



Human Factors (HF) Consult Memo

Consult Number: N/A – Interactive Review
Document Number: ICC1600853; BL 125640/0
Applicant: Grifols
Trade Name: Fibrin Sealant Grifols
Consult Type: Human Factors
Requestor: Rong Guo [RONG.GUO]
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Requested Consultant: N/A
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Consultant Home: CDRH\ ODE\ DAGRID\ HFPMET
Date Requested: 10/27/2017
Due Date: 11/01/2017
Instructions: HF/U Protocol Review during interactive (CBER)
Indications for use: *VeraSeal is a fibrin sealant (human) indicated as an adjunct to hemostasis for mild to moderate bleeding in adults (b) (4) undergoing surgery when control of bleeding by standard surgical techniques (such as suture, ligature, and cautery) is ineffective or impractical. VeraSeal is effective in heparinized patients.*
Key considerations for conducting a HF review: ICC/Q-SUB – Are there specific sponsor questions to be addressed?

Date consult sent: October 27, 2017

HF Recommendation: Please see below the comments to be communicated to the sponsor.

HF Consult Response to communicate to sponsor

Comment 1.

Based on your submitted Human Factors/Usability (HF/U) validation protocol of conducting your test in a simulated use environment and based on your proposed timeline, it appears that you intend to conduct the HF/U study separate from the planned pediatric clinical trial instead of as a subpart to the pediatric clinical trial as was previously agreed to. However, conducting your HF/U study separately may result in classification of this test to be a second Post-Market Requirement (PMR). Therefore, we recommend that you conduct a staged HF/U study that follows the phases of the pediatric clinical trial. For example, Phase/Stage 1 would include your HF/U test in a simulated use environment, while Phase/Stage 2 would include your final HF/U test in an actual use environment, incorporating, if any, relevant mitigations incorporated based on your Phase 1 results.

Comment 2.

You have provided in Table 4 (IG_PETC-000430_ING v1.pdf, pgs. 10-11) a table of use-related hazards along with their assessed severity levels. You have also stated in Table 5 (pgs. 12-13) that the majority of your critical tasks are mitigated by the Instructions for Use. However, in your test plan and Predetermined Surveys (Annex 1



and Annex 2), you do not directly test the user's comprehension of these critical tasks. As an example to facilitate your understanding, the third line in Table 4 (pg. 10) states that "thawing temperature exceeding 37°C" would cause "fibrin clot incorrectly formed." However, it does not appear that you test this critical task in your protocol. The agency requests in the 2016 Human Factors Guidance that those critical tasks that cannot be assessed by simulated use testing should be assessed via knowledge-based comprehensive tasks, so that all critical tasks may be appropriately assessed. Please provide an updated HF/U study plan that includes knowledge-based comprehensive tasks that will appropriately challenge user understanding of relevant critical tasks.

Comment 3.

You have stated that, "the study will involve at least 10 nurses (Group 1) and 10 surgeons (Group 2) according to their different roles in performing critical tasks correctly for use the product in a safe and effective manner" (pg. 7). The agency requests in the 2016 Human Factors Guidance that if the device has more than one distinct population of users, then the validation testing should include at least 15 participants from each user population. The FDA views user populations as distinct when their characteristics would likely affect their interactions with the device or when the tasks they perform on the device would be different. As it appears that surgeons and nurses will have different roles in performing critical tasks, please plan to recruit and test at least 15 nurses and 15 surgeons.

Comment 4.

You have provided a description of the training and study overview that you plan to provide to your HF/U participants, which will include "a study presentation with chart-diagrams of product preparation..." (IG_PETC-000430_ING v1.pdf, pg. 7). However, it is unclear whether this study presentation will correspond to real-world training expectations. The 2016 Human Factors Guidance states that "the training provided to the human factors validation test participants should approximate the training that actual users would receive" so that study results will be as accurate as possible. Please describe whether your planned training and study overview will be real-world representative and if not, modify your HF/U protocol to reflect expected training practices.

Additional Comment.

