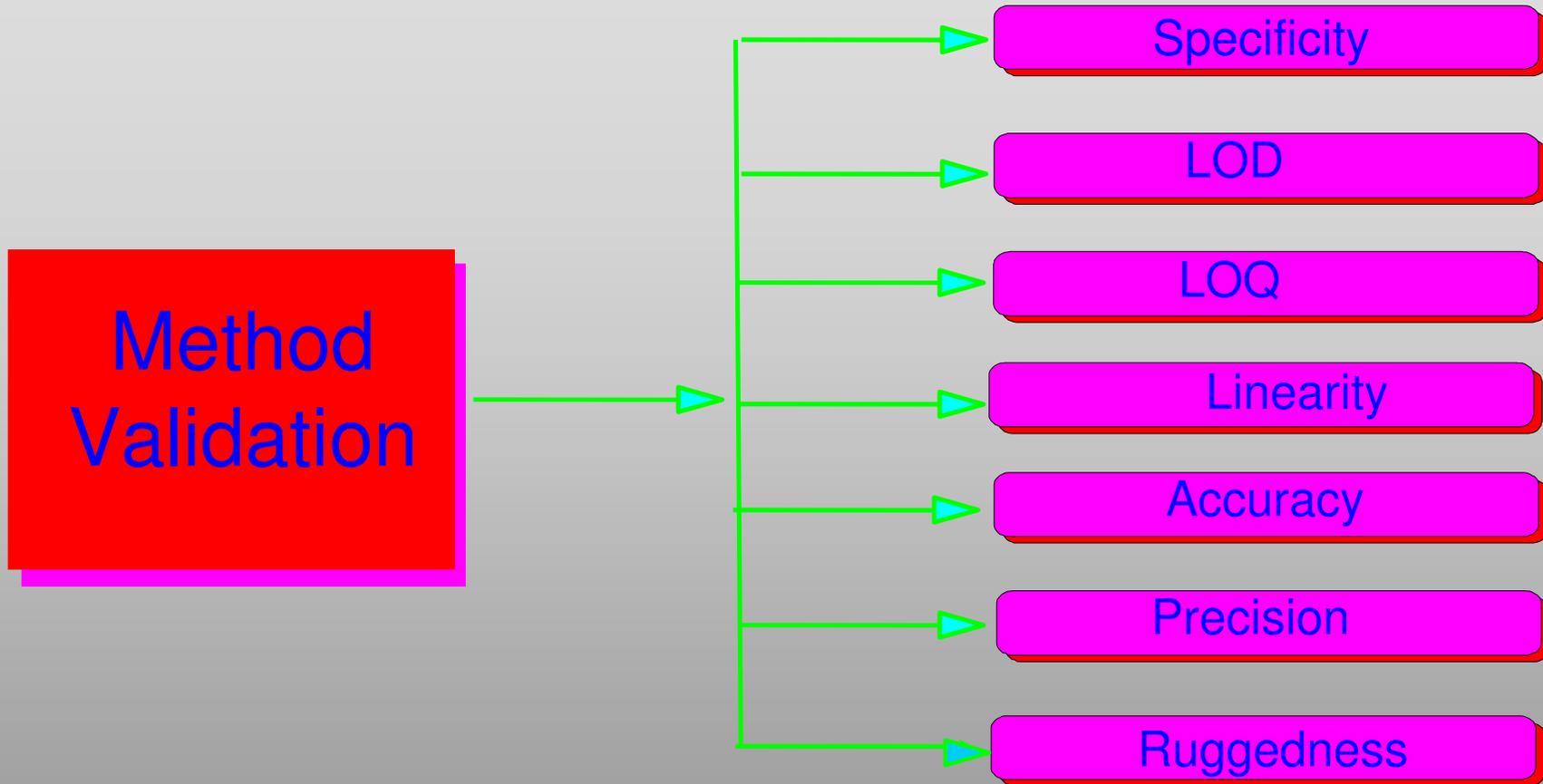
Inter-laboratory Method Validation

- Acceptable data from Min 8 different laboratories (generally min 12 lab)
- Blind duplicates
 - *spikes + blanks + naturally contaminated
 - *minimum of three levels of contamination

- ✓ **LOD & LOQ**
- ✓ **Linearity**
- ✓ **Accuracy (Recovery)**
- ✓ **Repeatability (r)**
- ✓ **Reproducibility (R)**



