Our STN: BL 125833/0

BLA APPROVAL
December 16, 2025

Grifols Therapeutics, LLC
Attention: Sharleen Xiong, PhD, RAC
Director, R&D Regulatory Strategy
79 TW Alexander Drive
4101 Research Commons, Research Triangle Park
Durham, NC 27709

Dear Dr. Xiong:

Please refer to your Biologics License Application (BLA) received December 27, 2024, submitted under section 351(a) of the Public Health Service Act (PHS Act) for fibrinogen, human–chmt.

LICENSING

We have approved your BLA for fibrinogen, human–chmt effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, fibrinogen, human–chmt under your existing Department of Health and Human Services U.S. License No. 1871. FESILTY is a human blood coagulation factor indicated for treatment of acute bleeding episodes in pediatric and adult patients with congenital fibrinogen deficiency, including hypo- or afibrinogenemia.

The review of this product was associated with the following National Clinical Trial (NCT) number: NCT02065882.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture fibrinogen, human–chmt at Biotest AG, Landsteinerstraße 3-5, 63303 Dreieich, Hesse, Germany, using cryoprecipitates manufactured at (b) (4) , and Grifols Therapeutics LLC., (b) (4) , USA. The diluent, sterile Water for Injections (sWFI), USP, will be manufactured at (b) (4) Nextaro v, 20/20 5 µm Transfer System will be manufactured at (b) (4) The co-packaged combination product, which contains one single-dose glass vial of the lyophilized fibrinogen, human-chmt drug product, one glass vial of 50 mL sWFI diluent, and one needleless Nextaro v, 20/20 5 µm Transfer System, will be assembled at Biotest AG, Landsteinerstraße 3-5,

63303 Dreieich, Hesse, Germany. You may label your product with the proprietary name FESILTY and market it in nominal dosage strength of 1g fibrinogen/vial.

ADVISORY COMMITTEE

We did not refer your application to the Blood Products Advisory Committee because our review of information submitted in your BLA, including the clinical study design and trial results, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

DATING PERIOD

The dating period for fibrinogen, human–chmt shall be 36 months from the date of manufacture when stored between 2°C and 30°C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The expiration date for the packaged product, FESILTY, fibrinogen, human-chmt, plus the diluent, sterile Water for Injection, shall be dependent on the shortest expiration date of any component.

FDA LOT RELEASE

Please submit final container samples of the product and each kit component in final containers together with protocols showing results of all applicable tests. You may not distribute any lots of product, until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

BIOLOGICAL PRODUCT DEVIATIONS

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to the Director, Office of Compliance and Biologics Quality, electronically through the eBPDR web application or at the address below. Links for the instructions on completing the electronic form (eBPDR) may be found on CBER's web site at https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/biological-product-deviations :

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

MANUFACTURING CHANGES

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of fibrinogen, human–chmt, in the manufacturing facilities.

LABELING

We hereby approve the draft content of labeling including the Package Insert submitted under amendment 68, dated December 15, 2025, and the draft package and container labels submitted under amendment 0 dated December 27, 2024 for the diluent, and under amendment 67, dated December 15, 2025, for the outer carton, inner carton, and vial.

WAIVER OF HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system, (eLIST) as described at Structured Product Labeling Resources | FDA. Content of labeling must be identical to the Package Insert submitted on December 15, 2025. Information on submitting SPL files using eLIST may be found in the guidance for industry SPL Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

PACKAGE AND CONTAINER LABELS

Please electronically submit final printed package and container labels identical to the package and container labels submitted on December 27, 2024, and December 15, 2025, according to the guidance for industry Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm333969.pdf.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125833 at the time of use and include implementation information on Form FDA 356h.

ADVERTISING AND PROMOTIONAL LABELING

You may submit proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

ADVERSE EVENT REPORTING

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and you must submit distribution reports as described in 21 CFR 600.81. For information on adverse experience reporting, please refer to the guidance for industry *Providing Submissions in Electronic Format —Postmarketing Safety Reports* at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-submissions-electronic-format-postmarketing-safety-reports and FDA's Adverse Event reporting System website at https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-electronic-submissions. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at https://www.fda.gov/vaccines-blood-biologics/lot-release/lot-distribution-database-ldd.

In addition, you must submit adverse event reports for any infectious disease transmission within 15 days after learning of the event. Infectious disease transmission refers to an adverse event that involves suspected or confirmed transmission of an infectious agent, whether the recipient develops the infectious disease or only has serologic or other evidence. If an infectious disease transmission event is serious and unexpected, you must submit a 15-day "alert report," as required under 21 CFR 600.80 (c)(1)(i). Infectious disease transmission events that do not meet criteria for expedited submission require periodic reports and must be submitted as individual safety case reports within 15 days, as authorized under 21 CFR 600.80(c)(2)(i). You should submit

reports for all other non-expedited adverse events under the periodic reporting requirements specified in 21 CFR 600.80(c)(2).

For information on the postmarketing safety reporting requirements for combination products as described in 21 CFR 4, Subpart B, and the dates by which combination product applicants must comply with these requirements, please refer to the Postmarketing Safety Reporting for Combination Products webpage available at https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products.

