

# THE RHEUMATOID DISEASE FOUNDATION®

5140 Revere Road, Parkwood § Durham, NC § 27714 § (919) 544-4040  
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John R.A. Simoons, Ph.D.  
President

March 26, 1984

Paul H. Spiekermann, M.D.  
Miles Pharmaceuticals  
400 Morgan Lane  
Westhaven, CT 06516

Dear Dr. Spiekermann:

Re: Systemic Use of Clotrimazole in Rheumatoid Arthritis

Thank you for your letter of March 13, 1984 which we only received on the 23rd and must have crossed our letter of March 12, 1984. In our letter of March 12th., we indicated that Dr. Turner would file the IND and PROTOCOL for the proposed double-blind study as soon as we have your approval of the availability of the compound.

It appears that Bayer AG is concerned about the side effects of Clotrimazole when this compound is administered orally over a long period of time for treatment of the above indication. We, of course, appreciate your concern but would kindly like to point out that our proposed PROTOCOL for the study would follow a completely different dosage regimen than previous studies reported so far.

Whereas H. WEUTA (Postgraduate Medical Journal, 1974(1), 50, 45-49) used daily doses of 60mg/Kg body weight for up to 28 days and J. WOJTULEWSKI (Annals of Rheumatic Diseases, 1980, 39 469-472) used 80mg/Kg in daily doses for up to 8 weeks, we intend to use only 20mg/Kg body weight divided in four doses and taken for two consecutive days per week for a period of not more than six weeks. All patients will be under strict medical observation and extensive clinical and laboratory assessment parameters and drug toxicity will be closely monitored during the entire study.

You must be aware of the fact that the FD&A will NOT approve the IND if the protocol fails to guarantee the safety of the patients, which first MUST be approved by the Medical Center's Human Research Committee, before submitting to the FDA.

We will assure you that Bayer AG nor you will be responsible for the study and kindly request to reconsider your decision. I would like to personally meet with you on April 13th. at your office in Westhaven before proceeding to Holland and would appreciate hearing from you at your earliest convenience.

Yours Sincerely,

John R.A. Simoons, Ph.D.  
cc: Dr. Robert Turner