January 10, 2019

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

Re: K182367
Trade/Device Name: DIASAFE®plusUS
Regulation Number: 21 CFR§ 876.5665
Regulation Name: Water Purification System for Hemodialysis
Regulatory Class: II
Product Code: FIP
Dated: December 4, 2018
Received: December 6, 2018

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/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Carolyn Y. Neuland -S

for
Benjamin R. Fisher, Ph.D.
Director
Division of Reproductive, Gastro-Renal,
and Urological Devices
Office of Device Evaluation
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)*

K182367

Device Name
DIASAFE®plusUS

Indications for Use *(Describe)*

The DIASAFE®plusUS is intended for the preparation of ultrapure dialysate from pre-treated water and is not intended to provide primary purification. Attention must still be given to the chemical and microbiological quality of water and concentrates and the maintenance of supply systems (e.g., RO system, central delivery system).

The microbiological quality (microbial count [CFU/mL] and endotoxin measurement [EU/mL]) of the incoming water should be < 200 CFU/mL and < 2 EU/mL, respectively.

The DIASAFE®plusUS can only be used with Fresenius Medical Care dialysis machines fitted for use with DIASAFE®plusUS.

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) 699-4479
Fax:	(781) 699-9635
Contact Person:	Denise Oppermann Senior Director, Regulatory Affairs – Devices
Preparation Date:	31 August 2018

5.2. Device Name

Trade Name:	DIASAFE®*plus*US
Common Name:	Subsystem, water purification
Regulation Name:	Water purification system for hemodialysis
Regulatory Class:	Class II per 21 CFR §876.5665
Product Code:	FIP
Classification Panel:	Gastroenterology/Urology

5.3. Legally Marketed Predicate Device

The legally marketed predicate device is the Dialysis Machine with Dialysate Ultrafilter (K944767), hereinafter referred to as "Diasafe Dialysate Ultrafilter". This predicate has not been subject to a design-related recall.

5.4. Device Description

5.4.1. Device Identification

The DIASAFE®*plus*US (P/N F00007039) is the subject of this Traditional 510(k).

5.4.2. Device Characteristics

The DIASAFE®*plus*US is a non-sterile dialysis fluid filter that produces ultrapure dialysate as defined in ANSI/AAMI/ISO 11663. The filter reduces microbial contaminants including endotoxins in the dialysate during hemodialysis treatment. The DIASAFE®*plus*US is installed and exchanged on 2008 Series hemodialysis machines using the DIAFIX™ Lock System. The DIAFIX™ Lock System is a standard feature on 2008 Series hemodialysis machines and is installed during machine production.

5.4.3. Environment of Use

The DIASAFE®*plus*US is used in environments where acute and chronic hemodialysis is performed.

5.4.4. Brief Description of the Device

Mixed dialysate is forced through an open filter port across the fibers of DIASAFE®*plus*US. A bypass valve at the other end is closed which forces the dialysate across the fiber membrane. Dialysate passes through the porous membrane and into the filtrate compartment where it is allowed to flow through the uncapped side ports and into the hemodialyzer. Microorganisms and molecules too large to pass through the membrane are trapped in the fibers until they are flushed out, and/or disinfected during a routine cleaning cycle

5.4.5. Materials of Use

The DIASAFE®*plus*US is classified as an externally communicating, blood path indirect, prolonged contact (>24 hours to 30 days) duration, Class II (Category B) 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).

A list of the DIASAFE®*plus*US components and materials is provided in Table 1.

Table 1: DIASAFE®*plus*US Components and Materials

Component	Material
Capillary fibers (fiber bundle)	Fresenius Polysulfone®, Polyvinylpyrrolidone
Filter housing	Polypropylene
PU-Resin (potting mass)	Polyurethane
Welded header (caps)	Polypropylene
O-ring	Silicone
Plastic tabs (tear-off brackets)	Silicone
Sealing disc-ring	Silicone

5.4.6. Key Performance Specifications/Characteristics

A description of the key DIASAFE®*plus*US performance specifications is provided in Table 2.

