April 17, 1964

Dr. Donald F. Klein
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Dear Don:

Thank you very much for sending back the depression paper so promptly. I liked your comments, and enclosed is the next draft. I did, as you suggested, take out all the EEG material which was not pertinent to the issue. The two tables that you inserted are quite good. The only question that I have about them, is whether it is necessary to include the statistical values in the table. While the original study was a random assignment, the patients that we are now extracting for the study are a sub-sample which is not matched. The statistics, then, are possibly a poor guide to the data. I think the tables speak for themselves.

As the content now stands, we present a description of the behavioral changes with each compound, the global ratings, and the rate and reactivity response. I wonder if we could bolster this with some additional data from the mood scales or some of the other depression scores. I liked what you did in the anxiety syndrome report and it may be worthwhile to add some similar information. Enclosed is a copy of those covariance analyses which were "depression sensitive". Perhaps we could include some of these or a table like this. Also, in the new scales which have been labeled Problem 13, numbers 1, 2, and 5 are depression sensitive just as the rate and reactivity score. It might be helpful to do a similar analysis for number 1 (perplexity), or 5 (tension).

While I deleted the EEG material, I believe the facts presented were correct. Before John left he did a review of the EEG data with chlorpromazine alone, and chlorpromazine and Kemadrin. Chlorpromazine, in general, produced more delta and theta activity, and the amount of beta was markedly decreased in contrast to the combined drug use. As for imipramine, we have done many analyses on the Hillside material and on additional experiments here. This is a fascinating study, because much of the expressed EEG changes are related to the pre-treatment record. In general, given a record with considerable amounts of alpha activity, this will decrease, there will be some theta activity and beta activity will appear significantly. In the presence of a record with slow wave activity already, especially in epileptic patients, the amount of seizure activity increases markedly and one does not see the

fast activity component. Our computer analysis programs have been working very well, and we are now completing an analysis of pentothal. I hope to take imipramine next, because I think it is a fascinating compound. Indeed, I have read your theoretical paper only once, and my first impression is that there may be some interesting neurophysiological material with imipramine which may fit with your models.

I read the paper on anxiety syndromes and found it very clear and interesting. It is precisely this sort of material which seems necessary today as the basis for a better understanding of drug action. I don't have such patients in our wards at the present time, but they probably exist in clinics and given the opportunity, I would like to bring your paper to the attention of some of the out-patient psychiatrists, hoping that they will try your recommendations.

Thanks once again for your help on the depression paper.

Sincerely yours,

Max Fink, M. D.
Director

MF/jb

Enc.