July 9, 2020

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

Re: K192928
Trade/Device Name: Optiflux Enexa F500 Dialyzer
Regulation Number: 21 CFR 876.5860
Regulation Name: High Permeability Hemodialysis System
Regulatory Class: II
Product Code: KDI
Dated: June 2, 2020
Received: June 4, 2020

Dear Denise M. 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 Director
DHT3A: Division of Renal, Gastrointestinal,
Obesity and Transplant Devices
OHT3: Office of GastroRenal, 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)*
K192928

Device Name
Optiflux Enexa F500 Dialyzer

Indications for Use *(Describe)*

Optiflux® Enexa™ dialyzers are intended for patients with acute kidney injury or chronic kidney disease when conservative therapy is judged to be inadequate.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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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) 996-9103
Fax:	(781) 699-9635
Contact Person:	Denise Oppermann, Senior Director Regulatory Affairs – Devices
Preparation Date:	16 October 2019

5.2. Device Name

Trade Name:	Optiflux Enexa F500 Dialyzer
Common Name:	Dialyzer
Regulation Name:	High permeability hemodialysis system
Regulatory Class:	Class II per 21 CFR §876.5860
Product Code:	KDI
Product Code Name:	Dialyzer, High Permeability With Or Without Sealed Dialysate System
Classification Panel:	Gastroenterology/Urology

5.3. Legally Marketed Predicate Device

The legally marketed predicate device is the Optiflux F160NR dialyzer cleared under K152367. This device is not currently subject to a design-related recall.

5.4. Device Description

5.4.1. Device Identification

The Optiflux Enexa F500 dialyzer is the subject of this 510(k).

5.4.2 Device Characteristics

The Optiflux Enexa F500 dialyzer is a high-flux, single-use, e-beam sterilized hemodialyzer that contains the additive Endexo SMM1 blended into the fiber. The dialyzer is provided blood pathway sterile and non-pyrogenic. The membrane surface area is 1.5 m^2.

5.2.2.1 Environment of Use

The Optiflux Enexa F500 dialyzers are used in environments where acute and chronic hemodialysis are performed.

5.4.2.2. Brief Written Description of the Device

The Optiflux Enexa F500 dialyzer is a high-flux, sterile device designed for single-use in acute and chronic hemodialysis. The dialyzer is 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 dialyzer contains 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 Optiflux Enexa F500 is classified as an externally communicating, blood path indirect, prolonged contact (> 24 hours to 30 days) duration, Class II device 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). Testing performed met or exceeded these requirements.

The Optiflux Enexa F500 dialyzer is composed of the following materials:

Component	**Material**
Housing	Polycarbonate
Potting Resin	Polyurethane
Fiber Bundle	Polysulfone w/Endexo SMM1
Screw Flange	Polycarbonate
O-Ring	Silicone
Blood Port Cap(s)	High Density Polyethylene
Dialysate Port Cap(s)	High Density Polyethylene

5.4.2.4. Key Performance Characteristics

Urea clearance is a key performance specification of the Optiflux Enexa F500 dialyzer. 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 Optiflux Enexa F500 dialyzer is provided in Table 1.

Table 1: *In vitro* Urea Clearance for the F500 Dialyzer*

Trade Name	Typical Urea Clearance (Sodium Used as Marker)
Optiflux Enexa F500	271

*Qb = 300 mL/min, Qd = 500 mL/min, Quf = 0 mL/min

5.5. Intended Use

Optiflux Enexa dialyzers are designed for single use acute and chronic hemodialysis.

5.6. Indications for Use

Optiflux® Enexa™ dialyzers are intended for patients with acute kidney injury or chronic kidney disease when conservative therapy is judged to be inadequate.

5.7. Comparison of Technological Characteristics with the Predicate Device

The following technological characteristics of the Optiflux Enexa F500 dialyzer are substantially equivalent to those of the predicate Optiflux F160NR dialyzer (K152367).

- Intended use
- Principle of operation
- Design characteristics
- Patient fluid-contacting materials

5.8. Performance Data

Performance testing was conducted in accordance with ISO 8637-1:2017 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.
Clearance – Sodium (marker for urea), Creatinine, Phosphate, Vitamin B_{12}, and Lysozyme	Calculated by analyzing test samples over the specified range of blood and dialysate flow rates.

