

From: Do, Yu
To: Joan.robertson@grifols.com
Subject: Information Request (With Response Due Date TBD): Original BLA, BL 125640/0, Fibrin Sealant (Human), Instituto Grifols, S.A.
Date: Monday, August 28, 2017 3:37:00 PM
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 have the following comments and requests for additional information to continue our review:

1. You have stated in your Human Factors study conducted in February 2017 that “there were some comments/suggestions to packaging (the outer pouch is difficult to open completely) and involving the Instructions for Use, mainly related to the product preparation (thawing time and cannula connection instructions), recorded during the evaluations.” (p. 20). In particular, all of the participants had comments to improve the step, “Connection operations are adequately described in preparation instructions.” Some of the participants also did not agree that the “thawing procedure is clear and easy to understand.” These steps are critical for the effectiveness of the device and thus for the timeliness of patients in critical condition receiving treatment. Please evaluate possible improvements to the labeling and/or instructions for use that would provide useful details for the user to complete these tasks with less difficulty or confusion. For example, you may use explanatory figures that show the different connection steps, and clarify the thawing procedure instructions (“immediately” should be defined). Please implement these changes and include the revised final IFU and labeling materials in your new Human Factors study.
2. Your new Human Factors study should address the following:
 - Recruit at least 15 clinicians to be participants in your study.
 - Describe what training, if any, will be provided to the participants.
 - Describe the use environment that participants are expecting to encounter (e.g., dim lighting, multiple alarm conditions, distractions, and multi-tasking).
 - Challenge each participant's understanding of each contraindication and warning in a knowledge-based test.
 - Provide an analysis of known use problems with your predicate device or devices with similar user interfaces. The findings from this analysis would feed into your use-related risk analysis and ensure that you have done a thorough risk analysis.
 - Describe the severity levels used in your use-related risk analysis in detail.

Please provide your complete UFMEA document and present the criteria that you used to identify the critical tasks (should be based only on severity and not occurrence levels).

- Include a subjective assessment portion, testing the participants using open-ended questions. Some examples include, “what did you think of the device overall?” and “Was anything confusing or did you have any trouble using the device? If so, what?”.
- Perform root cause analysis on all instances of failures, close-calls, and difficulties in performing critical tasks.

To save on resources, it may be in your best interest to consider running your new Human Factors study along with your planned pediatric clinical study

The review of this submission is ongoing, and issues may be added, expanded upon, or modified as we continue to review this submission. The due date for response will be determined based on discussion during the August 31, 2017, Late-Cycle Meeting.

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,

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