No report of this study was ever submitted to FDA by the William S. Merrell Company.

The results of our investigations were subsequently submitted to a Federal Grand Jury, and a twelve count true bill was returned on December 20, 1963, against the William S. Merrell Company and three employees, Dr. Harold W. Werner, Dr. Evert F. Van Maanew, and Dr. William M. King. All the defendants entered pleas of nolo contendere on June 4, 1964. The firm was sentenced to pay a total fine of $80,000, and the individuals were each placed on probation for a period of six months.

Thank you for the opportunity in allowing me to discuss my part in the MER/29 investigation. I will be glad to respond to any questions which the Committee may have.

AUGUST 19, 1959.

To: New Drug Branch. Attn: Dr. Epstein.
From: Division of Pharmacology.
Subject: NDA 12-066, M.E.R. 29, The Wm. S. Merrell Co.

This application lacks information on the safety of the drug in animals with respect to the selection of: (1) animals in chronic toxicity studies and (2) doses.

Since the drug may be used for long periods of time, one year oral studies in rats and three month studies in dogs would be desirable. In both groups a dose causing toxic effects should be included. The evidence presented in the NDA suggests that the margin of safety of the drug is low.

The chronic toxicity study in monkeys included in the application is helpful but lacks (1) a "toxic dose" and (2) enough animals to be significant, particularly for long term studies.

R. MEGIRIAN.

U.S. DEPARTMENT OF HEALTH,
EDUCATION, AND WELFARE,
Washington, D.C., September 14, 1959.

The WM. S. MERRELL CO.,
Lockland Station,
Cincinnati, Ohio.
(Attention of Dr. Joseph Murray.)

GENTLEMEN: Reference is made to your new drug application dated July 31, 1959, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for the preparation M. E. R.-29 (Triparanol Capsules).

This also acknowledges your letter of August 14, 1959.

The application is incomplete under section 505(b)(1) of the Act as follows:

The drug is by nature one which will receive chronic use. The data you have submitted suggests a low margin of safety. We feel that the following studies are in order to demonstrate safety.

A one year oral study in rats and a three month oral study in dogs should be performed. In both animal groups one dosage level should be selected to produce toxicity.

We shall reserve our comment on the labeling until the foregoing has been resolved.

Since the application is incomplete under section 505(b)(1) of the Act, it may not be filed as an application provided for in section 505(b).

Sincerely yours,

JEROME H. EPSTEIN, M.D.,
Medical Officer, New Drug Branch,
Bureau of Medicine.

THE WM. S. MERRELL CO.,
SCIENTIFIC DIVISION,
Cincinnati, Ohio, September 24, 1959.

JEROME H. EPSTEIN, M.D.,
New Drug Branch, Food and Drug Administration,
Washington, D.C.

DEAR DOCTOR EPSTEIN: I have your letter of September 14 advising us our New Drug Application for M. E. R.-29 (NDA 12-066) is incomplete. We are somewhat surprised by the statement that our data "suggest a low margin of safety."