



Memorandum

DATE November 19, 2025

FROM Jennifer Chan, PharmD, Consumer Safety Officer
Bioresearch Monitoring Branch (BMB)
Division of Inspections and Surveillance (DIS)
Office of Compliance and Biologics Quality (OCBQ)

THROUGH Kanaeko R. Sharp, MS, Chief BMB

THROUGH Carrie M. Mampilly, MPH, Director DIS

TO Sergey Akimov, PhD, Chair
Jennifer Dotson, DO, Clinical Reviewer
Fadi Nossair, MD, Clinical Reviewer
Candace Jarvis, RPM

SUBJECT Bioresearch Monitoring Final Discipline Review Memo
SPONSOR Grifols Therapeutics, LLC.
PRODUCT FESILTY (fibrinogen, human; BT524)
STN BLA 125833/0

FINAL SUMMARY STATEMENT

Bioresearch Monitoring (BIMO) inspections were issued for three foreign clinical investigator (CI) sites participating in the conduct of study Protocols 984 and 995. The inspections did not reveal significant issues impacting the data submitted in support of this Biologics License Application (BLA).

BACKGROUND

BIMO inspection assignments were issued for three foreign CI sites that participated in the study conduct of study Protocols 984 and 995. The sites were selected based on previous inspectional history, geographic location, and the data submitted in the BLA. The BLA review committee concurred with the sites selected for inspection. These inspections were conducted in accordance with FDA's Compliance Program (CP) 7348.811, Inspection Program for Clinical Investigators.

PROTOCOLS

Protocol 984: *A prospective, open-label, phase I/III study investigating pharmacokinetic properties of BT524 and efficacy and safety of BT524 in the treatment and prophylaxis of bleeding in patients with congenital fibrinogen deficiency*

Protocol 995: Randomized, Active-controlled, Multicenter, Phase III Study Investigating Efficacy and Safety of Intra-operative Use of BT524 (Human Fibrinogen Concentrate) in Subjects Undergoing Major Spinal or Abdominal Surgery (AdFlrst)

The inspection assignment included specific questions related to the study protocols, and information submitted in the BLA was compared to source documents at the clinical sites. Study 984 was conducted at six sites across Bulgaria, Egypt, Germany, and Tunisia, enrolling a total of 45 subjects in Parts 1 and 2 of the study combined. Study 995 was conducted at 15 sites across Czech Republic, Germany, Poland, Spain, Switzerland, and the United Kingdom, enrolling a total of 222 subjects. The three CI sites inspected in support of this BLA covered approximately 15% and 56% of the total study population enrolled in 984 and 995, respectively.

Note: Following the Late Cycle Meeting, the Sponsor withdrew the indication for BT524 as fibrinogen supplement in patients with acquired fibrinogen deficiency (AFD) from the application. As a result, the results of the two inspections in support of Protocol 995 were not included in the final BLA approval.

INSPECTION SUMMARY AND OUTCOME

The inspections verified the data reported in the BLA, including but not limited to subject eligibility, study drug administration, protocol deviations, and adverse events for the reviewed subjects enrolled at the inspected clinical site. No significant objectionable inspectional findings were observed during the inspections. The table below summarizes the BIMO inspections:

Protocol	Site ID	Study Site Name and Location	Form FDA 483 Issued?	Final Inspection Classification
984	12	Hôpital Aziza Othmana Service d'Hématologie Clinique Tunis, Tunisia 1004	No	No Action Indicated (NAI)
995	51	Fakultní nemocnice Královské Vinohrady Klinika Anesteziologie a Resuscitace Praha, Czech Republic 10034	Yes	Voluntary Action Indicated (VAI)
995	71	Hampshire Hospitals NHS Foundation Trust Basingstoke UK, RG24 9NA	No	NAI

Inspectional Findings:

The inspections did not reveal substantive issues that impact the data submitted in the BLA. However, the following issues were identified and shared with the BLA review committee:

- **Site 51:** A Form FDA 483 was issued at the close of the inspection for failure to maintain accurate case histories and failure to follow the protocol. Specifically, the source documentation for some subjects did not include information about adverse events (AEs) including causal relationship, severity, onset date, end date, and

outcome. Additionally, there were instances of underreported AEs, which were confirmed to have no impact on safety conclusions or benefit-risk assessment.

Sponsor Issues:

No significant sponsor issues were noted.

FINANCIAL DISCLOSURE

The CI CP directs the FDA investigators to ask the CI if and when he/she disclosed information about his/her financial interests to the sponsor and/or interests of any sub-investigators, spouses, and dependent children, and if and when the information was last updated. The information submitted to the BLA was verified at the inspected sites.

ADMINISTRATIVE FOLLOW-UP

No administrative follow-up is warranted at this time. Should you have any questions about the contents of this memo or any aspect of BIMO, please contact Jennifer Chan at (301) 348-1897.

Jennifer Chan, PharmD.
Consumer Safety Officer

DISTRIBUTION

Electronic Copies

CBER Connect BLA STN 125833/0

Sergey Akimov, PhD, Chair

Jennifer Dotson, DO, Clinical Reviewer

Fadi Nossair, MD, Clinical Reviewer

Candace Jarvis, RPM

Carrie M. Mampilly, MPH, Division Director, DIS

Kanaeko R. Sharp, MS, Chief, BMB

FDASubmissions@fda.hhs.gov

Gabrielle Swain, FDA Investigator

Dawn Olenjack, FDA Investigator

Lori Gioia, FDA Investigator

cberbimonotification@fda.hhs.gov

Chron file