November 1, 2019

Heraeus Medical GmbH
℅ Mary McNamara-Cullinane
Vice President of Regulatory Affairs
Alira Health
1 Grant Street
Framingham, Massachusetts 01702

Re: K191016
Trade/Device Name: COPAL® exchange G Hip Spacers
Regulation Number: 21 CFR 888.3390
Regulation Name: Hip joint femoral (hemi-hip) metal/polymer cemented or uncemented prosthesis
Regulatory Class: Class II
Product Code: KWY, KWL

Trade/Device Name: COPAL® exchange G Knee Spacers
Regulation Number: 21 CFR 888.3560
Regulation Name: Knee joint patellofemorotibial polymer/metal/polymer semi-constrained cemented prosthesis
Regulatory Class: Class II
Product Code: JWH

Dated: October 1, 2019
Received: October 2, 2019

Dear Ms. McNamara-Cullinane:

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,

Laurence D. Coyne, Ph.D.
Acting Director
DHT6C: Division of Restorative, Repair
and Trauma Devices
OHT6: Office of Orthopedic Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K191016

Device Name: COPAL® exchange G Hip and Knee Spacers

Indications for Use:

COPAL® exchange G Knee Spacer:
COPAL® exchange G knee (polymethylmethacrylate/gentamicin) is indicated for temporary use (maximum of 180 days) as a total knee replacement (TKR) in skeletally mature patients undergoing a two-stage procedure due to a septic process. COPAL® exchange G knee is applied on the femoral condyles and on the tibial plate following removal of the existing implant and radical debridement. The device is intended for use in conjunction with systemic antimicrobial antibiotic therapy (standard treatment approach to an infection).

COPAL® exchange G knee is not intended for use for more than 180 days, at which time it must be explanted, and a permanent device implanted, or another appropriate treatment performed (e.g., resection arthroplasty, fusion, etc.). COPAL® exchange G knee is only indicated for patientswho will consistently use traditional mobility assist devices e.g. crutches, walkers, canes) throughout the implantation period.

COPAL® exchange G Hip Spacer:
COPAL® exchange G hip (polymethylmethacrylate / gentamicin) is indicated for temporary use (maximum of 180 days) as a total hip replacement (THR) in skeletally mature patients undergoing a two-stage procedure due to a septic process. The device is inserted into the femoral medullary canal and acetabular cavity following removal of the existing implant and radical debridement. The device is assigned to be used in conjunction with systemic antimicrobial antibiotic therapy (standard treatment approach to an infection). COPAL® exchange G hip is not intended for use for more than 180 days, at which time it must be explanted, and a permanent device implanted, or another appropriate treatment performed (e.g., resection arthroplasty, fusion, perm etc.). COPAL® exchange G hip is only indicated for patients who will consistently use traditional mobility assist devices (e.g. crutches, walkers, canes) throughout the implantation period.

Prescription Use ___X___ AND/OR Over-The-Counter Use___
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

510(k) Summary for the Heraeus COPAL® exchange G Hip and Knee Spacers (per 21CFR 807.92)

1. SUBMITTER/510(K) HOLDER

Heraeus Medical GmbH
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Wehrheim Germany

Contact Person: Ljuba Litau Telephone: + 49 (0) 6181 / 35 – 23 39
Date Prepared: October 1, 2019

2. DEVICE NAME

Proprietary Name:	COPAL® exchange G Hip and Knee Spacers
Classification Name:	Hip and Knee Spacers
Common/Usual Name:	Hip and Knee Spacers

Classification Name:

• Knee joint patellofemorotibial polymer/metal/polymer semi-constrained cemented prosthesis.
• Hip joint femoral (hemi-hip) metal/polymer cemented or uncemented prosthesis.

Classification Regulation:	21 CFR 888.3560 and 21 CFR 888.3390
Product codes:	JWH, KWL and KWY

3. PREDICATE DEVICES

• Tecres Hip and Knee Spacers subject of K101356 (including its former versions K062274, K062273 and K031841)

4. DEVICE DESCRIPTION

The COPAL® exchange G Hip and Knee Spacers are combination products that provide patients, undergoing a two-stage revision procedure for an infected total joint, a temporary implant to l) allow for partial weight bearing and 2) provide an approximate natural range of motion. The devices also maintain a patient's soft tissue and joint space, preventing further complications such as muscular contraction. The gentamicin protects the device from bacterial colonization.

