Deacon's Challenge

No 152 - Answer

As part of the evaluation of a new serum creatinine assay a quality control sample is analysed in duplicate on twenty consecutive days with the following results (µmol creatinine/L serum):

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1st result	100	98	101	99	104	96	98	100	101	99	103	101	99	94	100	98	95	100	100	101
2nd result	102	96	104	101	101	94	101	104	96	97	104	99	102	97	101	96	94	101	99	103

Calculate the between-day imprecision.

The variance (s^2) of n values for x with mean m is given by the formula $\Sigma(x - m)^2/(n-1)$. However, if the above formula was applied to all 40 results using the *overall* mean then the result would be the *total* analytical variance which is made up of two components – the *within-day* and *between-day* variance. These two components can be separated if the appropriate mean values are used in the calculation (a classical two way analysis of variance).

Unlike question 151, where variation around daily means is used to eliminate between-day variation, the variation of daily means around the overall mean is used to eliminate within-day variation.

First calculate the overall mean by adding all 40 results together then dividing by 40:

$$\text{Overall mean} = \frac{100 + 102 + 98 + 96 \ldots\ldots\ldots + 103}{40} = \frac{3979}{40} = 99.5 \text{ µmol/L (to 3 sig figs)}$$

Next calculate the mean of each pair of duplicates. For day 1 the mean is (100 + 102)/2 = 101, for day 2 it is (98 + 96)/2 = 97 etc.

The between-day variance is then calculated from the standard formula using the overall mean and the individual daily means as values for each duplicate result i.e. for day 1 the results would be 101 and 101, for day 2 they would be 97 and 97 etc. Each daily mean is used twice. Since the daily means are used each day's data has only one degree of freedom so that the total number of degrees of freedom is the number of days minus one (because the overall mean is used in the calculation).

$$s^2_{\text{Between-day}} = \frac{(101 - 99.5)^2 + (101 - 99.5)^2 + (98 - 99.5)^2 + (98 - 99.5)^2 \ldots\ldots + (102 - 99.5)^2 + (102 - 99.5)^2}{20 - 1}$$

$$= \frac{2\{(101 - 99.5)^2 + (98 - 99.5)^2 \ldots\ldots + (102 - 99.5)^2\}}{19}$$

$$= \frac{258.475}{19} = \mathbf{13.6\ (\mu mol/L)^2} \quad \text{(to 3 sig figs)}$$

The standard deviation is the square root of variance:

$$s^2_{\text{Between-day}} = \sqrt{13.6} = \mathbf{3.7\ \mu mol/L} \quad \text{(to 2 sig figs)}$$

and the coefficient of variation is the standard deviation expressed as a percentage of the overall mean:

$$cv_{\text{Between-day}} = \frac{3.7 \times 100}{99.5} = \mathbf{3.7\%}$$

Question 153

An adult male (body weight 70 kg) is receiving an intravenous infusion of aminophylline (the diamine salt of theophylline) at a rate of 60 mL/h. The intravenous solution was prepared by adding two ampoules of aminophylline to 500 mL of 0.9% sodium chloride. Each ampoule contains 250 mg aminophylline in a volume of 10 mL. How long will it take to achieve a plasma theophylline concentration of 10 mg/L? Assume theophylline has a volume of distribution, V_d, of 0.5 L/kg and its elimination follows first-order kinetics with a half-life of 6 h. Aminophylline is 80% theophylline by weight.