

A Multiple Comparison Procedure for Comparing Several Treatments with a Control

Author(s): Charles W. Dunnett

Source: Journal of the American Statistical Association, Dec., 1955, Vol. 50, No. 272 (Dec., 1955), pp. 1096-1121

Published by: Taylor & Francis, Ltd. on behalf of the American Statistical Association

Stable URL: https://www.jstor.org/stable/2281208

JSTOR is a not-for-profit service that helps scholars, researchers, and students discover, use, and build upon a wide range of content in a trusted digital archive. We use information technology and tools to increase productivity and facilitate new forms of scholarship. For more information about JSTOR, please contact support@jstor.org.

Your use of the JSTOR archive indicates your acceptance of the Terms & Conditions of Use, available at https://about.jstor.org/terms



Taylor & Francis, Ltd. and American Statistical Association are collaborating with JSTOR to digitize, preserve and extend access to Journal of the American Statistical Association

A MULTIPLE COMPARISON PROCEDURE FOR COMPARING SEVERAL TREATMENTS WITH A CONTROL

CHARLES W. DUNNETT* American Cuanamid Company

I. INTRODUCTION

A COMMON problem in applied research is the comparison of treat-ments with a control or stondard. C ments with a control or standard. Such a situation may arise, for example, when an agronomist tests the effects on crop yield of the addition of chemicals to the soil, or when a pharmacologist assays drug samples to determine their potencies. In designing an experiment to measure the effects of such treatments, it is often desirable to include in the experiment a control in the form of either a dummy treatment. to measure the magnitude of the experimental response in the absence of the treatments under investigation, or some recognized standard treatment. Sometimes past experience with the control will suffice, but often this cannot be relied upon due to altered environmental conditions. Thus the agronomist may leave a few of his experimental plots untreated for comparison with the treated plots, and the pharmacologist may measure the response to a standard drug preparation of known potency concomitantly with the test samples in order to estimate the potencies of the latter.

We will consider the case where the numerical results of an experiment performed to compare p treatments with a control can be summarized in the form of a set of numbers $\overline{X}_0, \overline{X}_1, \cdots, \overline{X}_n$ and s, where the \overline{X} 's are means of p+1 sets of observations which are assumed to be independently and normally distributed, \overline{X}_0 referring to the control and \overline{X}_i to the *i*-th treatment $(i=1, \dots, p)$, and *s* is an independent estimate of the common standard deviation of the p+1 sets of observations. This paper presents a procedure for making confidence statements about the true (or expected) values of the p differences $\overline{X}_i - \overline{X}_0$, the procedure having the property that the probability of all p statements being simultaneously correct is equal to a specified value, P. Tables have been computed which enable the procedure to be used by the experimenter for P = .95 or .99 and p = 1(1)9. When the numbers of observations in each set are equal, the tables enable the experimenter

1096

This content downloaded from

200.144.62.89 on Sun, 07 Apr 2024 23:39:38 +00:00

All use subject to https://about.jstor.org/terms

^{*} I should like to express my appreciation to Frank Wilcoxon for suggesting this problem and for his constant encouragement throughout the course of the investigation. I am grateful for this opportunity to acknowledge also my indebtedness to Robert Bechhofer and to Milton Sobel. Were it not for my good fortune to be associated with them while working on an Air Force contract at Cornell University in 1952-3, this paper could not have been written.

I am indebted to Robert E. Bechhofer also for making the tables in reference [10] available to me.

to set one-sided upper (or lower) confidence limits on the true values of the p differences $\overline{X}_i - \overline{X}_0$ such that the probability is P that all p true values will actually be less than the upper limits set, or to set two-sided confidence limits on the true values of the p differences $\overline{X}_i - \overline{X}_0$ such that P is a lower bound to the probability that all p true values will actually be between the limits set. If the numbers of observations in each set are unequal, the tables may still be used but the associated Pwill be only approximate. The tables may also be used to set joint confidence limits on the potencies of p drugs relative to a common standard, the associated P being approximately equal to the probability that all statements will be correct when one-sided limits are set and approximately **a** lower bound to this probability when two-sided limits are set.

The problem of multiple comparisons with a control is a special case of the more general multiple comparisons problem considered by Tukey [17] and Scheffé [16]. Tukey's procedure based on the Studentized range and Scheffé's procedure based on the *F*-distribution enable the experimenter to make any number of comparisons among a set of sample means with the assurance that the probability of all confidence statements being correct will be equal to or greater than a specified value. When the experimenter only wishes to make comparisons between one of the means and each of the others, as in the case when one of the means represents a control, use of the Tukey or Scheffé procedure would result in confidence limits which are wider than necessary. The procedure described in this paper results in narrower confidence limits for the *p* comparisons $\overline{X}_i - \overline{X}_0$ than either the Tukey or the Scheffé procedure.

In an earlier paper, Roessler [15] considered the problem of multiple comparisons involving a control. However, he assumed that the p comparisons $\overline{X}_i - \overline{X}_0$ were independent which is incorrect since they all have \overline{X}_0 in common. In the present paper it is shown that, to obtain simultaneous confidence limits on the $\overline{X}_i - \overline{X}_0$, the multivariate analogue of Student's *t*-distribution defined by Dunnett and Sobel [4] is encountered. This same distribution was involved in a multiple decision procedure for ranking population means described by Bechhofer et al., [2], to which Tables 1a and 1b of the present paper are applicable. A multiple decision procedure for comparing several experimental categories with a control was formulated by Paulson [11]. Tables 1a and 1b of the present paper are also applicable to Paulson's procedure. The procedure described in the present paper may also be considered as a multiple decision procedure; it is compared with Paulson's in Section VII below. For the benefit of those who may be interested primarily in applications, the procedure is illustrated by two examples in Section II. The main part of the theory is given in Section III with a description of the construction of the tables in Section IV. In Section V, the question of the optimum allocation of available experimental resources between the control and the p treatments is considered. In Section VI, the procedure is applied to the problem of estimating the potencies of p drug samples relative to a common standard.

II. EXAMPLES

(a) The following example was adapted from one given by Villars [18]. The data represent measurements on the breaking strength of fabric treated by three different chemical processes compared with a standard method of manufacture.