Table 2: DIASAFE®*plus*US Features

Features	Specifications
Filtration Rate	≥ 300 mL/hr·mmHg ≥ 3.75 L/min·bar
Maximum Filtration Pressure	2 bar
Connection System	DIAFIX™ Lock System

Table 2: DIASAFE®*plus*US Features (Continued)

Features	Specifications
Surface Area	2.2m^2
Dialysis Fluid Purity (ultrapure dialysate)	<0.03 EU/mL < 0.1 CFU/mL

5.5. Intended Use/Indications for Use

The DIASAFE®*plus*US is intended for the preparation of ultrapure dialysate from pre-treated water and is not intended to provide primary purification. Attention must still be given to the chemical and microbiological quality of water and concentrates and the maintenance of supply systems (e.g., RO system, central delivery system).

The microbiological quality (microbial count [CFU/mL] and endotoxin measurement [EU/mL]) of the incoming water should be < 200 CFU/mL and < 2 EU/mL, respectively.

The DIASAFE®*plus*US can only be used with Fresenius Medical Care dialysis machines fitted for use with DIASAFE®*plus*US.

5.6. Comparison of Technological Characteristics with the Predicate Device

A comparison of the technological characteristics of the DIASAFE®*plus*US with the Diasafe Dialysate Ultrafilter (K944767) is provided in Table 3.

Table 3: DIASAFE®*plus*US Comparison of Technological Characteristics

Feature	Diasafe Dialysate Ultrafilter - Predicate Device (K944767)	DIASAFE®*plus*US - Proposed Device
Principle of Operation	The Diasafe Dialysate Ultrafilter reduces the level of bacteria and pyrogens in the dialysate for use in acute and chronic hemodialysis through membrane filtration and adsorption	The DIASAFE®*plus*US provides ultrapure dialysate for use in acute and chronic hemodialysis by reducing the level of bacteria and pyrogens through membrane filtration and adsorption
Environment of Use	The Diasafe Dialysate Ultrafilter is used in environments where acute and chronic hemodialysis is performed	The DIASAFE®*plus*US is used in environments where acute and chronic hemodialysis is performed
Membrane Surface Area	1.8 m^2	2.2 m²
Priming Volume (inside of capillaries)	110 mL	130 mL

Table 3: DIASAFE®*plus*US Comparison of Technological Characteristics (Continued)

Feature	Diasafe Dialysate Ultrafilter - Predicate Device (K944767)	DIASAFE®*plus*US - Proposed Device
Priming Volume (outside of capillaries)	310 mL	276 mL
Hemodialysis Machine Connection System	Dialyzer connections	DIAFIX™ Lock System
Device Packaging	Plastic overwrap with Tyvek® sterilized pouch	The filter is sealed with plastic tabs (tear-off brackets) and is packaged in a transparent Sealable PA/PE overwrap
Bleach Exposure	≤15 hours	≤ 30 hours (≤ 30 chemical disinfection cycles)
Shelf-life	3 years	3 years
Sterility	Ethylene Oxide sterilized	Non-sterile

5.7. Performance Data

Testing conducted to support the determination of substantial equivalence is summarized in Table 4.

Table 4: Performance Data Testing

Test Conducted	Test Method Description	Acceptance Criteria	Results / Conclusion
Bacteria Retention	Dialysis fluid spiked with bacteria that exceeded the allowable limit per ANSI/AAMI RD52 was filtered through the DIASAFE®*plus*US	The filter shall retain bacteria to produce ultrapure dialysate with a microbial count <0.1 CFU/mL (ANSI/AAMI/ISO 11663)	Pass, results within acceptance criteria
Endotoxin Retention	Dialysis fluid spiked with endotoxin that exceeded the allowable limit per ANSI/AAMI RD52 was filtered through the DIASAFE®*plus*US	The filter shall retain endotoxin to produce ultrapure dialysate with an endotoxin count <0.03 EU/mL	Pass, results within acceptance criteria

