

The Bulletins titled "Profit Improvement Promotional Program—'Indocin,'" are in memorandum form. Their form and contents would suggest that they are internal communications that are not intended to be distributed beyond the control of the firm.

These instructions to the detail force for increasing sales of Indocin recommend methods typical in the promotion of a variety of products with no public health implications. We regard the instructions as seriously misleading.

While there is considerable repetition (which in itself is a promotional tool) throughout the bulletins, the latter can be grouped for comparison into two time periods. For example, Indocin Bulletins 83, 84, 87, 88, 93 and 95 are dated between July 12 and August 4, 1965 (the period of introduction of the drug); and Indocin Bulletins 23, 66, 74, 80 and 85 are dated between April 5 and September 27, 1967.

The 1965 bulletins suggest generally to the detail men that they promote use of Indocin beyond approved indications, and play down side effects and other warnings present in the labeling. Some examples of passages from the bulletin are:

*Unwarranted Extension of Indications*

"... when there is Heat ... Redness ... Swelling ... and Pain in the muscles or joints ... 'Indocin' is usually effective."

"... treatment of the misery inflicted by arthritic diseases."

"Available to relieve pain, reduce fever tenderness and swelling, and increase joint mobility in patients with rheumatic disorders."

"... *Just Plain* musculoskeletal Aches and Stiffness ..."

In connection with the above, Bulletin 87 contains this admission:

"In fact, our guys are using a real expanded claim for 'Indocin' on inflammation. They are consistently telling their doctors that ... [as above]"

*Deemphasis of Side Effects, etc.*

"Therapy with 'Indocin' is safer ... a remarkable record of safety."

"... Side effects ... are usually minor and seldom constitute a problem. Usually they can be controlled by simple adjustment of dosage."

"With an extended margin of safety."

In relation to severity of side effects:

"Bothersome is probably as severe an adjective as we can use to describe these effects because in most patients they are tolerable, and transient."

The discussion of contraindications omits reference to the fact that Indocin is not recommended for use in children.

*Special Note*

Most reprehensible and significant in indicating the firm's disregard of the patient is the following passage:

"... it is obvious that 'Indocin' will work in that whole host of rheumatic crocks and cruds which every General Practitioner, Internist, and Orthopedic Surgeon sees everyday in his practice."

As you know, there were a series of events that occurred between 1965 and 1967 which involved our dealing with the firm regarding their advertising and promotion of Indocin. Merck was cited in regard to Indocin advertising, conferences were held with the firm's management in 1966 and the Assistant General Counsel of the Department spoke publicly regarding the misleading nature of an Indocin advertisement appearing in the *Journal of the American Medical Association*, and elsewhere. With such notice, the firm did take action to correct its forms of promotion which are subject to our control.

Notwithstanding such notice, however, we find in 1967 Indocin bulletins:

The expansion of indications for open-ended uses, "Wherever there is pain, inflammation, and swelling in or around the joint with a resultant limitation of motion. ..." [The remainder of this sentence mentions the approved indications but in context the listed indications are examples only and do not overcome the suggestion for expanded uses.]

The continued minimization of side effects and warnings, "Most of the adverse reactions which occur with 'Indocin' are common with any antirheumatic drug. They usually are transient, easily controlled, and often disappear on continued treatment." Also, "Gastric irritation can be minimized by giving the dose of 'Indocin' after meals."

While the foregoing comments are examples of things in the bulletins that have been given prominence by repetition or other emphasis, we believe that the