

## RECORD OF A TELE-CONFERENCE

**DATE:** Oct. 12, 1999/3:30 pm

**PARTICIPANTS:** Dr. DeLap, Ms. Walling/FDA and  
Dr. Walter Kernan/Yale U. (203-688-2984)

**SUBJECT:** Safety study of PPA for CHPA (NDMA)

Dr. Kernan called to report that the enrollment and the analysis of the study was complete and they planned to present the results to their Scientific Advisory Group on Sunday, Oct. 17. They intend to present it to the sponsors (CHPA) on Tuesday and they had hoped to present it to the FDA at the same time. He indicated that Lorna Tottman (CHPA) suggested that this be done in an open public meeting to be held on Tuesday, Oct. 19., which she would take the lead in setting up.

Dr. DeLap explained that it would take more than a few days to set up an open public meeting, including getting the notice into the Federal Register and inviting the appropriate people (including Dr. Temple as requested). He stated that if there was a significant safety issue it was very important that the agency know about it ASAP. He suggested that Dr. Kernan's group prepare a letter addressed to Dr. Ganley and copied to the CHPA, addressing the nature of the findings, specifically focusing on the safety issues that are persuasive and how (statistically) persuasive,, who is at risk and how bad the risk is, for example. He told Dr. Kernan that there was no predetermined format for such a report, but that he could use the Medwatch form if he wished. He indicated that the letter with the results would most likely have to be published as part of the meeting announcement and that the audience would include the public, the trade press, the members of CHPA, and FDA. Dr. DeLap said he would talk to Dr. Ganley and it would most likely a matter of several weeks or more until we had the meeting.

Dr. Kernan thanked us and said he would share the results with CHPA on Tuesday and agreed to send a letter copied to CHPA. He said to call his secretary Pam Doll at 203-785-4147 if we needed any information or to reach him.

On October 19, 1999 at 12:00, Drs. DeLap and Katz and Ms. Walling returned Dr. Walter Kernan's call (203-397-9481 h).

He had called to report that the Scientific Advisory Group recommend that additional analyses be done prior to sending the report of the findings of the study of PPA and the risk of hemorrhagic stroke.

He indicated that a letter was prepared with the findings but that there would be a delay of perhaps 2-3 days (Thursday of this week) in sending it. On the advice of their advisory group, one additional analysis would be done.

The sponsor (CHPA) had been notified. The Yale group would meet with the sponsor to discuss the results of the study as soon as was convenient.

A summary of the results thus far is as follows:

For the three coprimary endpoints-

1- any use 3 days prior to stroke (males and females)- the adjusted odds ratio (1.52) was not significant- 95% CI lower bound=0.94 and the p value= 0.078

2- use for cough/cold or appetite suppressant 3 days prior to stroke- male and female cough/cold adj. odds ratio= 1.23, CI lower bound = 0.75, and p= 0.246 AND for females as an appetite suppressant, the adj. odds ratio= 14.17, CI lower bound = 2.13 and the p= 0.011 (statistically sig)

3- females- first use stroke first day- (first use is defined as no use in prior 2 weeks and first dose is on index date or day before)- the adj. odds ratio= 3.53, CI lower bound = 1.19 and p= 0.028. They looked at males too but there were only 2. (statistically sig.)

The factors for adjustment were race, hypertension, cigarette smoking and cocaine use.

These analyses were drawn from 706 cases (which included 27 individuals exposed to PPA and 1383 matched controls (including 32 exposed to PPA).

The advisory group asked for a reanalysis based on using different definitions (consistent) of control groups (non-exposure was defined slightly differently in the three groups).

Dr. Kernan doesn't expect the results to change but he will send the letter with all of the information summarized when the reanalysis is done.

Dr. DeLap asked that he summarize in the letter who was studied, what were the findings, what was the statistical significance and what was the clinical significance. He also asked how the people that fell between more than 3 days post and less than 2 week exposure would be evaluated in the study, if they were counted neither as "exposed" or "not exposed".