

Division Director Memo

Division of Clinical Evaluation and Pharmacology / Toxicology
Office of Tissues and Advanced Therapies

Application: BLA 125640 / 0
 Applicant: Grifols Institute
 CBER Received Date: 11/3/2016
 PDUFA Date: 11/3/2017
 Review Date: 10/30/2017
 Established Name: Fibrin Sealant (Human)
 Trade Name: Proposed trade name Not acceptable
 Route: Topical
 INDICATION:

An adjunct to hemostasis for mild to moderate bleeding in adults undergoing surgery when control of bleeding by standard surgical techniques (such as suture, ligature, and cautery) is ineffective or impractical. Fibrin Sealant (Human) is effective in heparinized patients.

Review Team

Discipline/Review Activity	Reviewers and Consultants
<ul style="list-style-type: none"> • CMC - Product • CMC - Facilities • Facility Inspection 	Natalya Ananyeva, PhD, Svetlana Shestopal, PhD, and Ze Peng, PhD (OTAT/DPPT/HB) Christine Harman, PhD (OCBQ/DMPQ/BI) Christine Harman, PhD (OCBQ/DMPQ/BI) Natalya Ananyeva, PhD (OTAT/DPPT/HB)
<ul style="list-style-type: none"> • Clinical • Post-marketing safety epidemiological review • BIMO 	Agnes Lim, MD (OTAT/DCEPT/GMB1) Faith Barash, MD (OCBQ/DE/PB) Bhanu Kannan, MS (OCBQ/DIS/BMB)
<ul style="list-style-type: none"> • Statistical 	Min (Annie) Lin, PhD (OBE/DB/TEB)
<ul style="list-style-type: none"> • Toxicology • Developmental toxicology • Animal pharmacology 	John Jameson, PhD (OTAT/DCEPT/PTB2)
Labeling Review	Alpita Popat, PharmD (OCBQ/DCM/APLB)
<ul style="list-style-type: none"> • Extractables/Leachables, Chemistry and Identification/Quantification • QC, Test Methods, Product Quality • Lot Release Protocol/Testing Plan • QC, Sterility and Endotoxin Proprietary Name Review	Andrey Sarafanov, PhD (OTAT/DPPT/HB) Grainne Tobin, PhD, Ritu Agarwal, PhD, and Hsiaoling Wang, PhD (OCBQ/DBSQC/LACBRP) Varsha Garnepudi (OCBQ/DBSQC/QAB) Karla Garcia (OCBQ/DBSQC/LMIVTS) Oluchi Elekwachi (OCBQ/DCM/APLB)
<ul style="list-style-type: none"> • Delivery Device • Engineering, Delivery Device • Human Factors/Usability • Extractables/Leachables, Toxicological Assessment 	Deborah Trout (OCBQ/DMPQ/BI) Rong Guo, PhD (CDRH/ODE/DAGRID) Rita Lin, MS (CDRH/ODE/DAGRID) Evi Struble, PhD (OTAT/DPPT/PDB)
<ul style="list-style-type: none"> • Regulatory Project Manager 	Yu Do, MS (OTAT/DRPM/RPMBI)
<ul style="list-style-type: none"> • Advisory Committee summary 	Not presented to an advisory committee

REVIEW SUMMARY:

Please see primary reviews from the primary discipline reviewers for details.

In summary, the applicant conducted 3 randomized controlled trials, assessing the effect of Fibrin Sealant (Human) under different kinds of surgical procedures. The primary endpoint (proportion of subjects achieving hemostasis by 4 minutes, was met in the 3 trials. The applicant demonstrated that Fibrin Sealant was effective, in the context of these trials. The safety profile of this fibrin sealant is similar to currently licensed, similar fibrin sealant products. The benefit risk profile is favorable and the label, as revised with our input, is acceptable.

I concur with the review team's recommendation to issue an Approval Letter for this product.

There will be a PREA-related postmarketing required study, including a substudy component to assess human factors prior to the initiation of the actual pediatric study. Milestones dates proposed are acceptable.

OUTSTANDING ISSUES:

None