



| | Degrees of freedom | Sum of squares |
|-----------------------|--------------------|---|
| | $n - 1$ | $SS_{Total} = \text{td}(R_1^2 + \dots + R_d^2) - K$ |
| | $n - 1$ | $SS_{Total} = \text{td}(C_1^2 + \dots + C_d^2) - K$ |
| Completely randomised | $(nd - 1)(n - 1)$ | $SS_{Total} = SS_{Total} - SS_{Prep}$ |
| Randomised block | $nd(n - 1)$ | $SS_{Total} = SS_{Total} - SS_{Prep} - SS_{Block}$ |
| Latin square | $(nd - 1)(n - 1)$ | $SS_{Total} = SS_{Total} - SS_{Prep} - SS_{Block} - SS_{Row}$ |
| | $nbd + n - 1$ | $SS_{Total} = \sum_i (n - 1)^2$ |

formulae are only applicable if $n = nd$
 randomised designs
 one design

POTENCY AND CONFIDENCE

of the preparations can be

$$V_1 = \frac{6}{nd(2d+1)} \left(\frac{1}{d+1} + \frac{3}{h(d-1)} \right)$$
 (3.3.5.1-1)

$$V_2 = \frac{3(d+1)}{3(d-1) + h(d-1)}$$
 (3.3.5.1-2)

and similarly for each of the other
 from:

the test

$$R_1^* = \frac{3d(d+1)}{2d+1}$$
 (3.3.5.1-3)

by A_1 , the assumed potency of
 or to find the estimated potency
 cent doses was not identical for
 preparation, the potency has to be
 at, unlike the parallel-line analysis,
 fitted.

R_1^* is calculated from:

$$R_1^* = \frac{K^* + 1}{K^* - 2C^* R_1^*}$$
 (3.3.5.1-4)

and $K^* = (C^* - 1) V_1$
 variance and covariance of the
 of K^* . They can be obtained from:

$$V_1 = \frac{3}{2(2d+1) + nd(d-1)}$$
 (3.3.5.1-5)

$$C^* = \frac{1}{nd(d-1)}$$
 (3.3.5.1-6)

multiplied by A_1 , and if necessary by
 as for the $(hd - 1)$ design, with the



3.4. EXTENDED SIGMOID DOSE-RESPONSE CURVES

The logarithms of the
 concentration on the right. The responses are indicated on
 the vertical axis. The individual responses to each treatment
 are indicated with black dots. The 2 curves are the calculated
 (in)dose-response relationship for the standard and the test
 preparation.
 The general logistic function
 can be characterised by 4 parameters: The upper asymptote
 the lower asymptote, the slope factor (β), and the horizontal
 location (γ). This is a
 four-parameter model. The
 (in)dose-response curve is:

$$u = \delta + \frac{\alpha - \delta}{1 + e^{-\beta(x - \gamma)}}$$

For a valid assay it is necessary that the curves of the standard
 and the test preparations have the same slope factor, and the
 same maximum and minimum response level at the extremities.
 Only the horizontal location (γ) of the curves may be different.
 The horizontal distance between the curves is related to the
 "true" potency of the unknown. If the assay is used routinely,
 it may be sufficient to test the condition of equal upper and
 lower response levels when the assay is developed, and then to
 retest this condition directly only at suitable intervals when
 there are changes in materials or assay conditions.
 The maximum likelihood estimates of the parameters and their
 confidence intervals can be obtained with suitable computer
 programs. These computer programs may include some
 statistical tests reflecting validity. For example, if the maximum
 likelihood estimation shows significant deviations from the fitted
 model under the assumed conditions of equal upper and lower
 asymptotes and slopes, then one or all of these conditions may
 not be satisfied.



User Manual Version 6.0

The CombiStats User Manual

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