	Breaking Strength (lbs.)								
	Standard	Process 1	Process 2	Process 3					
	55	55	55	50					
	47	64	49	44					
	48	<u>64</u>	52	41					
Means	50	61	52	45					
Variances	19	27	9	21					

Here, p=3 and N=3. The average variance is $s^2=19$, which is an estimate of the common variance of the four sets with (p+1)(N-1)=8 degrees of freedom. It could be calculated directly as follows:

$$s^{2} = \frac{55^{2} + 47^{2} + 48^{2} + 55^{2} + \dots + 41^{2} - 3(50^{2} + 61^{2} + 52^{2} + 45^{2})}{8}$$
$$= \frac{152}{8} = 19.$$

The standard deviation is $s = \sqrt{19} = 4.36$ and the estimated standard error of a difference between two means is $s\sqrt{2/N} = 4.36\sqrt{2/3} = 3.56$. The quantity which must be added to and/or subtracted from the observed differences between the means to give their confidence limits has been called by Tukey [17] an "allowance" and is given by $A = ts\sqrt{2/N}$, where t is obtained from Table 1 if one-sided limits are desired or from Table 2 if two-sided limits are wanted. For p=3 and d.f. = 8, t=2.42 for one-sided limits and t=2.94 for two-sided limits for P=95%. Analogous values of t can be determined from the tables if P=99% confidence is required. For one-sided limits, the allowance is A = (2.42)(3.56) = 9 and the experimenter can conclude that:

- (i) The breaking strength using process 1 exceeds the standard by at least 61-50-9=2 lbs.
- (ii) The breaking strength using process 2 exceeds the standard by at least 52-50-9=-7 lbs.
- (iii) The breaking strength using process 3 exceeds the standard by at least 45-50-9=-14 lbs.

The joint statement consisting of the above three conclusions has a confidence coefficient of 95%, i.e., in the long run, 95% of such joint statements will actually be correct. Upper limits for the three differences could be obtained in an analogous manner.

For two-sided limits, the allowance is A = (2.94)(3.56) = 11 and the experimenter can conclude that:

- (i) The breaking strength using process 1 exceeds the standard by an amount between $61-50\pm11=0$ and 22 lbs.
- (ii) The breaking strength using process 2 exceeds the standard by an amount between $52-50\pm11=-9$ and 13 lbs.
- (iii) The breaking strength using process 3 exceeds the standard by an amount between $45-50\pm11=-16$ and 6 lbs.

The joint confidence coefficient for these three statements is greater than 95%. (Due to an approximation made in computing Tables 2a and 2b, the tabulated values of t are somewhat larger than necessary so that the actual P's attained are slightly greater than 95 and 99%. No such approximation was made in computing Tables 1a and 1b.)

(b) The following data are blood count measurements on three groups of animals, one of which served as a control while the other two were treated with two drugs. Due to accidental losses, the numbers of animals in the three groups are unequal.

	Blood Counts (Blood Counts (millions of cells per cubic millimeter)						
	Controls	Drug A	Drug B					
	7.40	9.76	12.80					
	8.50	8.80	9.68					
	7.20	7.68	12.16					
	8.24	9.36	9.20					
	9.84		10.55					
	8.32							
Sums:	49.50	35.60	54.39					
N:	6	4	5					
Means:	8.25	8.90	10.88					

1100 AMERICAN STATISTICAL ASSOCIATION JOURNAL, DECEMBER 1955 Computations:

$$s^{2} = \frac{7.40^{2} + 8.50^{2} + \dots + 9.20^{2} + 10.55^{2} - \frac{49.50^{2}}{6} - \frac{35.60^{2}}{4} - \frac{54.39^{2}}{5}}{(\sum N_{i}) - (p+1)}$$

 $=\!\frac{16.566}{15\!-\!3}\!=\!\frac{16.566}{12}\!=\!1.3805$

 $s = \sqrt{1.3805} = 1.175$

For d.f. = $(\sum N_i) - (p+1) = 12$ and P = 95%, t = 2.11 (one-sided) or t = 2.50 (two-sided).

"Allowances" for differences from the control:

One-sided: drug A:
$$(2.11)(1.175)\sqrt{1/6 + 1/4} = 1.60$$

drug B: $(2.11)(1.175)\sqrt{1/6 + 1/5} = 1.50$
Two-sided: drug A: $(2.50)(1.175)\sqrt{1/6 + 1/4} = 1.90$
drug B: $(2.50)(1.175)\sqrt{1/6 + 1/5} = 1.78$

If the experimenter is interested only in upper one-sided limits for the differences from the control, he can make the following statements:

- (i) Drug A raises the blood count by at most 8.90-8.25+1.60 = 2.25 millions per cmm.
- (ii) Drug B raises the blood count by at most 10.88-8.25+1.50=4.13 millions per cmm.

The joint confidence coefficient for these two statements is approximately 95%. (Since the tables of t were computed for equal numbers of observations per group, their use in the case of unequal numbers results in the desired probabilities being only approximately achieved.) Corresponding lower limits could be calculated in an analogous manner.

If the experimenter desires simultaneous upper and lower limits on the differences, he should use the two-sided allowances as follows:

- (i) Drug A raises the blood count by an amount between $8.90-8.25 \pm 1.90 = -0.25$ and 2.55 millions per cmm.
- (ii) Drug B raises the blood count by an amount between 10.88 $-8.25 \pm 1.78 = 0.85$ and 4.41 millions per cmm.

An approximate lower bound to the joint confidence coefficient of these statements is 95%.

III. THEORETICAL BASIS

Suppose there are available N_0 observations on the control, N_1 observations on the first treatment, \cdots , N_p observations on the *p*-th treatment. Denote these observations by X_{ij} $(i=0, 1, \cdots, p; j=1, 2, \cdots, N_i)$, and the *i*-th treatment mean, $\sum_{j=1}^{N_i} X_{ij}/N_i$, by \overline{X}_i . We make the assumptions usually made in the analysis of variance, namely, that the X_{ij} are independent and normally distributed with common variance σ^2 and means m_i . We assume also that there is available an estimate s^2 of σ^2 , independent of the \overline{X}_i , which is based on *n* degrees of freedom. For example, we may take

$$s^{2} = \sum_{i=0}^{p} \sum_{j=1}^{N_{i}} (X_{ij} - \overline{X}_{i})^{2} / n$$
(1)

where $n = (\sum_{i=0}^{p} N_i) - (p+1)$. Our problem is to obtain separate confidence limits for each of the differences $m_i - m_0$ $(i=1, 2, \dots, p)$, such that the joint confidence coefficient, i.e., the probability that all p confidence intervals will contain the corresponding $m_i - m_0$, is equal to a preassigned value, P (0 < P < 1).