The COPAL® exchange G Hip and Knee Spacers are placed into the joint to maintain normal joint space and alignment. They provide patient comfort and limited mobility while the infection is being treated. The COPAL® exchange G Hip and Knee Spacers are made with bone cement that are loaded with gentamicin antibiotics. The COPAL® exchange G Hip and Knee Spacers are temporary joint prostheses designed to temporarily replace an infected implant during a total hip or knee arthroplasty and provide the patient with limited mobility and predictable, consistent local antibiotic release

COPAL® exchange G Hip Spacer
COPAL® exchange G Hip Spacer is a single use device that mimics a hemi-hip prosthesis and is available in 8 sizes and usable for both left and right hips.

The COPAL® exchange G Hip Spacers are combination products made of fully formed polymethylmethacrylate (radiopaque PMMA with gentamicin). The COPAL® exchange G Hip Spacers contain an inner stainless steel (AISI 316L stainless steel) reinforcing structure. The mass used in the filling of the molds (the PMMA unformed resin) is prepared from a powder component and a liquid component. The liquid component consists of methyl methacrylate, N, N-dimethyl-p-toluidine, hydroquinone. The powder component consists of polymethymethacrylate, calcium carbonite, benzoyl peroxide, and gentamicin sulphate. The raw materials and a summary of the manufacturing process are found below.

COPAL® exchange G Knee Spacer
COPAL® exchange G Knee Spacer is a single use device that is comprised of a tibia and femur component and is available in 3 sizes to form one knee spacer that is usable for left and right knee.

5. INTENDED USE

COPAL® exchange G Knee Spacer:
COPAL® exchange G knee (polymethylmethacrylate/gentamicin) is indicated for temporary use (maximum of 180 days) as a total knee replacement (TKR) in skeletally mature patients undergoing a two-stage procedure due to a septic process. COPAL® exchange G knee is applied on the femoral condyles and on the tibial plate following removal of the existing implant and radical debridement. The device is intended for use in conjunction with systemic antimicrobial antibiotic therapy (standard treatment approach to an infection).

COPAL® exchange G knee is not intended for use for more than 180 days, at which time it must be explanted, and a permanent device implanted, or another appropriate treatment performed (e.g., resection arthroplasty, fusion, etc.). COPAL® exchange G knee is only indicated for patients who will consistently use traditional mobility assist devices e.g. crutches, walkers, canes) throughout the implantation period.

COPAL® exchange G Hip Spacer:
COPAL® exchange G hip (polymethylmethacrylate / gentamicin) is indicated for temporary use (maximum of 180 days) as a total hip replacement (THR) in skeletally mature patients undergoing a two-stage procedure due to a septic process. The device is inserted into the femoral medullary canal and acetabular cavity following removal of the existing implant and radical debridement. The device is assigned to be used in conjunction with systemic antimicrobial antibiotic therapy (standard treatment approach to an infection). COPAL® exchange G hip is not intended for use for more than 180 days, at which time it must be explanted, and a permanent device implanted, or another appropriate treatment performed (e.g., resection arthroplasty, fusion, perm etc.). COPAL® exchange G hip is only indicated for patients who will consistently use traditional mobility assist devices (e.g. crutches, walkers, canes) throughout the implantation period.

6. TECHNOLOGICAL CHARACTERISTICS

The Heraeus COPAL® exchange G Spacers are substantially equivalent to the predicate device with respect to the following:

The intended use is equivalent in that they are both indicated for temporary use (maximum of 180 days) as a total hip replacement (THR) or total knee replacement (TKR) for skeletally mature patients undergoing a two-stage procedure due to a septic process. The proposed and predicate devices are intended for use in conjunction with systemic antimicrobial antibiotic therapy (standard treatment approach to an infection).

The technological characteristics of the Heraeus COPAL® exchange G Spacers and the predicate product are identical in that they are all designed to mimic a permanent

implant that include an antibiotic for use in infected joints for a period of up to 180 days. The configurations consist of hip and knee components that mimic the intended anatomical space. The proposed Heraeus COPAL® exchange G Spacers and the predicate devices both contain an antibiotic component that helps to facilitate the healing process. The dressings are PMMA products which provide position and structure to the anatomical area. There are no major differences between the proposed and the predicate devices and are essentially identical in materials and design.

The operational characteristics of the Heraeus COPAL® exchange G Spacers are equivalent to the predicate device. Both Spacers provide patients, undergoing a two-stage revision procedure for an infected total joint, a temporary implant to: l) allow for partial weight bearing and 2) provide an approximate natural range of motion. The devices also maintain a patient's soft tissue and joint space, preventing further complications such as muscular contraction. The gentamicin protects the device from bacterial colonization.

