September 14, 1970

Dr. Norman Pitts
Chas. Pfizer & Co.
Groton, Connecticut 06340

Dear Norm,

I have read with interest the proposed guidelines for evaluating novel anti-anxiety compounds (received 9/8/70). Such an outline reflects prevailing practice, but makes no effort to either justify the practice as acceptable nor to highlight the hazards of our present practices. As a statement of present procedures, it is acceptable. The section on special studies is interesting and provides clues as to novel evaluating methods now under study.

Some specific comments are found on pages 3 and 4. In the introduction, the marked paragraph may be omitted as gratuitous; and on page 4, the section should be omitted since the NIMH-ACNP report is a discussion of problems and issues, not guidelines - and should not be so dignified, especially since the documents are not completed. Would it not be premature for the PMA Committee to incorporate an unpublished report before it is issued?

The initial single and multiple dose studies should be done in paid volunteers, to assess safety and not in patients (page 6).

What I miss most is a statement that would describe the steps leading to clinical trials, and criteria for a potentially effective therapeutic agent. The animal pharmacology which is used; the qualities (chemical and pharmacologic) of known anti-anxiety agents that seem common to this therapeutic group; and especially, those aspects of present drugs that need improvement. For example, all accepted anti-anxiety drugs are anti-convulsant, sedative (hypnotic), produce seizures on rapid withdrawal and tolerance. But other drugs have anti-anxiety qualities as various "anti-psychotic" drugs, some anti-depressants, calcium salts and such additional substances as ethyl alcohol, opiates etc.

In making these suggestions, I am reacting to the limited goal of these notes - i.e., minimum guidelines for clinical assay, as perhaps too limited for industry. By broadening the document to include animal pharmacology, criteria for early identification, and suggesting that the drugs are symptomatic (therefore, not easily categorized), PMA may highlight the complexity of the issues and minimize the utility of 1970 issued, rigid "guidelines".

I am also concerned with the lack of supporting citations for many of the introductory statements. A detailed, academic presentation would be a more powerful statement.

Thank you for the opportunity to read this document.

Sincerely yours,

Max Fink, M.D.
Professor of Psychiatry

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