

From: Do, Yu
To: Joan.robertson@grifols.com
Subject: Information Request (Response Due by Friday, September 8, 2017): Original BLA, BL 125640/0, Fibrin Sealant (Human), Instituto Grifols, S.A.
Date: Monday, August 07, 2017 9:42:00 AM
Attachments: [image001.png](#)
Importance: High

Dear Ms. Robertson:

We are reviewing your original November 3, 2016, submission to BLA 125640 for Fibrin Sealant (Human). We determined that the following information is necessary to continue our review:

1. Please provide the down-scale factor relative to the commercial-scale process in each of the viral clearance studies, and demonstrate that the scale-down studies are representative of commercial manufacturing.
2. Viral clearance studies for column chromatography need to be performed with fresh resins as well as resins that have been used for the specified maximum number of cycles. Please specify the number of cycles for the resins used in viral clearance studies *IG_ISVR-000156_ING* and *IG_ISVR-000161_ING*. If these studies were performed with fresh resins only, please submit results from studies performed using resins that have undergone the maximum number of cycles for the clearance of relevant and model viruses.
3. Please confirm if the (b) (4) test is used in post-use integrity test for the (b) (4) 35N/20N nanofilters used in the manufacture of human fibrinogen, and for the (b) (4) 15N nanofilters used in the manufacture of human thrombin.

The review of this submission is ongoing, and issues may be added, expanded upon, or modified as we continue to review this submission. Please submit your response as an amendment to this file by September 8, 2017, referencing the date of this request. If you anticipate you will not be able to respond by this date, please contact the Agency immediately so a new response date can be identified.

If we determine that your response to this information request constitutes a major amendment, we will notify you in writing.

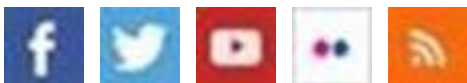
The action due date for this file is November 3, 2017.

Please acknowledge receipt of this request and contact me at (240) 402-8343 or Yu.Do@fda.hhs.gov if you have any questions.

Sincerely,

Yu Do, M.S.
Regulatory Project Manager
Office of Tissues and Advanced Therapies
Center for Biologics Evaluation and Research

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