THE
RHEUMATOID DISEASE FOUNDATION
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July 4, 1984

JOHN R. A. SIMOONS, Ph.D.
President

Mr. Perry A. Chapdelaine, Sr.
Rt.4, Box 137
Franklin TN, 37064

Dear Perry:

Thank you for your letter of June 29, 1984 with attachments and your comments on the proposed Protocol for the study.Please note that I will meet with Dr.Turner on July 13th., before arriving in Atlanta and that I will be able to report to our meeting of July 14,1984 of the ammendments in the protocol.I would appreciate receiving comments from our Physicians before the 13th. which I would then also discuss at our luncheon meeting.

Mr.Hal Smith will send me two advance copies of our Newsletter and I hope to obtain Turner's approval for the release.I will also discuss the terms of payment for the study based on a monthly disbursement of $10,000.- starting immediately until completion.

The "adverse experiences" and "Herxheimer" reactions will be listed and the Consent forms revised.The number of patients to enter the Phase 11 study as planned is adequate.Since this is a cross-over study, all 40 patients will eventually be treated with Clotrimazole and the "placebo" effect should not interfere with the statistical evaluation if we have significant results.Please note that ALL patients have three stages:, Drug, Placebo and Nothing,which means WASH-OUT period,also lasting 6 weeks.I have conducted several clinical studies and one study at Johns Hopkins in which we tested Cotazym-S in Cystic Fibrosis in only 18 patients was the best ever conducted.Most centers prefer only 24 patients because it becomes almost impossible to evaluate a large number of patients with several parameters.Phase 111, is a multi-center study, which will follow and in which Miles Pharmaceuticals will study "hundreds" of patients.Your age limit is also contrary to most inclusion criteria,especially when dealing with rheumatoid arthritis.

The dose of 20mg/Kg bodyweight cannot be increased without serious side-effects.Please read my letter of March 26, 1984 of which all board members had received a copy.Dr.Spiekermann and Prof.Krebs of Bayer AG ONLY agreed to participate after receiving my letter because they would not approve a higher dosage to patients in view of the toxicity of the drug.LEVAMISOLE, another Imidazole Compound was REJECTED because of the side-effects after the dosage was too high.We don't want to see that happening with Clotrimazole.I have studied at least 12 papers where Clotrimazole was administered orally and if you also review Wyburn-Mason's paper of Febr.28,1976,Lancet(Clotrimazole and rheumatoid arthr.) you will note that he suggested a dose of 10-12mg/Kg after he had serious side-effects using 25-100mg/Kg !!!

Over

Mr.Perry A. Chapdelaine, Sr. July 4, 1984

Clotrimazole is,however, the most potent anti-protozoal compound when tested "in vitro" and may become also the most effective drug for the treatment of rheumatoid arthritis.The dosage must be very carefully calculated and Dr.Wojtulewski who conducted the first double-blind study in England(Annals of the rheumatic diseases,1980,39,469-472) admitted to Dr.Wyburn-Mason and myself during our visit to him in August 1980 that he had far better results with lower doses than the dose used in the study of 40mg/Kg,first week then 80mg/Kg for another 7 weeks.

Drs.Blount,Bingham and Pybus have personal experience with Clotrimazole and I believe that they would agree.

Looking forward to meeting with you and the other Board members at our July 14,1984 meeting in Atlanta.

Cordially,

John R.A.Simoons, Ph.D.

cc:Dr.Blount
Dr.Bingham
Dr.Prosch
Dr.Pybus
Dr.Reich
Mr.Regelson
Mr.Swain
Mr.Smith
Dr.Reich
Dr.Wolcott