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November 21, 1983

Elaine C. Esber, M.D.
Director
Office of Biologic Research and Review
National Center for Drugs and Biologics
8800 Rockville Pike
Bethesda, Maryland 20205 HFN-800

6 DEC

Re: Antihemophilic Factor (Human)

Dear Dr. Esber:

The purpose of this letter is to amend our Antihemophilic Factor (AHF) (Human) Product License Application to include an optional "dry" heat-treatment step to our glycine precipitated process. Our glycine precipitated process with an option to "wet" heat-treat, reference 83-341, was submitted August 12, 1983, and is still pending at the Office of Biologics.

The manufacturing procedure used in the production of dry heat-treated Antihemophilic Factor (Human) is identical to reference 83-341 (submissions August 12, November 8 and 21, 1983) except for one significant process change. The process change is an option to dry heat-treat lyophilized AHF in final containers. The dry heat procedure is described in complete detail on PLA pages 5-1/7, 5-1/8, 5-1/9, 5-3/3 and 5-3/4 of our manufacturing procedure in Attachment X.

In support of this amendment, please see Attachments I through X. All of our support documents and revised PLA pages are contained in these attachments. New labeling and a package insert for the dry heat-treated product is also contained in Attachment X. All revisions and changes in this submission, as compared to reference 83-341, have been highlighted for your convenience in review.

Additionally, as requested, we have included as Attachment XI, an outline of the Phase IV clinical study for dry heat-treated Antihemophilic Factor (Human). A formal protocol for the study will be submitted under separate cover.

Under separate cover we are submitting samples and protocols Antihemophilic Factor (Human) qualification lots S8505, S8506 and S8' prepared by the dry heat-treatment process. Three month stability on S8505 have been generated and are included as Attachment IX. term stability on this lot and one other lot will be performed results submitted for your review annually.

We should note at this point, that we are requesting review and approval of this amendment independent of our August 12, 1983 submission, reference 83-341. After approval of both amendments, we will submit a consolidated manufacturing procedure including all approved manufacturing options.

Sincerely yours,

GRO-C

for Steven J. Ojala, Ph.D.
Director of Regulatory Affairs

SJO/PB/lf