Method Performance Characteristics

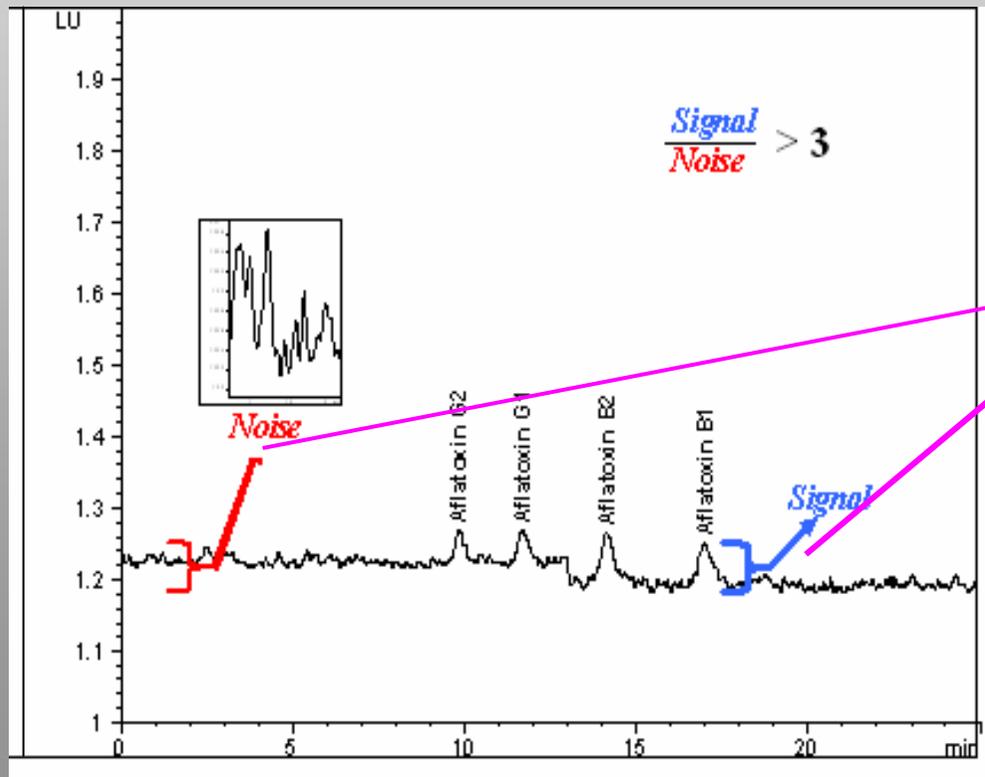


Actual validation effort depends on the analysis problem

What do you want to detect - in which matrix - at which detection limits

Limit of Detection (LOD)

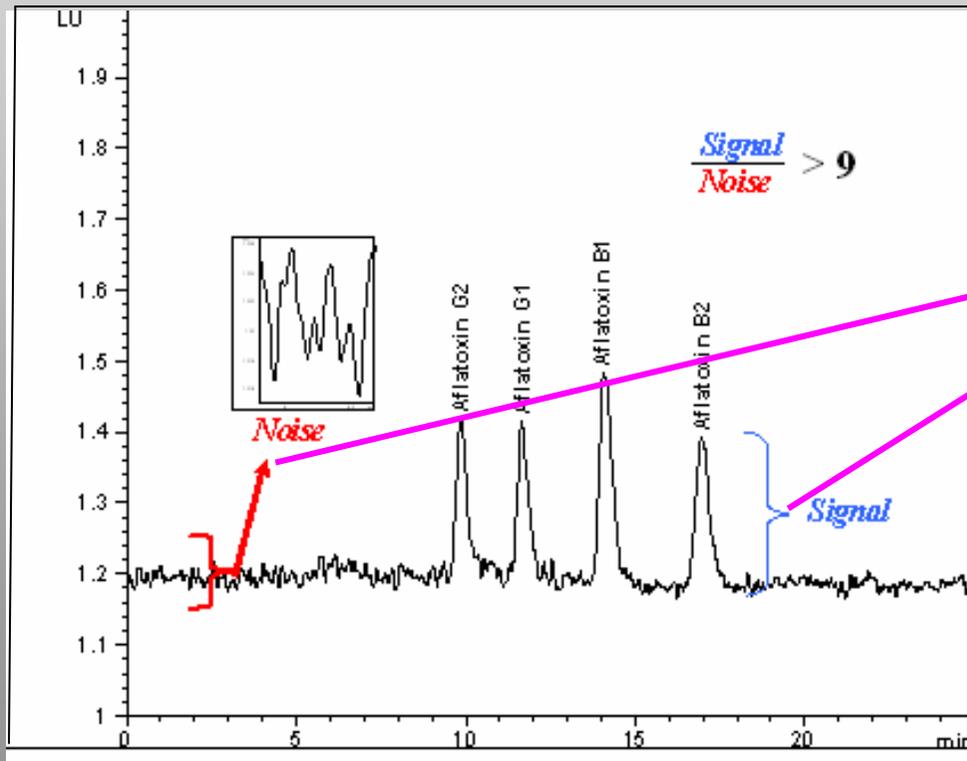
LOD, for a given analyte is the minimal amount needed, amount to be able to distinguish the analyte signal above the background detector noise.



