Reviewer's report

Title: Clinical Decision Support of Therapeutic Drug Monitoring of Phenytoin: Measured Versus Adjusted Phenytoin Plasma Concentrations

Version: 1 Date: 30 September 2011

Reviewer: John H Kalbfleisch

Reviewer's report:

These comments follow a request for statistical review.

Major Compulsory Revisions – none.

Minor Essential Revisions.

(1) Figure 1A and 1C. These are key presentations.
   a) Statistically compare the fitted-regression (dashed-line) with the line of identity (solid line). The result should support the authors conclusion (favor 1C over 1A).
   If added to the current manuscript, the Methods Section should indicate the procedure.
   b) Many of the data points are concentrated in the lower left section of the grid. If both scales are transformed to 'log' scales, the resulting plot should have more clarity for lower values and the correlation should be very similar.

(2) Figure 1B and 1D can remain, be eliminated or replaced by plots of all measurements beyond the first (which is 1A 1C).

Discretionary Revisions

(3) Figures 3 and 4. The slope of the fitted lines can be compared against “0" (which is the comparison of the fitted line versus the parallel line).

(4) In ‘Methods‘ the authors should indicate whether statistical analyses linked with Figure 5 were four separate procedures, or all four independent variate conditions tested for influence on the outcome (adj-freePHT) in a single analysis (similar to multiple regression)?

(5) I wondered if the authors considered using their data to determine a (non-linear) regression model (Y=PHTfree , X1 = PHTtotal, X2 = age(y), X3 = albumin and possible interaction terms)? Potentially, this determines another
adjustment formula.

(6) Can the categories in Figure 2 be linked with data points in Figure 1? (maybe ‘color’ can help, but I am not sure if readers would find this useful).

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests. John H. Kalbfleisch, Ph.D.