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***APPLICATION NUMBER:***

**20-659/S-13**

**20-680/S-11**

**STATISTICAL REVIEW(S)**

# DRAFT

## MEMORANDUM OF CONSULTATION

DATE:

BETWEEN: Kim Struble, Pharm.D.  
Division of Anti-Viral Drug Products, HFD-530

AND: Thomas Hammerstrom, Ph.D.  
Division of Biometrics, HFD-715

SUBJECT: RE-ANALYSIS OF NORVIR FINAL SUBMISSION FOR NDA-20-659  
and 20-680

I have verified the analysis of the final data from NDA-20-659 and 20-680 for Norvir. I have computed Kaplan-Meier curves and log-rank tests to compare progression free survival rates between the norvir and placebo arms in trial 247. I have also plotted the trajectory over time of HIV RNA and CD4 levels in both arms of trial 247 and in the Norvir, ZDV, and Norvir + ZDV arms of trial 245, together with 95% confidence intervals at each bimonthly period.

I concur with the findings in the applicant's submission with respect to both the statistical significance and the estimated magnitude of the treatment effects in these trials. The Norvir arm was superior to the placebo arm on progression, CD4 count, and HIV RNA levels in trial 247. The Norvir+ZDV arm was superior to the ZDV arm on CD4 count and HIV RNA levels in trial 245. The plots and tables in the applicant's submission are acceptable for use in the label.

Thomas Hammerstrom, Ph.D.  
Mathematical Statistician

Concur: Dr. Flyer

cc:  
HFD-530  
HFD-530/Dr. Jolson  
HFD-530/Dr. Birnkrant  
HFD-530/Dr. Struble  
HFD-725/Dr. Flyer  
HFD-725/Dr. Hammerstrom