Consider first the case p=1, where there is only one treatment to be compared with the control. The method of obtaining confidence limits for $m_1 - m_o$, as described in almost any statistics textbook, is based on Student's *t*-distribution. If we write

$$z = \frac{\overline{X}_{1} - \overline{X}_{0} - (m_{1} - m_{0})}{\sqrt{\frac{1}{N_{1}} + \frac{1}{N_{0}}}}$$

which is normally distributed with mean 0 and variance σ^2 , then t=z/s follows the Student *t*-distribution with *n* degrees of freedom. A lower limit on m_1-m_o with the desired confidence coefficient will be given by

$$\overline{X}_1 - \overline{X}_0 - d's \sqrt{\frac{1}{N_1} + \frac{1}{N_0}}$$

if d' is chosen so that

$$Prob (t < d') = P \tag{2}$$

Similarly, if an upper confidence limit is required, it will be given by

$$\overline{X}_1 - \overline{X}_0 + d's \sqrt{\frac{1}{N_1} + \frac{1}{N_0}} \cdot$$

On the other hand, if the experimenter wishes to have bounds on $m_1 - m_o$ in both directions, he may take

$$\overline{X}_1 - \overline{X}_0 \pm d''s \sqrt{\frac{1}{N_1} + \frac{1}{N_0}}$$

where d'' is chosen to satisfy

$$\operatorname{Prob}\left(\left|t\right| < d^{\prime\prime}\right) = P \tag{3}$$

The constant d' or d'' corresponding to the desired value of P can be obtained from tables of the percentage points of Student's *t*-distribution, which are widely available.

Now consider the general case where there are p treatments and a control. Write

$$z_i = \frac{\overline{X}_i - \overline{X}_0 - (m_i - m_0)}{\sqrt{\frac{1}{N_i} + \frac{1}{N_0}}}$$

and $t_i = z_i/s$, $i = 1, 2, \dots, p$. Then lower confidence limits with joint confidence coefficient P for the p treatment effects $m_i - m_0$ will be given by

$$\overline{X}_i - \overline{X}_0 - d_i' s \sqrt{\frac{1}{N_i} + \frac{1}{N_0}}, \ (i = 1, 2, \cdots, p),$$

if the p constants d_i' are chosen so that

Prob
$$(t_1 < d_1', t_2 < d_2', \cdots, t_p < d_p') = P.$$
 (4)

Similarly, upper confidence limits will be given by

$$\overline{X}_i - \overline{X}_0 + d_i' s \sqrt{rac{1}{N_i} + rac{1}{N_0}} \cdot$$

On the other hand, two-sided confidence limits having the desired joint confidence coefficient will be given by

$$\overline{X}_i - \overline{X}_0 \pm d_i''s \sqrt{\frac{1}{N_i} + \frac{1}{N_0}} \ (i = 1, 2, \cdots, p),$$

if the p constants d_i'' are chosen to satisfy

Prob
$$(|t_1| < d_1'', |t_2| < d_2'', \cdots, |t_p| < d_p'') = P.$$
 (5)

To find any set of constants d_i' or d_i'' satisfying these equations, the joint distribution of the t_i is required. It may be noted that the joint distribution of the z_i is a multivariate normal distribution with means 0 and variances σ^2 and where the correlation between z_i and z_j is given by

$$\rho_{ij} = 1/\sqrt{\left(\frac{N_0}{N_i} + 1\right)\left(\frac{N_0}{N_j} + 1\right)}.$$

The joint distribution of the t_i is thus the multivariate analogue of Student's *t*-distribution defined by Dunnett and Sobel [4].

To find solutions to (4) and (5), we require a tabulation of the multivariate Student *t*-distribution. We shall show now that the problem of tabulating the multivariate Student *t*-distribution can be reduced to the problem of tabulating the corresponding multivariate normal distribution. Consider first equation (4) above. It can be written

$$P = \text{Prob} (z_1 < d_1's, z_2 < d_2's, \cdots, z_p < d_p's)$$

= $\int_{-\infty}^{+\infty} F(d_1's, d_2's, \cdots, d_p's) p(s) ds$ (6)

where $F(z_1, z_2, \dots, z_p)$ is the multivariate normal c.d.f. of the z_i and p(s) is the probability density function of s. Thus, if F were tabulated, it would be fairly easy using a desk calculator to evaluate (6) by numerical integration for any set of fixed d_i' , and hence to find solutions to (4) as functions of P, p and n.

Similarly, (5) can be written

$$P = \text{Prob} \left(\left| z_{1} \right| < d_{1}''s, \left| z_{2} \right| < d_{2}''s, \cdots, \left| z_{p} \right| < d_{p}''s \right)$$
$$= \int_{-\infty}^{+\infty} G(d_{1}''s, d_{2}''s, \cdots, d_{p}''s)p(s)ds$$
(7)

where $G(z_1, z_2, \dots, z_p)$ is the c.d.f. of the $|z_i|$. Again, if G were tabulated, we could also evaluate (7) and determine the solutions to (5) as functions of P, p and n.

The functions F and G can be obtained for p=2 from K. Pearson's tables of the bivariate normal distribution [13], although the tabulation interval is not fine enough for numerical integration purposes. However, for p=2, (4) and (5) can be evaluated directly from the results of Dunnett and Sobel [4]. The function F has been tabulated for equal values of its arguments and for $p \leq 9$ by the National Bureau of Standards [10] for the special case $\rho_{ij}=1/2$. As will be explained in the next

section, Table 1 of this paper was based on this tabulation. It would be extremely useful for the purpose of the problem considered in this paper to have a corresponding tabulation of the function G.

Until exact tables are available, it will be necessary in general to rely upon approximations to the solutions of (4) and (5). From the results given by Dunnett and Sobel [5], we can write, when

$$\rho_{ij} = 1 / \sqrt{\left(\frac{N_0}{N_i} + 1\right) \left(\frac{N_0}{N_j} + 1\right)},$$

Prob $(t_1 < d_1', t_2 < d_2', \cdots, t_p < d_p') \ge \prod_{i=1}^p \operatorname{Prob} (t < d_i')$ (8)

and

Prob
$$(|t_1| < d_1'', |t_2| < d_2'', \cdots, |t_p| < d_p'')$$

$$\geq \prod_{i=1}^p \operatorname{Prob} (|t| < d_i'').$$
(9)

Thus, upper bounds to the constants d_i' and d_i'' can be determined by equating the right-hand sides of (8) and (9) to the desired value of P. These calculations involve only the probability integral of the univariate Student *t*-distribution, which has been tabulated most recently by Hartley and Pearson [8, 12].

Since (4) and (5) are each increasing functions of the correlations ρ_{ij} , alternative lower bounds which are closer than the lower bounds given in (8) and (9) may be obtained by taking $\rho_{ij}=0$. Pillai and Ramachandran [14] have tabulated solutions $d_1' = d_2' = \cdots d_p'$ to (4) and solutions $d_1'' = d_2'' = \cdots = d_p''$ to (5) for P = .95 and $\rho_{ij} = 0$. It would be useful to have a tabulation of such equicoordinate percentage points of the multivariate Student *t*-distribution in the important special case where $\rho_{ij} = 0$ for other values of P.

