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APPLICATION NUMBER:

125274Orig1s000

<u>STATISTICAL REVIEW(S)</u>

MEMORANDUM

DATE: August 28, 2008

FROM: Kun Jin, Ph.D.
      Statistical Team Leader, DBI

TO: File, BLA 125274

SUBJECT: Maintenance Effect at Week 8 an 12 in Study 51

I mostly concur with Dr. Siddiqui's conclusions, other than the one concerning the maintenance effect at Week 12 in Study 51. There are dropouts during the 12 week trial, and the significant p-value for the primary endpoints at Week 12 is based on the LOCF method to input missing data. Carrying on the earlier efficacy data to later weeks for the maintenance claim is inappropriate and potentially misleading. A difficult and long-standing problem in insomnia trials is how to access the long term maintenance effect when there are dropouts. At the present, we do not have a satisfactory solution to this problem, so we generally like the sponsor to do their best to keep patients in the trials and we would like to see significant OC results for the primary endpoint. The dropout problem is similar to those in insomnia trials. In Study 51, the corresponding OC p-value for the OC at Week 12 is 0.314. From this, I do not see convincing evidence to conclude that the efficacy is maintained through Week 12.