Reviewer’s report

Title: Human Physiologically Based Pharmacokinetic Model for Propofol: I) Description and validation of model.

Version: 1 Date: 1 July 2004

Reviewer: David Drover

Reviewer’s report:

General

The authors have presented their data and goals in a logical fashion and the manuscript is further to similar work he has published. This current work uses his modeling technique to help better understand the distribution and elimination of propofol. This article better helps to validate the utility of PKQuest with comparison of results previously determined by NONMEM. Many of my concerns have been addressed already by the author in the Discussion section of the manuscript. The reader will have to decide the significance of the drawbacks and assumptions that come with the use of PKQuest.

The authors note that they require only 2 parameters for fitting the data while NONMEM required 6 parameters for the same data set. This is not accurate; in the fitting process with PKQuest many (physiologic) parameters are present but have been "fixed". In other words, the author have taken best estimate of parameters from the literature for physiologic numbers and incorporated them in the model. They have not been called parameters only because the PKQuest program has not been allowed to optimize them to best fit the data. This requires assumptions about constancy of these parameters between subjects and between solutes.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

None

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1) The author notes for Figure 3 that 60% of the bolus is sequestered but it is not clear from the manuscript how this number was derived or optimized.
2) In table IV, the authors present data based on age. It is unclear if the values are significantly different by age. If not, they could be incorporated into a single value or else the significance should be established.

Discretionary Revisions (which the author can choose to ignore)

The authors present some result type discussion in the second last paragraph of the methods section; this may be best moved to the results section.

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No
Declaration of competing interests:

None