

28 November 1973

Robert E. Robinson, M.D.
Neuropharmacology Section
A. H. Robins Company
1407 Cummings Drive
Richmond, Virginia 23220

Dear Dr. Robinson:

I have just returned from a trip to Europe and have reviewed your letter regarding the EKG changes associated with lenperone (AHR-2277). I do not know how to interpret the data presented because we have become accustomed to finding such EKG changes with many of the anti-psychotic compounds. Some years ago Dr. Itil and I became concerned with this question and in a systematic study of thioridazine and chlordiazepoxide collected the data carefully and had them evaluated by two internists. We were impressed that the EKG changes induced by thioridazine were significantly greater than those induced by chlordiazepoxide. In a second study, patients receiving fluphenazine, thiothixene, and haloperidol were examined for EKG effects. In this study, the group of patients had fewer EKG changes than the patients who had received thioridazine. Since then I have followed the literature carefully and note the studies of Ban and Lehmann, Gallant, and Simpson. Each of these authors has indicated that the EKG changes following thioridazine were much greater than other anti-psychotic drugs.

When lenperone comes to Phase III testing, it might be advisable for you to consider a direct comparison of its cardiovascular effects with thioridazine and one other anti-psychotic compound.

With regard to our own work, our doses are much smaller and we anticipate no direct cardio-vascular difficulty. I thank you, however, for bringing this to my attention.

R. E. Robinson, M.D.

-2-

28 November 1973

We have continued our dose-finding studies and are now looking with greater detail at the EEG and behavioral effects of 3 and 6 mg doses.

My best regards,

Sincerely yours,

Max Fink, M.D.
Professor of Psychiatry

MF/cis