

1048-92-83

Cammeey Cole Manning* (ManningC@meredith.edu), Mathematics and Computer Science Department, 3800 Hillsborough Street, Raleigh, NC 27607. *Using Toxicokinetic Data to Develop Model Predictions for 4-Methylimidazole Chronic Exposure*. Preliminary report.

4-methylimidazole (4MI) is a light, yellow crystalline solid that has been under investigation by the National Toxicology Program. Exposure results from the use of 4MI as a starting material in the manufacture of various products including pharmaceuticals, dyes and pigments, and rubber; it is also a by-product in various food products including caramel and soy sauce. A physiologically based pharmacokinetic model representing the uptake, distribution, and metabolism of 4MI in rats and mice was developed to describe the processes involved in 4MI toxicokinetics. Model development was based on single-dose toxicokinetic data for male and female mice and rats. Most of the model parameters were obtained from estimates in the literature. However, the model had six parameters that did not have literature estimates. These parameters were estimated by least squares techniques. The model was fit to short timespan (less than 30 hours) intravenous injection and gavage toxicokinetic data. The fit model was used to make predictions of plasma concentrations of 4MI in feed dose study using a time scale of months. (Received January 26, 2009)