S/N 3

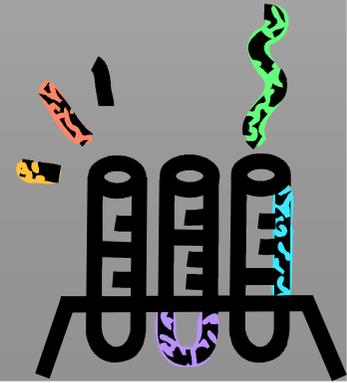
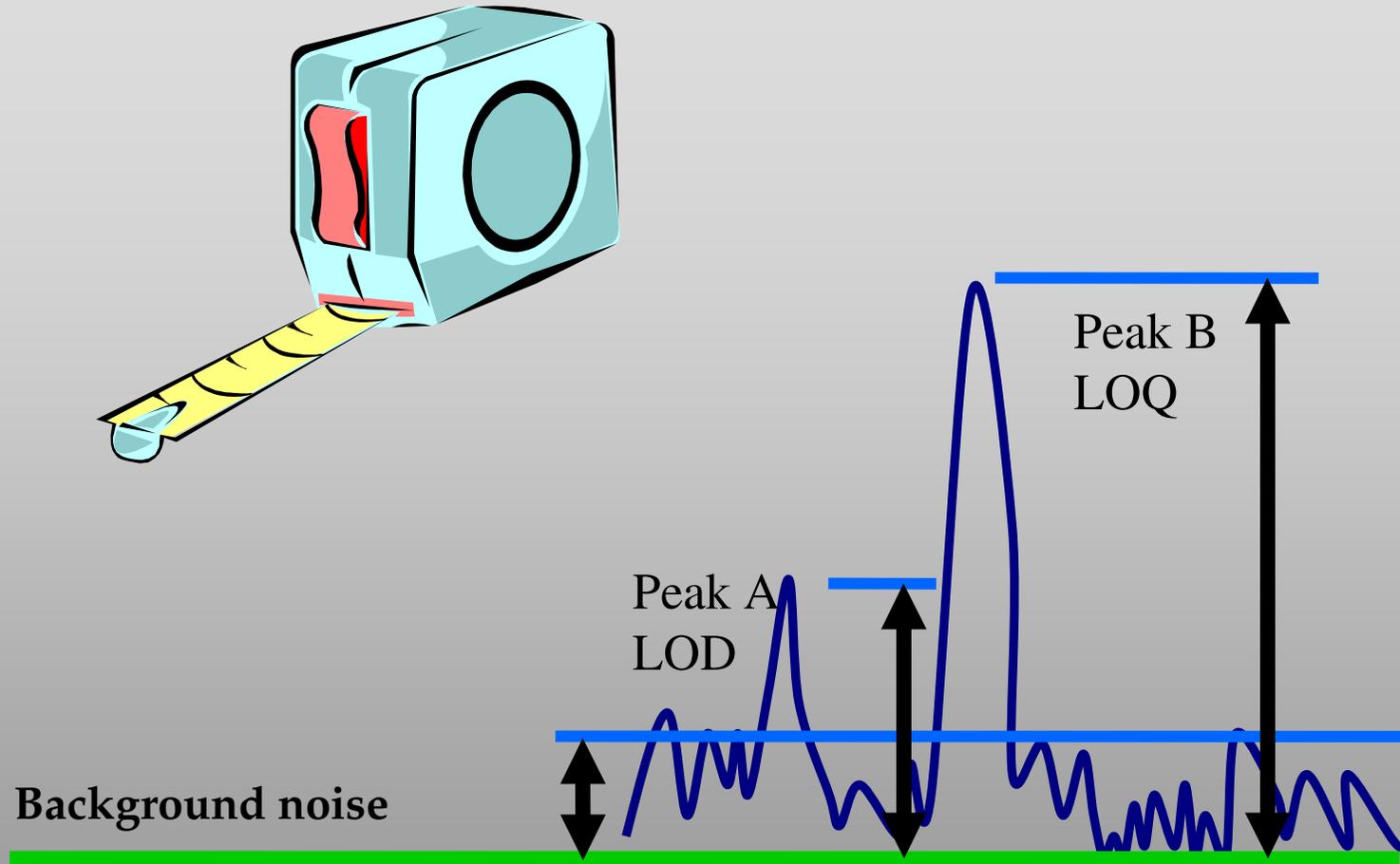
Limit of Quantitation (LOQ)

The limit of quantification of an analyte is the lowest amount of that analyte in a sample which can be accurately measured with reliability.



