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May 20, 2002

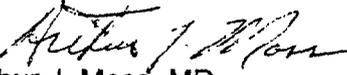
Joseph Kanapka, Ph.D.  
C. B. Fleet Company, Inc.  
P.O. Box 11349  
4615 Murray Place  
Lynchburg, VA 24506-1349

Dear Dr. Kanapka,

I have received the two volumes of material regarding protocol F00.20 on Phospho-soda Oral Solution. I reviewed the quantitative tabular data regarding the various ECG measurements including QTc. My interpretation of the findings are exactly the same as I previously reported to you in my letter dated April 6, 2002. That is, the mean QTc interval transiently increased by an average of 7.1msec and 11.3msec after the first and second dose of phospho-soda solution, respectively, with the overall mean QTc value remaining within normal limits. Twenty-nine percent of the study subjects had a borderline-prolonged QTc interval, and 8% had a slightly more prolonged QTc interval. The change in QTc values were inversely related to the change in serum potassium concentration, but the association was weak and not significant. There were no QTc outliers above 500msec., and thus no real concern. It is my opinion that there is a negligible risk for arrhythmias when sodium phosphate is used as a bowel cleansing agent.

The ECG equipment utilized in recording the electrocardiograms involved Marquette MAC-12 and MAC-PC recorders, and these are approved and acceptable recorders. The QT and RR intervals were measured manually by Dr. Lasseter and associates, with the QT corrected for heart rate (QTc) by the Bazett formula. The FDA may be concerned that only one representative complex was measured in each recorded ECG at baseline and at each follow-up recording after administration of Phospho-soda Oral Solution. The FDA frequently requires the measurement of several QRS-T complexes per ECG lead/tracing, and several baseline measurements at different times before starting therapy. Also, it may be important to know how the QT and RR measurements were checked. What is the degree of variability and reproducibility in the QT and RR measurements, and are a portion of the QT and RR measurements randomly checked by a second reader? You should obtain this information from Dr. Lasseter in case the FDA asks.

Sincerely,

  
Arthur J. Moss, MD  
Professor of Medicine (Cardiology)  
Director, Heart Research Follow-up Program