

February 27, 1967

Dr. Karl Rickels
University of Pennsylvania
School of Medicine
Department of Psychiatry
University Hospital
Philadelphia, Pennsylvania 19104

Dear Karl,

I am very pleased that our project has passed another hurdle. During the past two weeks I have read and re-read your proposed protocol and would like to share with you some questions and am enclosing a preliminary budget for your consideration.

If I understand the proposal, it is to compare two drugs, alone and combined with a placebo. Ratings will be done prior to drug administration, and after two and four weeks of treatment. This is not to be a crossover study and so the number of patients required will be at least 120. This indicates that the patient flow in your clinic is indeed large.

From the EEG point of view, the number of subjects and the sampling will be adequate. In these patients, one consideration might be that an initial record taken during the pre-treatment period should be discarded. In naïve subjects, an EEG recording is often accompanied by considerable anxiety and this is best alleviated by a recording and the overt demonstration that it is without risk.

Thus, if we plan on four recordings for each subject, the study will have a minimum of 500 useful records. From past experience with drop-outs, we should anticipate approximately one-third more records than we need - for a total of 650 records. If this is a realistic figure, then I would like to know approximately what the new patient admissions to the study are, so that we can realistically appraise the weekly number of records required. The sample length will be determined, in part, by the number of records to be run. Other things being equal, I would suggest at least twelve minutes of recording with eyes closed, and two minutes of eyes opened. The termination of each recording might be a hyperventilation, with a two minute post-hyperventilation record. In each instance, the recording will require at least a 7 to 10 minute settling period followed by a 15 minute actual recording.

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