Current Agency guidance applying human factors and usability engineering to medical devices can be found at: <http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm259760.pdf>



Reviewers Notes

Regulatory/Interaction History

See HF Consult History

Device Description

See HF Consult History

HF Activities

INTENDED USERS, USES, USE ENVIRONMENTS & TRAINING

From IG_PETC-000430_ING v1.pdf, pg. 7:

6.2 INTENDED DEVICE USERS

At least 20 Health Care Professionals (HCP) will participate in the study. The end-user will operate FS Grifols to evaluate the usability of the Medical Device (MD) according to the IFU. The study will involve at least 10 nurses (Group 1) and 10 surgeons (Group 2) according to their different roles in performing critical tasks correctly for use the product in a safe and effective manner. Nurses are in charge of preparing the kit and will evaluate the usability from initial package through thawing, preparation, transferring to the sterile field and cannula connection. Surgeons will evaluate usability of the product through application of the FS Grifols by both drip and spray methods.

The name of the end-user, affiliation and date of evaluation will be recorded in the usability report.

6.3 USE ENVIRONMENTS

It is intended that the FS Grifols Kit be used in a clinical setting and in a sterile field. A simulated used environment will be used to evaluate FS Grifols. In order to simulate as close as possible to clinical use, working teams will be formed by one person of each group (nurse and surgeon) to proceed with the evaluation of the product following IFU. The nurse will proceed with the preparation and handling and transfer the kit to the surgeon for its application in simulated-operation room.

The centers involved in the study of human factors study will be the same ones that participate in the pediatric clinical trial, so it faithfully reproduces the environment of real work zones, lighting, sound, alarms, etc.

6.4 TRAINING AND STUDY OVERVIEW

A study presentation with chart-diagrams of product preparation, handling, and administration tasks will be provided. The IFU will be supplied to each end-user before proceeding with the evaluation. The presentation documentation will be recorded in the final usability report.



Reviewer Analysis/Comments:

You have stated that, "the study will involve at least 10 nurses (Group 1) and 10 surgeons (Group 2) according to their different roles in performing critical tasks correctly for use the product in a safe and effective manner" (pg. 7). The agency requests in the 2016 Human Factors Guidance that if the device has more than one distinct population of users, then the validation testing should include at least 15 participants from each user population. The FDA views user populations as distinct when their characteristics would likely affect their interactions with the device or when the tasks they perform on the device would be different. As it appears that surgeons and nurses will have different roles in performing critical tasks, please plan to recruit and test at least 15 nurses and 15 surgeons.

You have provided a description of the training and study overview that you plan to provide to your HF/U participants, which will include "a study presentation with chart-diagrams of product preparation..." (IG_PETC-000430_ING v1.pdf, pg. 7). However, it is unclear whether this study presentation will correspond to real-world training expectations. The 2016 Human Factors Guidance states that "the training provided to the human factors validation test participants should approximate the training that actual users would receive" so that study results will be as accurate as possible. Please describe whether your planned training and study overview will be real-world representative and if not, modify your HF/U protocol to reflect expected training practices.

USER INTERFACE

Pg. 6:

5.7 INSTRUCTIONS FOR USE (IFU)

The IFU of FS Grifols will inform to the end-user of the medical device's intended purpose, proper use and of any precautions to be taken. It mainly contains information about the following particulars: indications and usage, dosage forms, contraindications, warnings and precautions, preparation and handling (thawing conditions, assembly device preparation before use), administration (drip or spray) and application precaution.

Reviewer Analysis/Comments: There have been many interactions with the labeling teams to improve the IFU based on the sponsor's last HF/U study results. The upcoming HF/U study(ies) will test the new IFU.

KNOWN USE PROBLEMS, FORMATIVE, IDENTIFICATION OF CRITICAL TASKS

Pgs. 8-13:



7. KNOWN USE PROBLEMS

A review of device failures for similar products (Tisseel[®] and Evice1[®]) were identified from the U.S. Food and Drug Administration’s Medical Device and User Facility Device Experience (MAUDE) database (<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/search.cfm>) (Table 1).

