**U.S. REGULATORY AFFAIRS** **FDA TELEPHONE CONVERSATION**

December 8, 1999

**Paxil (paroxetine hydrochloride) Tablets** **NDA 20-031**

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| Date & Time: | December 8, 1999: 3:00 P.M. |
| Conversation between: | Michael Seika and Thomas Kline |
| Title/Division: | Medical Reviewer, Division of Neuropharm Products |
| Phone Number: | (301) 594-5566 |
| Topic: | FDA Request for Deaths and Suicide Rates |

**Executive Summary:**

Dr. Seika requested clarification of several points addressed in SB's July 13th submission of death and suicide information involving paroxetine. Specifically, he inquired, and I confirmed, that the previously submitted data were derived from "depression" studies. He clarified several other issues, such as the collection of data from cross-over studies, and he's aware that SB will soon submit the updated information.

**Background:**

Per FDA's request of April 2, 1999, SB submitted on July 13, 1999 data pertaining to the death and suicide rate reported in the paroxetine safety database.

**Summary of Conversation:**

Mr. Seika called to clarify essentially two points relating to our July 13th submission. First, he inquired if the reported studies were restricted to the indication of "depression", which I confirmed. Secondly, he asked for clarification in the methods of classification used in our analysis, specifically if we included all patients within a 30 day window of last dose, and if our attribution for that particular event was assigned to the last treatment phase if it occurred within the 30 days post treatment in that particular phase. For example, if a patient were crossed-over to a placebo phase, (from initially a paroxetine phase), and if death occurred, for example, on day 29 of the placebo phase, Dr. Seika defines that patient as being a "paroxetine" death. I mentioned we would indeed confirm this, and inform him accordingly. He had the following additional requests for our update: (1) identify which studies were parallel or cross-over in design, and (2) identify which studies were North American versus non-North American studies. In addition, I raised a hypothetical example for his consideration. I inquired about his interpretation of classifying placebo-run deaths. Specifically, I asked if a patient were to die during placebo run-in, i.e. prior to randomization, should that patient be included in the calculation for placebo deaths. He clearly stated that such a patient should not be counted in our analyses, since such a patient would not comprise the "controlled" portion of a trial. In closing, Dr. Sevka is fully aware that FDA's request is demanding considerable effort by SB, he further realizes that several cases in the July 13th response were unblinded and that we have been

evaluating these in more detail and that the incidence rates will be revised accordingly. He also was made aware that SB's updated information is being finalized and is scheduled to be submitted shortly. Finally, Dr. Sevka suggested that we don't hesitate to call him if we have any questions needing clarification.

**Action(s):**

- Clinical (D. Burnham) to confirm data methodology and provide additional information per FDA's request
- U.S. Regulatory Affairs (T. Kline) to arrange phone call to FDA if needed, and to coordinate submission accordingly

Thomas Kline
Assistant Director
U.S. Regulatory Affairs