April 24, 2020

Dr. Franz Kohler Chemie GmbH
Clifton Czarnojon
Quality Manager
Werner-von-Siemens-Strabe 14-28
Bensheim, Hessen 64625
GERMANY

Re: K192408
Trade/Device Name: Custodiol HTK Solution
Regulation Number: 21 CFR 876.5880
Regulation Name: Isolated Kidney Perfusion and Transport System and Accessories
Regulatory Class: II
Product Code: KDL, MSB
Dated: March 23, 2020
Received: March 25, 2020

Dear Clifton Czarnojon:

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,

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)*
K192408

Device Name
CUSTODIOL® HTK Solution

Indications for Use *(Describe)*
CUSTODIOL® HTK solution is indicated for perfusion and flushing of donor kidneys, liver, pancreas and heart prior to removal from the donor or immediately after removal from the donor. The solution is left in the organ vasculature during hypothermic storage and transportation to the patient. CUSTODIOL® HTK solution is not indicated for continuous machine perfusion of donor organs.

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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K192408

1. General Info

Submission Date	**2019-03-23**
Device's Name	**CUSTODIOL® HTK Solution**
Submitter	**Dr. Franz Köhler Chemie GmbH** Werner-von-Siemens-Straße 14-28 64625 Bensheim Germany Tel.: +49 6251 1083-0 Fax: +49 6251 1083-146 E-Mail: info@koehler-chemie.de Internet: www.koehler-chemie.de
Official Contact Person	**Clifton Czarnojon** Quality Manager Tel.: +49 6251 1083-242 E-Mail: c.czarnojon@koehler-chemie.de
Common Device Name	**Set, Perfusion, Kidney, Disposable**
Classification Name	**Isolated kidney perfusion and transport system and accessories**
Classification Panel	**Gastroenterology/Urology**
Product Code	**KDL, MSB**
Regulation Number	21 CFR 876.5880
Device Class	**2**

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2. Summary of Legally Marketed Devices

In the table below is listed the predicate device deemed substantially equivalent to Dr. Franz Köhler Chemie GmbH CUSTODIOL® HTK Solution.

Subject Device	Predicate Device 1			
	Trade Name	Model Number	510(k) N°	510(k) Holder
CUSTODIOL® HTK Solution	CUSTODIOL® HTK Solution	N.A.	K043461	Dr. Franz Köhler Chemie GmbH

3. Device Description

The CUSTODIOL® HTK solution is intended for perfusion and flushing donor kidney, liver, heart, and pancreas prior to removal from the donor and for preserving these organs during hypothermic storage and transport to the recipient. CUSTODIOL® HTK solution is based on the principle of inactivating organ function by withdrawal of extracellular sodium and calcium, together with intensive buffering of the extracellular space by means of histidine/histidine HCI, so as to prolong the period for which the organs will tolerate interruption of blood and oxygen supply. Only a small portion of the osmolality of the CUSTODIOL® HTK solution is due to the sodium and potassium. The composition of HTK is similar to that of extracellular fluid. All of the components of the CUSTODIOL® HTK solution occur naturally in the body. The CUSTODIOL® HTK solution is relatively low in potassium concentration so that residual solution in the transplanted organ poses no danger to the recipient. This is particularly important in organs that take up relatively large amounts of the perfusate, which may find its way into the recipient's circulation. The CUSTODIOL® HTK solution has a low viscosity, even at low temperatures. This characteristic assures rapid flow rates during initial perfusion, allowing the organ to be quickly cooled.

3.1. Indication for Use

CUSTODIOL® HTK solution is indicated for perfusion and flushing of donor kidneys, liver, pancreas and heart prior to removal from the donor or immediately after removal from the donor. The solution is left in the organ vasculature during hypothermic storage and transportation to the patient. CUSTODIOL® HTK solution is not indicated for continuous machine perfusion of donor organs.

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4. Product Info

CUSTODIOL® HTK contains:

Component	Ingredient	Function
Active Components	Sodium chloride	Electrolyte
	Potassium chloride	Electrolyte
	Magnesium chloride hexahydrate	Electrolyte
	Calcium chloride dihydrate	Electrolyte
	Histidine	Buffering agent
	Histidine hydrochloride monohydrate	Buffering agent
	Tryptophan	Cell protective agent
	Mannitol	Osmolytic agent
	α-ketoglutaric acid	Cell protective agent
Excipients	Potassium hydroxide	pH adjusting agent
	Water for injections	Solvent

5. Subject / Predicate /Reference Devices Comparative Tables

5.1. Indication for Use Comparison

Indication for Use	Intended User
Subject Device / Dr. Franz Köhler Chemie GmbH / Product Code KDL/MSB / 510(k) N° - / CUSTODIOL® HTK Solution	
CUSTODIOL® HTK solution is indicated for perfusion and flushing of donor kidneys, liver, pancreas and heart prior to removal from the donor or immediately after removal from the donor. The solution is left in the organ vasculature during hypothermic storage and transportation to the patient. CUSTODIOL® HTK solution is not indicated for continuous machine perfusion of donor organs.	Federal law restricts sale of this device to or on the order of a physician or licensed practitioner.
Predicate Device 1 / Dr. Franz Köhler Chemie GmbH / Product Code KDL/MSB / 510(k) N° K043461 / CUSTODIOL® HTK Solution	
CUSTODIOL® HTK Solution is indicated for perfusion and flushing donor kidneys, liver, pancreas, and heart prior to removal from the donor or immediately after removal from the donor. The solution is left in the organ vasculature during hypothermic storage and transportation (not for continuous perfusion) to the recipient.	Federal law restricts sale of this device to or on the order of a physician or licensed practitioner.
Results after Predicate Device 1 Comparison	
Substantially Equivalent	Substantially Equivalent

5.1.1. Indication for Use Conclusions

As clearly demonstrated, in the table above, there are no differences between candidate and predicate device Indication for Use. Therefore, Indication for Use are deemed substantially equivalent.

