
**Appendix A - Further details**

**A performance standard based on LR percentiles**

Instead of focusing on the 50th percentile in equation (1), consider testing hypotheses for the pth percentile $\mu_{LR} + z_p \sigma_R$ of the normally distributed LRs for a disinfectant,

\[
\begin{align*}
H_0 &: \mu_{LR} + z_p \sigma_R \leq LR_{target,p} \\
H_a &: \mu_{LR} + z_p \sigma_R > LR_{target,p}
\end{align*}
\]

\[ (A1) \]

where $z_p$ is the pth percentile from a standard normal distribution. The true reproducibility SD of the LRs is denoted by $\sigma_R$ (and estimated by $S_R$ in equation (4)). Note that for $p < 0.5$, $z_p < 0$.

The rejection region for a single test is

\[ (A2) \]

\[
RR_1 = \begin{cases} 
LR \geq LR_{PS, p} \\
LR - \mu_{LR} \geq LR_{PS, p} - (LR_{target,p} - z_p \sigma_R)
\end{cases}
\]

\[
= \begin{cases} 
\frac{LR - \mu_{LR} - z_p \sigma_R}{\sigma_R} \geq \frac{LR_{PS, p} - LR_{target,p}}{S_R} \\
\frac{S_R^2}{\sigma_R^2}
\end{cases}
\]

\[
= \left\{ T \geq \frac{LR_{PS, p} - LR_{target,p}}{S_R} \right\}
\]

Thus, when the LRs are normally distributed, $T \sim t(df_R, \lambda = -z_p) = t(df_R, \lambda = z_{1-p})$. This shows that the pass-error rate is (cf. equation (10))

\[
\alpha_1 = Pr(Rejecting H_0 \mid \mu_{LR} = LR_{target,p})
= Pr(T \geq t_1 \mid df_R, \lambda = z_{1-p})
\]

where $t_1$ is calculated similar to equation (9). Similar calculations show that the fail-error rate for testing the hypotheses in (A1) using the rejection region in (A2) is (cf. equation (11))

\[
\beta_1 = Pr(T \leq t_1 \mid df_R, \lambda = \lambda_1 + z_{1-p}).
\]

**Alternate Step 5: Error rates for a performance standard that requires that a disinfectant passes tests on the average for a single microbe**

Instead of evaluating the hypotheses in (1) by requiring that a disinfectant pass all of multiple tests, one could instead impose a PS on the observed mean LR across multiple tests. Consider the case where $K$ multiple tests are performed at each of $L$ laboratories. The rejection region is
\[
RR_{\text{mean}} = \{\text{mean}(LR) \geq LR_{\text{PS}}\} = \{(\text{mean}(LR) - LR_{\text{target}})/SE_{\text{mean}} \geq (LR_{\text{PS}} - LR_{\text{target}})/SE_{\text{mean}}\} = \{T \geq t_{\text{mean}}\},
\]

where \(t_{\text{mean}} = (LR_{\text{PS}} - LR_{\text{target}})/SE_{\text{mean}}\). The value for \(t_{\text{mean}}\) differs in a single fundamental respect from the value \(t_1\) for a single test PS presented in equation (9). The denominator is now occupied by \(SE_{\text{mean}}\), the standard error of the mean LR. To use all available data, \(SE_{\text{mean}}\) is found by pooling \(SE_{\text{collab}}\), the standard error obtained from the existing collaborative study, with \(SE_{\text{future}}\), the standard error to be observed in \(K\) future tests performed at each of \(L\) laboratories as required by the PS. Each of these standard errors is defined next. First,

\[
SE_{\text{future}} = [S_{\text{future,lab}}^2/L + S_{\text{future,test}}^2/(LK)]^{1/2},
\]

has \(df_{\text{future}} = L - 1\) degrees of freedom (23, pp 958-976), with the variance components \(S_{\text{future,lab}}^2\) and \(S_{\text{future,test}}^2\) calculated from the future \(K\) tests performed at each of \(L\) laboratories. Note that \(SE_{\text{future}}\) can be estimated from the variance components \(S_{\text{lab}}^2\) and \(S_{\text{test}}^2\) from the existing collaborative study of \(J\) tests performed at each of \(I\) laboratories by

\[
SE_{\text{collab}} = [S_{\text{lab}}^2/L + S_{\text{test}}^2/(LK)]^{1/2}.
\]