Lower bounds based on the bivariate Student *t*-distribution can also be obtained, as shown in [5]. Taking $d_1' = d_2' = \cdots = d_p' = d'$, $d_1'' = d_2'' = \cdots = d_p'' = d''$, and $\rho_{ij} = \rho \ge 0$, these can be written

Prob
$$(t_1 < d', t_2 < d', \cdots, t_p < d' | \rho_{ij} = \rho)$$

$$\geq [Prob (t_1 < d', t_2 < d' | \rho_{12} = \rho)]^{p/2}$$
(10)

and

Prob
$$(|t_1| < d'', |t_2| < d'', \dots, |t_p| < d'' | \rho_{ij} = \rho)$$

$$\geq [Prob (|t_1| < d'', |t_2| < d'' | \rho_{12} = \rho)]^{p/2}$$
(11)

The probability within the square brackets can be determined from the probability integral of the bivariate Student-*t* distribution [4] with correlation ρ . The bounds obtained from these inequalities are sharper than those given by (8) and (9), and in most cases will also be sharper than those obtained by using the Pillai and Ramachandran tables [14].

There are, of course, infinitely many solutions to (4) and (5). For the applications considered in this paper, we will take the constants to be equal, viz., $d_1'=d_2'=\cdots=d_{p'}(=d', \operatorname{say})$ and $d_1''=d_2''=\cdots=d_{p''}(=d'', \operatorname{say})$. Besides greatly simplifying the computational problem, there are some theoretical grounds for doing so in the case where $\rho_{ij}=\rho\geq 0$, which occurs frequently in practice. For example, it can be shown that $\sum d_i''$ and $\sum d_i'''$ are each minimized by this choice.

IV. CONSTRUCTION OF THE TABLES

Tables 1a and 1b give solutions $d' = d_1' = \cdots = d_p'$ to (4) for P = .95and .99, respectively, for $p \leq 9$ and $\rho_{ij} = 1/2$. They are applicable to the situation where there are equal numbers of observations on the control and the p treatments, viz, $N_0 = N_1 = \cdots = N_p$. These tables were constructed by numerical evaluation of the integral in (6) using tables of the function F computed by the National Bureau of Standards [10]. The method used was as follows: For n = 5, 10, 20, 25 degrees of freedom, the integral in (6) was calculated for three successive values of d'differing by 0.1 such that the desired value of P was bracketed. The required value of d' was then determined to 3 decimal places by 3-point inverse interpolation. For $n = \infty$ degrees of freedom, the values given in tables computed by Bechhofer [1] were used. For the intermediate degrees of freedom, the values were obtained by interpolation with 1/nas argument. An accuracy of 1 in the second decimal place should be achieved by this method.

Tables 2a and 2b give solutions $d''=d_1''=\cdots=d_p''$ to the righthand side of (11) for P=.95 and .99, respectively, for $p \leq 9$ and $\rho_{ij}=1/2$. The method of constructing these tables was as follows: For n=5, 10, 20, 40, ∞ degrees of freedom, the probability in the square brackets of (11) was calculated for three successive values of d'' differing by 0.1 such that the desired value of P was bracketed, using the expressions developed in [4] for the probability integral of the bivariate Student *t*-distribution. The required value of d'' was then determined by 3-point inverse interpolation to 3 decimal places. For the intermediate degrees of freedom, the required values were obtained by interpolation using 1/n as argument. An accuracy of 1 in the second decimal place should be achieved by this method.

V. OPTIMUM ALLOCATION OF OBSERVATIONS BETWEEN CONTROL AND TREATMENTS

The tables given in this paper were prepared to handle the case where equal numbers of observations are available on each of the p treatments and on the control. In many practical situations, the experimenter will, in fact, wish to allocate the available number of observations equally to each group. Where it is feasible, however, it may be advantageous to do otherwise. In this section, we will consider the consequences of allocating N_0 observations to the control and N_1 observations to each of the other treatment groups, i.e., we will take $N_1 = N_2 = \cdots = N_p$ and $N_0 \neq N_1$.

Lower confidence limits to the $m_i - m_0$ will be given by

$$\overline{X}_i - \overline{X}_0 - d's \sqrt{\frac{1}{N_1} + \frac{1}{N_0}} \qquad (i = 1, 2, \cdots, p),$$

where d' is chosen to satisfy

Prob
$$(t_i < d', i = 1, 2, \cdots, p) = P,$$
 (12)

the t_i having the multivariate Student t-distribution with

$$\rho_{ij} = 1 \bigg/ \bigg(\frac{N_0}{N_1} + 1 \bigg).$$

We will consider the allocation N_0/N_1 optimum if it maximizes P for fixed value of

$$d'\sqrt{\frac{1}{N_1}+\frac{1}{N_0}}$$

and fixed total number of observations, $N_0 + pN_1$. It may be noted that fixing the total number of observations also fixes *n*, the number of degrees of freedom associated with the multivariate *t*-distribution, if *s* is defined by (1). Let

$$h = d' \sqrt{\frac{1}{N_1} + \frac{1}{N_0}} \cdot$$

Then (12) can be written

Prob
$$\left(t_{i} < \frac{h}{\sqrt{\frac{1}{N_{1}} + \frac{1}{N_{0}}}}, i = 1, 2, \cdots, p\right) = P$$
 (13)

From (13), it is evident that P can be increased for fixed h by decreasing

$$\sqrt{\frac{1}{N_1} + \frac{1}{N_0}} \cdot$$

It is easy to show, as has been pointed out by several authors, see, for example, Finney [7], that

$$\sqrt{\frac{1}{N_1} + \frac{1}{N_0}}$$

attains a minimum for fixed $N_0 + pN_1$ when $N_0/N_1 = \sqrt{p}$. However, this choice makes $\rho_{ij} < 1/2$, which operates to decrease P.

In order to investigate numerically the effect of different allocations on P, the curves shown in Figs. 1 and 2 computed. Fig. 1 shows P as a function of N_0/N_1 for p=2 and $n=1, 2, 5, 10, \infty$, with h chosen in each case to make P=.95 when $N_0/N_1=1$. Fig. 2 shows P as a function of N_0/N_1 for p=2, 4, 9 and $n=\infty$, with h again chosen to make P=.95when $N_0/N_1=1$. The curves for finite n were computed from formulas given in [4]. The curves for $n=\infty$ were computed by numerical integration using tables of the normal distribution [9], with certain points for p=2 checked against Pearson's bivariate normal tables [13].

Figs. 1 and 2 indicate that the optimum allocation occurs where N_0/N_1 is only slightly less than \sqrt{p} except when the number of degrees of freedom is small. Some further computations carried out by the author for the case of $n = \infty$ degrees of freedom indicated that the point of optimum allocation becomes even closer to \sqrt{p} when h is chosen to make P = .99 for $N_0/N_1 = 1$. However, for h chosen to make P = .75 for $N_0/N_1 = 1$, it was found that P < .75 for $N_0/N_1 = \sqrt{p}$ and the optimum value of N_0/N_1 was considerably less than \sqrt{p} . For practical purposes, we can thus conclude that, if the experimenter is working with a joint confidence coefficient in the neighborhood of P = .95 or greater, then the experiment should be designed so that $N_0/N_1 = \sqrt{p}$ approximately, where N_0 is the number of observations on the control and N_1 the number on each of the p treatments.

