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**Memorandum**

**Date:** January 12, 2009

**FROM:** Joseph P. Manik, Bioresearch Monitoring Branch, HFM-664

Division of Inspections and Surveillance

Office of Compliance and Biologics Quality

**THROUGH:** Patricia A. Holobaugh

Bioresearch Monitoring Branch Chief, HFM-664

**TO:** Roman T. Drews, Ph.D., Committee Chair, HFM-392

Pratibha Rana, Regulatory Project Manager, HFM 380

**SUBJECT:** Bioresearch Monitoring Final Review memo

STN: BLA 125284/0

Sponsor: GTC Biotherapeutics, Inc.

Product: ATryn® (antithrombin alfa rhAT)

**FINAL SUMMARY STATEMENT**

Results of four bioresearch monitoring inspections of four clinical sites did not reveal problems that impact the data submitted in the application.

**BACKGROUND**

Inspections of four clinical investigators were performed in support of this Biologics License Application (BLA). Information from the BLA was compared to source documents during the inspections. The inspections focused on specific questions concerning two pivotal studies.

**PROTOCOL :** GTC AT HD 012-04

**STUDY TITLE:** A Multicenter, Multinational Study to Assess the Safety and Efficacy of Antithrombin alfa in Hereditary Antithrombin (AT) Deficient Patients in High-Risk Situations for Thrombosis

**Inspection of clinical sites and outcome for GTC AT HD 012-04**

Study Site Number	Study Site	Location	Number of Subjects	Form FDA 483 Issued	Final Classification
01-06	Yale-New Haven Hospital	New Haven , Connecticut	01	No	NAI
01-04	Weill Medical College of Cornell University	New York , New York	01	No	NAI

NAI – No Action Indicated, VAI – Voluntary Action Indicated, EIR – Establishment Inspection Report

**PROTOCOL:** GTC AT III 01002

**STUDY TITLE:** A Multicenter, Multinational Study to Assess the Incidence of Deep Vein Thrombosis (DVT) Following Prophylactic Intravenous Administration of Recombinant Human Antithrombin (rh AT) to Hereditary Antithrombin Deficient Patients in High-Risk Situations

**Inspection of clinical sites and outcome for GTC AT III 01002**

Study Site Number	Study Site	Location	Number of Subjects	Form FDA 483 Issued	Final Classification
81	Northwest Georgia Oncology Centers	Marietta , Georgia	02	No	EIR Pending
83	Children's Hospital Medical University of South Carolina	Charleston , South Carolina	01	No	EIR Pending

NAI – No Action Indicated, VAI – Voluntary Action Indicated, EIR – Establishment Inspection Report

#### **SPONSOR ISSUES**

No sponsor or monitoring issues were noted.

#### **INSPECTIONAL FINDINGS**

Clinical Investigator (CI) issues:

Study Site # 01-06: The inspection revealed no deviations from applicable federal regulations governing investigational drugs but the FDA investigator discussed two items at the conclusion of the inspection, including the importance of recording observations in ink and the importance of properly documenting any changes that are made to recorded observations so that accurate study records are maintained.

Study Site # 01-04: The inspection revealed no deviations from applicable federal regulations governing investigational drugs.

As of this date inspections have been completed for Study Site # 81, Northwest Georgia Oncology Centers, and Study Site # 83, Children's Hospital Medical University of South Carolina, but the Establishment Inspection Report (EIR) is pending. The Bioresearch Monitoring Branch has contacted the investigators who conducted each of these inspections and has obtained the following information:

Study Site # 81 : The inspection revealed no deviations from applicable federal regulations governing investigational drugs. No FDA 483 was issued.

Study Site # 83: The inspection covered informed consent, a comparison of source documents and CRFs, a comparison of the safety and efficacy assessments provided with the assignment to the data contained in the case report forms/source documents, in addition to the C.P. 7348.811 coverage requirements of protocol adherence, IRB approval and correspondence, sponsor correspondence, and test article accountability. The inspection found only one subject screened for the study. No objectionable conditions were found during the inspection. No FDA 483 was issued.

#### **BIMO ADMINISTRATIVE FOLLOW-UP**

Close out letters were issued to Study Site # 01-04 and Study Site # 01-06.

Correspondence will be issued to Study Site # 81 and Study Site # 83 after complete review of the establishment inspection reports and final classification.

Should you have any questions or comments about the contents of this memorandum or any aspect of Bioresearch Monitoring, please contact me at (301) 827-6335.

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Joseph P. Manik  
Consumer Safety Officer

**Return to**

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