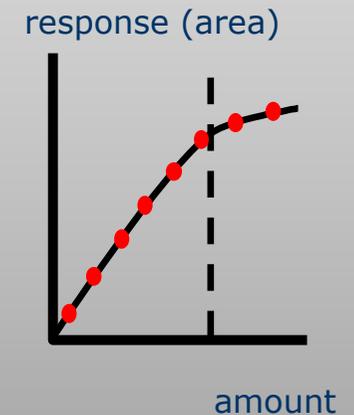
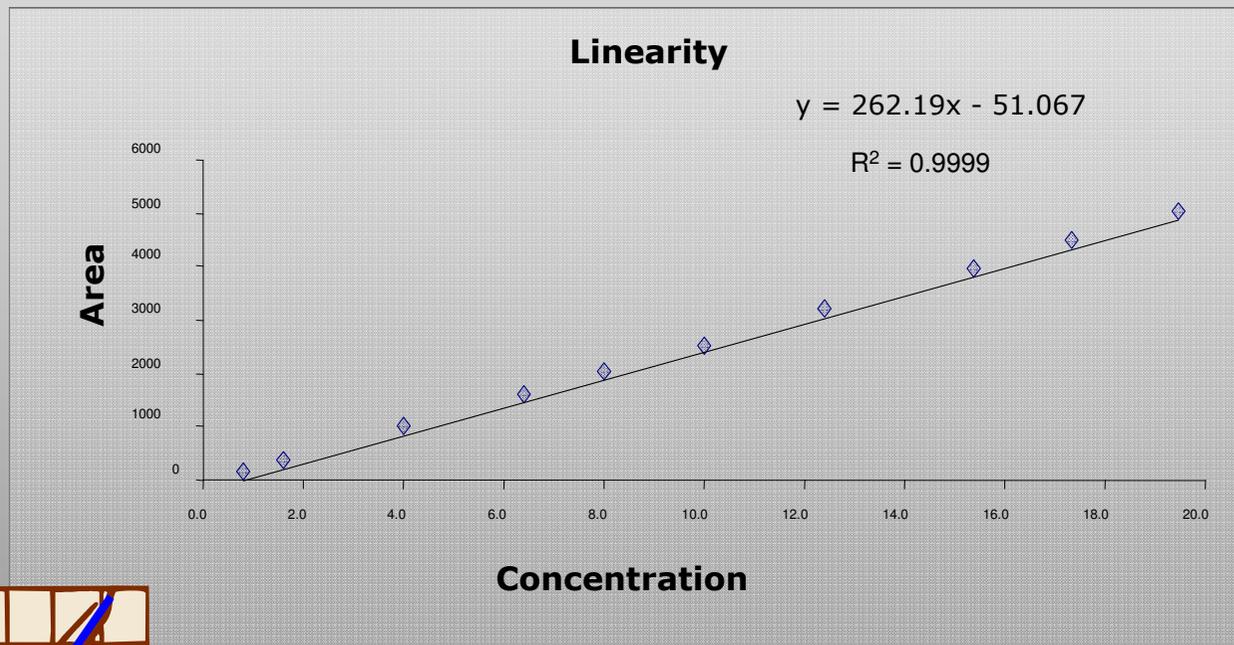
S/N 9
3 x LOD = LOQ