VI. APPLICATION TO BIOLOGICAL ASSAY

An important example involving the multiple comparison of several treatments with a control arises in the biological assay of several drug samples relative to a common standard. In the "parallel line" type of biological assay, regression lines $Y = a_0 + bX$ and $Y = a_1 + bX$ are fitted



FIG. 1.—In plotting these curves, $d'\sqrt{(1/N_1)+(1/N_0)}$ was fixed for each n so that P = .95 for $N_0 = N_1$, where $d's\sqrt{(1/N_1)+(1/N_0)}$ is the difference between $\overline{X}_{\bullet} - \overline{X}_0$ and its lower confidence limit. The dotted curve indicates where the optimum occurs for each n; the vertical dashed line is drawn at $N_0/N_1 = \sqrt{p} = \sqrt{2}$.

to data representing observed responses Y at several log-dose levels X of a standard drug preparation S and a test sample U. The estimated log-potency of U relative to S is represented by the horizontal distance between the two regression lines,

$$M = \frac{a_1 - a_0}{b} = \overline{X}_0 - \overline{X}_1 + \frac{Y_1 - Y_0}{b}$$
(14)



FIG. 2.—In plotting these curves, $d'\sqrt{(1/N_1)+(1/N_0)}$ was fixed for each p so that P = .95 for $N_0 = N_1$, where $d'\sigma\sqrt{(1/N_1)+(1/N_0)}$ is the difference between $\bar{X}_* - \bar{X}_0$ and its lower confidence limit. The black arrows indicate where the optima occur; the white arrows indicate the points where $N_0/N_1 = \sqrt{p}$.

where \overline{X}_0 and \overline{X}_1 are the mean log-dose levels, and \overline{Y}_0 and \overline{Y}_1 are the mean observed responses, of S and U respectively. On the other hand, the true log-potency may be represented by

$$\overline{M} = \overline{X}_0 - \overline{X}_1 + \frac{m_1 - m_0}{\beta} \tag{15}$$

where m_0 , m_1 and β are the expected values of \overline{Y}_0 , \overline{Y}_1 and b, respectively. Assuming that the responses Y are independent and normally distributed with common variance σ^2 and means $m_0 + \beta(X - \overline{X}_0)$ and $m_1 + \beta(X - \overline{X}_1)$ for S and U respectively, we can obtain confidence limits for \overline{M} by Fieller's [6] method by considering 1110 AMERICAN STATISTICAL ASSOCIATION JOURNAL, DECEMBER 1955

$$z = \frac{\overline{Y}_{1} - \overline{Y}_{0} - (\overline{M} - \overline{X}_{0} + \overline{X}_{1})b}{\left[\frac{1}{N_{1}} + \frac{1}{N_{0}} + (\overline{M} - \overline{X}_{0} + \overline{X}_{1})^{2}c^{2}\right]^{1/2}}$$
(16)

Here, N_0 and N_1 are the numbers of responses observed on S and U respectively, and $c^2\sigma^2$ is the variance of the common slope b. Then z is normally distributed with mean 0 and variance σ^2 . If s^2 is an estimate of σ^2 independent of z, based on n degrees of freedom, then z/s has Student's *t*-distribution with n degrees of freedom. Hence, confidence limits for \overline{M} with confidence coefficient P can be obtained by equating z^2/s^2 to t^2 , where t is the P-percentage point of Student's t, and solving the resulting quadratic equation for \overline{M} . The solution may be found, for example, in Bliss [3].

Now suppose there are p unknown drug samples: $U_1, U_2 \cdots, U_p$, to be compared with a common standard, S. Extending the above notation in an obvious way, we define the p variables,

$$z_{i} = \frac{\overline{Y}_{i} - \overline{Y}_{0} - (\overline{M}_{i} - \overline{X}_{0} + \overline{X}_{i})b}{\left[\frac{1}{N_{i}} + \frac{1}{N_{0}} + (\overline{M}_{i} - \overline{X}_{0} + \overline{X}_{i})^{2}c^{2}\right]^{1/2}}, i = 1, 2, \cdots, p \quad (17)$$

The z_i have a joint *p*-variate normal distribution with means 0, common variance σ^2 and correlation between z_i and z_j given by

$$\rho_{ij} = (1 + \epsilon_i \epsilon_j) / \sqrt{\left(\frac{N_0}{N_i} + 1 + \epsilon_i^2\right) \left(\frac{N_0}{N_j} + 1 + \epsilon_j^2\right)}$$

where $\epsilon_i = \overline{M}_i - \overline{X}_0 + \overline{X}_i c \sqrt{N_0}$. For the *p* pairs of confidence limits on the \overline{M}_i to have a joint confidence coefficient equal to *P*, we are led to consider the joint distribution of the z_i/s , which is the multivariate Student *t*-distribution as in Section III, with this important difference: the correlations ρ_{ij} are no longer known exactly since they involve the unknown parameters \overline{M}_i and \overline{M}_j . Fortunately, ϵ_i may be expected to be fairly small in most cases since it is common practice in designing a biological assay experiment to try to arrange the dose levels so that $\overline{X}_0 - \overline{X}_i$ is close to \overline{M}_i . Thus, we can obtain confidence limits for the \overline{M}_i which have approximately the desired confidence coefficient by assuming the ϵ_i to be negligible, whence

$$\rho_{ij} = 1 / \sqrt{\left(\frac{N_0}{N_i} + 1\right) \left(\frac{N_0}{N_i} + 1\right)}.$$
(18)



This takes the value $\frac{1}{2}$ in the usual situation where $N_0 = N_i$ $(i=1, 2, \cdots, p)$, in which case the tables in this paper are applicable.

The contour curves in Fig. 3 show the effect of ϵ_i and ϵ_j on ρ_{ij} when $N_0 = N_i = N_j$. In most practical situations, the log-dose levels chosen by the experimenter for each drug will cover a wide enough range so that



FIG. 4

the ϵ_i are numerically small, in which case they do not exert much influence on the value of ρ_{ij} . In Fig. 4, curves are drawn for degrees of freedom equal to 5 and ∞ showing the actual *P* attained as a function of ρ in the case of estimating the log-potencies of two drugs (p=2)when $N_0=N_1=N_2$ and the tables are used applicable to $\rho=\frac{1}{2}$ and P = 95%. It may be seen that for a wide range of values of ρ around $\rho = \frac{1}{2}$, P does not differ much from the value 95%.