The degrees of freedom associated with \(SE_{\text{collab}}\) is given by

\[
(A3) \quad df_{\text{collab}} = \frac{(H + \frac{1}{K})^2}{I-1} \cdot \frac{(1-K)^2}{J^2} \cdot \frac{1}{IJK(1-\frac{1}{J})^2}.
\]

In (A3), for the UDM example, \(I = 5\) is the number of laboratories in the existing UDM collaborative study; \(J = 3\) is the number of repeated tests in each laboratory in the UDM collaborative study; \(H = S_{\text{lab}}^2/S_{\text{test}}^2\), where both \(S_{\text{lab}}^2\) and \(S_{\text{test}}^2\) are the variance components from the UDM collaborative study; and \(K\) is the number of tests in each laboratory in future UDM tests of the disinfectant. Equation (A3), found via Satterthwaite’s approximation, is a modification of Mee’s (22) formula (cf. equation (5)). The resulting pooled standard error of the mean is

\[
(A4) \quad SE_{\text{mean}} = \sqrt{\frac{df_{\text{collab}} SE_{\text{collab}}^2 + (L-1)SE_{\text{future}}^2}{df_{\text{collab}} + L-1}}.
\]

Thus, the degrees of freedom associated with \(SE_{\text{mean}}\) is

\[
(A5) \quad df_{\text{mean}} = df_{\text{collab}} + L - 1.
\]

To evaluate (A4) and then estimate the error rates, since we do not have \(SE_{\text{future}}\), we set \(SE_{\text{future}} = SE_{\text{collab}}\), in which case \(SE_{\text{mean}} = SE_{\text{collab}}\), with degrees of freedom given by (A5). Now, the pass-error rate for a PS on the average over all \(K\cdot L\) tests is
\( \alpha_{\text{mean}} = Pr(T \geq t_{\text{mean}} \mid df_{\text{mean}}, \lambda = 0) \).

The fail-error rate for a highly effective product (for which \( \mu_{LR} = LR_{\text{high}} \)) is
\[
\beta_{\text{mean}} = Pr(T < t_{\text{mean}} \mid df_{\text{mean}}, \lambda = \lambda_{\text{mean}}).
\]

with non-centrality parameter given by
\[
\lambda_{\text{mean}} = (LR_{\text{high}} - LR_{PS})/SE_{\text{mean}}.
\]

Computer code for these calculations is provided in Appendix B.

**Appendix B - Computer code**

The error rate calculations presented in this manuscript for the UDM example were generated using the statistical software package R (33), package *mvtnorm* (25, 34). The R code is presented in the same order that the calculation steps were presented in this paper: by first showing how to calculate the error rates for a PS on a single test, then for a PS that requires passing all tests, and then based on passing multiple tests on average. The following R code, presented in this font, should be sequentially entered directly into R’s command line.

The following R function generates the LR associated with the number of positive carriers for a semi-quantitative method (cf. equation (4)):

```r
GetLR=function(N,TestLD=6,NumTot=60)
{LR = TestLD - log10(-log(((NumTot - N+.5)/(NumTot + 1)))
return(LR)
}
```

Following the example presented earlier, for a single UDM test, the pass-error rate \( \alpha_1 \) for the current PS is calculated for each microbe using equation (10) by the following code. The first three lines are only for semi-quantitative methods.

```r
PS1 = 1                                  # This corresponds to the current UDM PS used in the example
LR.PS1 = GetLR(PS1)
LR.target = GetLR(PS1+1)
SR_Pa = 0.5348   # UDM reproducibility SD for P. aeruginosa
SR_Sa = 0.3162   # UDM reproducibility SD For S. aureus
df1_Pa = 6.9          # For P. aeruginosa via equation (5)
df1_Sa = 13.8       # For S. aureus via equation (5)
t1_Pa = (LR.PS1 - LR.target)/SR_Pa
alpha1_Pa = 1 - pt(t1_Pa,df1_Pa)
t1_Sa = (LR.PS1 - LR.target)/SR_Sa
alpha1_Sa = 1 - pt(t1_Sa,df1_Sa)
```