LOD, LOQ and S/N



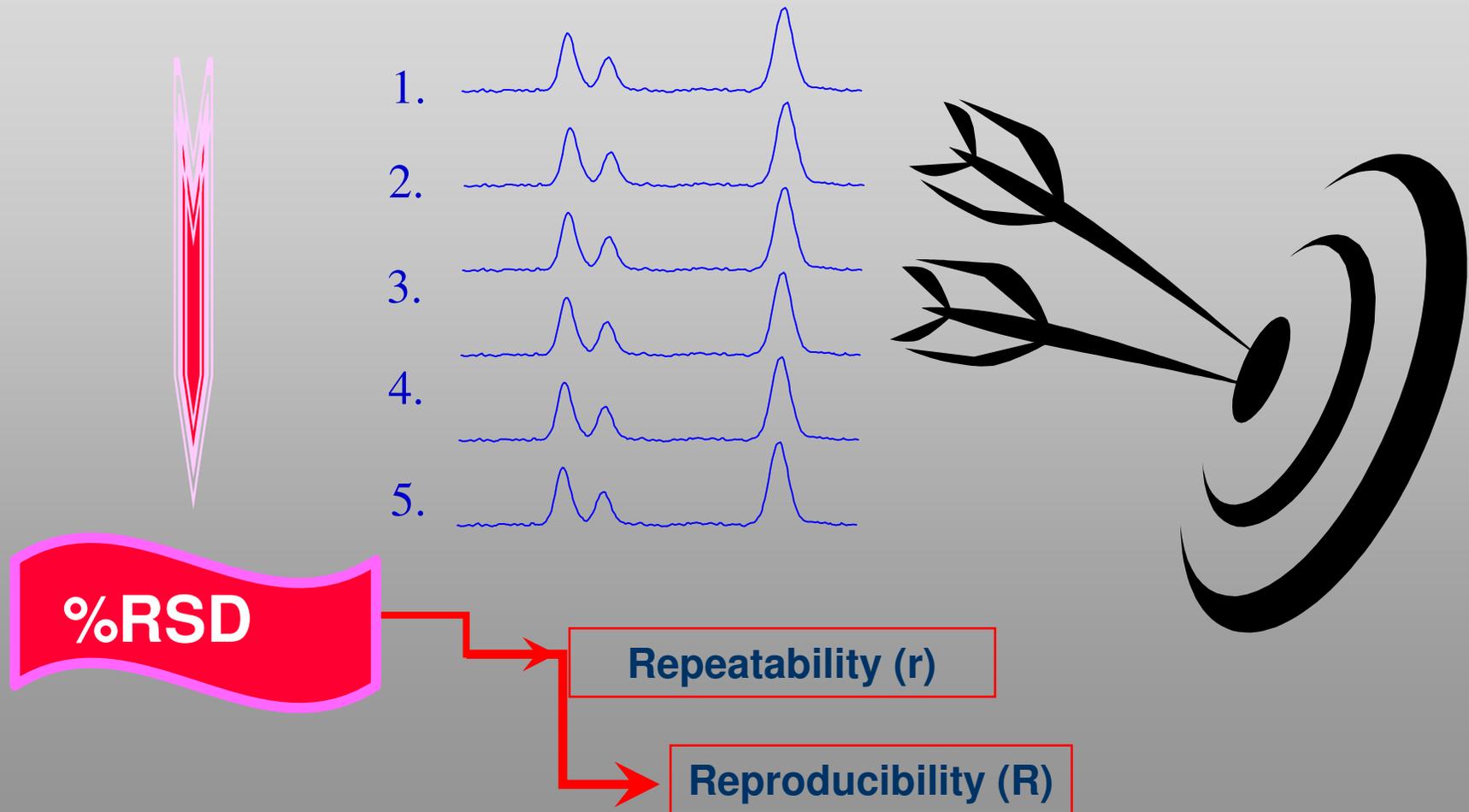
Linearity

The linearity of an analytical procedure is the extent to which (within a give range) the measured signals are directly proportional to the concentration of the analyte in the sample.



Precision (*Repeatability and/or Reproducibility*)

The precision of an analytical procedure expresses the closeness of agreement between a series of measurements obtained from multiple sampling of the same homogenous sample under prescribed conditions.



Precision (*Repeatability and/or Reproducibility*)

Same operation conditions over a short interval time

Repeatability, r



Same analyst
Same Instrument
Same reagents
Same laboratory

Expresses the precision between different laboratories

Reproducibility, R



Different analyst
Different laboratory
Different equipment
Different sources of reagents

Precision (*Repeatability*)

