

July 28, 1970

Mr. Robert Marlin  
Sandoz Pharmaceuticals  
Hanover, New Jersey 07936

Dear Bob,

Separately I am sending you a summary report and statistical data of our two EEG studies of S 42,548 in volunteers. In the first study, reported December 22, 1969, we defined a dose of 4.0 mg of S 42,548 as adequate to alter the behavior of our volunteer subjects.

In the second study, reported here, we compared the EEG profile of S 42,548 to placebo. While many differences, particularly in behavior and systolic blood pressure were observed, we were unable to establish an EEG profile. As we discussed, the failure may relate to the sample size or dose of S 42,548 - or to the possibility that its central effects are variable and unsystematic (at this dose).

There are two options that are of interest to us and meet some of your needs. One is to extend this study by additional subjects at 4.0 mg or by an additional 6-12 subjects at 6.0 mg, in comparison to placebo, following this design. This will either demarcate an EEG profile, or failing to do so, satisfy the statisticians who may question our sample size.

The second is to accept this data and proceed with a direct comparison with dextroamphetamine in a larger sample. This compound was the principal comparison in animal studies. If we define a profile for dextroamphetamine and not for S 42,548, we can be confident that the CNS effects of S 42,548 are less than amphetamine. Failure to define a profile for dextroamphetamine will raise doubts as to our technique.

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Before concluding the present study, however, you may wish to arrange a review of our data with other investigators of S 42,548, both within and outside Sandoz Pharmaceuticals. I am leaving for my holidays in August, and would be pleased to participate in such a meeting in early September.

I would also be pleased to meet with your statisticians to review their analyses of the data, trusting that their results are similar (but hoping they find more than we did).

Incidentally, the study took much longer than I anticipated largely by our need to improve our statistics and programs. Now that these are fully operational, I am sure we can proceed with greater ease.

My thanks for your cooperation in this study - and my best regards.

Sincerely yours,

Max Fink, M.D.  
Professor of Psychiatry

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