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Trueness-related uncertainty

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Overview

- Definitions of trueness and bias
- Expressing bias and recovery
- Reference values for evaluating recovery
- Estimating uncertainty associated with recovery
- Assessing significance of recovery
- Discussion based on Eurachem/CITAC guide “Evaluation of measurement uncertainty from in-house precision and recovery data”

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Why is trueness-related uncertainty important?

- Precision doesn't capture systematic effects
- Data can be precise but consistently 'wrong'
- Ignoring systematic effects potentially underestimates measurement uncertainty
- Trueness studies estimate systematic effects

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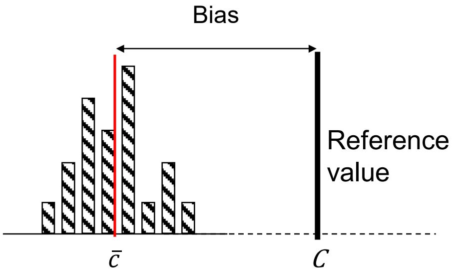
Evaluating bias

- **Bias**: difference between observed mean value and reference value
- Bias is a measure of *Trueness*
- Expression of bias
  - As an absolute value $b = \bar{c} - C$
  - As a fraction or percentage
    - $b_{rel} = (\bar{c} - C)/C$
    - $b(\%) = 100 \times (\bar{c} - C)/C$
- Expression of recovery
  - $R = \bar{c}/C$ (or %, $R(\%) = 100 \times \bar{c}/C$)



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Sources of reference values

- Certified reference material
- Laboratory spiked samples
  - Blank or containing native analyte
- Proficiency test materials
  - Check metrological traceability of assigned value
    - Especially if it is assigned by consensus of participant results
- Test items characterise by another method
- Materials should be representative of routine test materials
  - Analytes, analyte level, matrix

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Categories of reference value for trueness-related uncertainty estimation

- Reference materials independent of the laboratory
  - Certified reference materials
  - Proficiency test materials
  - Spiked blank samples
- Spiked samples containing native analyte
  - Requires measurements before and after spiking

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General approach for recovery evaluation

- Assume systematic effects are proportional to analyte level
- Calculate the mean recovery, $\bar{R}$, for the test material
- Determine whether mean recovery is significantly different from 1
  - Taking into account the uncertainty in the mean recovery

- How can we calculate the uncertainty in the recovery?

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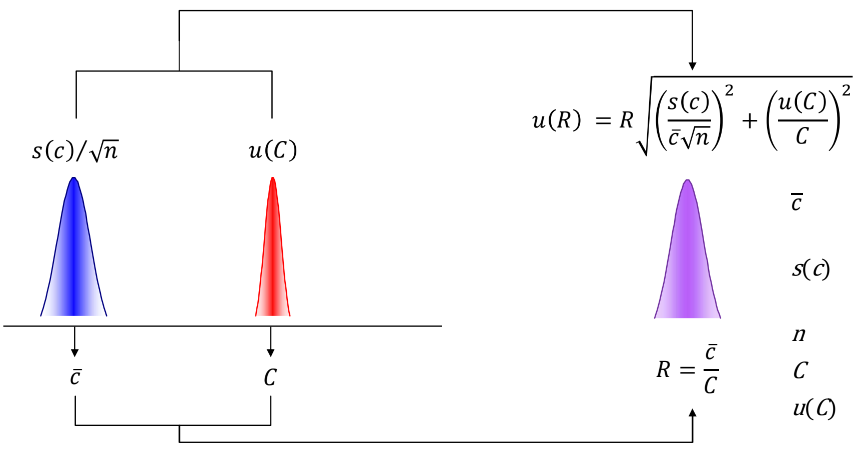
Uncertainties associated with recovery



$\bar{c}$	mean of observations of reference material
$s(c)$	standard deviation of observations of reference material
n	number of observations
C	reference value
$u(C)$	standard uncertainty of reference value

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Approach for multiple reference materials independent of laboratory