Day 1

100.6

100.8

100.1

100.3

100.5

100.4

Day 2

99.5

99.9

98.9

99.2

99.7

99.6

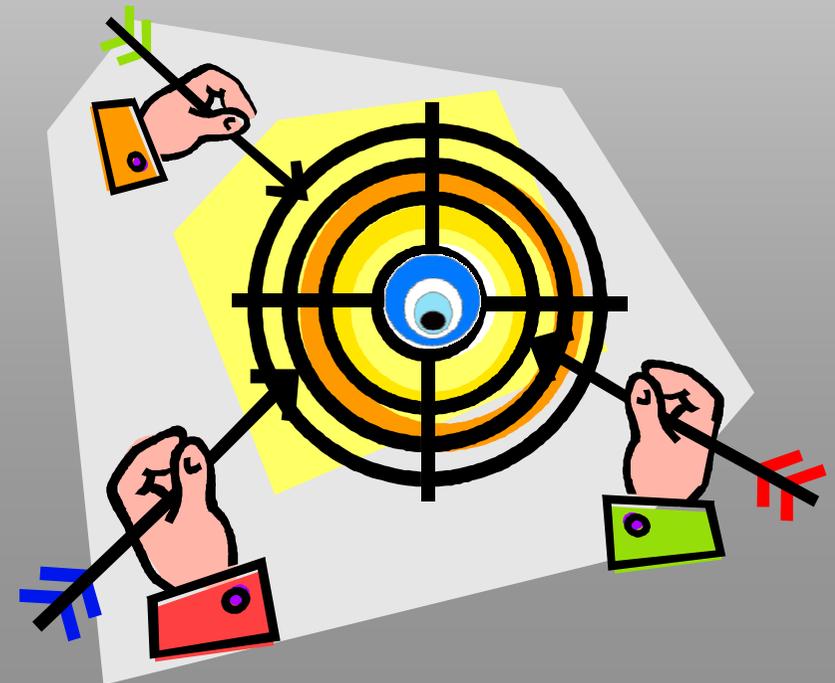
Mean = 100.5
RSD = 0.24%
CI = 100.5 ± 0.24

Mean = 99.5
RSD = 0.36%
CI = 99.5 ± 0.36

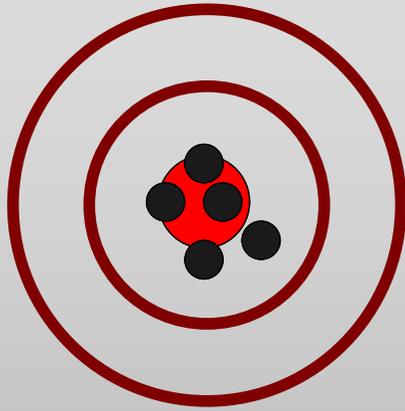
Accuracy

The closeness of a measured level of an analyte to the known true level

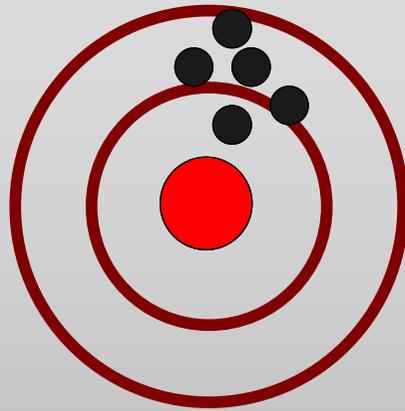
Accuracy, frequently reported as % recovery of known, added amount, or difference between the mean and true value, with confidence intervals



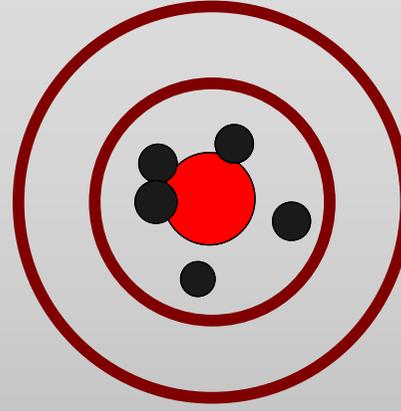
Accuracy and Precision Relation



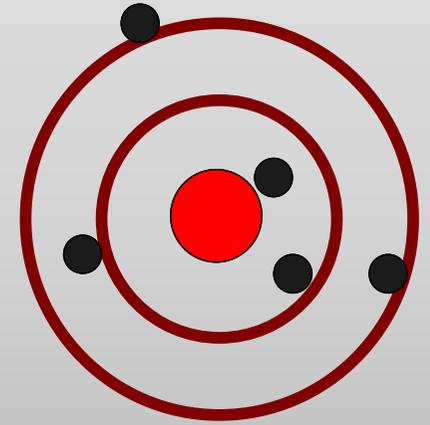
A



B



C



D

- A** Accuracy is good, precision is good
- B** Accuracy is poor, precision is good
- C** Accuracy is good, precision is poor
- D** Accuracy and precision are poor