TABLE 1
Known incidents of similar devices

Report number	Event date	Event type	Device failure type
6746501	2017/07/14	Malfunction	Error in preparation

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8. FORMATIVE HUMAN FACTORS STUDIES

Users’ comments/suggestions of previous human factor studies (IG ITEC-002747_ING. Fibrin Sealant. Usability and IG ITEC-002779_ING. Fibrin Sealant Grifols: Usability) are included in Table 2.

TABLE 2
Identified suggestions

User’ comments/suggestions	Potential event type	Potential device failure type
Spillage of product in the transfer from nurse to the surgeon	Malfunction	Decreased dose administered
Difficulty to open the outer pouch	Malfunction	Delay of the administration
More detailed instructions or explanatory figures for the different connection steps	Malfunction	Applicator would not dispense
Clear information about the state “FS Grifols should be used immediately” once thawed	Operational misunderstanding	Applicator would not dispense

Taking into account user’s comments/suggestions shown in Table 2, a revised version of IFU is being generated that includes improvements to the instructions for use to provide greater clarity and to avoid areas of confusion that were previously identified. This revised final IFU will be used in the human factors study as outlined in this protocol. The IFU will be included in the final report with all the results, comments, suggestions of the HCP and a detailed evaluation of these observations will be performed.

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TABLE 3
Severity level

Severity level	Description and potential clinical impact
Catastrophic (S1)	Injury to the patient
Critical (S2)	Loss of efficacy of the product
Marginal (S3)	Allergic reactions due to the product
Negligible (S4)	Kit unsuitable for use. Need of another kit or procedure applied to stop the loss of blood

Use-related hazards identified are shown in Table 4.

TABLE 4
Use-related hazards

Severity level	Risk analysis identifier	Potential cause of failure	Potential effect of failure
S4	RA-990	Storage conditions outside of the prescribed ones	Kit unsuitable for use
S2	RA-985	Inappropriate thawing method	Fibrin clot incorrectly formed
S2	RA-987	Thawing temperature exceeding 37 °C	Fibrin clot incorrectly formed

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TABLE 5
Risk analysis

Critical task	Potential use error(s)	Description of harm (Clinical impact)	Level	Mitigations
Check storage conditions	Expired kit	Kit unsuitable for use	S4	Instructions for use
Open packaging	Damage to device	Delay of administration. Unusable kit	S4	Instructions for use
	Difficulty to open			
	Loss of instructions or components			
Thaw product	Inappropriate thawing method	Fibrin clot incorrectly formed; loss of efficacy	S2	Instructions for use
	Time to thaw exceeded			
	Temperature to thaw exceeded			
	Product not totally thawed	Delay in administration	S4	Instructions for use
	Product removed from the outer pouch before thawing			

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Critical task	Potential use error(s)	Description of harm (Clinical impact)	Level	Mitigations
Cannula connection	Inability to connect	Delay of administration	S4	Instructions for use
	Use of non-recommended tip applicators	Reduced efficacy	S2	Tip packaged with the device. Instructions for use
Administration to targeted tissue	Use the product disassembled	Unusable kit	S4	Instructions for use
	Unable to depress plunger	Unusable kit	S4	Product requirement specification (force of application) (b) (4)
	Intravascular application	Thromboembolic complications	S1	Instructions for use
Spray delivery	Spray the product at lower than the recommended distance	Potential air or gas embolism	S1	Instructions for use
	Sprays the product at higher than the recommended pressure			
	Sprayed the product with air			
	Spray the product at lower than the recommended pressure	Reduced efficacy	S2	Instructions for use
	Spray the product at a higher than the recommended distance			

Reviewer Analysis/Comments: I contacted Dr. Agnes Lim, the clinician on this file, and she agrees that any risk that could cause loss of efficacy of the product (sponsor’s defined severity level S2), should also be considered a critical task in addition to S1 tasks, and evaluated accordingly.