PEDIATRIC REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

This product is appropriately labeled for use in ages 0 to 18 years for this indication. Therefore, no additional studies are needed in this pediatric group.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We acknowledge your written commitments as described in your letters of November 20, 2025, November 26, 2025, December 3, 2025, and December 10, 2025, as outlined below:

1. Grifols commits to conduct a leachables risk assessment ((b) (4) for the Drug Product (DP) using actual DP lots (b) (4) PPQ lots: (b) (4)) to be tested in the ongoing stability study. This assessment will cover storage at 25°C for the 36-months DP shelf life. In this study, for DP reconstitution, actual diluent supplied in the kit and aged to not less than the DP at the respective time point will be used. The reconstituted DP will be held in the Nextaro Transfer Device under in-use (clinical preparation) conditions at maximal hold time and temperature until sample preparation and analysis.

   The final results will be submitted as a “Postmarketing Study Commitment - Final Study Report”.

   Final Study Report Submission: February 29, 2028

2. Grifols commits to complete validation of the (b) (4) assay, according to (b) (4) , as a reference method for Fibrinogen (b) (4) determination in FESILTY Drug Product to be used on stability testing, in addition to the

(b) (4) assay. Grifols also commits to update SOP-Q-00227 with description of verification of the (b) (4) results for Fibrinogen (b) (4) by the (b) (4) method in stability studies.

The Method Validation Report and updated SOP-Q-00227 will be submitted as a Prior Approval Supplement (PAS) titled as a "Postmarketing Study Commitment" – Final Study Report to fulfill the commitment by March 31, 2026.

Prior Approval Supplement Submission: March 31, 2026

3. Grifols commits to:

   a. Develop and validate a calibration model based on the statistical advice in the FDA Information Request dated October 28, 2025. For the calibration model validation, (b) (4)). The validation will determine where the model applies "as suitable for the circumstances" and specify situations requiring model (b) (4) with the reference method.

      The results of this development and validation will be submitted to FDA for review prior to starting method validation as a "Postmarketing Study Commitment – Status Update" by March 2, 2026.

   b. Validate the (b) (4) method as a quantitative method for the determination of (b) (4) for release and stability testing of FESILTY Drug Product. The method validation will be performed according to (b) (4) , including assay specificity, linearity, precision (repeatability and intermediate precision), limits of quantitation, accuracy, and robustness. The method validation will be conducted using a (b) (4) assay suitability and performance.
      The Method Validation Protocol will be submitted to FDA for review prior to starting method validation as a "Postmarketing Study Commitment – Status Update" by March 2, 2026.The Method Validation Report will be submitted as a Prior Approval Supplement (PAS) titled as a "Postmarketing Study Commitment – Final Study Report" to fulfill the commitment by May 31, 2026.

      Prior Approval Supplement Submission: May 31, 2026

4. Grifols commits to revise Qualification Report BE-232-24/00 "Control sample establishment of Fibrinogen Concentrate (BT524) for SOP-Q-00438" dated

November 14, 2025. The revised version of the Report will include the following sections:

a. Preparation
b. Characterization/Qualification with predefined Acceptance Criteria
c. Qualification of the in-house Fibrinogen control sample (reference sample) Lot (b) (4) for determination of Fibrinogen (b) (4) using the current (b) (4) as control.
d. Stability Program/Storage of the in-house reference material.

The submission will also include a Qualification Protocol for implementation of future lots of the in-house Fibrinogen control sample (reference sample).

The updated Qualification Report BE-232-24/00 and the Qualification Protocol will be submitted as a Prior Approval Supplement titled "Postmarketing Study Commitment – Final Study Report" to fulfill the commitment by March 31, 2026.

Final Study Report Submission: March 31, 2026

5. Grifols commits to update the Use-Related Risk Analysis (URRA) based on the Human Factor Advice in FDA Information Request dated November 26, 2025, to appropriately capture the clinical impact associated with identified use errors or task failures.

   The updated URRA will be submitted as "Postmarketing Study Commitment – Final Study Report" to fulfill the commitment by February 28, 2026.

   Final Report Submission: February 28, 2026

We request that you submit information concerning nonclinical and chemistry, manufacturing, and control postmarketing commitments and final reports to your BLA, STN BL 125833. Please refer to the sequential number for each commitment.

Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Status Update**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment – Final Study Report**

For each postmarketing commitment not subject to the reporting requirements of 21 CFR 601.70, you may report the status to FDA as a **Postmarketing Commitment – Status Update**. The status report for each commitment should include:

- the sequential number for each study as shown in this letter;
- the submission number associated with this letter;
- describe what has been accomplished to fulfill the non-section 506B PMC; and,
- summarize any data collected or issues with fulfilling the non-section 506B PMC.

When you have fulfilled your commitment, submit your final report as **Postmarketing Commitment – Final Study Report** or **Supplement contains Postmarketing Commitment – Final Study Report**.

POST APPROVAL FEEDBACK MEETING

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, please contact the Regulatory Project Manager for this application.

Sincerely,

For
Asha Das, MD
Acting Director
Office of Clinical Evaluation
Office of Therapeutic Products
Center for Biologics Evaluation and Research