Welcome to the Webinar!

Measurement Uncertainty & Decision Rules

Presented by:
Susan Audino, PhD
S.Audino & Associates, LLC

February 20, 2024
1:00-2:00 PM EST

PJLA

Webinar Overview

DISCUSS THE IMPORTANCE OF

- Overview of ISO/IEC 17025 requirements MU and decision rules
- How to obtain MU and what factors to consider
- Applying Decision Rules

Webinar Housekeeping

- This webinar will be recorded
- All PJLA webinars are made available on our website & YouTube channel

  https://www.pjlabs.com/training/pjla-webinars/past-webinars
- All attendees are muted
- Please utilize the question tool bar to submit questions to be answered at the end of presentation

Meet Our Presenter

- Dr. Susan Audino is a chemist/chemometrician and independent consultant to chemical and biological laboratories. As a contractor for Accreditation Bodies, Dr. Audino assesses laboratories to and is an instructor for multiple ISO/IEC standards including ISO 17025. In addition to serving as science advisor to the AOAC International Cannabis Analytical Science Program (CASP), she was a contributing member of the NCIA Guide for Laboratory Testing, is a faculty member of Teachable Medicine, Trustee of Hood College, Board Member of The Center for Research on Environmental Medicine, advisor to Emerald Scientific, board member of cannabis/hemp testing laboratories, and has been an invited speaker at many domestic and international scientific conferences. Her clients have included government regulatory bodies, cannabis laboratories, and advocacy organizations. Dr. Audino is principal at S. Audino & Associates, LLC, principal at RWD, LLC, principal at Executive Quality Management, LLC, has several patents pending, and is a contributing author to Cannabis Laboratory Fundamentals.

Measurement Uncertainty and Decision Rules

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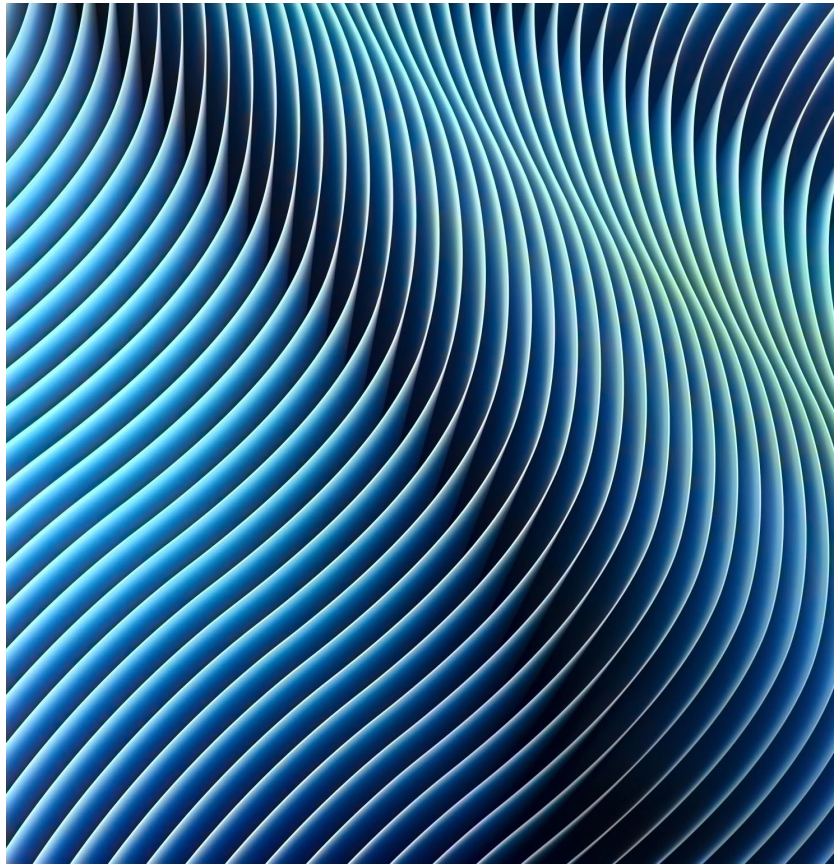
- Webinar sponsored by PJLA on February 20, 2024

To be or Not to be in this session …

- [x] Broad discussion on Measurement Uncertainty and its role in Decision Rules
- [x] How we ‘get to’ MU
- [ ] How to calculate MU
- [x] Evaluation of Conformity Specifications
- [x] Hypothetical Data includes assumptions that will not be reviewed
- [ ] Specific calculations and methods to calculate MU



Decision Rules

"Rule that describes how measurement uncertainty is accounted for when stating conformity with a specified requirement." ISO/IEC 17025:2017

