

LEAST COST FORMULATIONS, LTD.

824 Timberlake Drive, Virginia Beach, VA 23464-3239

Tel: (757) 467-0954 Fax: (757) 467-2947

E-mail: office@lcfld.com URL: <http://lcfld.com/>

TECHNICAL REPORT

NUMBER: TR310

DATE: 2010 June 28

TITLE: Statistical analysis of interlaboratory studies. XXVIII. Calculation of dLPOD and 95% confidence interval for two microbiological methods compared on unmatched or matched test portions in a multicollaborator study.

AUTHOR: R. A. LaBudde

ABSTRACT: Formulas are given for estimating the difference dLPOD in detection probabilities across collaborators for two quantal methods, and an associated approximate 95% confidence interval, when the methods are matched or unmatched on test portions.

KEYWORDS: 1) QUANTAL 2) dLPOD 3) PAIRED 4) LPOD

REL.DOC.: TR296, TR298, TR309

REVISED:

INTRODUCTION

Frequently two or more methods (e.g., “candidate”, and “reference” or “alternate”) are evaluated in the same in a multicollaborator study.

Multiple collaborators each use the methods on randomized replicate test portions. If two methods are performed on the *same* test portions, the study is described as “paired” (or, more generally, “matched”) on test portions. If the two methods are performed on *different* test portions, the study is described as “unpaired” or “unmatched”. In microbiological quantal methods, pairing is accomplishable if, e.g., the first enrichment can be used in common for the two methods.

The chief benefit of matching on test portions occurs when concentrations below 5 CFU/test portion are used, and the possibility of no CFU being present in a test portion is measurably greater than zero. For this case, particularly for concentrations between 0.2 and 2.0 CFU/test portion, matching on test portions will create high positive correlation among results, if the methods used are sensitive to a single CFU. If the methods under test are insensitive to concentrations below 5 CFU/test portion, distribution of CFUs across test portions is no longer critically important, and it is unlikely that matching on test portions will have useful benefit compared to unmatched test portions.

The chief statistical advantage of matching is the standard error of the difference in method performance will be lower if positive correlation between methods is present at 0.5 or greater, as compared to the standard error of the difference of individual mean values when matching is not used. It should be noted that matching may result in *larger* standard error if anti-correlation of methods is present. Other issues include simplified logistics lower repeatability degrees of freedom when matched test portions are used.

TERMINOLOGY

In what follows, it will be assumed that the measures of effect and variance of TR296, TR298 and TR309 are being used. These include:

- POD: Probability of detection at a specific concentration for a given method, as measured by the proportion of positive results on test portions obtained by a single collaborator.
- LPOD: Probability of detection across collaborators at a specific concentration for a given method, as measured by the average proportion of positive results across collaborators.
- dPOD: Difference in probability of detection at a specific concentration between two given methods, as measured by the difference of proportion of positive results on test portions obtained by a single collaborator.
- dLPOD: Difference in probability of detection at a specific concentration between two given methods, as measured by the difference of average proportion of positive results on test portions across collaborators.
- L: Number of collaborators in the study
- n_k : Number of replicate test portions used by collaborator $k = 1, 2, \dots, L$. It will be assumed that all $n_k = n$, a common value, or close to this, for each collaborator.
- C, R: Assume two methods are being compared, denoted “C” for “Candidate” and “R” for “Reference” or “Alternate”. There is no assumption here that either method is known a priori to be more accurate than the other.

RECOMMENDATIONS

UNMATCHED TEST PORTIONS

For unmatched test portions, POD_C and POD_R are independently estimable, each based on n different replicate test portions, so

$$dPOD_{CR} = POD_C - POD_R \quad (1)$$

If the 95% confidence interval for the expected value of POD_C is (LCL_C, UCL_C) , and the corresponding interval for the expected value of POD_R is (LCL_R, UCL_R) , then the recommended confidence interval for $dPOD_{CR}$ is (see TR296):

$$LCL_{dPOD} = dPOD_{CR} - \sqrt{ \{ [POD_C - LCL_C]^2 + [POD_R - UCL_R]^2 \} } \quad (2a)$$

$$UCL_{dPOD} = dPOD_{CR} + \sqrt{ \{ [POD_C - UCL_C]^2 + [POD_R - LCL_R]^2 \} } \quad (2b)$$

The difference in method across collaborators is measured by (TR296)

$$dLPOD_{CR} = \Sigma dPOD_{CR,k} / L \quad (3)$$

and the standard error across collaborators of (TR296)

$$S_{dLPOD} = \sqrt{ \{ \Sigma [dPOD_{CR,k} - dLPOD_{CR}]^2 / (L - 1) \} } \quad (4)$$

Finally, a 95% confidence interval on the expected value of $dLPOD_{CR}$ is given by

$$LCL_{dLPOD} = \max \{ -2, dLPOD_{CR} - t_{0.975} S_{dLPOD} / \sqrt{L} \} \quad (5a)$$

$$UCL_{dLPOD} = \min \{ +2, dLPOD_{CR} + t_{0.975} S_{dLPOD} / \sqrt{L} \} \quad (5b)$$

and $t_{0.975}$ is the 97.5% quantile of the student-t distribution for $L-1$ degrees of freedom (TR296).

Confidence intervals for the single method POD and LPOD values are given in TR296.

MATCHED TEST PORTIONS

For matched test portions by a single collaborator, let

$$d_j = x_{C,j} - x_{R,j} \quad j = 1, 2, \dots, n \quad (6)$$

denote the numerical difference of the two method results on test portion j . Note that d_j may take on only the values -1 , 0 or $+1$.

The recommended method (TR309) for estimating $dPOD_{CR}$ for this collaborator is the mean of the differences d_k :

$$dPOD_{CR} = \Sigma d_k / n \quad (7)$$

The recommended (TR309) approximate 95% confidence interval is the usual student-t based interval, with the standard error of $dPOD_{CR}$ computed from the replicate differences:

$$s_d = \sqrt{\{\Sigma [d_k - dPOD_{CR}]^2 / (n - 1)\}} \quad (8a)$$

$$SE_{dPOD} = s_d / \sqrt{n} \quad (8b)$$

and

$$LCL_{dPOD} = dPOD_{CR} - t_c SE_{dPOD} \quad (9a)$$

$$UCL_{dPOD} = dPOD_{CR} + t_c SE_{dPOD} \quad (9b)$$

where t_c is the 97.5% quantile of the student-t distribution for $n-1$ degrees of freedom, and the 95% confidence interval is (LCL, UCL).

The difference in method across collaborators $dLPOD_{CR}$ is measured by eq.(3), the same as for unmatched test portions, but with $dPOD_{CR}$ values from eq.(7) instead of eq.(1). The standard error of $dLPOD_{CR}$ is given by eq.(4) using the $dPOD_{CR}$ values from eq.(7). Finally, a 95% confidence limit on the expected value of $dLPOD_{CR}$ is given by eqs.(5).

Again, confidence intervals for the single method POD and LPOD values are given in TR296, and are the same formulas for both matched and unmatched test portions.