Name of Payee: Anna H. Hanes Research Fund, Department of Medicine, payable to Dr. Grace P. Kerby.
Street Address: Duke University School of Medicine.
City: Durham, N.C., 27706.
Sincerely yours,

GRACE P. KERBY, M.D.

UNIVERSITY OF OREGON MEDICAL SCHOOL,
DEPARTMENT OF PHARMACOLOGY,
Portland, Oreg., February 25, 1964.

Dr. NELSON H. REAVEY CANTWELL,
Merck Sharp & Dohme Research Laboratories,
West Point, Pa.

DEAR DR. CANTWELL: Herewith are the special case reports for 11 cases who have had trial of the "Indocin" capsules. The number of the cases are from 3518 to 3528. For the record, I am retaining the additional case record forms that you sent and numbered from 3529 to 3567. These unused forms will be used for any additional cases that are placed on "Indocin" capsules. However, if you wish these blank case forms returned, I can do that.

As you know, I sent you a copy of the individual case records for all the patients (21 cases) who have received both the tablets and the capsules of "Indocin". I am currently writing this up as a short report for possible publication as a research note in CURRENT THERAPEUTIC RESEARCH. When I complete this short note, I shall forward you a copy for your inspection.

I hope that your case reports for the capsules are coming in satisfactorily and you can get off the material to the FDA. Good Luck!

With best wishes,

NORMAN A. DAVID, M.D.
Professor of Pharmacology.

STATEMENT OF SENATOR NELSON—Resumed

One of our witnesses, Dr. Donald Mainland, a medical doctor and one of the most famous biostatisticians in this country, has recommended that the evaluation of drugs be taken entirely out of the hands of the pharmaceutical industry, an idea which merits study. Even if the drug firms continue to do animal, and to some extent clinical studies, approval for marketing by the FDA should be based, at the very least, on studies under its direction. Perhaps it may be a good idea to establish a national drug institute, the purpose of which would be to evaluate drugs, in-house and/or by contract. In other words, it seems reasonable that there should be an independent, careful and scientific evaluation of a drug to secure FDA's approval. We are studying this problem and may be prepared to propose legislation in this field sometime soon.

The second problem is FDA's requirements for evidence of safety and efficacy. The statute requires "substantial evidence" of safety and efficacy which means "evidence consisting of adequate and well-controlled investigations." On December 7, 1964, the medical officer in charge of the New Drug Application for Indocin stated in her summary that "There is a paucity of controlled studies in this massive NDA." On March 15, 1967, Dr. David Hurwitz, M.D. of the FDA's Bureau of Medicine in referring to claims of efficacy in osteoarthritis of the joints, other than the hips and muscular skeletal disorders, found that "136 out of 137 studies are deficient in technique and incapable of standing up to critical examination; it is unfortunate that the company and its investigators do not use the more sophisticated investigative techniques that have been evolved to evaluate new drugs."

Dr. Hurwitz also stated that:

"In view of the wide-spread acceptance of Indocin and its seeming benefit in Rheumatoid Arthritis, it is an unwarranted conclusion to say at this time that the drug is of no usefulness in this disease. However, since these excellent studies by Cooperating Clinics Committee and by Donnelly et al. in the British Medical Journal cast considerable doubt on the efficacy of Indocin, further studies of equal or better quality and of longer duration are in order to determine the place of this drug in the physician's Armamentarium. This re-evaluation is particularly necessary given the toxicity of Indocin which renders the drug totally unfit for use if a significant therapeutic benefit cannot be established."

The question then arises whether a "significant" therapeutic benefit has been