

From: James P McCafferty/DEV/PHRD/SB\_PLC  
To: SallyL@stimedinfo.com  
Subject: RE: Paroxetine adolescent depression study is now finalized  
Date: 07/19/1999 15:03:51 (GMT-05:00)

Sally,

I reviewed the latest version of the manuscript and have some comments. Two are minor but one is of some concern.

Minor:

1) The statement that most subjects had a "family history of depression" is based on data in Table 1 that shows that 90% of the patients had a positive family history of "major depression". However, you may recall, that these data were collected using an instrument that asked the parents whether any first degree relative of the patient had shown "signs or symptoms of depression". This is not the same as a diagnosis of major depression. I suggest we remove the term "major" from the table.

2) In the discussion we express the sentiment that future clinical trials with TCAs are unlikely to be conducted because of 1) expired patents and 2) cardiovascular liabilities. Using expired patents as a reason not to conduct a trial seems too commercial, although there is some truth to this. Perhaps we could describe that there is less interest in TCA trials as these are "older therapies", rather than use the patent expiry argument. Or more important than the patent situation, is the consistent finding in clinical trials of little or no benefit with TCAs, once again supported by the results of the present study.

Major:

Safety. It seems incongruous that we state that paroxetine is safe yet report so many SAEs. I know the investigators have not raised an issue, but I fear that the editors will. I am still not sure how to describe these events. I will again review all the SAEs to make myself feel comfortable about what we report in print.