For a single UDM test, the fail-error rate \( \beta_1 \) is calculated using equations (11) and (12) by the following code. The first line pertains only to semi-quantitative methods.

```r
LR.0 = GetLR(0)
lambda1_Pa = (LR.0 - LR.target)/SR_Pa
lambda1_Sa = (LR.0 - LR.target)/SR_Sa
beta1_Pa = pt(t1_Pa,df1_Pa,ncp=lambda1_Pa)  # for P. aeruginosa
beta1_Sa = pt(t1_Sa,df1_Sa,ncp=lambda1_Sa)  # for S. aureus
```
When a PS requires that a disinfectant passes all of $KL$ uncorrelated tests (this means that each test is performed in a different laboratory in the case of $P. \text{aeruginosa}$), then the pass-error rate $\alpha_{KL}$ and the fail-error rate $\beta_{KL}$ are calculated using a multivariate $t$ via equations (13) and (14) by:

$$
\text{library(mvtnorm)}
\text{K = 1 \ # Number of } P. \text{aeruginosa} \text{ tests at each lab}
\text{L = 3 \ # Number of labs}
\text{TotTests = K*L \ # Total number of tests}
\text{alphaKL = pmvt(lower=rep(t1_Pa, TotTests ),upper=rep(Inf, TotTests ),df=df1_Pa)}
\text{betaKL = 1- pmvt(lower=rep(t1_Pa, TotTests ),upper=rep(Inf, TotTests ),df=df1_Pa,delta=lambda1_Pa)}
$$

The error rate calculations are more complicated when multiple tests of a single microbe are performed in the same laboratory in the presence of a significant among-laboratories variance component $S^2_{lab}$, in which case the correlation matrix amongst the tests must be inputted in order to evaluate equations (13) and (14). For example, the error rates for two $P. \text{aeruginosa}$ tests performed in each of two labs are calculated by:

```r
##### An R function to generate the correlation matrix for tests of a single microbe
GenCorrMatrix<-
function(NumTests,NumLabs=1,VarLab=.175,VarExp=.111)
{Z = matrix(0,NumTests,(NumTests+1))
Z[,1]=1
for (i in 1:NumTests)
{Z[i,i+1]=1}
Psi=diag(c(rep(VarLab,1),rep(VarExp,NumTests)))
Vblk=2%*%Psi*%2
N = NumTests*NumLabs \ # total number of data points across all labs and exps
V=matrix(0,N,N)
for (i in 0:(NumLabs-1))
{index=(i*NumTests+1):((i+1)*NumTests)
V[index,index]=Vblk \ # construct the covariance matrix first
}
V = V/V[1,1]
return(V)
}
##### End of function
L = 2 \ # Number of labs
K = 2 \ # Number of tests in each of the labs
TotTests = K*L
R_Pa = GenCorrMatrix(K,1)
alphaKL = pmvt(lower=rep(t1_Pa, TotTests ),upper=rep(Inf, TotTests ),df=df1_Pa,delta=lambda1_Pa)
betaKL = 1- pmvt(lower=rep(t1_Pa, TotTests ),upper=rep(Inf,TotTests ),df=df1_Pa,delta=lambda1_Pa)
```

