

From: Do, Yu
To: Joan.robertson@grifols.com
Subject: Information Request (Response Due by Friday, August 18, 2017): Original BLA, BL 125640/0, Fibrin Sealant (Human), Instituto Grifols, S.A.
Date: Thursday, August 03, 2017 10:47:00 AM
Attachments: [image001.png](#)
(b) (4) [CBER Template-05-2012.doc](#)
(b) (4) [Endpoint_CBER Template.doc](#)
Importance: High

Dear Ms. Robertson:

We are reviewing your original November 3, 2016, submission to BLA 125640 for Fibrin Sealant (Human). We have the following comments and requests for additional information to continue our review:

Please revise your Lot Release Protocol template to address the comments stated below:

1. On page 1, please structure the section “Summary of the History of Manufacture” as follows and verify the proposed definitions with your definitions of Total Filling Time and Total Processing Time, including their time limits:
 - Human Fibrinogen Lot Number
 - Human Thrombin Lot Number
 - Sterile Filtration/Filling Date
 - Total Filling Time
 - Total Filling Time is defined as the time from the beginning of Thrombin sterile filtration to the last Fibrinogen syringe filled and includes sterile filtration and filling of both components. Total Filling Time should not exceed (b) (4).
 - Total Processing (Filling + Packaging) Time
 - Total Processing (Filling + Packaging) Time is defined as the time from the beginning of Thrombin sterile filtration to the freezing of the last Fibrin Sealant (Human) kit. Total Processing Time should not exceed (b) (4).
 - Volume
 - Number of kits manufactured
 - Number of kits rejected
 - Number of kits intended for market release
 - Storage temperature
2. On pages 1, 2, and 3 of 3, please add cc line at the top of every page (i.e., cc: STN/License No. -C, -B, or -FC).
3. On pages 1, 2, and 3 of 3, please remove trade name from the Licensed Name of Product. Only the proper name “Fibrin Sealant (Human)” should be written on that line.
4. On page 2 of 3, please remove the trade name VERASEAL from the statement under Final Container Analysis.

5. On pages 2 and 3 of 3, under Fibrin Sealant, Fibrinogen Component, and Thrombin Component, please add a column “Test Date” for each test.
6. On page 2 of 3, under Fibrinogen Component, please insert space after (b) (4), Appearance of Frozen Product, Appearance of Solution (After Thawing), and Identification for better readability.
7. On pages 2 and 3 of 3, under Fibrinogen and Thrombin Components, please update specification for the Appearance of Solution (After Thawing) as follows: “Colourless or pale yellow solution, essentially free of particles” [refer to July 5, 2017, submission (Amendment 33)].
8. On page 2 of 3, under Fibrinogen Component for (b) (4), TNBP, and Polysorbate 80 specifications, please replace <= with = . For Volume specification, please replace >= with respective ranges for each fill size [refer to July 5, 2017, submission (Amendment 33)].
9. On page 3 of 3, under Thrombin Component for TNBP and Polysorbate 80 specifications, please replace <= with = . For Volume specification, please replace >= with respective ranges for each fill size [refer to July 5, 2017, submission (Amendment 33)].
10. On page 2 of 3, under Fibrinogen Component for TNBP, Polysorbate 80, Volume, and Endotoxins, please replace “ml” with “mL” for consistency.
11. On page 3 of 3, under Thrombin Component for Thrombin, Albumin, Glycine, TNBP, Polysorbate 80, Volume, and Endotoxins, please replace “ml” with “mL” for consistency.
12. On page 2 of 3, under Fibrinogen Component, please provide detailed results for Sterility for (b) (4) Final Container in a similar manner to that of the Thrombin Component data. In addition, please add “Result” and “Specification” in the sterility template, and state a method type (i.e., USP 88 or 21 CFR 610).
13. On pages 2 and 3 of 3, under Fibrinogen and Thrombin Components for Endotoxins, please add detailed results, using the attached CBER (b) (4) templates.
14. On page 3 of 3, for Sterility please provide a method type (i.e., USP 88 or CFR 610). Also, please add “Result” and “Specification” in the template.
15. On page 2 of 3, under Fibrinogen Component, please add the parameter “Total Protein” and its respective specification [refer to July 5, 2017, submission (Amendment 33)].
16. On page 3 of 3, please remove the General Safety table [refer to July 5, 2017, submission (Amendment 33)].

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 August 18, 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.
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Office of Medical Products and Tobacco
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