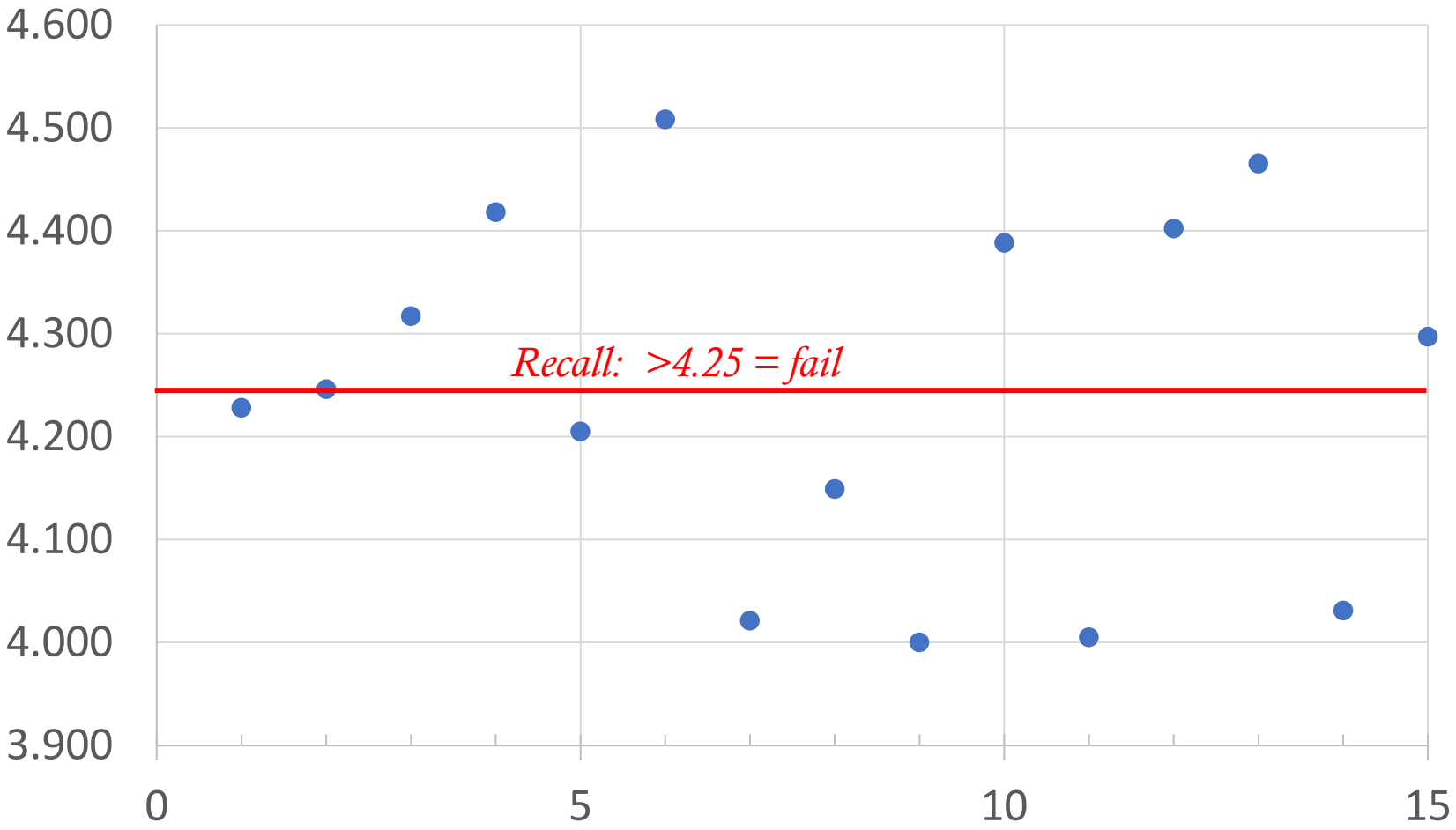
Typically binary

- Pass/Fail
- In Spec/ Out of Spec

Hypothetical Test Results

- ✓ Some specification says “Acceptable Value for this plastic is **4.25”** *(>4.25 = “fail”)*
- ✓ *CRM for this Plastic is **4.5***
- ✓ Lab prepared 15 independent samples and tested on some instrument.

Now let's look at the data



Sample	Result	Decision?
1	4.228	P
2	4.246	P
3	4.317	F
4	4.418	F
5	4.205	P
6	4.508	F
7	4.021	P
8	4.149	P
9	4.000	P
10	4.388	F
11	4.005	P
12	4.402	F
13	4.465	F
14	4.031	P
15	4.297	F

Arithmetic mean = **4.245**

Standard deviation = **0.17423**

Can we Confidently State Conformity?

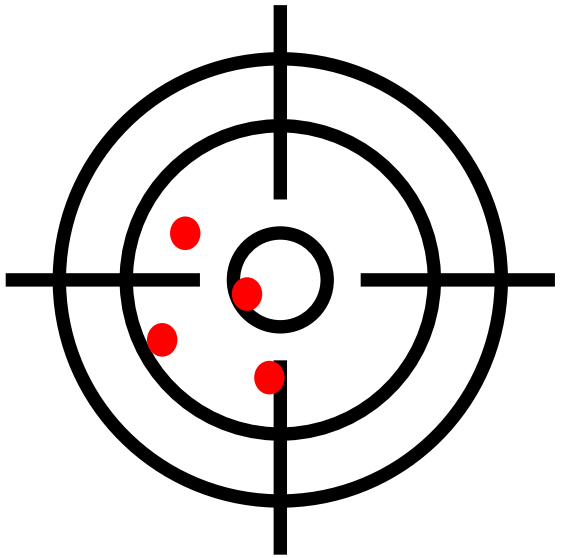
- Measurement Error
  - "How correct is the test result?"

