

January 14, 1971

Dr. Jack Freund
A. H. Robins Co.
Richmond, Virginia

Dear Jack,

Enclosed is an answer from Paul Janssen to my inquiry about sulpiride. It is of little help.

Separately, I received two reports about clozapine from Dr. Hippus. Stille and Hippus is a pharmacological review and indicates that clozapine has distinctive activity on a variety of tests, interpreted by Stille as characteristic for antipsychotic drugs. Angst et al. is a clinical report in 126 patients with diagnoses of acute schizophrenia and mania. The essay is presented as a demonstration of the applicability of the collaborative, computerized data collection and analysis system, so that much of the text is devoted to technical features. But they are impressed that clozapine has distinct antipsychotic activity with two important features: no effect on muscle tone (i.e., no parkinsonism) and a marked improvement of sleep disturbances. The separation of antipsychotic and parkinson features is considered sufficiently novel as to become the basis of a test of the accepted theory that all antipsychotic drugs must produce parkinsonism. Clozapine is described as not having antidepressant or antimanic features.

If these data are verified, the compound should be active. They refer to a comparison with levomepromazine and with thioridazine, claiming that clozapine is at least as effective an antipsychotic as these compounds; noting also that it has not been compared to the piperazine phenothiazines.

An additional report not available to me is Gross and Langner, *Arzneimittel-Forschung* 19:496-498, 1969.

It sounds like an interesting compound (better perhaps than the reports of sulpiride).

My best.

Sincerely yours,

Max Fink, M.D.