August 23, 2019

Fresenius Medical Care Renal Therapies Group, LLC
Denise Oppermann
Senior Director, Regulatory Affairs
920 Winter Street
Waltham, MA 02451

Re: K190459
Trade/Device Name: Hemoflow™ F3 and F4 Dialyzers
Regulation Number: 21 CFR 876.5820
Regulation Name: Hemodialysis system and accessories
Regulatory Class: Class II
Product Code: FJI
Dated: July 25, 2019
Received: July 26, 2019

Dear Denise Oppermann:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

for Carolyn Y. Neuland, Ph.D.
Assistant Division Director
DHT3A: Division of Renal, Gastrointestinal, Obesity and Transplant Devices
OHT3: Office of Gastro-Renal, ObGyn, General Hospital and Urology Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*

K190459

Device Name
Hemoflow™ F3 and F4 Dialyzers

Indications for Use *(Describe)*
The Hemoflow F3 and F4 dialyzers are intended for hemodialysis of patients, including pediatric patients, with acute or chronic renal failure when conservative therapy is judged to be inadequate. Consider body and dialyzer surface area, blood flow, body weight, and extracorporeal blood volume when selecting dialyzers for use with pediatric patients.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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5. 510(K) SUMMARY

This 510(k) Summary is in accordance with the requirements of the Safe Medical Device Act (SMDA) of 1990. The content of this 510(k) summary is provided in conformance with 21 CFR § 807.92.

5.1. Submitter's Information

Name:	Fresenius Medical Care Renal Therapies Group, LLC
Address:	920 Winter Street Waltham, MA 02451-1457
Phone:	(781) 699-4479
Fax:	(781) 699-9635
Contact Person:	Denise Oppermann, Senior Director Regulatory Affairs – Devices
Preparation Date:	22 February 2019

5.2. Device Name

Trade Name:	Hemoflow F3 and F4 Dialyzers
Common Name:	Dialyzer
Regulation Name:	Hemodialysis system and accessories
Regulatory Class:	Class II per 21 CFR § 876.5820
Product Code:	FJI
Product Code Name:	Dialyzer, Capillary, Hollow Fiber
Classification Panel:	Gastroenterology/Urology

5.3. Legally Marketed Predicate Device

The legally marketed predicate devices are the Fresenius Hemoflow F3, F4 dialyzers cleared under K874872. These devices have not been subject to a design-related recall.

The Gambro Polyflux 6H Hemodialyzer (K051520) and Fresenius Optiflux Dialyzers (K152367 and K162488) are used as reference devices.

5.4. Device Description

5.4.1. Device Identification

The Hemoflow F3 and F4 dialyzers are the subject of this 510(k).

5.4.2. Device Characteristics

The Hemoflow F3 and F4 dialyzers are low-flux, single-use, ethylene oxide (EO) sterilized hemodialyzers. The dialyzers are provided blood pathway sterile and non-pyrogenic. The membrane surface areas of the F3 and the F4 dialyzers are 0.3 m^2 and 0.7 m^2, respectively.

5.4.2.1. Environment of Use

The Hemoflow F3 and F4 dialyzers are used in environments where acute and chronic hemodialysis are performed.

5.4.2.2. Brief Written Description of the Device

The Hemoflow F3 and F4 dialyzers are low-flux, sterile devices designed for single-use acute and chronic hemodialysis. The dialyzers are configured to connect to a bloodline set which connects to a patient's vascular access system when used with a hemodialysis machine equipped with ultrafiltration control. During hemodialysis, blood is pumped from the patient's body through an extracorporeal circuit, one component of which is the dialyzer. The dialyzers contain a semi-permeable membrane that allows for diffusion and/or ultrafiltration to transport toxins and excess fluid from the blood compartment (fiber lumen) to the dialysate compartment. Dialyzers utilize a counter-current flow in which dialysate and blood flow in opposite directions in the dialyzer. The counter-current flow maintains the concentration gradient across the membrane for waste and fluid removal.

5.4.2.3. Materials of Use

The Hemoflow F3 and F4 dialyzers are classified as externally communicating, circulating blood, prolonged contact (> 24 hours to 30 days) duration, Class II (Category B) devices in accordance with FDA guidance *Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"* (16 June 2016).

The Hemoflow F3 and F4 dialyzers' components are composed of the following materials:

Component	Material
Housing	Polycarbonate
Potting Resin	Polyurethane
Fiber Bundle	Polysulfone
Screw Flange	Polycarbonate
O-Ring	Silicone
Blood Port Cap(s)	High Density Polyethylene

5.4.2.4. Key Performance Characteristics

Urea clearance is a key performance specification of the Hemoflow F3 and F4 dialyzers. FMCRTG uses sodium clearance as a marker for urea clearance because sodium and urea exhibit similar movement across a membrane. Sodium clearance data from the Instructions for Use (IFU) for the Hemflow F3 and F4 dialyzers are provided in Table 1.

Table 1: *In vitro* Urea Clearance for the F3 and F4 Dialyzer Models*

Trade Name	Typical Urea Clearance (Sodium Used as Marker)
Hemoflow F3 Dialyzer	117
Hemoflow F4 Dialyzer	155

*Qb = 200 mL/min, Qd = 500 mL/min, Quf = 0 mL/min

5.5. Intended Use

Hemoflow F3 and F4 dialyzers are designed for single use acute and chronic hemodialysis.

