Appendices for
Parker, Hamilton and Tomasino (2014). A Statistical Model for Assessing Performance Standards for Quantitative and Semi-quantitative Disinfectant Test Methods. *JAOAC*, 97(1):58-67.

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 p^{th} percentile $\mu_{LR} + z_p\sigma_R$ of the normally distributed LRs for a disinfectant,

(A1) H_0: $\mu_{LR} + z_p\sigma_R \leq LR_{target,p}$
H_a: $\mu_{LR} + z_p\sigma_R > LR_{target,p}$

where z_p is the p^{th} percentile from a standard normal distribution. The true reproducibility SD of the LRs is denoted by σ_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)
$$\begin{aligned} RR_1 &= \{\mathbf{LR} \geq LR_{PS,\,p}\}, \\ &= \{\mathbf{LR} - \mu_{LR} \geq LR_{PS,\,p} - (LR_{target,p} - z_p\sigma_R)\} \\ &= \left\{ \frac{\frac{\boldsymbol{LR}-\mu_{LR}}{\sigma_R} - z_p}{\sqrt{\frac{\boldsymbol{S_R}^2}{\sigma_R{}^2}}} \geq \frac{LR_{PS,p} - LR_{target,p}}{S_R} \right\} \\ &= \left\{ \boldsymbol{T} \geq \frac{LR_{PS,p} - LR_{target,p}}{S_R} \right\}. \end{aligned}$$

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

$$\begin{aligned} \alpha_1 &= Pr(\text{Rejecting } H_0 \mid \mu_{LR} = LR_{target,\,p}) \\ &= Pr(\boldsymbol{T} \geq t_1\,;\, df_R, \lambda = z_{1-p}) \end{aligned}$$

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))

$$\beta_1 = Pr(\boldsymbol{T} \leq t_1\,;\, df_R, \lambda = \lambda_1 + z_{1-p}).$$

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

$$RR_{\text{mean}} = \{\mathbf{mean(LR)} \geq \text{LR}_{\text{PS}}\}.$$
$$= \{(\mathbf{mean(LR)} - \text{LR}_{\text{target}})/\ \boldsymbol{SE}_{\mathbf{mean}} \geq (\text{LR}_{\text{PS}} - \text{LR}_{\text{target}})/\ SE_{\text{mean}}\}$$
$$= \{\boldsymbol{T} \geq t_{\text{mean}}\},$$

where $t_{\text{mean}} = (\text{LR}_{\text{PS}} - \text{LR}_{\text{target}})/\ SE_{\text{mean}}$. The value for t_{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_{mean}, the standard error of the mean LR. To use all available data, SE_{mean} is found by pooling SE_{collab}, the standard error obtained from the existing collaborative study, with SE_{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,

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

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

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

The degrees of freedom associated with SE_{collab} is given by

(A3) $$df_{collab} = \frac{\left(H+\frac{1}{K}\right)^2}{\frac{\left(H+\frac{1}{J}\right)^2}{I-1}+\frac{\left(1-\frac{K}{J}\right)^2}{IJK^2\left(1-\frac{1}{J}\right)^2}}.$$

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; $H = S^2_{\text{lab}}/S^2_{\text{test}}$, where both S^2_{lab} and S^2_{test} 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) $$SE_{\text{mean}} = \sqrt{\frac{df_{collab}\,SE^2_{collab}+(L-1)SE^2_{future}}{df_{collab}+L-1}}.$$

Thus, the degrees of freedom associated with SE_{mean} is

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

To evaluate (A4) and then estimate the error rates, since we do not have SE_{future}, we set $SE_{\text{future}} = SE_{\text{collab}}$, in which case $SE_{\text{mean}} = SE_{collab,}$ 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

(A6) $\alpha_{mean} = Pr(\boldsymbol{T} \geq t_{mean}\ ;\ df_{mean}, \lambda = 0)$.

The fail-error rate for a highly effective product (for which $\mu_{LR} = LR_{high}$) is

(A7) $\beta_{mean} = Pr(\boldsymbol{T} < t_{mean}\ ;\ df_{mean}, \lambda = \lambda_{mean})$.

with non-centrality parameter given by

$$\lambda_{mean} = (LR_{high} - LR_{PS})/SE_{mean}).$$

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)):

```
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 α_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.

```
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 β_1 is calculated using equations (11) and (12) by the following code. The first line pertains only to semi-quantitative methods.

```
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 $K \cdot L$ uncorrelated tests (this means that each test is performed in a different laboratory in the case of *P. aeruginosa*), then the pass-error rate α_{KL} and the fail-error rate β_{KL} are calculated using a multivariate *t* via equations (13) and (14) by:

```
library(mvtnorm)
K = 1  # Number of P. aeruginosa tests at each lab
L = 3 # Number of labs
TotTests = K*L  # Total number of tests
alphaKL = pmvt(lower=rep(t1_Pa, TotTests ),upper=rep(Inf, TotTests),df=df1_Pa)
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. aeruginosa* tests performed in each of two labs are calculated by:

```
##### 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=Z%*%Psi%*%t(Z)
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,L)
alphaKL = pmvt(lower=rep(t1_Pa, TotTests),upper=rep(Inf, TotTests ),df=df1_Pa,corr=R_Pa)
betaKL = 1-pmvt(lower=rep(t1_Pa, TotTests),upper=rep(Inf,TotTests),df=df1_Pa,corr=R_Pa,delta=lambda1_Pa)
```

When a PS requires that all tests from both *P. aeruginosa* and *S. 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:

```
#####  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] sepcifies 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]
index2=(NumTests[1]+1):sum(NumTests)
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-pmvt(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
SEmean = 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)/SEmean
alpha_mean = 1-pt(tmean,dfmean)
lambda_mean = (LR.0-LR.PSmeanplus1)/SEmean
beta_mean = pt(tmean,dfmean,ncp=lamda_mean)
```