Reply

To the Editor:

In my review of Fig. 1, there appears to be a small by systematic bias of the predicted erythromycin breath results over 1 hour (i.e., ERMBT 1-hour values) during conditions of extreme inhibition (i.e., at very low ERMBT 20-minute measured values). Thus, equation 4 will improve the interpretation of the breath test. However, upon further reflection, is there really a need for such a conversion? It appears that calculation of ERMBT has changed over the years from an AUC determination over 135 minutes,[1] to one over 60 minutes,[2-4] to a single breath test at 20 minutes.[5,6] With a half-life of 1 to 2 hours, the ERMBT (in any of these forms) does not represent the clearance of erythromycin. Instead, the significance of ERMBT determination lies with its ability to measure hepatic CYP3A activity. Because a good correlation is found between 20-minute ERMBT values and 1-hour ERMBT values, why not just simply report the 20-minute ERMBT values and avoid the conversion altogether? I believe that this would make more sense, be an easier approach, and would still allow for treatment comparisons within a subject by representing the data as percentage of control. For treatment comparisons between subjects, both methods (i.e., 20-minute ERMBT values or conversion to 1-hour ERMBT values) would have the same advantages and disadvantages.

With respect to the article by Cheng et al.,[7] upon reanalysis using equation 4, the results were essentially the same. For example, the mean ± SD values of parameter estimates for inhibition of ERMBT by delavirdine plasma concentrations were (compare with Table VI in Cheng et al.[7]): predose ERMBT of 2.85% ± 1.16% ^{14}C exhaled/hr (3.1-fold range), I_{max} of 84.5% ± 5.2% inhibition (1.3-fold range), and IC_{50} of 0.933 ±0.854 μmol/L (49.5-fold range). Updated figures and tables are available on request. It should be appreciated that all of our original conclusions remain intact.

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References

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13/8/90463