Table 4: Performance Data Testing (Continued)

Test Conducted	Test Method Description	Acceptance Criteria	Results / Conclusion
		(ANSI/AAMI/ISO 11663)	
Ultrafiltration Rate	DIASAFE®*plus*US filter samples were evaluated for aqueous K_{UF}	The aqueous ultrafiltration rate shall be >300 mL/hr mmHg (3.75 L/min bar) at 37°C	Pass, results within acceptance criteria
Dialysis Fluid Composition	Dialysate was passed through the filter at varying flow rates simulating typical in-use conditions. Dialysate composition was measured before and after filtration	Dialysate composition shall not be adversely affected after passing through the DIASAFE®*plus*US	Pass, results within acceptance criteria
Filter Integrity	Filter integrity was evaluated after simulated ship testing	The filter connectors, caps, housing, and welding shall not leak at a filtration pressure <2 bar and at a temperature of 20 ± 5°C	Pass, results within acceptance criteria
Membrane Integrity	Membrane integrity was evaluated after simulated ship testing	The membrane shall be intact at a transmembrane pressure <2 bar and at a temperature of 20 ± 5°C	Pass, results within acceptance criteria
Chemical Contaminants	The DIASAFE®*plus*US was evaluated for elemental and ionic chemical contaminants listed in ANSI/AAMI/ISO 13959:2014	The DIASAFE®*plus*US should not contribute unacceptable levels of chemical contaminants	Pass, results within acceptance criteria for each defined element/ion

5.7.1. Biocompatibility Testing

The following testing was performed to support the biological safety of the DIASAFE®*plus*US.

- Chemical characterization
- Cytotoxicity, ISO Elution Method with MEM
- Sensitization, Guinea Pig Maximization
- Intracutaneous Irritation
- Material Mediated Pyrogenicity
- Hemocompatibility, ASTM Hemolysis (Indirect) – Contact
- Subchronic Intravenous Toxicity
- Risk assessment of potential toxicity
- PVP Testing

5.7.2. Stability Design Verification

The DIASAFE®*plus*US is provided non-sterile and will be labeled with a 36 months (3-year) product shelf life. The shelf life is supported by accelerated aging equivalent to 3-year real-time and 24 months real-time.

5.7.3. Shipping Verification

Shipping verification was conducted to support that the DIASAFE®*plus*US can withstand the distribution environments it is subjected to during actual use. Initial shipping verification was performed to evaluate pallet shipping configurations according to ASTM D4169-14 using an assurance level II with distribution cycle 6. A subsequent gap assessment between the ASTM D4169-14 and ASTM D4169-16 confirmed that the previous requirements of ASTM D4169-14 satisfied the requirements of ASTM D4169-16.

Additional shipping verification was then performed to evaluate single packaging shipping configurations according to ASTM D4169-16 using an assurance level II with distribution cycles 3 and 13.

Membrane and filter integrity testing were performed after ship testing to evaluate gross mechanical damage to the fiber/filter.

5.7.4. Human Factors Testing

Formative and validation studies were conducted to address both labeling comprehension and user interaction with the DIASAFE®*plus*US. Execution of the human factors process is consistent with the requirements of ANSI/AAMI/IEC 62366-1:2015 and FDA guidance *Applying Human Factors and Usability Engineering to Medical Devices* (03 February 2016).

5.7.5. Software Verification and Validation Testing

This section is not applicable. The DIASAFE®*plus*US does not contain software.

5.7.6. Animal Studies

No animal studies were performed.

5.7.7. Clinical Studies

No clinical studies were performed.

5.8. Conclusion

The intended use, principle of operation, environment of use, and design of the DIASAFE®*plus*US are substantially equivalent to those of the predicate device. FMCRTG concludes that within the meaning of the Medical Device Amendments Act of 1976, the DIASAFE®*plus*US is safe and effective for its intended use