

From: Do, Yu
To: Joan.robertson@grifols.com
Subject: CORRECTION: Information Request (Response Due by Monday, September 18, 2017) - Original BLA, BL 125640/0, Fibrin Sealant (Human), Instituto Grifols, S.A.
Date: Tuesday, August 29, 2017 4:12:00 PM
Attachments: [image001.png](#)
Importance: High

From: Do, Yu
Sent: Tuesday, August 29, 2017 4:04 PM
To: Joan.robertson@grifols.com
Subject: Information Request (Response Due by Friday, September 18, 2017): Original BLA, BL 125640/0, Fibrin Sealant (Human), Instituto Grifols, S.A.
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:

Fibrinogen and Thrombin Components

- Determination of Tri-n-Butyl Phosphate (TNBP) by (b) (4)

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1. Regarding the Method validation reports for the determination of TNBP in fibrinogen product (Document IG_IVMA-000261_ING) and thrombin product (Document IG_IVMA-000237_ING):

- In your method validation for the TNBP assay, the range of the assay as based on linearity, accuracy, and precision results is (b) (4) for fibrinogen product and (b) (4) for thrombin product. Since TNBP is present as an impurity in your product, it is critical to have an assay range that includes the upper specification limit of (b) (4). Please provide linearity and accuracy from fibrinogen and thrombin samples to show that TNBP can be quantitated at the proposed upper specification limit of the assay.

Fibrinogen Component only

- Determination of Glutamic Acid, Glycine, Arginine, and Isoleucine by (b) (4)

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2. Regarding the Method validation report, Document IG_IVMA-FGD1358C_ING:

- In your (b) (4) assay for the quantitation of amino acids, glycine is measured as an impurity. Therefore, during the study of validation characteristics, it is critical to include the data point at the defined specification limit of (b) (4). As mentioned in our Information Request dated July 10, 2017, please provide the requested data to permit a complete review of your assay.

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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 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.

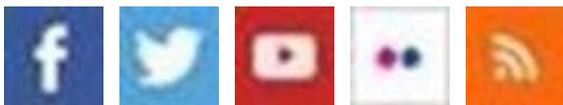
If we determine that your response to this information request constitutes a major amendment, we will notify you in writing.

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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