

J. Peeters

March 29, 1979

Turan Itil, M.D.
HZI Research
Tarrytown, New York

Dear Turan,

I have had a chance to read the Final Report of the ACNP-FDA Task Force on Bioavailability with some attention to the details, and I am writing because I believe the report is less sanguine than need be with regard to the methods already available to us to assess bioavailability and pharmacodynamics of drugs. Specifically, the section 7.2.2 should be expanded in some way to reflect the state of knowledge presented at our sessions. You may recall that two methods were discussed at length as reflecting the changes in brain function induced by drugs which crossed the blood-brain barrier, that of pupillography and of quantitative electroencephalography. These methods provide valid end-points to the effects of drugs on the brain, and are as quantitative as established biochemical methods in this regard.

Would you consider amending the paragraph 7.2.2 by the addition of the following:

" . . . There is currently no recognized standard approach, although pharmacodynamic methods such as the quantitative EEG and pupillography, which are responsive to the effects of drugs which cross the blood-brain barrier, provide the most logical opportunity for such development."

Quantitative EEG methods provide indices for the assessment of benzodiazepines (diazepam, bromazepam), mianserin, doxepin, thiothixene, phenytoin, among others, in studies from my laboratory alone. Others have made similar contributions, and the negative statement of 7.2.2 ought to reflect this experience.

My best regards.

Sincerely yours,

Max Fink, M.D.
Professor of Psychiatry

J. Ellen

April 10, 1978

Turan Itil, M.D.
HZI Research 1
150 White Plains Road
Tarrytown, New York

Dear Turan,

It was nice seeing you again, and we did enjoy the visit with Ellen. I felt a bit better after the debacle in Ottawa since we did have the occasion to talk again.

I enclose the reprints from the recent work by Bolwig. It is the clearest data that ECT produces an increase in permeability of the blood-brain barrier, and is quite compelling. Maybe it could be used in the TRP problem.

My best regards.

Sincerely yours,

Max Fink, M.D.