Recall: CRM = 4.5

Contributions:

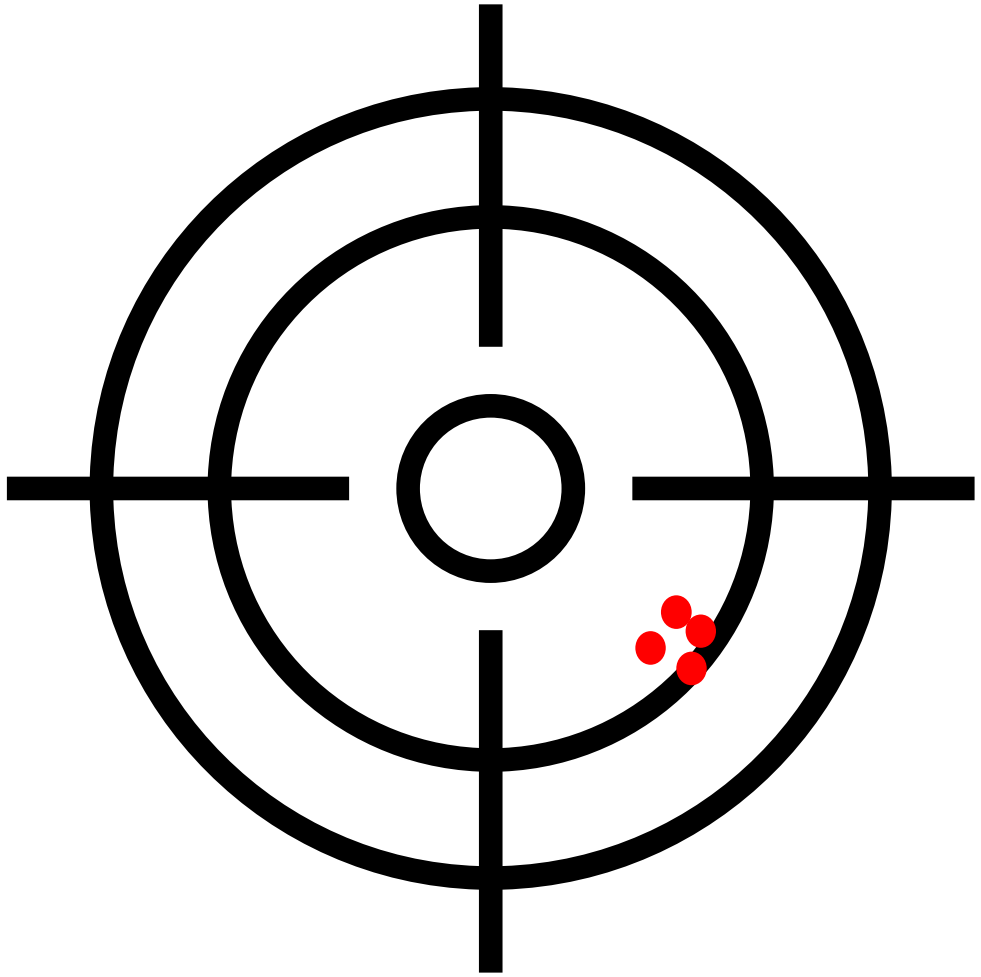
✓Systematic Errors

✓Random Errors



Measurement Accuracy

Sample	Result	Error
1	4.228	-0.272
2	4.246	-0.254
3	4.317	-0.183
4	4.418	-0.082
5	4.205	-0.295
6	4.508	0.008
7	4.021	-0.479
8	4.149	-0.351
9	4.000	-0.500
10	4.388	-0.112
11	4.005	-0.495
12	4.402	-0.098
13	4.465	-0.035
14	4.031	-0.469
15	4.297	-0.203