You have provided in Table 4 (pgs. 10-11) a table of use-related hazards along with their assessed severity levels. You have also stated in Table 5 (pgs. 12-13) that the majority of your critical tasks are mitigated by the Instructions for Use. However, in your test plan and Predetermined Surveys (Annex 1 and Annex 2), you do not directly test the user's comprehension of these critical tasks. As an example to facilitate your understanding, the third line in Table 4 (pg. 10) states that "thawing temperature exceeding 37°C" would cause "fibrin clot incorrectly formed." However, it does not appear that you test this critical task in your protocol. The agency requests in the 2016 Human Factors Guidance that those critical tasks that cannot be assessed by simulated use testing should be assessed via knowledge-based comprehensive tasks, so that all critical tasks may be appropriately assessed. Please provide an updated HF/U study plan that includes knowledge-based comprehensive tasks that will appropriately challenge user understanding of relevant critical tasks.



HF VALIDATION STUDY PROTOCOL & METHOD

Pgs. 13-15:

10 ANALYSIS AND EVALUATIONS

10.1 MEASURES

Our measurement plan includes the human factor triad of measurements-performance, behavior, and subjective experience.

During each session, observers will follow the performance and behaviors of each participant. Success, failure, errors, confusions, and other indices of mal-interaction that could result in incorrect use of the device will be recorded. Participants will be also actively interviewed to provide a subjective narrative of their experience, any difficulties they experienced, and their opinions of the device and instructional materials.

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Pg. 17:

2. Subjective assessment:

What do you think of the device overall?

Did you have any problem(s) using it? If yes, what kind of problem(s) did you have?

Was anything confusing? If yes, what was confusing?

Reviewer Analysis/Comments: See above for comment regarding knowledge-based comprehensive tasks.



Materials Reviewed

- IG_PETC-000430_ING v1.pdf

End of Review

Consultant

Concurrence



Appendix: HF Consult History

ICC1600853, CON178638

Date: May 29, 2017

Consultant: Rita Lin

HF Consult Response to communicate to sponsor

Deficiency 1:

You have provided your list of “parameters” (Table 2, Protocol). However, the criteria you have used to choose your critical tasks is not clear. Of note, since it is difficult to estimate probability of occurrence accurately in the premarket stage, you should use severity level alone to identify the critical task associated with the subject device. Please 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. If there are no critical tasks associated with the subject combination product, then you can provide the use-related risk analysis results as justification for not including Human Factors data as a part of the pre-market submission.

- a. In your list of “parameters,” you have listed a few prompts that should be evaluated by use testing or knowledge tasks and not by self-evaluation. For example, “contraindications and warnings are clearly described” and “connection operations are adequately described in preparation instructions” do not give any evidence that objectively, the contraindications and warnings are clear and that the steps are adequately described. If these are critical tasks, they should aim to challenge the user’s knowledge and/or ability to locate the information. Please provide in more detail if this and like tasks will be evaluated via use testing, through knowledge test, or other applicable test. If appropriate, please conduct additional HF/U testing.

Deficiency 2:

You have recruited 5 surgeons for your final HF/U validation study. However, FDA guidance states that a minimum of 15 participants per distinctive user group should be included in the HF validation study. Please adjust your protocol to include a minimum of 15 participants per distinctive user group and conduct additional HF/U testing as required.

Deficiency 3:

You did not describe in detail the planned training provided to the test participants, including the content and delivery modes and the length of time that will elapse prior to testing (decay window). Because retention of training decays over time, testing should not occur immediately following training; some period of time should elapse. Please provide a description of the planned training, if any, including content and delivery modes.

Deficiency 4:

Human Factors Consult Memo | page i of Appendix



Appendix: HF Consult History

Under your Objective section, you have stated that you plan to analyze the usability of the combination product regarding the intended uses “under the expected working conditions.” However, you have not described what are the “expected working conditions.” The conditions under which simulated-use HF/U validation testing is conducted should be sufficiently realistic so that the results of the testing are generalizable to actual use. The need for realism is therefore driven by the analysis of risks related to the device’s specific intended use, users, use environments, and the device user interface. To the extent that environmental factors might affect users’ interactions with elements of the device user interface, they should be incorporated into the simulated use environment (e.g., dim lighting, multiple alarm conditions, distractions, and multi-tasking). Please describe your use environment.