VII. MULTIPLE DECISION PROCEDURES FOR COMPARING TREATMENTS WITH A CONTROL

A multiple decision procedure for selecting the "best" of p+1 categories when comparing p experimental categories with a control has been developed by Paulson [11]. Paulson gives a method for making one of the following p+1 decisions:

 $\begin{cases} D_0: \text{ select the control as best} \\ D_i: \text{ select the } i\text{-th category as best} \end{cases} (i=1, 2, \cdots, p)$

If $\overline{X}_0, \overline{X}_1, \cdots, \overline{X}_p$ represent the p+1 means, each based on N observations, \overline{X}_0 being the control, then Paulson's method consists in picking out $\overline{X}^* = \max(\overline{X}_1, \cdots, \overline{X}_p)$ and if $\overline{X}^* - \overline{X}_0 \geq \lambda_n s \sqrt{2/N}$ the decision D^* corresponding to \overline{X}^* is made, whereas if $\overline{X}^* - \overline{X}_0 < \lambda_n s \sqrt{2/N}$ the decision D_0 is made. The constant λ_n is chosen so that the probability of making decision D_0 , when all p treatments are equivalent to the control, is equal to a pre-assigned value P. Clearly, $d_i' = \lambda_n$ must be a solution of (4). Thus, Tables 1a and 1b of this paper give the required values of λ_n for P = .95 and .99.

In some situations it may be appropriate to consider the following set of possible decisions from which a choice is to be made:

The following procedure is proposed for choosing one of the above 2^p decisions on the basis of the p+1 observed means $\overline{X}_0, \overline{X}_1, \cdots, \overline{X}_p$, each based on N observations, and the independent estimate s of the common standard deviation:

By choosing d to satisfy (4), we will be assured that the probability of accepting D_0 when all the treatments are equivalent to the control is equal to a pre-assigned value P. In fact, d will then be identical with Paulson's λ_n . Table 1 gives the required values of d for P = .95 and .99.

It is also possible to determine the size N of sample required to achieve a specified probability of accepting some other decision when all the treatments are not equivalent to the control. For example, suppose all the treatments are equivalent to the control except one, say the first one, which is better than the control. The correct decision to make would then be D_1 . Suppose $m_0 = m_2 = m_3 = \cdots = m_p = m_1 - \delta$. Then the probability of making decision D_1 can be written

$$P_{1} = \Pr \left(D_{1} \mid m_{0} = m_{2} = \cdots = m_{p} = m_{1} - \delta\right)$$

$$= \Pr \left(\overline{X}_{1} - \overline{X}_{0} \ge ds\sqrt{2/N}, \quad \overline{X}_{2} - \overline{X}_{0}\right)$$

$$< ds\sqrt{2/N}, \cdots, \overline{X}_{p} - \overline{X}_{0} < ds\sqrt{2/N}\right)$$

$$= \Pr \left(t_{1} \ge d, t_{2} < d, \cdots, t_{p} < d\right)$$
(19)

where

$$t_i = \frac{\overline{X}_i - \overline{X}_0}{s\sqrt{2/N}} \qquad (i = 1, 2, \cdots, p)$$

We note that t_2, \dots, t_p are Student *t*-variates, but t_1 is a non-central *t*-variate.

To obtain bounds for P_1 , write

$$\overline{P}_1 = \Pr (t_1 < d, t_2 < d, \cdots, t_p < d)$$

$$\geq \Pr (t_1 < d) \cdot \Pr (t_2 < d, \cdots, t_p < d)$$
(20)

This inequality follows from Dunnett and Sobel [5]. Since

$$P_1 + \overline{P}_1 = \Pr(t_2 < d, \cdots, t_p < d), \qquad (21)$$

it follows that an upper bound for P_1 is given by

$$P_1 \leq \Pr(t_1 \geq d) \cdot \Pr(t_2 < d, \cdots, t_p < d).$$
(22)

On the other hand, an obvious upper bound on \overline{P}_1 is

$$\overline{P}_1 \leq \Pr\left(t_1 < d\right) \tag{23}$$

From (21) and (23), we get the following lower bound for P_1 ,

$$P_1 \ge \Pr(t_2 < d, \cdots, t_p < d) - \Pr(t_1 < d).$$
 (24)

The difference between the bounds given by (22) and (24) is



FIG. 5

Pr $(t_1 < d) \cdot [1 - \Pr(t_2 < d, \dots, t_p < d)]$ which will be small in the region of interest where P_1 is fairly large. In Fig. 5, the two bounds for P_1 are plotted as functions of $\sqrt{(N/2)}\delta/\sigma$ for d.f. = ∞ , p=2 and 9, and where d is chosen in each case so that P=.95. To compute the probability involving t_2, \dots, t_p , in (22) and (24), tables of the multivariate normal distribution computed by the Bureau of Standards [10] were used. If it were desired to compute the bounds on P_1 for a finite number of degrees of freedom, the probability involving t_2, \dots, t_p could be computed by numerical integration on the Bureau of Standards tables. However, since in most practical situations the number of degrees of freedom will be large, it may be sufficient to assume d.f. = ∞ and use the Bureau of Standards tables directly.

Using Fig. 5, it is possible to determine the required value of N corresponding to any given values of δ/σ and P_1 . The following table shows the value of $\sqrt{N}\delta/\sigma$ corresponding to p=1(1)9 to achieve $P_1=.80$ for P=.95 and d.f. = ∞ .

Contraction of the Address of the Ad		the second	
	p	$\sqrt{N}\delta/\sigma$	
	1	3.52	
	2	4.05	
	3	4.30	
	4	4.46	
	5	4.58	
	6	4.67	
	7	4.74	
	8	4.81	
	9	4.86	
		1	

For example, suppose that the experimenter has p=5 treatments to compare with a control. Table 1a will provide the value of d to give a probability of P=.95 that none of the treatments will be declared superior to the control when, in fact, all are equivalent to the control. If, in addition, the experimenter wants to achieve a probability of $P_1=.80$ of correctly selecting a superior treatment, if there is one which is, say, one standard deviation better than the control, the above table shows that $\sqrt{N}\delta/\sigma=4.58$ whence N=21 on substituting $\delta/\sigma=1$. Thus 21 observations should be taken on each of the treatments and on the control. This will provide (p+1)(N-1)=120 degrees of freedom for estimating the variance, so that d=2.26 from table 1a. While the table used above to determine N is based on d.f. = ∞ , the result should not be much different for d.f. = 120. The experimenter would then take 21 observations in each group, observe \overline{X}_0 and \overline{X}_i $(i=1, 2, \dots, 5)$, calculate s^2 from equation (1), and declare any treatment superior to the control which gives a mean \overline{X}_i greater than $\overline{X}_0+2.26s\sqrt{2/21}$.

