The revised mailing piece is also under review. It was not approved by us in the form in which it issued. Our impression is that it is more a promotional piece than a warning letter. As to the gout claims, our position is as stated in New Drugs (1966). As to the omitted warning information, please compare the approved brochure with the advertisement.

Very truly yours,

WILLIAM W. GOODRICH,
Assistant General Counsel, Food and Drug Division.

[U.S. Government Memorandum]

NOVEMBER 2, 1966.

To: Herbert L. Ley, Jr., M.D., Director, Bureau of Medicine. Through: H. I. Weinstein, M.D., Acting Associate Director for Medical Review.
From: Acting Director, Division of Medical Advertising/OMR.
Subject: Misleading promotional labeling piece under guise of apparent "Dear Doctor" letter re Indocin.

By first class mail, a letter (copy attached) was sent 10/4/66 by the firm in an envelope flagged for the physician's attention by a beguiling euphemism, "Safety," in very large red letters.

It contained the attached new FPL submitted, under 130.9 (presumably "justified" because it only added warning ideas), by 9/2/66 Company letter to Dr. John Jennings. Whether this was a legitimate act is open to serious question since revision of the FPL was under serious dispute in several details at the last meeting of BuMed and Company personnel on 7/15/66.

The 9/2/66 letter (copy attached) affirmed the intent to put the FPL into use O/A October 31, 1966, without awaiting approval as would be necessary if it were a suplemental NDA submitted under regulation 130.4—this is spite of the fact the 9/2 letter was really a "negotiating" communication turning down a number of specific requests made at the same 7/15/66 meeting.

The above must also be viewed from the perspective that the Company therein rather imperiously turned down at least two important requests for "warnings" by BuMed—see paragraphs "2)" and "3)" of the letter's page 2. Their unwillingness to state, "*NOT FOR USE IN CHILDREN*," appears irresponsible in the face of their knowledge of deaths in children—deaths not prevented by the old FPL language they even here aver to be adequate.

Further, they jumped the implied 10/31/66 "use" date by putting the FPL into use via the 10/4/66 letter to the medical profession.

Misleading features of subject "October, 1966" letter: 1. The first sentence sets the tone of the letter as blatantly promotional. It is both out of place and a non-sequitur, since experience in 98 of the 99 countries is largly if not solely beside the point. This is especialy improper because of the tie-in to the second sentence's idea that presumably only this massive "global" experience with circa 150 million patient days therapy resulted in the few and new additional warning idea "reflected in the revisions . . ." in the included FPL.

2. The Company's decision to highlight "one change in particular," namely the "potential of masking . . . ," must be judged against the following:

a. It represents a unilateral act of rejection of a BuMed proposal to warn of the "Possible activation of latent infection." (See 9/2/66 letter, page 3.)

b. The above "change" constitutes a minimized alert to a standard idea, which, while important, has competed successfully in the Company's "mind" against the prominent inclusion of the following *new* FPL contraindications and side effect ideas:

(1) Contraindicated in aspirin-sensitive asthmatics and during lactation.
(2) Convulsion, depersonalization.
(3) Jaundice, hepatitis.
(4) Angiitis, elevated blood pressure.
(5) Acute respiratory distress.
(6) Agranulocytosis.
(7) Hyperglycemia.

3. It subtly promotes use of the drug more widely than the FPL permits:

a. Re: end of first sentence, ". . . in the treatment of *arthritic* disorders . . . ."—and the end of the last sentence, ". . . next to aspirin, the most frequently prescribed *antirheumatic drug* . . . ." (underscoring added);