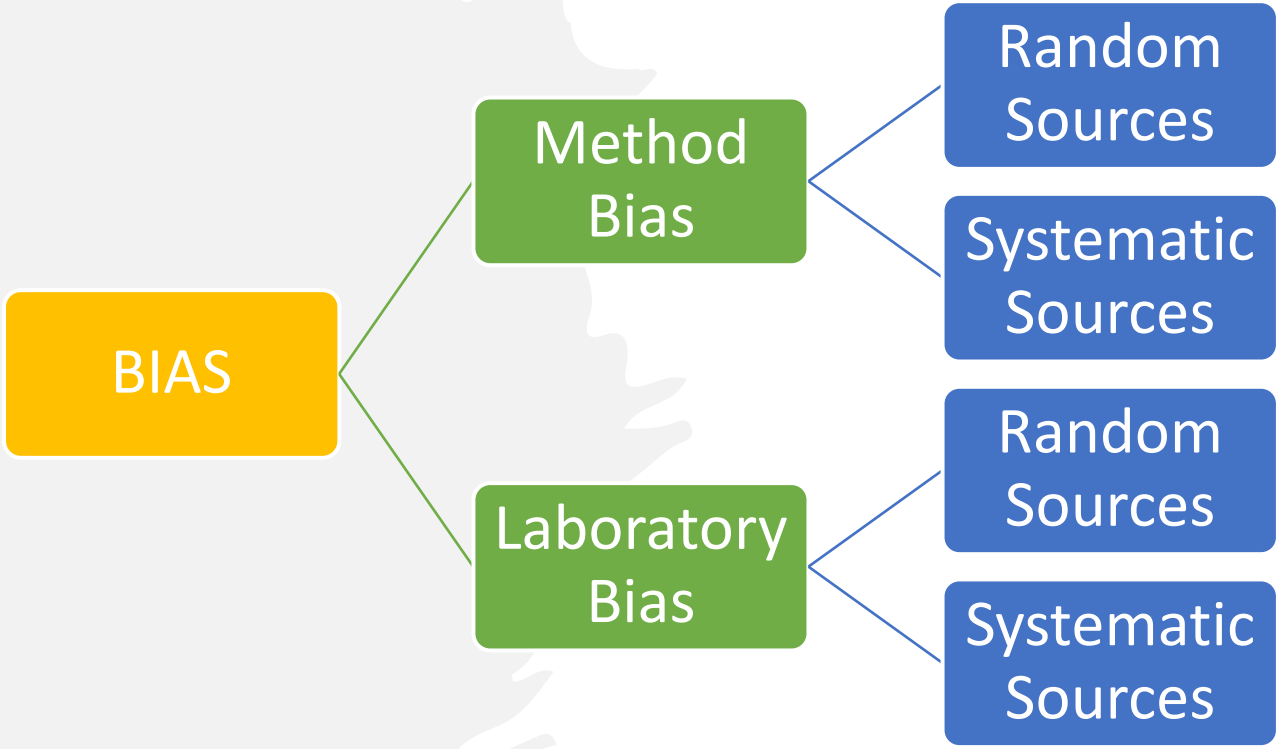


Precision

- Measurement Precision
  - Spread or dispersion of results
  - Measurement repeatability
  - Measurement reproducibility

To Infinity and Beyond?

- Can we correctly measure trueness or correctness of our test results?



Determination of Bias

- Reference Materials
- Recovery Studies
- Comparison with other methods

Recall: CRM = 4.5

Our hypothetical data:

- Mean = 4.245
- Standard Deviation = 0.17423

Bias = mean – CRM

4.2 – 4.5 = -0.25

Bias % = (mean – CRM)/CRM * 100

= (4.25 – 4.5)/4.5) * 100
= -5.66%

Let’s take a closer look

<u>What we know:</u>

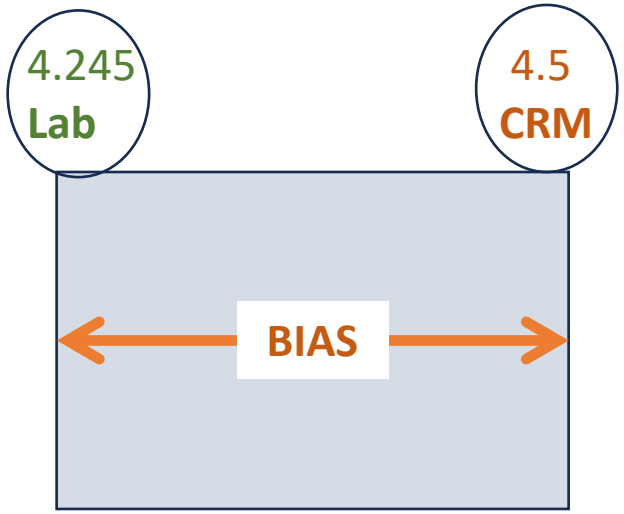
Specification Level = 4.25

CRM = 4.5

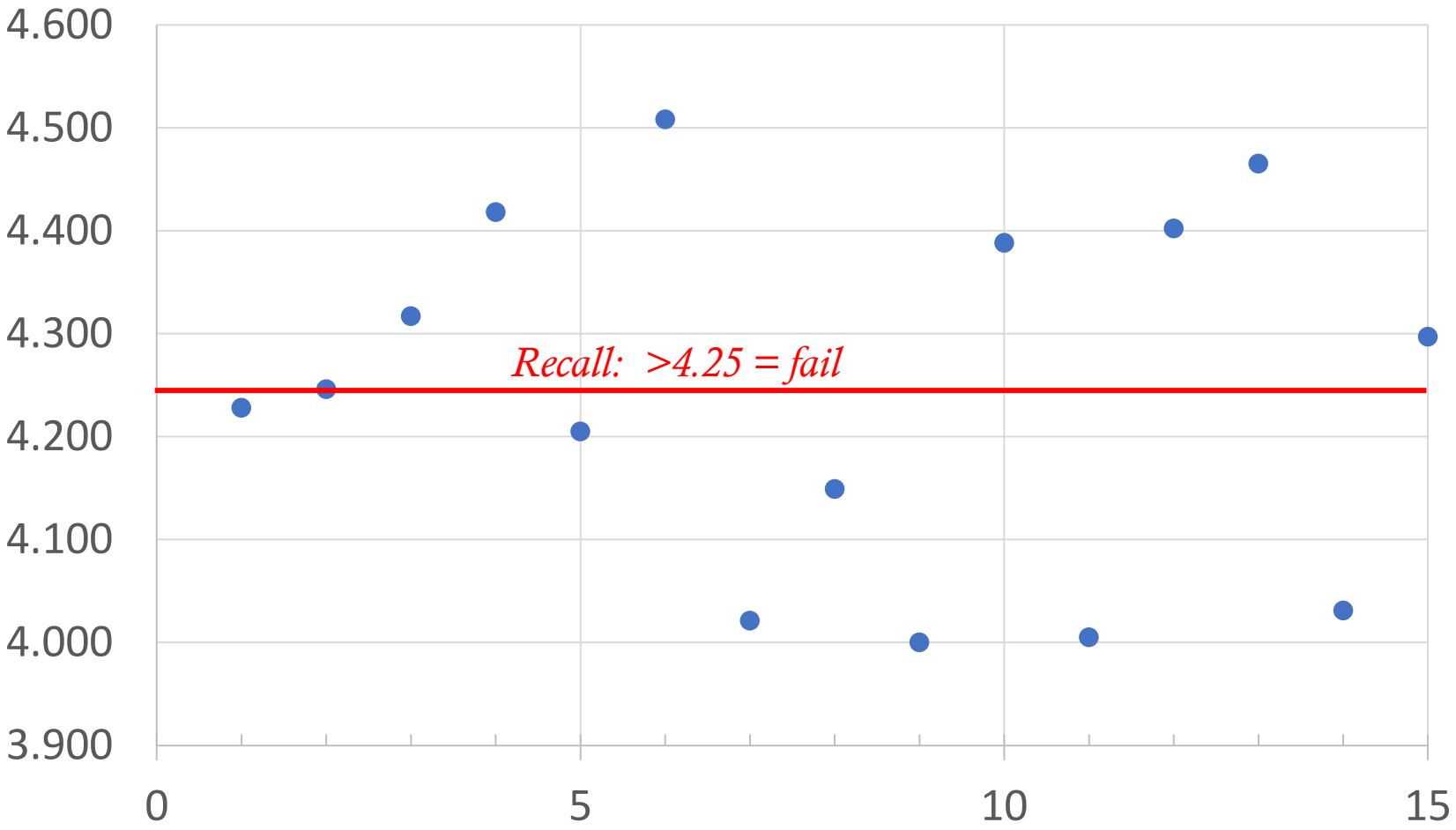
Laboratory Mean = 4.245

Laboratory Bias = -0.246

Laboratory Bias = -5.67%



How confident are we that these values are ‘real’?



Sample	Result
1	4.228
2	4.246
3	4.317
4	4.418
5	4.205
6	4.508
7	4.021
8	4.149
9	4.000
10	4.388
11	4.005
12	4.402
13	4.465
14	4.031
15	4.297

MEASUREMENT UNCERTAINTY:

"parameter, associated with the result of a measurement, that characterizes the dispersion of the values that could reasonably be attributed to the measurand."

ISO 19036:2019

Really Asking…

What is the range of values within which the true value lies?

Or

"How confident am I that my test result of 4.2 really is 4.2?"