TABLE 1a*

TABLE OF t FOR ONE-SIDED COMPARISONS BETWEEN p TREAT-MENT MEANS AND A CONTROL FOR A JOINT CONFIDENCE COEFFICIENT OF P=95%

p, Number Of Treatment Means (Excluding The Control)									
d.f.	1	2	3	4	5	6	7	8	9
5	2.02	2.44	2.68	2.85	2.98	3.08	3.16	3.24	3.30
6	1.94	2.34	2.56	2.71	2.83	2.92	3.00	3.07	3.12
7	1.89	2.27	2.48	2.62	2.73	2.82	2.89	2.95	3.01
8	1.86	2.22	2.42	2.55	2.66	2.74	2.81	2.87	2.92
9	1.83	2.18	2.37	2.50	2.60	2.68	2.75	2.81	2.86
10	1.81	2.15	2.34	2.47	2.56	2.64	2.70	2.76	2.81
11	1.80	2.13	2.31	2.44	2.53	2.60	2.67	2.72	2.77
12	1.78	2.11	2.29	2.41	2.50	2.58	2.64	2.69	2.74
13	1.77	2.09	2.27	2.39	2.48	2.55	2.61	2.66	2.71
14	1.76	2.08	2.25	2.37	2.46	2.53	2.59	2.64	2.69
	}								
15	1.75	2.07	2.24	2.36	2.44	2.51	2.57	2.62	2.67
16	1.75	2.06	2.23	2.34	2.43	2.50	2.56	2.61	2.65
17	1.74	2.05	2.22	2.33	2.42	2.49	2.54	2.59	2.64
18	1.73	2.04	2.21	2.32	2.41	2.48	2.53	2.58	2.62
19	1.73	2.03	2.20	2.31	2.40	2.47	2.52	2.57	2.61
20	1.72	2.03	2.19	2.30	2.39	2.46	2.51	2.56	2.60
24	1.71	2.01	2.17	2.28	2.36	2.43	2.48	2.53	2.57
30	1.70	1.99	2.15	2.25	2.33	2.40	2.45	2.50	2.54
40	1.68	1.97	2.13	2.23	2.31	2.37	2.42	2.47	2.51
60	1.67	1.95	2.10	2.21	2.28	2.35	2.39	2.44	2.48
120	1.66	1.93	2.08	2.18	2.26	2.32	2.37	2.41	2.45
inf.	1.64	1.92	2.06	2.16	2.23	2.29	2.34	2.38	2.42
	1	1	1		1		1		1

* Table 1a gives a solution $d_{i'} = t$ to equation (4) in the text for P = .95 for the case $\rho_{ij} = 1/2$.

TABLE 1b*

TABLE OF t FOR ONE-SIDED COMPARISONS BETWEEN p TREAT-MENT MEANS AND A CONTROL FOR A JOINT CONFIDENCE COEFFICIENT OF P = 99%

p, Number Of Treatment Means (Excluding The Control)									
d.f.	1	2	3	4	5	6	7	8	9
5	3.37	3.90	4.21	4.43	4.60	4.73	4.85	4.94	5.03
6	3.14	3.61	3.88	4.07	4.21	4.33	4.43	4.51	4.59
7	3.00	3.42	3.66	3.83	3.96	4.07	4.15	4.23	4.30
8	2.90	3.29	3.51	3.67	3.79	3.88	3.96	4.03	4.09
9	2.82	3.19	3.40	3.55	3.66	3.75	3.82	3.89	3.94
10	2.76	3.11	3.31	3.45	3.56	3.64	3.71	3.78	3.83
11	2.72	3.06	3.25	3.38	3.48	3.56	3.63	3.69	3.74
12	2.68	3.01	3.19	3.32	3.42	3.50	3.56	3.62	3.67
13	2.65	2.97	3.15	3.27	3.37	3.44	3.51	3.56	3.61
14	2.62	2.94	3.11	3.23	3.32	3.40	3.46	3.51	3.56
15	2 60	2 91	3 08	3 20	3 29	3 36	3 42	3 47	3 52
16	2.58	2.88	3 05	3 17	3 26	3 33	3 39	3.44	3.48
17	2.57	2.86	3 03	3 14	3 23	3 30	3 36	3.41	3.45
18	2 55	2.84	3 01	3 12	3.21	3.27	3.33	3.38	3.42
19	2.54	2.83	2.99	3.10	3.18	3.25	3.31	3.36	3.40
20	2.53	2.81	2.97	3.08	3.17	3.23	3.29	3.34	3.38
24	2.49	2.77	2.92	3.03	3.11	3.17	3.22	3.27	3.31
30	2.46	2.72	2.87	2.97	3.05	3.11	3.16	3.21	3.24
4 0	2.42	2.68	2.82	2.92	2.99	3.05	3.10	3.14	3.18
60	2.39	2.64	2.78	2.87	2.94	3.00	3.04	3.08	3.12
120	2.36	2.60	2.73	2.82	2.89	2.94	2.99	3.03	3.06
inf.	2.33	2.56	2.68	2.77	2.84	2.89	2.93	2.97	3.00

* Table 1b gives a solution $d_i' = t$ to equation (4) in the text for P = .99 for the case $\rho_{ij} = 1/2$.

TABLE 2a*

TABLE OF t FOR TWO-SIDED COMPARISONS BETWEEN p TREAT-MENT MEANS AND A CONTROL FOR A JOINT CONFIDENCE COEFFICIENT OF P=95%

p, Number Of Treatment Means (Excluding The Control)									
d.f.	1	2	3	4	5	6	7	8	9
5	2.57	3.03	3.39	3.66	3.88	4.06	4.22	4.36	4.49
6	2.45	2.86	3.18	3.41	3.60	3.75	3.88	4.00	4.11
7	2.36	2.75	3.04	3.24	3.41	3.54	3.66	3.76	3.86
8	2.31	2.67	2.94	3.13	3.28	3.40	3.51	3.60	3.68
9	2.26	2.61	2.86	3.04	3.18	3.29	3.39	3.48	3.55
10	9.93	2 57	2 81	2 07	2 11	3 91	2 21	2 20	3 46
10	2.20	2.57	2.01	2.01	3 05	3 15	3 94	3 31	3 38
12	2.18	2.50	2.70	2.88	3 00	3 10	3 18	3 25	3 32
12	2.10	2.48	2.69	2.84	2.96	3 06	3 14	3 21	3 27
14	2.10	2.10	2.67	2.81	2.00	3 02	3 10	3 17	3 23
	2.11	2.10	2.01	2.01	2.00	0.02	0.10	0.11	0.20
15	2.13	2.44	2.64	2.79	2.90	2.99	3.07	3.13	3.19
16	2.12	2.42	2.63	2.77	2.88	2.96	3.04	3.10	3.16
17	2.11	2.41	2.61	2.75	2.85	2.94	3.01	3.08	3.13
18	2.10	2.40	2.59	2.73	2.84	2.92	2.99	3.05	3.11
19	2.09	2.39	2.58	2.72	2.82	2.90	2.97	3.04	3.09
20	2.09	2.38	2.57	2.70	2.81	2.89	2.96	3.02	3.07
24	2.06	2.35	2.53	2.66	2.76	2.84	2.91	2.96	3.01
30	2.04	2.32	2.50	2.62	2.72	2.79	2.86	2.91	2.96
40	2.02	2.29	2.47	2.58	2.67	2.75	2.81	2.86	2.90
60	2.00	2.27	2.43	2.55	2.63	2.70	2.76	2.81	2.85
120	1.98	2.24	2.40	2.51	2.59	2.66	2.71	2.76	2.80
inf.	1.96	2.21	2.37	2.47	2.55	2.62	2.67	2.71	2.75
	1 - / • •			1	=	= . • -		1	