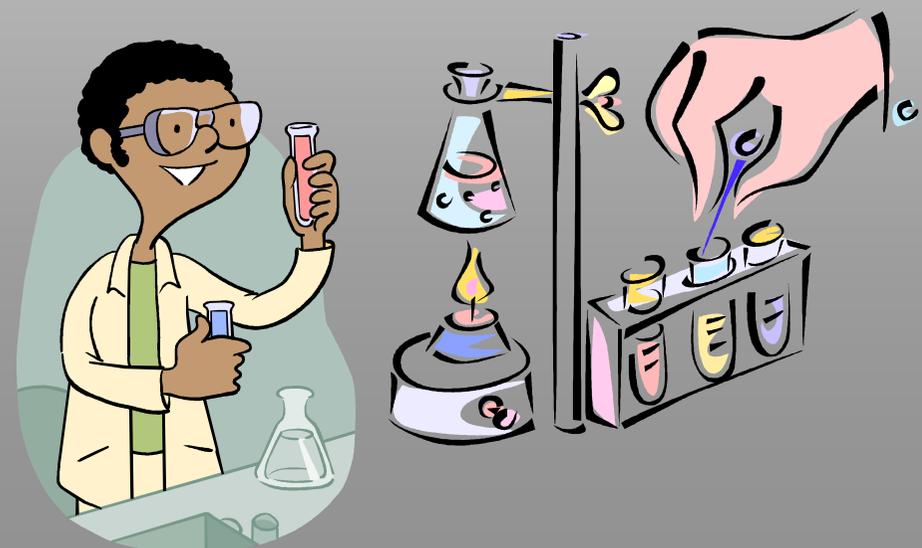
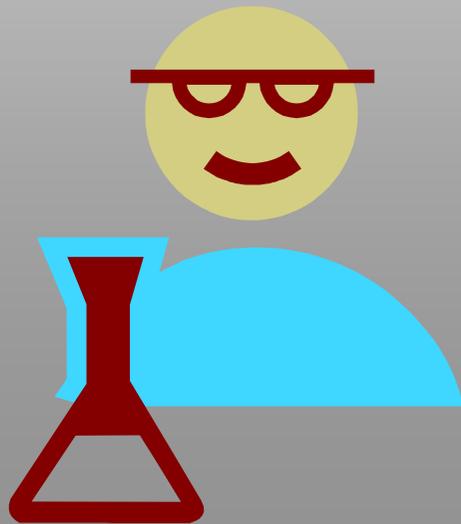


Summarize Measurement Quality Objectives

- **Statement of performance or requirement for a particular method performance characteristic – can be quantitative or qualitative**
 - **quantification capability (expressed as the *limit of quantitation* - LOQ)**
 - **detection capability (expressed as the *limit of detection* - LOD)**
 - **applicable analyte concentration range - method's ability to measure analyte over some specified range**
 - ***method specificity* - ability of method to measure the analyte in the presence of interferences**
 - ***method ruggedness* - relative stability of method performance for small variations in method parameter values**

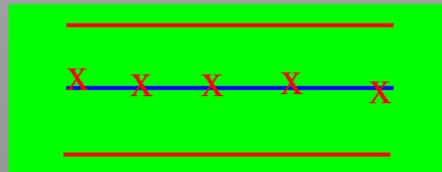
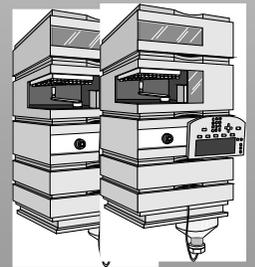
Why are quality systems important?

- ❖ Improve accuracy, consistency, reliability of data
- ❖ Improve efficiency through standard procedures
- ❖ Required by customers, e.g. accreditation
- ❖ Required by regulations
- ❖ Image and reputation of organization
- ❖ Image and reputation of individual scientists



Common Elements of Quality Systems in Laboratories

- ❖ (Standard) Operating Procedures
- ❖ Equipment computer/validation, calibration, maintenance
- ❖ Method validation
- ❖ Documentation of tasks, procedures, results, deviations (measurement uncertainties)
- ❖ People qualification
- ❖ Use of qualified reference material
- ❖ Internal audits
- ❖ Records



Key Principles of ISO/IEC 17025:2005

- **Internal quality control** scheme
- Participation in **proficiency testing** or other interlaboratory comparisons
- **Working procedures** or **Standard operating procedures (SOPs)**
- Regular use of **traceable standard reference materials** and/or in-house quality control using sub-references
- **Instruments** which are well maintained and calibrated
- **Validated methods**
- **Reporting measurement uncertainty**
- **Qualified personnel**
- **Recording and reporting**

ISO17025



Validation and accreditation

- Accreditation requires use only of validated methods (in-house or full study)
- Enforcement requires use only of validated methods
 - minimum performance specified



Relation Between Validation and Accreditation

Method validation is the process that provides evidence that a given analytical method, when correctly applied, produces results that are fit for purpose.

