(h) We request that you provide us with the names of all monitors involved in the clinical investigation of Voranil, and the dates during which they served in such capacity.

(i) There does not seem to be a consistent pattern for the numbering of Case Report Forms. Will you please advise us as to the methods employed—especially in those cases where a chronological order was not observed.

ROBERT O. KNOX, M.D.,
Division of Neuropharmacological Drugs.

MEMORANDUM

U.S. GOVERNMENT,
February 12, 1970.

To: John Jennings, M.D.
From R. Newberry
Subject: NDA 16-880 Voranil (Clortermine hcl) tablets.

Original NDA—Not approvable letter based on inadequacies in almost all areas.

Although the letter does not actually say so, it is apparent that the evidence so far does not show sufficient benefits to justify the risks involved. I am wondering if we should encourage further clinical studies at all.

As I read between the lines, this drug appears to be a good candidate for drug abuse.

FOOD AND DRUG ADMINISTRATION,
February 19, 1970.

Ciba Pharmaceutical Co.
Summit, N.J.
(Attention Joseph S. Harun, M.D.).

NDA 16-880—AF 20-232

Gentlemen: Reference is made to your undated new drug application submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for the preparation Vorenil (clortermine hydrochloride) Tablets. The application was received on July 29, 1969.

We also acknowledge receipt of your additional communication dated July 31, 1969.

We have completed our review and find that the information presented is inadequate and the application is not approvable. The deficiencies may be summarized as follows:

The application is inadequate under section 505(b) (1) and (6) of the Act in the absence of data which show that the drug is safe and effective in use under the conditions prescribed, recommended or suggested.

Concomitant therapy is not covered adequately on the same report forms. If none was given, the record should so state.

In several studies there are apparent discrepancies with respect to the hematological data submitted; further clarification is required.

The bases for the opener's analyses of clinical laboratory data are subject to question because of the bread range and the possibility of sex differences.

Bias has been introduced into the statistical analyses by deleting data from certain investigators in such a manner as to exclude unfavorable findings. With request to Dr. Sinkins' letter of February 1, 1968, we request that you submit a copy of your January 23, 1968 letter to him. His letter refers to an additional eight patients he intends to forward; these additional eight case report forms should be submitted to us.

The patient populations used are not described adequately to permit proper evaluation of case material and experiental design.

Studies submitted are of insufficient duration to support long term administration. Most of the controlled studies are limited to eight weeks duration or less, whereas the proposed labeling does not indicate a time limitation.

The names of all clinical monitors and the dates during which they served should be provided.

The method used for numbering case report forms should be provided, particularly in these cases where a chronological order was not observed.