Comment

This is proof of the criticism I expressed over the previous paragraphs. I therefore conclude this summary with the statement that the presently approved labeling is grossly inadequate and would serve to mislead the practicing physician. I might add that the advertisement for Lomotil which appeared in the July, 1964 issue of the Virginia Medical Monthly on page 23 could also serve to mislead. This advertisement promotes both tablet and liquid and nowhere in these two volumes of the NDA did I see any data or anything in the approved labeling that would substantiate the use of the liquid.

JOHN O. NESTOR, M.D.

REFERRALS AND RECOMMENDATIONS

ISSUANCE DATE MAY 25, 1964

To: Division of Toxicological Evaluation,

Please review Dr. Nestor's & Dr. Moling's comments. Do you have further comments? Thank you.

M. J. ELLENHORN.
NDSnB.

M.J.E. My summary states my view and points in detail but I will list some briefly below:

1. The promotional material in PDR is labeling and the source of the material is the firm. My understanding is the firm submits the material in exactly the form it is to be printed.
2. The animal studies were performed only on one ingredient and not on the final product as marketed.
3. The clinical data are grossly inadequate in all age groups but especially in children.
4. The investigators were not fully and adequately identified. Many individual case reports were not submitted. There were only 43 in the whole NDA.
5. Finally, two children died as the result of ingesting this drug.
6. In my opinion the data to substantiate safety and efficacy are grossly deficient and the drug should come off the market.

J. O. NESTOR, M.D.
July 8, 1964.

REFERRALS AND RECOMMENDATIONS

ISSUANCE DATE MAY 18, 1964

To: J. H. Moling.

Do you have any comments on this summary (of Dr. Nestor) or the NDA?

M. J. ELLENHORN.

M. J. Ellenhorn: Have reviewed Dr. Nestor's summary and major portions of NDA 12-462. Dr. Nestor notes the factual deficiencies in the clinical work in this NDA as usual. The toxicity studies apparently were on the diphenarylate Hcl only but the drug is marketed with a small atropine content, possibly to prevent overdosage. This obviously was not effective in the two deaths reported. D.P. would perhaps like to comment further on the toxicity studies in this light. The case histories are tabulated rather than being submitted in original form but it would appear that the pediatric experience was wanting as Dr. Nestor suggests. Hepatic toxicity is alluded to in the labeling but the hazard of such is not thoroughly explored in the clinical data submitted. These data and deficiencies should be satisfied or the labeling modified to exclude the younger age groups. The NDA is effective as it exists but efficacy may be questioned in Oct. if not safety.

J. H. MOLING, M.D.