Deficiency 5:

You have not provided an analysis of known use problems with your predicate device or devices with similar user interfaces. You should address any known post-market human factors issues known to exist for using your device or similar devices. Examples of human factors issues include, but are not limited to, actions requiring substantial dexterity or strength, good visual acuity, or familiarity with uncommon practices. Information on post-market issues may be found by reviewing your internal user complaint files, the published literature, the FDA’s Medical Device Reporting (MDR) system, and FDA Safety Alerts and Public Health Notifications. The findings from this analysis would feed into your use-related risk analysis and ensure that you have done a thorough risk analysis. Please provide this analysis.

Deficiency 6:

You have not provided details of how your performance data was analyzed, specifically if you have analyzed all instances of failures, close-calls, and difficulties in performing critical tasks. The protocol should include a subjective assessment portion, testing the user interface using open-ended questions. Please conduct root cause analysis on the task failures, close calls, and difficulties and provide this analysis as well as proposed mitigations.

- a. You have noted in your Discussion (pg. 20) that “there were some comments/suggestions to packaging.. and involving the Instructions for Use, mainly related to the product preparation.” Please evaluate whether any of these suggestions would mitigate use-related risks, such as being able to quickly and effectively prepare the product for use during surgery. If these suggestions are potential mitigations, please provide an explanation for why they were not pursued.

Additional comment: Current Agency guidance applying human factors and usability engineering to medical devices can be found at: <http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm259760.pdf>



Appendix: HF Consult History

Reviewers Notes

Regulatory/Interaction History

N/A

Device Description

From IG_ITEC-002779_ING_USABILITY_FEB2017.pdf, pgs. 3-4:

Fibrin Sealant (FS) Grifols is composed of two syringes containing sterile frozen solutions of human fibrinogen (component 1) and human thrombin with calcium chloride (component 2) assembled on one syringe holder. The FS Grifols is intended for local application and a local effect. Intended benefits of the fibrin sealant application are to support local hemostasis, to “glue” surface of injured tissues in order to obtain adaptation or sealing of surfaces, to support sutures, or to improve repair or healing. The application by dripping is generally used to seal specific sites such as anastomosis in cardiac and vascular surgeries. Spray application is generally limited to stop great hemorrhages. The surgery fields where fibrin sealants have been extensively applied include cardiac and vascular surgery, thoracic surgery, neurosurgery, plastic and reconstruction surgery, gastrointestinal surgery, hepatic and splenic surgery, and dental surgery.

The tip applicator has been designed to allow a simple and homogeneous application. It consists of two polycarbonate pieces (syringe holder and plunger) produced through (b) (4). The syringe holder is clipped onto the two (b) (4) syringes, filled with fibrinogen and thrombin/calcium chloride, and it is intended to hold the syringes during transport, storage and application. The plunger link is connected to the syringe holder. It ensures that the plungers of the syringes are connected and move at the same rate during the application of the fibrinogen and thrombin with calcium chloride, resulting in a simultaneous application (Figures 1 and 2).



Appendix: HF Consult History

FIGURE 1

Description of the device components

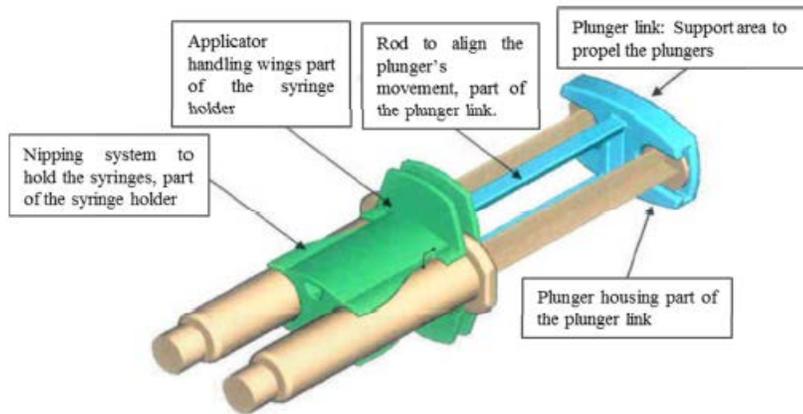


FIGURE 2

Tip applicator



HF Activities

Intended Use, Users, Use Environments, Training

From IG_ITEC-002779_ING_USABILITY_FEB2017.pdf, pgs. 3-4:



Appendix: HF Consult History

This updated report describes the usability test that was performed on Fibrin Sealant Grifols by incorporating new end-users surgeons. For this, five surgeons from three independent sites (Hospital Germans Trias y Pujol, Spain; Hospital Clinic, Spain; and Hospital de Mataró, Spain), were involved in the study. The Instructions for Use (IFU) that accompany the device were read carefully, to finally test the product on an animal model surgery, to give their medical opinion about the FS Grifols usability.

2. OBJECTIVE

This report describes the usability test that was performed on Fibrin Sealant Grifols by end-users surgeons to analyze the usability of the combination product regarding the intended uses under the expected working conditions to give the best possible care to patients.

Reviewer Analysis/Comments:

You have recruited 5 surgeons for your final HF/U validation study. However, FDA guidance states that a minimum of 15 participants per distinctive user group should be included in the HF validation study. Please adjust your protocol to include a minimum of 15 participants per distinctive user group and conduct additional HF/U testing as required.

You did not describe in detail the planned training provided to the test participants, including the content and delivery modes and the length of time that will elapse prior to testing (decay window). Because retention of training decays over time, testing should not occur immediately following training; some period of time should elapse. Please provide in your test protocol a description of the planned training, including content and delivery modes, and please include a minimum of 1 hour break time between the training and the testing.

Under your Objective section, you have stated that you plan to analyze the usability of the combination product regarding the intended uses “under the expected working conditions.” However, you have not described what are the “expected working conditions.” The conditions under which simulated-use HF/U validation testing is conducted should be sufficiently realistic so that the results of the testing are generalizable to actual use. The need for realism is therefore driven by the analysis of risks related to the device’s specific intended use, users, use environments, and the device user interface. To the extent that environmental factors might affect users’ interactions with elements of the device user interface, they should be incorporated into the simulated use environment (e.g., dim lighting, multiple alarm conditions, distractions, and multi-tasking). Please describe your use environment.

Device User Interface



Appendix: HF Consult History

From IG_ITEC-002779_ING_USABILITY_FEB2017.pdf, pg. 6:

7.3 MATERIAL

Human fibrinogen and thrombin are filled into (b) (4) glass syringes with bromo-butyl-rubber plunger stopper. Syringes are closed with appropriate sized tip cap made of bromo-butyl-rubber. Glass material, plunger stopper and tip cap meet the requirements of the (b) (4). The syringes, tip caps and plunger stoppers (b) (4) syringes) are purchased from (b) (4), (b) (4).

(b) (4)
(b) (4). The cannula is manufactured by (b) (4), (b) (4). This applicator was cleared by FDA under (b) (4) and has since been reclassified as a class 1 product. It is attached to the luer connectors of the syringes and channels the fibrinogen and thrombin/calcium chloride components as they are dispensed from the syringes.

Spray Applicator (FibriJet[®] Aerosol Applicator): The spray applicator (Micromedics spray, applicator kit reference SA-6205 and Micromedics compressed air regulator reference SA-6030) is an optional component of the system and provided separately. It is manufactured by Micromedics Inc. The spray applicator is intended for use in applying two non-homogenous fluids to a treatment site. The spray applicator is attached to the luer connectors of the syringes and a medical gas supply line. It channels the fibrinogen and thrombin/calcium chloride components as they are dispensed from the syringes and sprayed onto the treatment site.

The Instructions for Use (IFU) of FS Grifols (Annex) inform the device user of the medical device's intended purpose and proper use and of any precautions to be taken. It mainly contains information about the following particulars: indications and usage, dosage forms, contraindications, warnings and precautions, preparation and handling (thawing conditions, assembly device preparation before use), administration (drip or spray) and application precautions.

