To whom it may concern,

Thank you for the opportunity to comment on the OSU Abbreviated Class Update on Newer Drugs for Insomnia. Overall, we found the methodology to be sound, and the conclusions fair. Our comments consist, for the most part, of pointing out minor transcription errors.

Page 1:
In the conclusions regarding tasimelteon and suvorexant (final two bullet points) please include the dosages and treatment times being described.

Page 8:
Again, please state the time point for which outcomes are reported. This summary appears to be using 12-month outcomes. These were not ranked as the key efficacy outcomes in the study. Subjective Total Sleep Time (sTST) and subjective Time to Sleep Onset (sTSO) during the first month (using weekly averages of Weeks 1, 2, 3, and 4) were secondary objectives; all other efficacy endpoints were exploratory

An extra Zero was added to one of the p values "p=0.000009"

The second time a p value of 0.000009 is reported, the reported value was actually p<0.00001.

In several places, study NCT01097629 is reported as "NCT101097629"

Please revise accordingly.

Page 9:
The Drug Enforcement Agency has completed its evaluation of suvorexant. It is considered a Schedule 4 agent. Please revise.

Page 10:
Again, efficacy results are reported only for Month 12. If this is the time point of most interest to the P&T Committee, then it should be reported, obviously, but please also acknowledge that other time points are available.

Under Withdrawals due to ADE, P should be 22/259, not 23/259.

Although the power calculations were not described in the publication of study NCT01021813, both Good Clinical Practice and regulatory requirements dictate that they be performed. Based upon variability and missing data estimates obtained from four prior studies conducted on another compound, marginal power estimates for detecting various differences between treatments with respect to sTSTm and sTSOm (averaged over Weeks 1, 2, 3 and 4) were obtained based upon LDA ANCOVA methodology using a 2-sided, 5%-level test, and are summarized in Table 9-3 below.

Table 9-3

Power Estimates for Detecting Various Differences
Between Treatments in sTSTm and sTSOm During 1 Month of Treatment

Variable	Delta (Improvement)	Power†
sTSTm	20	>99%
	15	95%
	12	82%

sTSOm	12 10 8	>99% 97% 87%
† Based upon N=500 on MK-4305 and N=250 on Placebo; 2-sided, 5%-level test; estimates of covariance matrix and missing data rates based upon prior in-house studies of MK-0928 (Protocols 003, 014, 10403 and 005)		

Page 11:
Under Sleep Efficiency for Night 1, p should equal 0.002 for 10mg. For the remaining dosages, p<0.001. For Night 28, p=0.003 for 10mg and <0.001 for the remaining dosages.

Under Safety Results, the table states “No ADE significantly higher than placebo. “ Somnolence was significantly greater than placebo for suvorexant 20, 40 and 80mg.

Under Patient Population, polysomnography was run on nights 1 and 7 of the placebo run-in period. As written, the text implies that polysomnography was conducted during the treatment period. Please revise.

We believe that attrition in NCT00792298 was low, rather than moderate as stated in the table. Analysis was performed on the full analysis set as stated in the publication, not the per protocol set as stated in the table. The publication (Herring et al., 2012) states “The population for the efficacy analyses was the full analysis set, which included all randomized patients who received at least 1 dose of study medication and had a baseline and at least1 postrandomization measurement.” This amounted to 249 patients in the full analysis set of the 254 who were randomized. Thus, only 2% of randomized patients were excluded. We request that the study quality assessment be revised accordingly.

Thank you again for providing this comment opportunity

Sincerely,

Richard Chapell
For the Merck Insomnia Comment Team

Richard Chapell
Assoc. Director: HTA/CER
CORE US Outcomes Research
Merck and Co Inc.