vised, as well as close observation and artificial respiration. A follow-up report dated 7/14/66 stated that the child had recovered.

Impression: Reaction from Lomotil overdosage.

H. Searle Case # LO 2–67 dated 3/2/67 and 4/19/67

Report of a fatality in a 2 year old child who accidentally ingested approximately 8 Lamotil tablets 12 hours prior to arriving at the Shawnee Mission Hospital, Shawnee, Kansas, D.O.A.

An autopsy was performed which revealed pulmonary congestion consistent with the picture of interstitial viral pneumonitis, reticuloendothelio hyperplasia, and a hypoplasia of the adrenal cortex. The final diagnosis of cause of death is listed as acute pneumonitis. "The results of toxological examination of the stomach contents show no atropine nor diphenoxylate to be present. The blood sample was insufficient for evaluation (quantitative) of diphenoxylate. Histological findings are consistent with those seen in children dying of acute viral pneumonitis and it is felt that the cause of death in this child is of this etiology."

Impression: Death probably not due to drug but viral pneumonitis.

I. Searle Case # LO 4–67 dated 4/19/67 and 4/27/67

Case of fatality from Lomotil overdosage in a 2½ year old girl treated at the University Hospital, Western Reserve University, Cleveland, Ohio. She allegedly ingested 8 tablets of Lomotil. Heroic symptomatic and supportive therapy given.

Follow-up autopsy by the Coroner's Office, Cleveland, Ohio yielded the following:

a. Lungs: Hemorrghagic bronchopneumonia.

b. Stomach: Acute ulcer.

c. Kidney: Renal tubular necroses. Protein casts. (Most of tubular epithelium is preserved).

d. Brain: Marked cerebral and cerebellar edema. Subarachnoid hemorrhage, focal, slight.

The tissue forwarded to Searle for laboratory analysis was received by the firm in such poor condition as to make them useless for analysis.

Impression: Possible death from Lomotil overdosage.

MARVIN SEIFE, M.D.,
Acting Director, Division of Cardiopulmonary Renal Drugs/ODS.

PHARMACOLOGIST'S SUMMARY

Date Summary Completed: July 21, 1967, NDA 12–699.

Company: G. D. Searle & Co., Chicago, Ill.

Original Effective Date: September 19, 1960 (12–699 OED 1/17/61).

Name of Drug.—Lomotil.

Generic Name.—Diphenoxylate hydrochloride with atropine sulfate.

Category.—Antiperistalic agent.

Dosage.—To 20 mg/day for adults in divided doses, orally.

Material Reviewed.—

Report of Acute Oral Toxicity of Lomotil Liquid dated July 12, 1967.

These are useless studies on the toxicity of the components of the vehicle of Liquid Lomotil. We requested "acute and subacute studies of toxicity in the newborn and adult to determine the relative toxicity of the mixture of drugs (2.5 mg diphenoxylate and 0.025 mg atropine sulfate) as the dry powder and as the syrup." Studies of the vehicle or components of the vehicle do not give any information as to a possible difference in absorption of the drug in the presence of the liquid vehicle.

The studies which were requested should be submitted.

LOUISE L. PHILLIPS, Ph. D.

ADDENDUM TO SUMMARY OF SUPPLEMENT NDA 12–699, DATED AUGUST 17, 1967, REGARDING REPORT DATED AUGUST 16, 1967

Report on NDA 12–699 (Lomotil Liquid) entitled "Acute Oral Toxicit Study—Weanling Rats, Diphenoxylate RCL–R1132, Lomotol Power, Lomotil Liquid—Final Report" dated 16 August 1967 and signed by Herbert Helling, Food and Drug Administration Liaison Coordinator. The report supplements the previous incomplete report.