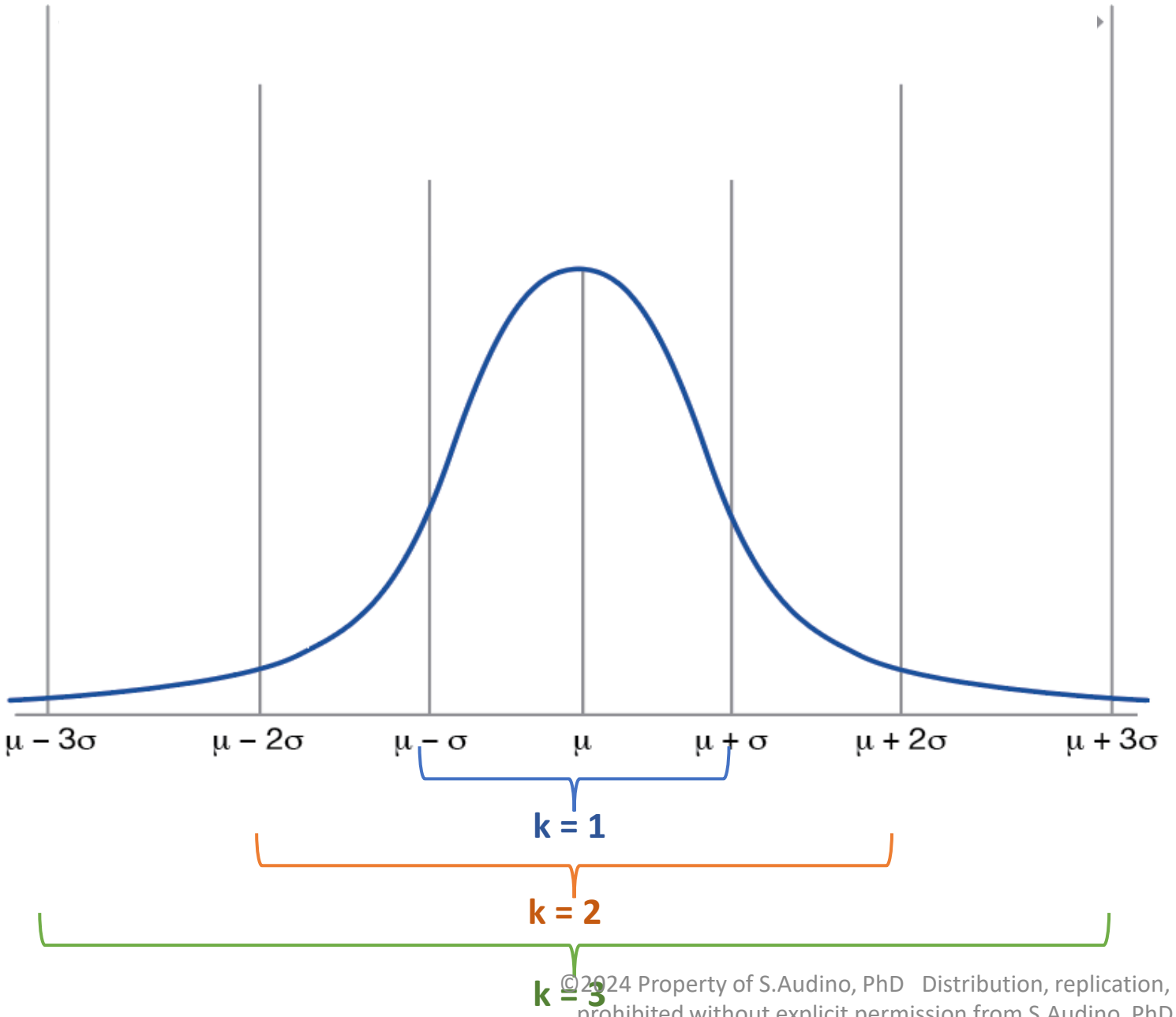
ISO/IEC 17025:2017

Clause 7.6 requires …

- Identification of contributions to uncertainty
- Evaluation of uncertainty

Clause 7.8 requires…

- Documentation of decision rule employed
- Evaluation of risk level (i.e., false accept, false reject)
- Statistical assumptions



Putting this into perspective …

- One way to calculate Uncertainty:
  - Σ = sum
  - X_i = i^{th} measurement
  - μ = data set mean
  - n= number of measurements in the data set

Uncertainty (U) = $\frac{\sqrt{\Sigma(x_i - \mu)^2}}{\sqrt{n(n-1)}}$

$U_{Expanded}$ = U * k

Reviewing our data with confidence boundaries

Our Hypothetical Data:

$U = 0.045$

$U_{Exp,\ k=2} = 0.0900$

$U_{Exp,\ k=3} = 0.135$

Sample	*LL*	Result	*UL*	K=2	K=3
1	4.093	4.228	4.363	P → P	P → P
2	4.111	4.246	4.381	P → P	P → P
3	4.182	4.317	4.452	F → IND	F → IND
4	4.283	4.418	4.553	F → F	F → F
5	4.070	4.205	4.340	P → IND	P → IND
6	4.373	4.508	4.643	F → F	F → F
7	3.886	4.021	4.156	P → P	P → P
8	4.014	4.149	4.284	P → P	P → P
9	3.865	4.000	4.135	P → P	P → P
10	4.253	4.388	4.523	F → F	F → IND
11	3.870	4.005	4.140	P → P	P → P
12	4.267	4.402	4.537	F → F	F → F
13	4.330	4.465	4.600	F → F	F → F
14	3.896	4.031	4.166	P → P	P → P
15	4.162	4.297	4.432	F → IND	F → IND

Decision Rules

"Rule that describes how measurement uncertainty is accounted for when stating conformity with a specified requirement." ISO/IEC 17025:2017

Typically binary

- Pass/Fail
- In Spec/ Out of Spec

Statements of Conformity and 17025

- **Clause 7.1.3:**

"When the customer requests a statement of conformity to a specification or standard for the test or calibration (e.g. pass/fail, in-tolerance/out-of-tolerance) the specification or standard, and the decision rule shall be clearly defined. Unless inherent in the requested specification or standard, the decision rule selected shall be communicated to, and agreed with, the customer."

→Cannabis labs, Statements of Conformity generally are made in relation to samples submitted for "compliance" testing.