* Table 2a gives a solution $d_i'' = t$ which makes the right-hand side of inequality (11) in the text equal to .95 for the case $\rho = 1/2$. This may be used as an approximate solution to equation (5) in the text for P = .95 for the case $\rho_{ij} = 1/2$.

TABLE 2b*

TABLE OF t FOR TWO-SIDED COMPARISONS BETWEEN p TREAT-MENT MEANS AND A CONTROL FOR A JOINT CONFIDENCE COEFFICIENT OF P=99%

p, Number Of Treatment Means (Excluding The Control)									
d.f.	1	2	3	4	5	6	7	8	9
5	4.03	4.63	5.09	5.44	5.73	5.97	6.18	6.36	6.53
6	3.71	4.22	4.60	4.88	5.11	5.30	5.47	5.61	5.74
7	3.50	3.95	4.28	4.52	4.71	4.87	5.01	5.13	5.24
8	3.36	3.77	4.06	4.27	4.44	4.58	4.70	4.81	4.90
9	3.25	3.63	3.90	4.09	4.24	4.37	4.48	4.57	4.65
10	3 17	3 53	3 78	3 95	4 10	4 21	4 31	4 40	4 47
11	3 11	3 45	3 68	3 85	3 98	4 09	4 18	4 26	4 33
12	3.05	3.39	3 61	3 76	3 89	3 99	4.08	4.15	4 22
13	3.01	3.33	3.54	3.69	3.81	3.91	3.99	4.06	4.13
14	2.98	3.29	3.49	3.64	3.75	3.84	3.92	3.99	4.05
		00	0.120	0.01		0.01	0.00-		
15	2.95	3.25	3.45	3.59	3.70	3.79	3.86	3.93	3.99
16	2.92	3.22	3.41	3.55	3.65	3.74	3.82	3.88	3.93
17	2.90	3.19	3.38	3.51	3.62	3.70	3.77	3.83	3.89
18	2.88	3.17	3.35	3.48	3.58	3.67	3.74	3.80	3.85
19	2.86	3.15	3.33	3.46	3.55	3.64	3.70	3.76	3.81
20	2.85	3.13	3.31	3.43	3.53	3.61	3.67	3.73	3.78
24	2.80	3.07	3.24	3.36	3.45	3.52	3.58	3.64	3.69
30	2.75	3.01	3.17	3.28	3.37	3.44	3.50	3.55	3.59
40	2.70	2.95	3.10	3.21	3.29	3.36	3.41	3.46	3.50
60	2.66	2.90	3.04	3.14	3.22	3.28	3.33	3.38	3.42
120	2.62	2.84	2.98	3.08	3.15	3.21	3.25	3.30	3.33
inf.	2.58	2.79	2.92	3.01	3.08	3.14	3.18	3.22	3.25

* Table 2b gives a solution $d_i'' = t$ which makes the right-hand side of inequality (11) in the text equal to .99 for the case $\rho = 1/2$. This may be used as an approximate solution to equation (5) in the text for P = .99 for the case $\rho_{ij} = 1/2$.

REFERENCES

- Bechhofer, Robert E., "A single-sample multiple decision procedure for ranking means of normal populations with known variances," Annals of Mathematical Statistics, 25 (1954), 16-39.
- [2] Bechhofer, Robert E., Dunnett, Charles W., and Sobel, Milton, "A twosample multiple decision procedure for ranking means of normal populations with a common unknown variance," *Biometrika*, 41 (1954), 170-6.
- [3] Bliss, C. I., The Statistics of Bioassay. New York, Academic Press, 1952.
- [4] Dunnett, Charles W., and Sobel, Milton, "A bivariate generalization of Student's t-distribution, with tables for certain special cases," *Biometrika*, 41 (1954), 153-69.
- [5] Dunnett, C. W., and Sobel, M., "Approximations to the probability integral and certain percentage points of a multivariate analogue of Student's *t*-distribution," *Biometrika*, 42 (1955), 258-60.
 [6] Fieller, E. C., "A fundamental formula in the statistics of biological assay,
- [6] Fieller, E. C., "A fundamental formula in the statistics of biological assay, and some applications," *Quarterly Journal of Pharmacy and Pharmacology*, 17 (1944), 117-23.
- [7] Finney, D. J., Statistical Method in Biological Assay. New York: Hafner Publishing Company, 1952.
- [8] Hartley, H. O., and Pearson, E. S., "Table of the probability integral of the t-distribution," Biometrika, 37 (1950), 168-72.
- [9] National Bureau of Standards, Tables of Normal Probability Functions. Washington: U. S. Government Printing Office, 1953.
- [10] National Bureau of Standards, Unpublished tables.
- [11] Paulson, Edward, "On the comparison of several experimental categories with a control," Annals of Mathematical Statistics, 23 (1952), 239-46.
- [12] Pearson, E. S., and Hartley, H. O., Biometrika Tables for Statisticians, Vol. I. Cambridge: Cambridge University Press, 1954.
- [13] Pearson, K., Tables for Statisticians and Biometricians, Part II. Cambridge: Cambridge University Press, 1931.
- [14] Pillai, K. C. S., and Ramachandran, K. V., "On the distribution of the ratio of the *i*th observation in an ordered sample from a normal population to an independent estimate of the standard deviation," Annals of Mathematical Statistics, 25 (1954), 565-72.
- [15] Roessler, E. B., "Testing the significance of observations compared with a control," Proceedings of the American Society for Horticultural Science, 47 (1946), 249-51.
- [16] Scheffé, Henry, "A method for judging all contrasts in the analysis of variance," Biometrika, 40 (1953), 87-104.
- [17] Tukey, John W., "The problem of multiple comparisons." Unpublished notes in private circulation. Princeton University.
- [18] Villars, Donald Statler, Statistical Design and Analysis of Experiments for Development Research. Dubuque, Iowa: Wm. C. Brown Company, 1951.