Reviewer's report

Title: Identification of cryptolepine metabolites in rat and human hepatocytes and metabolism and pharmacokinetics of cryptolepine in Sprague Dawley rats

Version: 1 Date: 08 May 2017

Reviewer: Melanie Felmlee

Reviewer's report:

1) The sex of the cryopreserved hepatocytes from humans and rats should be listed. The authors should also indicate if these were pooled or single donor samples.

2) Page 4 line 35: List the final concentration of DMSO in metabolite profiling experiments.

3) Page 5, line 28: Harlan Laboratories is now Envigo.

4) Page 5: Intravenous drug administration through which vein (jugular, tail vein etc). Also which vein for blood sampling.

5) Please clarify how bioavailability was calculated for animals 3 and 4. There was no iv data from these animals to make this calculation. Bioavailability could be calculated from the pooled data from both animals for each administration route.

6) The X-axis should be truncated for Figures 4 and 5. This would allow the reader to better evaluate the profiles. It also appears that the compound undergoes biliary recycling based on the profiles, but this was not mentioned in the results or discussion.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

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.

Yes

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.

Not relevant to this manuscript

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

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