TABLE I.—INDOCIN REVIEW—CONTROLLED BLIND STUDIES FROM ORIGINAL NDA

Author	Date	Volume	Number of patients	Type	Results	Comment
Hart, F. D., and Boardman, P. L. (British Medical Journal, 11:1281, 1965).	1965	30	18	Double-blind crossover comparison with Phenylbutazone 56 days.	(1) Little difference between drugs in therapeutic or adverse effects; (2) Indocin had greater effect on reduction of joint swelling; (3) no serious reactions.	Data not included with study (has been published with adequate data).
Percy, J. S., Stephenson, P., Thompson, M. (Ann. Rheum. Dis.) (23:226, May 1964).	1964	30	24	Double-blind crossover sequential comparison with Phenylbutazone.	(1) No significant difference between drugs in patient preference or grip strength; (2) Phenylbutazone had lower incidence of adverse reactions (none serious in either group).	Data incomplete as regards grip measurement or preference, it would be desirable to see how parameters were measured and actual figures; without these we are unable to tell if the patients improved.
Wenka, J., Jones, L., Wood, P., Dixon, A.	1964	30	22	Double-blind crossover comparison with placebo 6 weeks.	(1) Patients preferred Indocin but no measurable difference in grip strength; (2) no significant reactions.	The ARA Committee has noticed a feelins of well-being in patients on Indocin; is this the case here? No objective benefit was noted in the single measured parameter-grip strength.
Ward, J. R.	1965	30	Studies: (1) 29; (2) 40.	2 studies double-blind crossover comparison with placebo. In study No. 1, unlimited and irregular use of aspirin and steroids was permitted. Study No. 2, all patients on fixed aspirin and prednisone, dosage 4 months.	(1) Indocin group had less tenderness and morning stiffness; (2) Indocin group had significant decrease in pain, morning stiffness, swelling, tenderness; (3) no significant reactions.	(1) Results variable, uncontrolled use of aspirin and prednisone in study No. 1 make it invalid. (2) data scant, inadequate placebo effect (nil); validity of statistics, questionable dosage of other medications unspecified (Study No. 2).
Smyth, C. J.	1965	47	55	Single-blind variable time several weeks to several months.	Indocin effective in several parameters as compared to placebo.	(1) Well-developed response criteria; (2) large, unwieldy amount of data; (3) poorly controlled, variable dosage and length of administration; (4) results only suggestive to efficacy.
Bode, J. J.		80	27 total, 15 on Indocin.	Double-blind 3 months	(1) Indocin group had decrease joint tenderness and pain, no difference in parameters; (2) no serious reactions.	(1) Did patients use other medications during this long study?

TABLE II.—INDOCIN—NEW STUDIES QUESTIONING EFFICACY

Pinals, R. S., Frank, S. (NEJM March).	1967		24	Double-blind crossover comparison with aspirin 2 months.	(1) No difference between Indocin and aspirin; (2) no serious reactions.	(1) No baseline data; (2) neither drug had any clinical effect which makes results difficult to interpret; authors did not discuss this point; (3) 5 patients on steroids.
Donnelly, P., Lloyd, K., Campbell, H. (British Medical Journal, January 1967).	1967		30	Double-blind crossover comparison with placebo 1 month.	(1) No statistical significant difference between Indocin and placebo; (2) some delay in onset of fatigue on Indocin but not statistically significant; (3) no serious reactions.	(1) Well-designed study, well-controlled; (2) used aspirin in all patients but amount was recorded and evaluated statistically.
Mainland et al. (Clin. Pharm. and Therapeutics, January 1967).	1967		141	Double-blind comparison with placebo 3 months.	(1) No statistically significant difference between Indocin and placebo; (2) no serious reactions.	Use of aspirin reduces sensitivity of experiment and may mask small differences between placebo and Indocin.