



Our STN: BL 125640/0

BLA FILING NOTIFICATION

January 2, 2017

Instituto Grifols, S.A.
Attention: Joan Robertson
Vice President, Regulatory Affairs
Grifols Shared Services North America, Inc.
8368 U.S. Highway 70 West
Clayton, NC 27520

Dear Ms. Robertson:

This letter is in regard to your Biologics License Application (BLA) submitted under section 351 of the Public Health Service Act.

We have completed an initial review of your application dated November 03, 2016, for Fibrin Sealant (Human) to determine its acceptability for filing. Under 21 CFR 601.2(a) we have filed your application today. The review classification for this application is Standard. Therefore, the review goal date is November 03, 2017. This acknowledgment of filing does not mean that we have issued a license nor does it represent any evaluation of the adequacy of the data submitted.

We are reviewing your application according to the processes described in the *Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products*. Therefore, we have established internal review timelines as described in the guidance, which include the time frames for FDA internal milestone meetings. We plan to hold our internal mid-cycle review meeting on April 13, 2017. Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process.

We will contact you regarding your proposed labeling no later than October 05, 2017. If postmarketing study commitments (506B) are required, we will contact you no later than October 05, 2017.

We are not currently planning to hold an advisory committee meeting to discuss this application.

While conducting our filing review, we identified the following potential review issues:

Chemistry, Manufacturing, and Controls (CMC)

1. We acknowledge your commitments to the following:
 - a. To submit the Design History File including all elements as per 21 CFR 820.30 and Design Control data for your combination product by February 15, 2017 (with reference made to the December 12, 2016, Amendment).
 - b. To provide two additional lots of Fibrin Sealant (Human) Finished Drug Product (FDP) and their lot release data for CBER's in-support testing by Week 16 to Week 18 of 2017 (with reference made to the December 07, 2016, teleconference and December 23, 2016, Amendment).
2. Please submit the following information:
 - a. A consolidated list of all FDP lots manufactured to date and their use (e.g., developmental, preclinical, clinical, and process validation) with respective clinical and preclinical study numbers.
 - b. Description of changes in the manufacturing process, from material used in clinical trials to commercial production lots.
 - c. Summary information on Hold times during the manufacturing process, if any, and their validation.
 - d. Description and validation of the analytical methods which were used for viral safety and immunogenicity testing in clinical studies. Please include information on the laboratories where clinical laboratory tests were performed.
 - e. Overall CTD Table of Contents for eCTD Section 2.1 and Section 3.1. In Section 3.1, please include a guide to the location of specific information within Module 3.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our complete review. Issues may be added, deleted, expanded upon, or modified as we review the application. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application. Following a review of the application, we shall advise you in writing of any action we have taken and request additional information if needed.

If you have any questions, please contact the Regulatory Project Manager, Yu Do, at (240) 402-8343 or Yu.Do@fda.hhs.gov.

Sincerely,

Wilson W. Bryan, MD
Director
Office of Tissues and Advanced Therapies
Center for Biologics Evaluation and Research