Reviewer Analysis/Comments: Sponsor data is adequate. The spray applicator is an optional component sold separately, but should be tested for HF/U because it was noted in the Introduction that “spray application is generally limited to stop great hemorrhages (pg. 3)”, which is likely a critical task.



Appendix: HF Consult History

Summary of Known Use Problems

Reviewer Analysis/Comments: You have not provided an analysis of known use problems with your predicate device or devices with similar user interfaces. You should address any known post-market human factors issues known to exist for using your device or similar devices. Examples of human factors issues include, but are not limited to, actions requiring substantial dexterity or strength, good visual acuity, or familiarity with uncommon practices. Information on post-market issues may be found by reviewing your internal user complaint files, the published literature, the FDA's Medical Device Reporting (MDR) system, and FDA Safety Alerts and Public Health Notifications. The findings from this analysis would feed into your use-related risk analysis and ensure that you have done a thorough risk analysis. Please provide this analysis.

Analysis of Hazards/Risks

Reviewer Analysis/Comments:

See first Deficiency.

Summary of Preliminary Analysis and Evaluation

From IG_ITEC-002779_ING_USABILITY_FEB2017.pdf, pg. 3:

A previous usability study (report IG_ITEC-002747_ING) involving five vascular surgeons from three independent sites that tested and gave their medical opinion about the dripping application of FS, had been performed. The usability of the product was considered correct and the FS Grifols could be easily applied and it could be used for the intended uses under the expected use conditions.

Reviewer Analysis/Comments: One previous formative test. Not clear if other evaluation was performed.

Description/Categorization of Critical Tasks

From IG_ITEC-002779_ING_USABILITY_FEB2017.pdf, pg. 9:



Appendix: HF Consult History

TABLE 2
Evaluation performed by Dr. Joan Francesc Julian:

Parameter	Yes/No	Comments
Have you used other commercial FS?	Yes	A lot (among them Tisseel)
The syringe label information identifies: product concentration, batch, expiration date	Yes	
The external box is closed enough to prevent loss instructions, kits, and cannula.	Yes	
Indications and usage are clearly described	Yes	
FS dosage forms are described	Yes	
Contraindications and warnings are clearly described	Yes	Too explicit
Dosage instructions are clear and easy to understand	Yes	
Thawing procedure is clear and easy to understand	Yes	Temperature above 37 °C could be specified
Stability after thawing is correctly described	Yes	

...

Reviewer Analysis/Comments:

Regarding your critical tasks:

- b. You have provided your list of “parameters” (Table 2, Protocol). However, the criteria you have used to choose your critical tasks is not clear. Of note, since it is difficult to estimate probability of occurrence accurately in the premarket stage, you should use severity level alone to identify the critical task associated with the subject device. Please 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.
- c. In your list of “parameters,” you have listed a few prompts that should be evaluated by use testing or knowledge tasks and not by self-evaluation. For example, “contraindications and warnings are clearly described” and “connection operations are adequately described in preparation instructions” do not give any evidence that objectively, the contraindications and warnings are clear. These tasks should aim to challenge participant knowledge. Please provide in more detail if this and like tasks will be evaluated via use testing, through knowledge test, or other applicable test.



Appendix: HF Consult History

Details of HF Validation Testing

Reviewer Analysis/Comments:

You have noted in your Discussion (pg. 20) that “there were some comments/suggestions to packaging.. and involving the Instructions for Use, mainly related to the product preparation.” Please evaluate whether any of these suggestions would mitigate use-related risks, such as being able to quickly and effectively prepare the product for use during surgery. If these suggestions are potential mitigations, please provide an explanation for why they were not pursued.

You should provide details on how the performance data will be analyzed, specifically to analyze all instances of failures, close-calls, and difficulties in performing critical tasks. The protocol should include a subjective assessment portion, testing the user interface change overall using open-ended questions. Conduct root cause analysis on the task failures, close calls, and difficulties and discuss it in your report.

Materials Reviewed

- IG_ITEC-002779_ING_USABILITY_FEB2017.pdf

End of Review (ICC1600853, CON178638, 05-29-17)