March 24, 1964

Dr. Sol Goldberg
Psychopharmacology Service Center
National Bank Building
Bethesda, Maryland

Dear Sol:

I have read the research plan on depression dated February, 1964, and find it very exciting. I have a few comments, however, and I am sharing these with you so that some of the questions which may come up at the committee meeting will be anticipated.

With regard to the research plan itself, I believe that it would be advisable to specifically answer the following questions regarding previous treatment (page 5). When the record indicates that the patients will be kept off anti-depressants for 72 hours, what action will be taken for those patients admitted to the hospital receiving medication from a previous practitioner? What about patients who received ECT in the days or weeks preceding admission? (In the Hillside study, we arbitrarily excluded all patients who had received medication and ECT within three weeks of referral. (This was an arbitrary decision and I know of no satisfactory data to support this action).

The administration of chlorpromazine in doses up to 600 mg. will carry with it in some patients overt rigidity and Parkinsonism. In our study, we tried a number of anti-Parkinsonian agents and we concluded that the concurrent administration of procyclidene would prevent the Parkinsonian features. We published this in one of Jonathan's bulletins. On page 7, you indicate that all medication will be discontinued at the end of the 5th week. This should be done in gradual fashion because we observed unpleasant side effects when this was done suddenly.

These three comments are the only significant ones that I want to make about the proposal itself. I would like to suggest that you add to your list of references concerning imipramine being superior to placebo those enclosed, which reflect the work done at Hillside Hospital. On page 2, you review the various placebo

controlled studies and conclude that such studies have not resulted in useful information concerning the types of depressed patients responding to the drug. I am taking the liberty of enclosing an early draft of my study at Hillside, in which we described the responders in that population. It may be useful to review this report as the basis for selection of some of the rating scales which will be applied in this study program.

I might suggest that some of the differences in the 13 controlled double blind study lists may be related to such mundane matters as dosage, duration and numbers of subjects. In the past few weeks I have been reviewing the EEG changes induced by various drugs and it has been an eyeopener to realize that some men summarize data in a very assertive way even though the actual numbers involved are few. A review of these 13 studies may give a somewhat different picture.

My best regards.

Sincerely yours,

Max Fink, M.D.
Director

MF/jb

cc: Dr. Jonathan Cole