Job Aid 1: Uncertainty Hierarchy [1505v2]

Practical Suggestions for Gaussian Distributions (Normal and Log-normal)

Standard uncertainty (μ = 1 SD = μ_{SD})
In Gaussian distribution, standard deviation = standard uncertainty

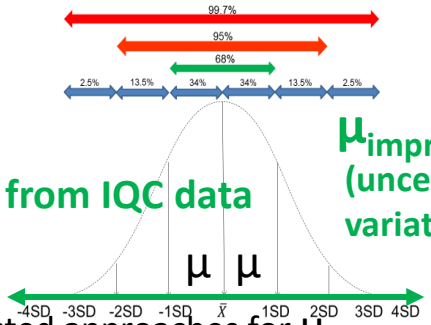
Combined uncertainty
$\mu_c = \sqrt{(\mu_{imprecision}^2 + \mu_{bias}^2)}$

Expanded uncertainty
$U_{exp} = k * \mu_c$,
Coverage factor
k = 2 (95% coverage; 2 SD)
k =3 (99% coverage; 3 SD)

WHERE WE ARE

$\mu_{combined} = \mu_{procedure}$

If bias is ignored or considered insignificant (e.g. SDI < 2), then $U_{imprecision} = U_{procedure}$



$\mu_{imprecision}$ (uncertainty involving randomness or variation; $\mu_{analytical}$)

from IQC data

Suggested approaches for $\mu_{imprecision}$:

Initial Verification

- Use total imprecision from CLSI EP15-A2 5x3 design

$\alpha_{total}^2 = \alpha_{within\text{-}run}^2 + \alpha_{between\text{-}run}^2 = \alpha^2_{within\text{-}laboratory}$ where α^2 is the variance and α is the SD

OR

- Collect over 30 QC data points (i.e. month) during the verification experiments,

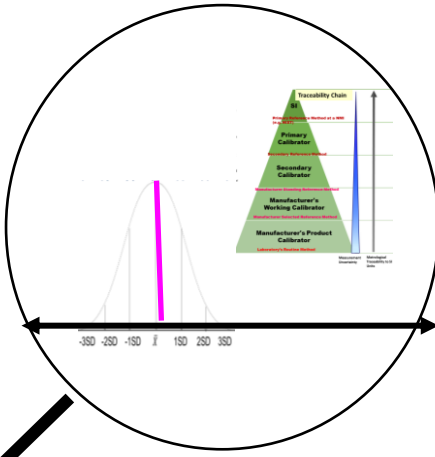
Continue to evaluate until long-term can be established

Long-term Verification

Utilize a top-down approach using long-term SD or CV data (i.e. your internal QC data over six months). Because the QC data points are collected from an extended time period capturing variation from known events (e.g. maintenance, reagent and operator changes), the observed measurements probably reflect the uncertainty from the calibrator materials. If you are unable to incorporate μ_{bias} , then focus on the μ at the cut-off levels, reference intervals, or the difference between serial results needed for patient management.

Relative standard measurement uncertainty;
Coefficient of variation uncertainty
$\mu_{rel} = (\mu_{SD}/value)*100\%$ $\mu_{rel} = (\mu_{SD}/X_{IQC})*100\% = \%CV_{IQC}$

μ_{bias} (uncertainty involving bias correction)

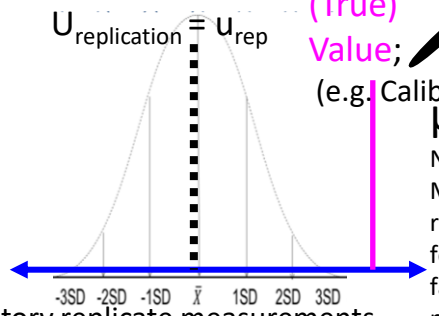


➢ Calibrator or CRM data
(CRM=certified reference material)

$\mu_{Bias} = \sqrt{(\mu_{reference}^2 + \mu_{replication}^2)}$

SEM = standard error of the mean for replicate measurements (a.k.a. standard uncertainty of the mean; standard deviation of the mean); the confidence interval of the mean; the uncertainty in the true value of the mean

SD/√n =
$U_{replication} = u_{rep}$



In-laboratory replicate measurements

Target (True) Value;
(e.g. Calibrator, CRM, higher-order standard)

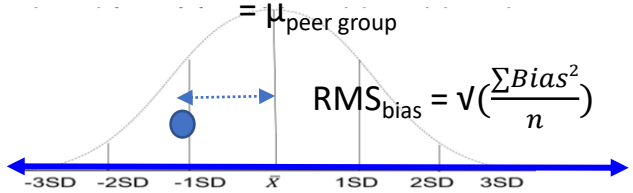
$\mu_{reference} = \mu_{ref}$

Noted in CRM certificate or calibrator certificate. May be available from manufacturer, if requested. If the value given represents U_{exp}, for the calibrator, then divide by k (coverage factor) to determine its standard uncertainty. If not stated, assume k=2.

➢ PT peer data or QC interlaboratory data

$\mu_{Bias} = \sqrt{(RMS_{bias}^2 + \mu_{peer\ group}^2)}$

$SD_{peer\ group}/\sqrt{n_{participating\ laboratories}} = \mu_{peer\ group}$



$RMS_{bias} = \sqrt{(\frac{\sum Bias^2}{n})}$

If your PT provider reports μ, then replace $\mu_{peer\ group}$ with μ_{ref}