



8 February, 2003

Dockets Management Branch (HFA-305),  
Food and Drug Administration,  
5630 Fishers Lane, rm. 1061,  
Rockville, MD 20852.

Dear Sir or Madam,

In your draft guidance, named "Guidance for Industry and Reviewers Estimating the Safe Starting Dose in Clinical Trials for Therapeutics in Adult Healthy Volunteers", the first part of Appendix C ought to be simplified to the following:

Power equation:  $(mg) = aW^b$ .

Given the weights of animal and human, and animal dose in mg/kg, solve for HED in mg/kg:

Let  $H$  = mg/kg dose in humans,  $A$  = mg/kg dose in animals,  $W_h$  = weight of human, and  $W_a$  = weight of animal.

For animal  $(mg) = aW_a^b$ , replace mg  $A \times W_a = aW_a^b$ . Likewise for human  $H \times W_h = aW_h^b$ .  
Divide the equation for human by that for animal to get  $(H/A) \times (W_h/W_a) = (W_h/W_a)^b$ .  
Solve for  $H$ :  $H = A \times (W_a/W_h)^{(1-b)}$ .

The current version makes an unnecessary log-transformation and getting the final solution by an often algebraically erroneous step, i.e., equating a constant.

Sincerely,

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