

March 29, 1971

Dr. Fred Kagan
Manager, CNS Research
Upjohn Company
Kalamazoo, Michigan 49001

Dear Fred,

Since our last note, we have established a dosage for diazepam, and begun our defined classification study of U 28,773. It should take 8 weeks for the data collection, and 2-3 for the analyses, so that I anticipate our report by mid-June.

Your notes on the duration of action of U 28,773 are most interesting, for with so clear a duration effect, we may wish to approach the clinical effects in a study of a different design. A compound with a flat extended duration of action would be most powerful as an antianxiety agent. Our present problems with diazepam and chlordiazepoxide are their relative short duration of action, requiring repeated dosage, repeated risk of sedation, and the development of tolerance, requiring more frequent administrations in some patients. An effective, flat dosage regimen may avoid some of these difficulties. Your note, that a half-life > 24 hours would make you "bearish" is puzzling. Such a feature may increase the risks of uncontrolled use, but may be more useful in reducing the euphorogenic risks. The higher risks, higher euphorogenic action, and higher addiction liability of heroin compared to methadone are documented. Both drugs effectively reduce opiate hunger, opiate withdrawal symptoms, and may usefully substitute, one for the other. Yet, methadone is considered the safer drug, with its longer duration of action. The extended duration of action enables some useful applications.

Come visit New York soon. Meanwhile, even if the rubidium fever has cooled, the enclosed announcement may be of interest to someone on your staff. I'll try to be there and will send you a summary if no-one else is able to go.

See you soon.

Sincerely yours,

Max Fink, M.D.
Professor of Psychiatry

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