**APPENDIX E:**

## Example Calculation of $PD_{20}$

The equations of Sterk et al[1], Juniper et al[2] and Cockcroft et al[3] to calculate the interpolated $PC_{20}$ can be adapted to the calculation of $PD_{20}$;

where

$D_1$ = the dose at the second to last methacholine step (ie, step preceding the final step)

$D_2$ = the dose at the final methacholine step (ie, step resulting in a 20% or greater fall in $FEV_1$)

$R_1$ = % fall in $FEV_1$ after $D_1$

$R_2$ = % fall in $FEV_1$ after $D_2$

$$PD_{20} = \text{antilog}\ \left[ \text{Log } D_1 + \frac{[(\log D_2 - \log D_1)(20 - R_1)]}{(R_2 - R_1)} \right]$$

The lung delivered dose is based on the nebulizer output characteristics and the duration of inhalation at each concentration.

Dose = rate of output X respirable fraction X duration of inhalation X Ti/Ttot

Where respirable fraction is that of the aerosol carried in particles less than 5 μm and Ti/Tot is the respiratory duty cycle assumed to be 0.4[4]

Exponential models are better than linear models for interpolating between concentrations or doses[5].

Example of calculations:

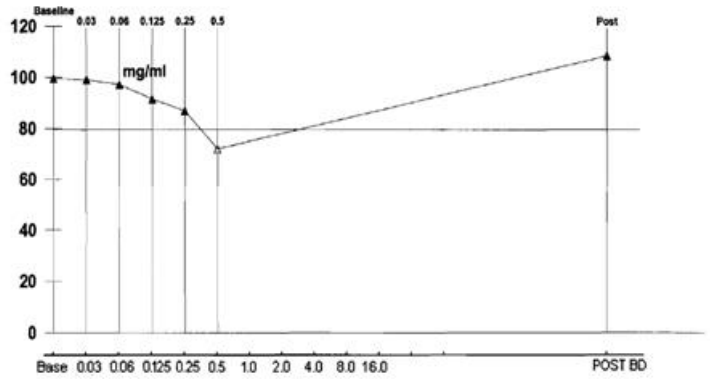
In the test data shown graphically below, the $FEV_1$ fell 13% ($R_1$) at a concentration step of 0.25 mg/mL and 28% ($R_2$) at a concentration of 0.5 mg/mL

If the dosing protocol used is known to deliver 16 μg at a concentration of 0.25 mg/mL and 32 μg at 0.5 mg/mL, then $D_1$=16 and $D_2$=32

$$PD_{20} = \text{antilog}\ \left[\log 16 + \frac{[(\log 32 - \log 16)(20 - 13)]}{(28 - 13)}\right] = 22\ \mu g$$

**Methacholine Challenge Report**

| | Ref | Pre | Level 1 | Level 2 | Level 3 | Level 4 | Level 5 | Level 6 | Level 7 | Level 8 | Level 9 | Level 10 | Level 11 | Post |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Conc | | | 0.03 | 0.06 | 0.125 | 0.25 | 0.5 | | | | | | | |
| FEV1 | 2.16 | 1.91 | 1.77 | 1.73 | 1.63 | 1.55 | 1.28 | | | | | | | 1.93 |
| % Chg | | 8 | -0 | -2 | -8 | -13 | -28 | | | | | | | 9 |




[1] Sterk PJ, Fabbri LM, Quanjer PH, *et al.* Airway responsiveness. Standardized challenge testing with pharmacological, physical and sensitizing stimuli in adults. *Eur Respir J* 1993; 6: Suppl. 16, 53–83.

[2] Juniper EF, Cockcroft DW, Hargreaves FE, *et al.* Histamine and Methacholine Inhalation Tests: Tidal Breathing Methods. Laboratory Procedure and Standardization. Lund, Astra Draco, 1994.

[3] Cockcroft DW, Murdock KY, Mink JJ. Determination of histamine PC20: comparison of linear and logarithmic interpolation. *Chest* 1983; 84: 505–506.

[4] Coates AL, Leung K, Dell SD. Developing alternative delivery systems for methacholine challenge tests. *J Aerosol Med Pulmon Drug Deliv* 2014; 27: 66–70.

[5] Verlato G, Cerveri A, Villani A, *et al.* Evaluation of methacholine dose-response curves by linear and exponential mathematical models: goodness-of-fit and validity of extrapolation. *Eur Respir J* 1996; 9: 506–511.