When a PS requires that all tests from both $P. \text{aeruginosa}$ and $S. \text{aureus}$ must be passed, the error rate calculations via equations (19) and (20) look similar as for the single microbe case, but now the correlation matrix must contain a between-microbe correlation. For example, when three tests of each microbe are performed in one lab, the error rates are calculated by:

```r
##### An R function to generate the correlation matrix for tests of two microbe
GenCorrMatrix_Microbe<-
function(NumTests,NumLabs,CorrMicrobe,VarLab=c(.175,0),VarExp=c(.111,.1))
{PaBlock=GenCorrMatrix(NumTests[1],1,VarLab[1],VarExp[1])
SaBlock=GenCorrMatrix(NumTests[2],1,VarLab[2],VarExp[2])
Vblk = matrix(CorrMicrobe,sum(NumTests),sum(NumTests))
index1=1:NumTests[1]
Vblk[index1,index1]=PaBlock
Vblk[index2,index2]=SaBlock}
```

When a PS requires that all tests from both $P. \text{aeruginosa}$ and $S. \text{aureus}$ must be passed, the error rate calculations via equations (19) and (20) look similar as for the single microbe case, but now the correlation matrix must contain a between-microbe correlation. For example, when three tests of each microbe are performed in one lab, the error rates are calculated by:

```r
##### An R function to generate the correlation matrix for tests of two microbe
# NumTests is a 2x1 vector, NumTests[1] specifies number of tests for Pa in each lab
# NumTests[2] specifies number of tests for Sa in each lab
# VarLab is a 2x1 vector, VarLab[1] is for Pa, VarLab[2] is for Sa
# VarExp is a 2x1 vector, VarExp[1] is for Pa, VarExp[2] is for Sa
GenCorrMatrix_Microbe<-
function(NumTests,NumLabs,CorrMicrobe,VarLab=c(.175,0),VarExp=c(.111,.1))
{PaBlock=GenCorrMatrix(NumTests[1],1,VarLab[1],VarExp[1])
SaBlock=GenCorrMatrix(NumTests[2],1,VarLab[2],VarExp[2])
Vblk = matrix(CorrMicrobe,sum(NumTests),sum(NumTests))
index1=1:NumTests[1]
Vblk[index1,index1]=PaBlock
Vblk[index2,index2]=SaBlock}
```
N = sum(NumTests)*NumLabs  # total number of data points across all labs and exps
V=matrix(0,N,N)
for (i in 0:(NumLabs-1))
{index=(i*sum(NumTests)+1):((i+1)*sum(NumTests))
  V[index,index]=Vblk}
return(V)

##### End of function
L = 1  # Number of labs
K_Pa = 3  # Number of P. aeruginosa tests in each of the labs
K_Sa = 3  # Number of S. aureus tests in each of the labs
R = GenCorrMatrix_Microbe(c(K_Pa,K_Sa),L,0.25)
vecblk = c(rep(t1_Pa,K_Pa),rep(t1_Sa,K_Sa))
lower.vec = rep(vecblk,L)
deltablk = c(rep(lambda1_Pa,K_Pa),rep(lambda1_Sa,K_Sa))
delta.vec = rep(deltablk,L)
TotTests = (K_Pa + K_Sa)*L
alphaKL = pmvt(lower=lower.vec,upper=rep(Inf,TotTests),df=df1_Pa,corr=R)
betaKL = 1-pmv(t(lower=lower.vec,upper=rep(Inf,TotTests),df=df1_Pa,corr=R,Delta=delta.vec)

The error rates for a PS on the average over K multiple tests performed at each of L labs are calculated using equations (A3)-(A7):

PSmean = 1
L = 3  # Number of labs required by the PS
K = 10  # Number of future tests in each lab
S2_lab = 0.175  # For P. aeruginosa, use S2_lab = 0.000 for S. aureus
S2_test = 0.111  # For P. aeruginosa, use S2_test = 0.100 for S. aureus
dfcollab = 3.06
SMean = sqrt(S2_lab/L + S2_test/(L*K))
dfmean = dfcollab + L - 1
LR.PSmean = GetLR(PSmean)
LR.PSmeanplus1 = GetLR(PSmean+1)
tmean = (LR.PSmean - LR.PSmeanplus1)/SMean
alpha_mean = 1-pt(tmean,dfmean)
lambda_mean = (LR.0-LR.PSmeanplus1)/SMean
beta_mean = pt(tmean,dfmean,ncp=lambda_mean)