- Calculate the recovery for each reference material/blank spiked sample
- Calculate the mean recovery (N reference materials)
  - $\bar{R} = \frac{\sum_{i=1}^{N} \frac{\bar{c}_i}{C_i}}{N}$
- Calculate the standard uncertainty
  - $u(\bar{R}) = \sqrt{\sum_{i=1}^{N} \left\{ \left(\frac{\bar{c}_i}{C_i}\right)^2 \left[\left(\frac{s(c_i)}{\bar{c}_i \sqrt{n_i}}\right)^2 + \left(\frac{u(C_i)}{C_i}\right)^2 \right] \right\}} \Big/ N$

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Example – ortho-phosphate in fresh water

- Experiments to evaluate recovery
  - 2 x certified reference materials
  - 1 x proficiency testing material

	Reference value			Measured value		
Material	**C_i /mg L^{-1}**	**$U(C_i)$ (k=2, 95%) /mg L^{-1}**	**$u(C_i)$ /mg L^{-1}**	**$\bar{c}_i$ /mg L^{-1}**	**$s(c_i)$ /mg L^{-1}**	**n**
CRM 1	2.24	0.10	0.10/2 = 0.050	2.31	0.11	12
CRM 2	1.000	0.050	0.05/2 = 0.025	1.032	0.090	10
PT	1.77	0.23	0.23/2 = 0.115	1.70	0.014*	1
*From known relative intermediate precision						

Example from Eurachem/CITAC Guide

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Example - Calculations

- Calculate mean recovery
  - $\bar{R} = \frac{\frac{2.31}{2.24}+\frac{1.032}{1.000}+\frac{1.70}{1.77}}{3} = 1.008$
- Calculate the standard uncertainty
  - $u(\bar{R}) = \sqrt{\left\{\left(\frac{2.31}{2.24}\right)^2\left[\left(\frac{0.11}{2.31\sqrt{12}}\right)^2+\left(\frac{0.050}{2.24}\right)^2\right]\right\}+\left\{\left(\frac{1.032}{1.000}\right)^2\left[\left(\frac{0.090}{1.032\sqrt{10}}\right)^2+\left(\frac{0.025}{1.000}\right)^2\right]\right\}+\left\{\left(\frac{1.70}{1.77}\right)^2\left[\left(\frac{0.14}{1.70\sqrt{1}}\right)^2+\left(\frac{0.115}{1.77}\right)^2\right]\right\}\Big/3} = 0.03705$

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Approach for spiked samples with native analyte

- Calculate the recovery for each spiked sample
- Calculate the mean recovery
  - $\bar{R} = \frac{\sum_{i=1}^{N}\frac{\bar{c}_i-\bar{c}_{0i}}{c_{+i}}}{N}$
- Calculate the standard uncertainty
  - $u(\bar{R}) = \sqrt{\sum_{i=1}^{N}\left\{\left(\frac{\bar{c}_i-\bar{c}_{0i}}{c_{+i}}\right)^2\left[\frac{\frac{s^2(c_i)}{n_i}+\frac{s^2(c_{0i})}{m_i}}{(\bar{c}_i-\bar{c}_{0i})^2}+\left(\frac{u(c_{+i})}{c_{+i}}\right)\right]\right\}\Big/N}$

$\bar{c}_{0i}$	mean of observations of unspiked material
$\bar{c}_i$	mean of observations of spiked material
c_{+i}	spiked value
n	number of observations of spiked sample
m	number of observations of unspiked sample
$u(c_{+i})$	standard uncertainty of spiked value

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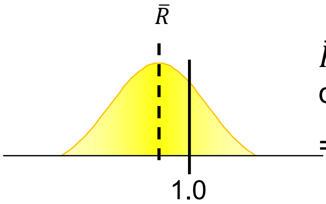
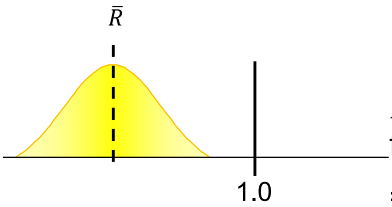
Is the mean recovery acceptable?

