

GLAXO LABORATORIES LTD.
FERMENTATION RESEARCH DIVISION
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YOUR REFERENCE
PLEASE ADDRESS REPLY TO
JFR/T/EMS.



TELEPHONE: FULMER 155
Registered Offices:
GREENFORD MIDDLESEX

9th March, 1956.

Prof. Sir Ronald A. Fisher, Sc.D., F.R.S.,
Department of Genetics,
University of Cambridge,
Whittingehame Lodge,
14, Storey's Way,
Cambridge.

Dear Professor Fisher,

Thank you for your letter of the 3rd instant in which you kindly give us the formulae for the case of 3 and 3 D.F. Unfortunately, however, N_1 and $N_2 = 4$ in the letter of 1st instant refer to the degrees of freedom and not to the number of treated plants. We apologise for the confusion in paragraphs 1 and 2 in this respect.

We note with interest that your recent work has produced explicit formulae for the case where both degrees of freedom are small odd numbers and this would help in those cases where our experiments have 5 and 5 D.F., but not, unfortunately, in the more usual case of 4 against 4 D.F.

These experiments with such small replication arose from a misunderstanding as to the replication required. This misunderstanding has been corrected and we do not anticipate that the problem will arise again. In the meantime we are tackling the interpretation of the results by enumerating the number of ways that the observed results could be rearranged to give an equal or greater difference between control and treated than the difference actually observed and comparing this number with the total arrangements possible. (We know the treatment cannot make matters worse, so a one tailed test is adequate). In view of the small replication and the fact that we cease to enumerate as soon as either the significance is established or not established as the case may be at the 5% level, this method, though tedious, is not impracticable. We are, in fact, working on a systematic way of enumerating the possible "swop-overs" by means of a laid out proforma such that the operations can be done at sight, the system ensuring exhaustiveness.

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Our experiments are concerned with comparing the intensity of a disease by means of total lesion counts on various leaflets as between control plants and plants treated with chemicals that enter the leaflets by translocation from the site of application. Our evidence suggests that in the absence of the chemicals the standard error is proportional to the mean lesion count but that with intermediate levels of chemical or intermediate times allowed for translocation, the variance of the treated plants is inflated, presumably because the amount of chemical entering the leaflets under these conditions is marginal and somewhat erratic in controlling the disease. In any event the relationship between mean lesion count and variance appears complex and our evidence is not sufficient to postulate a definite functional relationship upon which a transformation could be based.

Even assuming the \bar{d} test had been tabulated for small degrees of freedom, the general question of significance tests for a number of means in excess of two from populations of different variances would remain unanswered. We have read the papers by James [(1951), *Biometrika*, 38, (3) & (4), p.324] and Welch [*Ibid*, p.330] from which it appears that their modified χ^2 and F tests are not likely to be accurate for small degrees of freedom.

In respect of your suggestion that our company might care to finance the computation of \bar{d} tables from (1,1) to (7,7) we would certainly like to consider this, though at this stage we would prefer not to commit ourselves for a number of reasons not least of which is that the company is currently investigating its computation requirements on the accounting and business side with a view to getting a suitable electronic computer. This computer will probably be available for a certain amount of scientific work when the needs of the accounting work have settled into a satisfactory routine, though allowing for the time required to formulate the computers requirements, to get the machine constructed and to accommodate the accounting work on a routine basis, we would anticipate a delay of two to three years before scientific work can be undertaken.

In the meantime our thoughts on this matter (including the tentative possibility that the company might consider computation elsewhere) would be assisted if you could tell us (or put us in touch with the appropriate person in Yates Department) exactly what is entailed. As you will appreciate we cannot authorise the work ourselves, but armed with the necessary details we can present the case for the company's consideration.

Yours sincerely,


J.P.R. TOOTILL


A.T. DUNN