Deacon's Challenge
No 134 - Answer

Replicate analyses are often employed in an attempt to overcome poor assay imprecision.

a) What is the imprecision (expressed as a percentage of the imprecision for a single measurement) for a mean calculated from duplicate measurements?

b) Calculate the minimum number of replicate measurements required to produce a mean value with an imprecision of one half of the value which would be obtained for single measurements.

---

a) Each individual measurement (value of x) has a standard deviation (s value) equal to the within-run analytical s of the assay.

If the assay is performed in duplicate then two results (x_1 and x_2) are obtained, each with their own standard deviations (s_1 and s_2).

The mean of the two duplicate measurements $= \dfrac{(x_1 + x_2)}{2}$

When two values are added their combined s is the square root of the sum of the squares of the individual s values (see Question 125). Furthermore when a value is divided by a constant then the s value must also be divided by the same constant. Therefore the s value for the mean (s_m) calculated from two values is given by:

$$s_m = \frac{\sqrt{(s_1^2 + s_2^2)}}{2}$$

However, $s_1 = s_2$ which is the within-run analytical imprecision of the assay (s). Therefore the above expression can be simplified:

$$s_m = \frac{\sqrt{(s^2 + s^2)}}{2} = \frac{\sqrt{2s^2}}{2} = \frac{\sqrt{2} \times s}{2} = \frac{s}{\sqrt{2}} = \frac{s}{1.414}$$

To obtain s_m as a percentage of s simply substitute $s = 100$:

$$s_m = \frac{100}{1.414} = \mathbf{71\%} \quad \text{(2 sig figs)}$$

Therefore performing the assay in duplicate has only reduced the imprecision to 71% of that obtained with single measurements.

b) An expression can be derived in a similar way to cover the generalised case where n replicate measurements are made with values x_1, x_2........ x_n which have standard deviations s_1, s_2...... s_n:

$$\text{Mean } (m) = \frac{(x_1 + x_2 + ...x_n)}{n}$$

$$s_m = \frac{\sqrt{(s_1^2 + s_2^2 + ...s_n^2)}}{n} = \frac{\sqrt{ns^2}}{n} = \frac{\sqrt{n} \times s}{n} = \frac{s}{\sqrt{n}}$$

s_m is also referred to as the standard error of the mean (SE_m) and its formula is well worth committing to memory:

$$SE_m = \frac{s}{\sqrt{n}}$$

To find a value for n which reduces the imprecision by a half, substitute $s = 1$ and $SE_m = 0.5$ then solve for n:

$$0.5 = \frac{1}{\sqrt{n}}$$

$$\sqrt{n} = \frac{1}{0.5} = 2$$

$$n = 2^2 = 4$$

Therefore to reduce the imprecision obtained for single measurements by a half at least four replicate analyses are required.

Question 135

A teenage male presents to A&E after a session of "binge drinking" with a plasma sodium concentration of 125 mmol/L and a body weight of 72 Kg. As no other cause can be found for his hyponatremia a diagnosis of "beer potomania" is made. Stating any assumptions you make, estimate the fluid excess in litres.