

From: Do, Yu
To: Joan.robertson@grifols.com
Subject: Information Request (Response Due by Monday, February 27, 2017): Original BLA, BL 125640/0, Fibrin Sealant (Human), Instituto Grifols, S.A.
Date: Monday, February 06, 2017 11:33:00 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 qualification data to support package integrity and seal strength of the blisterpak packaging. Please note that this testing should be performed on the blisterpak after all final packaging activities and after freezing of the final packaged product.
2. Please provide (or indicate location in submission) details and results of the filling process for fibrinogen and thrombin manufacturing. These details should include a listing of the critical process parameters that are monitored during filling (i.e., (b) (4) [REDACTED]) and the acceptance criteria that ensure consistency in the filling process.
3. Please provide a listing of all product contact equipment used in the Fibrin Sealant (Human) manufacturing process and indicate if the equipment is shared vs. dedicated and/or disposable. For shared and/or dedicated equipment, please indicate the cleaning method and/or sterilization method used if applicable.
4. Please provide details with regard to the preparation of the glass syringes and stoppers prior to (b) (4) sterilization. Additionally, please indicate how the glass syringes are depyrogenated and if endotoxin testing is performed on the glass syringes and stoppers.
5. Please indicate the IQ status and provide summaries (in English) of the OQ/PQ of the following equipment:
 - (b) (4) [REDACTED]
 - (b) (4) [REDACTED]
 - (b) (4) [REDACTED]
 - (b) (4) [REDACTED]
 - Syringe filling machine (b) (4) [REDACTED]
 - Syringe feeding machine (b) (4) [REDACTED]
 - Syringe labeling machine (b) (4) [REDACTED]
 - (b) (4) [REDACTED]
 - (b) (4) [REDACTED]
 - Sterilizer equipment (b) (4) [REDACTED]

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 February 27, 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.

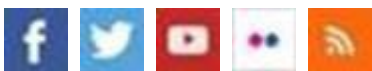
If we determine that your response to this information request constitutes a major amendment, we will notify you in writing.

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
Office of Medical Products and Tobacco
Food and Drug Administration
(240) 402-8343
Yu.Do@fda.hhs.gov



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