5.6. Indications for Use

The Hemoflow F3 and F4 dialyzers are intended for hemodialysis of patients, including pediatric patients, with acute or chronic renal failure when conservative therapy is judged to be inadequate. Consider body and dialyzer surface area, blood flow, body weight, and extracorporeal blood volume when selecting dialyzers for use with pediatric patients.

5.7. Comparison of Technological Characteristics with the Predicate Device

The following technological characteristics of the Hemoflow F3 and F4 dialyzers are equivalent to those of the predicate Fresenius Hemoflow F3 and F4 dialyzers (K874872).

- Intended use
- Principle of operation
- Design characteristics
- Sterilization method
- Patient fluid-contacting materials: polysulfone, polycarbonate, polyurethane, and silicone

5.8. Performance Data

Performance testing was conducted in accordance with ISO 8637:2010 and *Guidance for the Content of Premarket Notifications for Conventional and High Permeability Hemodialyzers, August 1998*. Testing conducted to support the determination of substantial equivalence is summarized in Table 2.

Table 2: Performance Testing Summary

Test Conducted	Test Method Description
Blood Compartment Volume	Calculated, considering the fiber inner diameter, fiber crimp, the minimum and maximum blood volume, O-ring compression volume, dialyzer housing length, and polyurethane height.

Table 2: Performance Testing Summary

Test Conducted	Test Method Description
Clearance – Sodium (marker for urea), Creatinine, Phosphate, and Vitamin B12	Calculated by analyzing the test samples over the specified range of blood and dialysate flow rates.
Ultrafiltration	Calculated as the slope from a plot of the measured ultrafiltration rate UFR (over the applied transmembrane pressure (TMP) range) versus the applied TMP.
Pressure Drop	The dialysate and blood compartments were filled with dialysate and bovine blood, respectively. Inlet and outlet pressures of the blood and dialysate compartments were measured across the range of flow rates with the dialyzers in a horizontal configuration.
Structural Integrity	The positive and negative pressure decay was measured by a pressure monitor connected at one end of the dialyzer while applying 900 mmHg and -700 mmHg from opposite ends.
Blood Compartment Integrity	Air and water were added to the top blood port and the dialysate side, respectively. A pressure differential was applied across the dialyzer membrane.
Simulated Shipping and Distribution	Testing was conducted per ASTM D4169-16. Performance testing was conducted before and after simulated shipping to demonstrate that the product and package integrity and sterility are maintained throughout the intended product shelf life.

All testing met predetermined acceptance criteria. Results of the proposed devices' design verification tests met the requirements and demonstrated that, like the predicate device, the Hemoflow F3 and F4 dialyzers are safe and effective for their intended use.

5.8.1. Biocompatibility Testing

Testing was performed to support the biological safety of the Hemoflow F3 and F4 dialyzers.

- Chemical analysis – extractables and leachables
- Cytotoxicity, ISO Elution Method with MEM
- Sensitization, Guinea Pig Maximization
- Intracutaneous Irritation
- Acute Systemic Toxicity
- Systemic Toxicity, Short-Term Repeated Exposure
- Material-Mediated Pyrogenicity

- Genotoxicity, Bacterial Reverse Mutation Assay
- Genotoxicity, *in vitro* Mouse Lymphoma Gene Mutation Assay
- Genotoxicity, Mouse Micronucleus *in vivo* Assay
- Hemocompatibility, ASTM Hemolysis (Direct and Indirect – Extract)
- Hemocompatibility, Complement Activation – SC5b-9 fragment
- Hemocompatibility, ASTM Partial Thromboplastin Time
- Hemocompatibility, Mechanical Hemolysis
- Hemocompatibility, *in vitro* Thrombogenicity Assay
- PVP Testing

A toxicological risk assessment was also performed.

5.8.2. Human Factors Validation Testing

The Hemoflow F3 and F4 dialyzers were validated for safe and effective use in accordance with FDA guidance *Applying Human Factors and Usability Engineering to Medical Devices* (03 February 2016).

5.8.3. Electrical Safety and Electromagnetic Compatibility (EMC)

Not applicable. The Hemoflow F3 and F4 dialyzers are not electrical mechanical devices.

5.8.4. Software Verification and Validation Testing

Not applicable. The Hemoflow F3 and F4 dialyzers do not contain software.

5.8.5. Mechanical and Acoustic Testing

No mechanical or acoustic tests were performed.

5.8.6. Animal Studies

No animal studies were performed.

5.8.7. Clinical Studies

A retrospective data analysis performed on the Hemoflow F3 and F4 dialyzers included 10 pediatric ESRD patients on HD treated for 12 consecutive weeks. Hemoflow F3 and F4 dialyzers provided adequate clearance with a mean spKt/V of 1.78 and 2.18, respectively, and were well tolerated.

5.9. Conclusion

The intended use, principle of operation, design characteristics, sterilization method and patient fluid-contacting materials of the Hemoflow F3 and F4 dialyzers are substantially equivalent to that of the predicate devices. FMCRTG concludes that within the meaning of the Medical Device Amendments Act of 1976, the Hemoflow F3 and F4 devices are safe and effective for their intended use.