- Taking into account $u(\bar{R})$, is $\bar{R}$ significantly different from 1?
  - $\frac{|1-\bar{R}|}{u(\bar{R})} \leq t_{\nu}^{0.95}$
  - Typically an approximation of $t_{\nu}^{0.95} = 2$ is used



$\bar{R}$ not significantly different from 1

=> no significant bias



$\bar{R}$ significantly different from 1

=> significant bias

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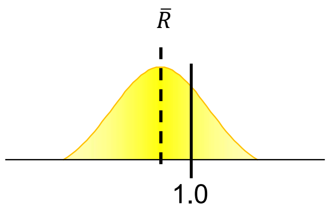
Including recovery in uncertainty estimates: Scenario 1

- No significant bias
- $\bar{R}$ not significantly different from 1
- Assume $\bar{R} = 1$ with an uncertainty, $u(\bar{R})$



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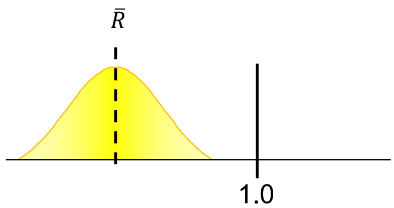
Including recovery in uncertainty estimates: Scenario 2

- Significant bias – correction applied
- $\bar{R} \neq 1$, results corrected by $\bar{R}$
- Corrected result, c_c
  - $c_c = c/\bar{R}$
- $u(\bar{R})$ included in uncertainty estimate for corrected results, $u(c_c)$
- 'GUM' approach
  - Not always applied in chemical analysis



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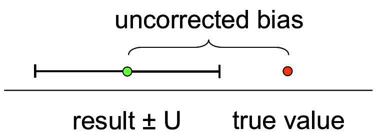
Including recovery in uncertainty estimates: Scenario 3

- Significant bias – correction not applied
- Uncertainty is a range which includes the true value…..



- …so significant bias should not be ignored

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Scenario 3 options

- Is bias 'practically significant'?
  - A statistically significant bias may be insignificant compared to precision uncertainty
    - => no correction or additional uncertainty component required
- Modify method to remove/reduce bias
- Report recovery and its uncertainty separately
  - End-user can apply correction if needed
- Increase reported uncertainty to take account of the uncorrected bias

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Allowing for uncorrected bias

- Still a contentious issue!
- In addition to $u(\bar{R})$ need an uncertainty component to account for uncorrected bias
- Different approaches proposed
  - mean squared error (MSE) ← See Eurachem/CITAC guide for details
  - mean bias
  - bias divided by coverage factor, k
- All have pros and cons

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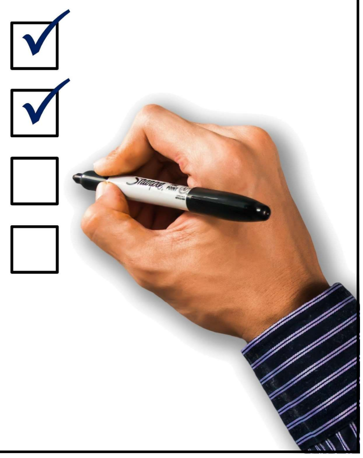
Conclusions

- Systematic effects should be evaluated as part of uncertainty estimation
- Evaluated via bias/recovery studies
- Reference value required
- Evaluate recovery and its uncertainty
- Combine uncertainty with precision component of uncertainty
- Assess whether recovery is ‘fit for purpose’



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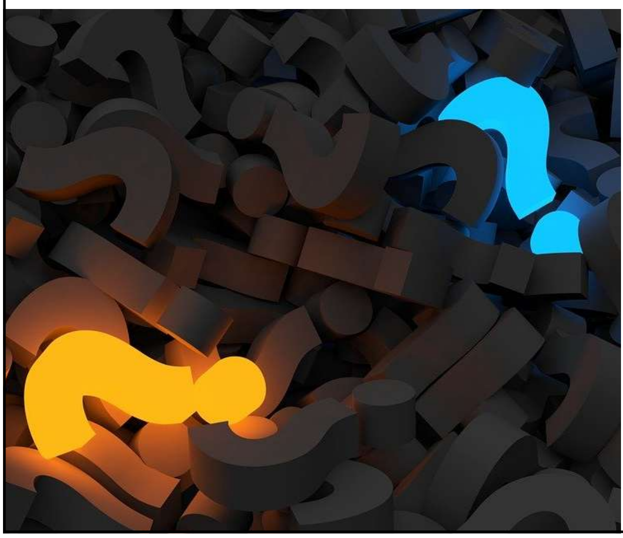

Any Questions?

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