No matter how well a method performs elsewhere, analysts need to confirm that the method is valid when applied in their laboratory.

There is now much greater emphasis on method validation in the ISO/IEC 17025 accreditation standard.



What is Accreditation?

Accreditation is both a status and a process.



As a status, accreditation provides public notification that an institution or program meets standards of quality set forth by an accrediting agency.

As a process, accreditation reflects the fact that in achieving recognition by the accrediting agency, the institution or program is committed to self-study and external review by one's peers in seeking not only to meet standards but to continuously seek ways in which to enhance the quality of education and training provided.

Relation Between Validation & Accreditation

Analyst need to confirm that;

- produces results “*fit for purpose*”
- the method is *valid*



Greater emphasis on method validation in the ISO/IEC 17025 accreditation standard.

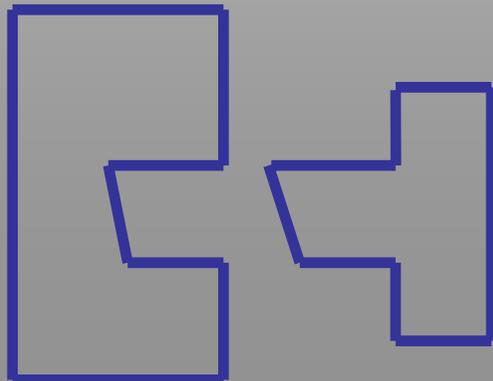
Summarize Validation & Accreditation

Validation and accreditation

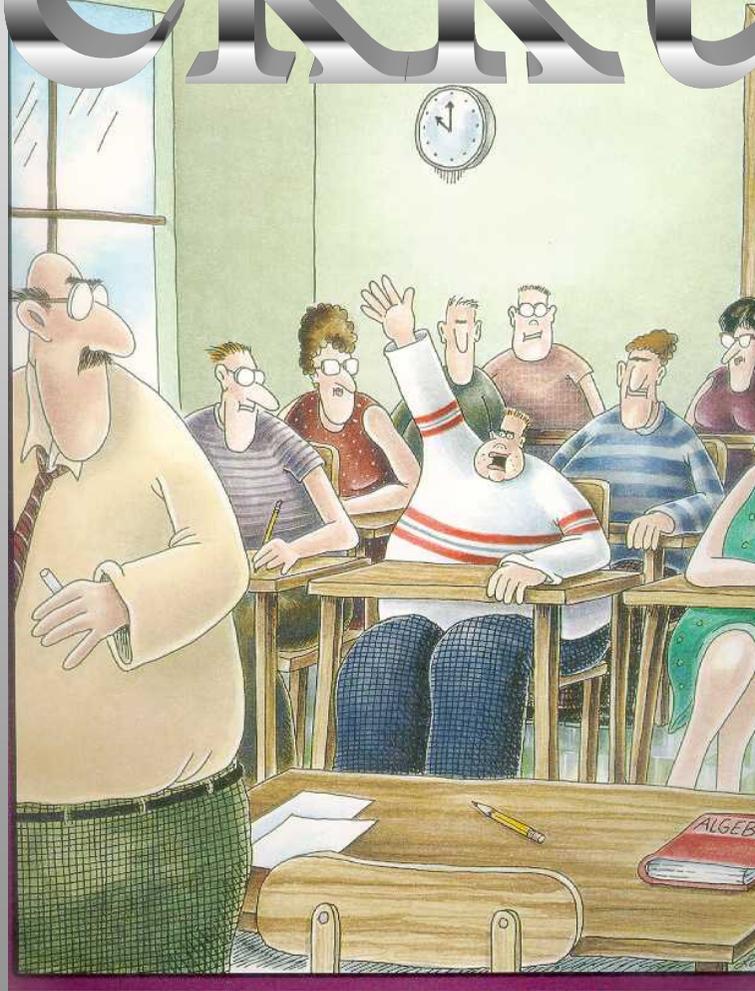
Accreditation requires use only of validated methods (in-house or full study)

Enforcement requires use only of validated methods

- minimum performance specified



teşekkürler



“Mr. Osborne, may I be excused? My brain is full.”



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