Test Conducted	Test Method Description
Protein Sieving Coefficient	The test circuit was stabilized for blood and filtrate flows. All air was removed from the dialyzer. Paired samples for blood and filtrate flows were collected after 15 min. Samples were taken again after another 15 min. Sieving coefficient was calculated in accordance with Section 5.6.2.4 of ISO 8637-1:2017.
Ultrafiltration	Calculated as the slope from a plot of the measured transmembrane pressure versus the ultrafiltration rate.
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 position.
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 the opposite end.
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 product and package integrity and sterility are maintained throughout the intended product shelf life.

All testing met predetermined acceptance criteria. Results of the proposed device design verification tests met the requirements and demonstrated that, like the predicate device, the Optiflux Enexa F500 dialyzer is safe and effective for its intended use.

5.8.1. Biocompatibility Testing

The following testing was performed to support the biological safety of the Optiflux Enexa F500 dialyzer:

- Chemical Analysis – Extractables and Leachables
- Cytotoxicity, ISO Elution Method with MEM
- Sensitization, Guinea Pig Maximization
- Intracutaneous Irritation
- Acute Systemic Toxicity
- Subchronic Toxicity, Dual Routes of Parental Administration

- Material-Mediated Pyrogenicity
- Genotoxicity, Bacterial Reverse Mutation Assay
- Genotoxicity, *in vitro* Mouse Lymphoma Gene Mutation Assay
- Genotoxicity, ISO *in vitro* Mouse Lymphoma Gene Mutation Assay
- Hemocompatibility, ASTM Hemolysis (Direct and Indirect – Extract)
- Hemocompatibility, Complement Activation – C3a and SC5b-9 fragment
- Hemocompatibility, ASTM Partial Thromboplastin Time
- Hemocompatibility, Mechanical Hemolysis
- Hemocompatibility, *in vitro* Thrombogenicity Assay
- PVP Assay
- SMM1 Assay
- *In vivo* Toxicity Studies

A toxicological risk assessment was also performed.

5.8.2. Human Factors Validation Testing

Human Factors (HF) validation testing was leveraged for the Optiflux Enexa F500 dialyzer to demonstrate its 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 Optiflux Enexa F500 dialyzer is not an electrical mechanical device.

5.8.4. Software Verification and Validation Testing

Not applicable. The Optiflux Enexa F500 dialyzer does not contain software.

5.8.5. Animal Studies

No animal studies were performed.

5.8.6. Clinical Studies

Eighteen (18) hemodialysis (HD) subjects with chronic renal failure were administered 664 HD treatments with the Optiflux® Enexa™ F500 in a prospective, multi-center, open-label clinical study. Mean treatment duration was 207 ± 20 min, blood flow rate 447.7 ± 37.7 mL/min, and dialysate flow rate 698 ± 62.8 mL/min. Mean Kuf was 16.36 ± 9.92 mL/hr/mmHg, and spKt/V 2.06 ± 0.42. Mean urea and ß2-microglobulin removal rates were 81.49 ± 5.95% and 63.04 ± 16.86%, respectively. Mean pre-HD serum albumin levels remained unchanged; an increase from 3.94 ± 0.21 g/dL to 4.23 ± 0.41 g/dL was observed from pre-HD to post-HD. There was no evidence of overt complement activation as C5a and C3a levels remained largely unchanged from pre-HD levels. A decrease in mean C3a levels from 1318.8 ± 886.7 ng/mL to 1301.2 ± 335.7 ng/mL and in mean C5a levels from 8.8 ± 6.1

ng/mL to 7.62 ± 4.7 ng/mL was observed pre-HD and 30 mins post-HD. A slight increase in mean sC5b- 9 level from 224.3 ± 51.3 ng/mL to 304.22 ± 71.6 ng/mL was observed at 30 min post-HD. No clinically meaningful changes were observed in hematologic parameters and mean platelet counts. Adverse events that occurred during the study were not related to the device. Eleven (11) out of the 18 subjects (61.1%, 32 AEs) reported at least 1 AE during the study. No deaths or AEs leading to discontinuation were reported during the study. Three (3) serious adverse events were reported but none were related to the device. The mean thrombus score (1-4, clear to fully clotted) was 1.29 ± 0.52. None of the treatments with the Optiflux® Enexa™ F500 showed a Grade 4 Thrombus.

5.9. Conclusion

The intended use, principle of operation, design characteristics, and patient fluid-contacting materials of the Optiflux Enexa F500 dialyzer are substantially equivalent to that of the predicate device. FMCRTG concludes that within the meaning of the Medical Device Amendments Act of 1976, the Optiflux Enexa F500 device is safe and effective for its intended use.