Statements of Conformity and 17025

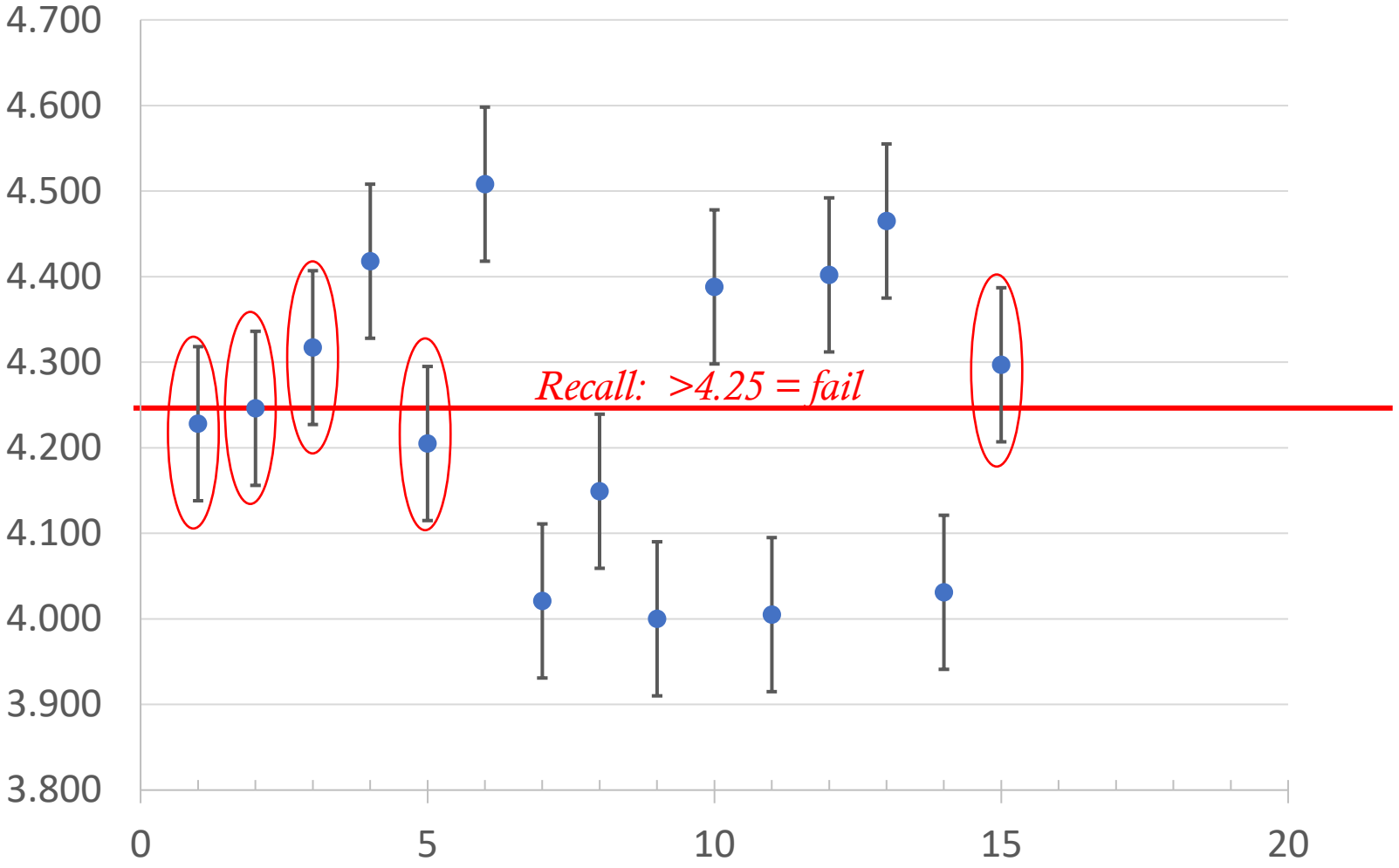
- **Clause 7.8.3.1b:**

"…Test reports shall, where necessary for the interpretation of the test results, include where relevant, a statement of conformity with requirements or specifications…"

Clause 7.8.6.1:

"When a statement of conformity to a specification or standard is provided, the laboratory shall document the decision rule employed, taking into account the level of risk (such as false accept and fall reject and statistical assumptions) associated with the decision rule employed, and apply the decision rule."

How confident are we that these values are ‘real’?



Sample	Result	K=2
1	4.228	P → P
2	4.246	P → IND
3	4.317	F → IND
4	4.418	F → F
5	4.205	P → IND
6	4.508	F → F
7	4.021	P → P
8	4.149	P → P
9	4.000	P → P
10	4.388	F → F
11	4.005	P → P
12	4.402	F → F
13	4.465	F → F
14	4.031	P → P
15	4.297	F → IND

Sources of Measurement Uncertainty

- Bias
- Equipment
- Environment
- Instrument
- Matrix
- Sampling (from the population)
- Method

