Reviewer’s report

Title: A mechanism-based pharmacokinetic model of fenofibrate for explaining increased drug absorption after food consumption

Version: 0 Date: 29 Sep 2017

Reviewer: Kathleen Job

Reviewer's report:

Overall Comments
This manuscript describes a mechanistic gastro-intestinal absorption model evaluating food effects on fenofibrate absorption utilizing clinical data from 24 participants in a three-way crossover study. I applaud the authors for their work in modeling fenofibrate pharmacokinetics, as accounting for food effects is an important consideration for this drug. There are, however, several improvements that need to be made to the manuscript. Generally, clarification figure adjustment in regards to the figures (specifically figure 1), description of the study cohort in the text, and restructuring of the discussion and results section will significantly improve this manuscript. Additionally, the manuscript would benefit review by a technical writer. Please see below for additional comments.

METHODS: Data collection
Additional information is needed regarding the three-way crossover study, including description of the sampling time points. When was this study run? Please provide general demographic data information in words in addition to by supplemental table (e.g. age, weight, ethnicity) either here or in the results.

PK Modeling
Please revise Figure 1 to clarify where interactions are occurring and to include Ebile. Please also define all terms (e.g. T, V, MPAST, etc).

RESULTS/DISCUSSION:
A significant portion of the discussion describes what was done rather than the significance of the models, potential future improvements/applications, etc. These portions should be included in the results or methods sections and additional comments made in the discussion.

TABLES/FIGURES:
Table 5: I suggest including the numerical parameters in addition to the percent changes.

Table 3: Parameters are listed differently than in other figures and text.

Figure 1: Please extend the description in the figure caption and make additions to the figure as described above.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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