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5.2. Biological Characteristics Comparison

Nature of Body Contact - Type		Nature of Body Contact - Category	Nature of Body Contact - Contact	Contact Duration
Subject Device / Dr. Franz Köhler Chemie GmbH / Product Code KDL/MSB / 510(k) N° - / CUSTODIOL® HTK Solution				
Direct ☒	Indirect ☐	Implant device	Tissues, blood, circulating blood	B – Prolonged (>24 h to 30 d)
Predicate Device 1 / Dr. Franz Köhler Chemie GmbH / Product Code KDL/MSB / 510(k) N° K043461 / CUSTODIOL® HTK Solution				
Direct ☒	Indirect ☐	Implant device	Tissues, blood, circulating blood	B – Prolonged (>24 h to 30 d)
Results after Predicate Device 1 Comparison				
Substantially Equivalent		Substantially Equivalent	Substantially Equivalent	Substantially Equivalent

5.2.1. Biological Characteristics Conclusions

Biological comparison has been provided in the aforementioned table. As clearly demonstrated, there are no differences between candidate and predicate device. Therefore, biological characteristics are deemed substantially equivalent.

5.3. Design / Technical Characteristics Comparison

Image	Delivery Status	Material	Packaging
Subject Device / Dr. Franz Köhler Chemie GmbH / Product Code KDL/MSB / 510(k) N° - / CUSTODIOL® HTK Solution			
	Sterile	Sodium chloride Potassium chloride Potassium hydrogen 2-ketoglutarate Magnesium chloride · 6H₂O Histidine · HCl · H₂O Histidine Tryptophan Mannitol Calcium chloride · 2H₂O	Bottles of 500 ml Bottles of 1000 ml Bags of 1000 ml Bags of 2000 ml Bags of 5000 ml
Predicate Device 1 / Dr. Franz Köhler Chemie GmbH / Product Code KDL/MSB / 510(k) N° K043461 / CUSTODIOL® HTK Solution			
	Sterile	Sodium chloride Potassium chloride Potassium hydrogen 2-ketoglutarate Magnesium chloride · 6H₂O Histidine · HCl · H₂O Histidine Tryptophan Mannitol Calcium chloride · 2H₂O	Bottles of 500 ml Bottles of 1000 ml
Results after Predicate Device 1 Comparison			
N.A.	Substantially Equivalent	Substantially Equivalent	Different; Substantial Equivalence demonstrated through non-clinical testing [a)]

a) Plastic materials used for infusion bags conform to Ph. Eur. Monographs 3.2 "Containers for pharmaceutical use" and 3.1 "Materials for the manufacture of containers for pharmaceutical use" requirements.
To comply with the USP<1663> Assessment of Extractables associated with pharmaceutical packaging/delivery systems, an extractable and leachable study has been carried out. Furthermore, CUSTODIOL® HTK solution has been tested for cytotoxicity, irritation and sensitization.
Compatibility of plastic materials used in infusion bags was confirmed for CUSTODIOL® HTK solution. The results of the comparative investigations performed with the plastic materials of the infusion bags permit the conclusion that the applied conditions of sterilization procedure have no influence on the quality of the product.

5.3.1. Design / Technical Characteristics Conclusions

Design/Technical comparison has been provided in the aforementioned table. As clearly demonstrated, differences between candidate and predicate device were evaluated through non-clinical testing, which supported that the devices are substantially equivalent.

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6. Summary of Performance Testing

6.1. Bench Testing

6.1.1. Biocompatibility

CUSTODIOL® HTK systemic toxicity, genotoxicity as well as hemocompatibility are considered to be satisfactorily demonstrated by available data.
Biological evaluation has been proved in accordance with:

- USP <85>, USP <87>, USP <88>, USP <381>, USP <661>, USP <1663>, EU.Ph 2.2.1, EU. Ph. 2.2.2, Eu. Ph. 2.2.25, Eu. Ph.3.1, EU. Ph. 3.2, Eu. Ph. 3.2.2, Eu.Ph. 3.2.9, ISO 10993-11 (Tests performed on packaging / solution)

CUSTODIOL® HTK cytotoxicity, irritation and sensitization additional tests were performed according to the ISO 10993-1/2/5/10/12 and are considered to be satisfactorily demonstrated.

6.1.2. Sterilization

CUSTODIOL® HTK Solution is supplied in STERILE via steam sterilization.

6.1.3. Shelf-Life

CUSTODIOL® HTK Solution shelf life has been validated up to 12 months through stability studies, biocompatibility testing, and packaging validation.

6.2. Animal Testing

Animal tests are deemed not necessary to demonstrate safety of CUSTODIOL® HTK Solution.

6.3. Clinical Testing

Clinical data are available and able to demonstrate reliability of CUSTODIOL® HTK Solution. To support the substantial equivalence for this 510(k), no further clinical data were required. The safety and efficacy of CUSTODIOL® HTK Solution as an organ preservation solution has not been clinically demonstrated in extended criteria donors (ECD), donation after cardiac arrest (DCD) or other marginal donor populations.

7. 510(k) Summary Conclusions

Based on the available 510(K) information, Dr. Franz Köhler Chemie GmbH CUSTODIOL® HTK solution is considered "substantially equivalent" to selected predicate device. Differences concerning the clinical application, intended use, biological aspects, design, technical features as well as performance specifications do not lead to any new risks. Both tests and validations performed on our devices support our statements.