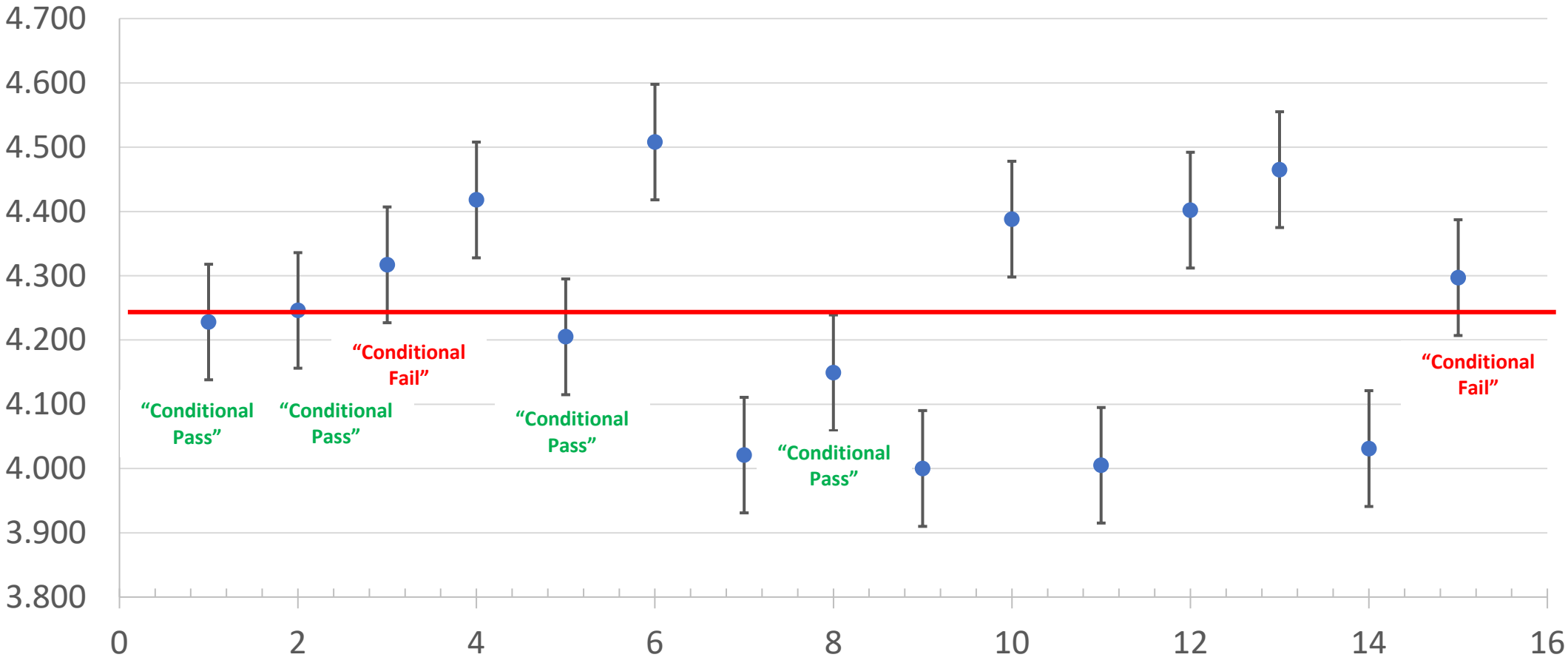
What's happening in cannabis?

Many regulations have conformity standards or decision rules that labs must state on CoAs.

Some challenges to the labs:

- Requirement for lab to make a decision on CoA on basis of a single value, without regard for MU
- Several requirements are inherently flawed when labs are forced to quantitate test values when such values are less than the LOQ
- Inter-laboratory differences
- Laboratory-regulatory differences

Do these Statements of Conformity Make Sense?



How can cannabis labs navigate …

- Requirement to impose a decision on:
  - A single value
  - In isolation
  - Oftentimes unreliable from the start (i.e., <LOQ)

Consider…

Hypothetical COA for sample ID 1UP:

Test Results	**Specification**
Plastic = 4.31	"FAIL: as per Regulatory Group Yikes"

Could include …
"The calculated expanded uncertainty for a 95% level of confidence is 0.09"

Or

"Based on expanded measurement uncertainty for a 95% level of confidence, this test result is considered 'conditional fail' or 'indeterminant"

Or

"The calculated expanded uncertainty for a 95% level of confidence is 0.09. This means that the true value of plastic is expected to be between 4.22 and 4.40"

Shift in Thought is Needed

Customers use test results to make business decisions.

Test results and relevant data should be made available to customers and other interested parties.

MU is an essential component of the method’s fitness for intended use.

References

- ISO/IEC 19036:2019
- ISO/IEC 17025:2017
- Eurachem/CITAC Guide: Measurement uncertainty arising from sampling: A guide to methods and approaches. Second Edition (2019)
- Eurachem Guide: The Fitness for Purpose of Analytical Methods: A Laboratory Guide to Method Validation and Related Topics. Second Edition (2014)
- ISO/IEC Guide 98-3, Uncertainty of measurement – Part 3: Guide to the expression of uncertainty in measurement (GUM:1995)
- ISO/IEC Guide 98-4, Uncertainty and measurement – Part 4: Role of measurement uncertainty in conformity assessment.
- ILAC G8:09/2019: Guidelines on Decision Rules and Statements of Conformity
- UKAS LAB 48, Edition 2: Decision Rules and Statements of Conformity (2020)

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Join us for Future Free Workshops and Webinars!

Tuesday, March 19, 2024 – 1:00-3:00pm ET
Risk Based Thinking
Free Live Workshop presented by Matthew Sica

Monday, March 25, 2024 - 1:00-2:00pm ET
A Look at the ISO/IEC 17025:2017 Requirements Concerning Document Control and Control of Records

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Thank You!