APPENDIX II

APPENDIX B

Alpha THERAPEUTIC CORPORATION®
5555 Valley Boulevard, Los Angeles CA 90032
(213) 225-2221 TLX: GRO-C

November 2, 1989

Mr. K. J. Ayling
Superintendent Medicines Inspector
Medicines Inspectorate, Room 1804
Department of Health and Social Security
Market Towers
1 Nine Elms Lane
London, SW8 5NQ
England

Reference: Inspection of Alpha Therapeutic Corporation, U.S.A.

Dear Mr. Ayling:

On October 6, 9 and 10, Mr. D. Warburton and Dr. M. Kavanagh conducted an inspection of our biological product manufacturing facilities at 5555 Valley Boulevard, and 2410 Lillyvale Avenue. At the conclusion of the inspection, Mr. Warburton and Dr. Kavanagh discussed with us one critical, three major, and eleven other inspectional observations.

At this time, we wish to respond to these observations, and confirm our commitment to take appropriate corrective action. Enclosed is a listing of each observation followed by our response. We are naturally extremely concerned at the possibility of action being taken against our UK Product License because of our inability to respond as fully as we would like to the critical observation made by the inspectors. Despite our best endeavors to expedite the change to solvent detergent product, we feel that an unfortunate series of technical problems has caused the delay in our submission of the variation to the UK Product License. We wish to emphasize that obtaining data to support the US and UK license variations has been the top priority at Alpha since the last UK inspection in February 1988. In relation to the other points made by the inspectors regarding the n-heptane area, we believe the responses attached exemplify the sincerity and commitment which the company has to satisfying the concerns of the inspectors.

Alpha Therapeutic has always prided itself on the safety and quality of its products. These aspects in particular have contributed to UK

physician's confidence in Profilate Heat-Treated to the extent that we currently supply well in excess of 80% of UK commercial factor VIII requirements. Since the UK inspectors visit in February 1988, we have been working hard to provide as rapidly as possible a quality Factor VIII product improved over the existing product in terms of both its method and manufacture and its viral safety. We fully realize that the shortcomings of the manufacturing facilities for the existing n-heptane product may pose a dilemma for the UK Licensing Authority.

However, we believe we have now taken every feasible step to ensure the current product is as safe as possible. We are convinced that the solvent-detergent product (for which an application has now been submitted) is a superior product and that it has been developed as rapidly as possible. Finally, because of our majority share of the commercial UK Factor VIII market, we consider that the effect of action against our license for the n-heptane Factor VIII product will be a considerable blow to the UK hemophiliac community. We respectfully ask for time to allow the Licensing Authority to process the solvent-detergent variation application.

We take this opportunity to thank Mr. Warburton and Dr. Kavanagh for the highly professional and courteous manner in which they conducted the inspection.

If you have any questions in this regard, please contact me at (213) 225-2221.

Sincerely,

GRO-C

Marietta Carr
Vice President
Regulatory Affairs

LNB:dl
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Enclosures

cc: Mr. D. Warburton
Dr. M. Kavanagh