These findings have been discussed with our consultant, Dr. Joel G. Brunson of the University of Mississippi Medical School, who advises that such corneal changes are common in the laboratory rat. Dr. Brunson has studied sections of the eyes of rats autopsied at Merrell and he feels that the changes are inflammatory and he reports the presence of acute inflammatory cells in the sections.

I regret that this information was not available to us at the time we submitted data on corneal changes.

Sincerely yours,

F. JOS. MURRAY.

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
Washington, D.C., March 28, 1960.

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

GENTLEMEN: Reference is made to your new drug application dated July 21, 1959, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for the preparation "M.E.R.–29 (Triparanol Capsules)."

We also acknowledge receipt of your additional communications dated January 26, 1960, February 4, 12, 22, and 29, 1960, and March 7, 1960.

We also acknowledge receipt of a communication dated February 5, 1960, from Maumee Chemical Co., 2 Oak Street, Toledo 5, Ohio, outlining the methods, facilities, and controls they will employ in manufacturing the new drug substance, 1-p-(beta-diethyl (aminoethyl) phenyl-1-(p-tolyl)-2-(p-chlorophenyl) ethanol, they will supply you.

We have not received any statement from Strong-Cobb-Arner concerning their methods, facilities, and controls they will employ in encapsulating the material for you.

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

It fails to report the clinical studies in full detail.

The reports should include detailed information pertaining to each individual treated, including age, sex, conditions treated, dosage, frequency of administration, duration of administration of the drug, results of clinical and laboratory examinations made, and a full statement of any adverse effects and therapeutic results observed.

As brought out in our meeting of March 7, 1960 with representatives of the Wm. S. Merrell Co., we are unable to resolve the apparent discrepancy in interpretation of the pharmacologic studies in dogs between your people and ours. Because of this dispute, because of the potential hazard of liver toxicity with this drug, and further because of the highly theoretical value of taking such a drug as MER-29 (to our minds) we are making the application incomplete until longer term clinical studies have been made utilizing periodic liver function studies to show that this blocker of intermediate cholesterol metabolism is not producing liver damage.

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,

FRANK J. TALBOT, M.D.,
Medical Officer, New Drug Branch,
Bureau of Medicine.

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
Washington, D.C., April 19, 1960.

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

GENTLEMEN: Reference is made to your new drug application dated July 21, 1959, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for the preparation "M.E.R.–29 (Triparanol)."

We also acknowledge receipt of your additional communication dated March 31, 1960.

Our action in allowing this application to become effective is based solely on the evidence of the safety of the drug. All claims are on your own responsibility.