The Heraeus COPAL® exchange G Spacers and the predicate devices are placed into the joint to maintain normal joint space and alignment. They provide patient comfort and limited mobility while the infection is being treated. The COPAL® and predicate Spacers are made with bone cement and the Tecres spacers are loaded with gentamicin antibiotics.

The technological characteristics of the proposed Heraeus COPAL® exchange G Spacers are equivalent to the predicate device: the Hip Spacers are comprised of PMMA, gentamicin and a stainless-steel inlay and the Knee Spacers are comprised of PMMA and gentamicin. The design and operational characteristics are equivalent for the proposed and predicate devices in that they mimic the permanent implants and are intended to be used as temporary implants in conjunction with systemic antibiotic therapy. The proposed and predicate devices are provided in a range of sizes that are compatible with skeletally mature adults. All of these technological characteristics are equal fit, form and function resulting in the Heraeus COPAL® exchange G Spacers being substantially equivalent to the Tecres Hip and Knee Spacers.

7. PERFORMANCE TESTING

Testing was conducted according to the FDA recognized standards in order to demonstrate equivalence to the predicate devices. These tests include:

Biocompatibility testing is performed in accordance with the FDA Guidance, “Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1.

The following testing was conducted according to the FDA recognized standards in order to demonstrate equivalence to the predicate devices:

- Biocompatibility testing was performed in accordance with the FDA Guidance, “Use of International Standard ISO 10993-1-2016, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"” including cytotoxicity, irritation, hypersensitivity, acute and subchronic systemic toxicity and mutation assays.

    - The in vitro cytotoxicity was performed according to ISO 10993-5-2009. No leachable substances were dissolved in cytotoxic amounts under the test conditions.
    - An irritation test according to ISO 10993-10, -1, -12 (Intracutaneous Reactivity) was carried out. Under the conditions of the test the polar as well as the nonpolar extracts of the test item caused no signs of irritation. The test item is classified as not irritant.
    - A test for delayed-type hypersensitivity (Guinea Pig Maximization Test) was carried out according ISO10993- 10, -1, -12. Under the conditions of the test, no reactions were identified as sensitization.
    - A test of acute systemic toxicity was performed according to the guidelines ISO 10993-11, -1, -12 and ASTM F750-87 (reapproved 2012). Under the conditions of the study, it can be stated that the test item showed no acute systemic toxic characteristics.
    - A reverse mutation assay was carried out according ISO10993-3, -1, -12. The results are considered to be non-mutagenic.
    - An in vitro mammalian cell gene mutation assay was carried out according to ISO10993-3 -1, -12. Under the conditions of the assay, the extracts of the test item are considered to be non-mutagenic.
    - A femoral bone implantation study combined with an assessment of subchronic systemic toxicity were carried out according to ISO10993- 6, 11, -1, -12. At the implantation sites, there were no inflammatory or degenerative findings encountered.
    - In summary, it can be stated that the COPAL® exchange G spacers are biocompatible according to ISO10993-2016. The proposed COPAL® exchange G spacers and the predicate devices were both tested for biocompatibility according to ISO10993.

- Sterilization Validation was performed in accordance to ISO 11135 and AAMI TIR 28. The sterilization was carried out by gassing with ethylene oxide. The sterilization cycle is designed to deliver sterile units, starting with a defined bioburden and ending with a sterility assurance level (SAL) of 10^{-6}.

Based on the tests performed and the results obtained, the chosen sterilization process can be considered as valid.

- The shelf life of the COPAL® exchange G spacers was tested at 25 ± 2 °C over a period of 36 months. The test times were 0 months, 3 months, 6 months, 9 months, 12 months, 24 months and 36 months. The sterility according to DIN EN ISO 11737, Part 2, the compressive strength according to ISO 7206-6 and ISO 14879-1, the gentamicin content and the content of gentamicin impurities were tested with an HPLC analysis method. All examined hip spacers and knee spacers were sterile throughout the storage period. The compressive strength of the hip spacers and knee spacers was within the specified range. The gentamicin content and gentamicin impurities remained within the specified range over the entire storage period. In summary, the COPAL® exchange G spacers were stable at a temperature of 25 ± 2 ° and a humidity of 50 % for a period of 36 months.

- Validation of the sterile barrier were performed according to ISO 11607-1 and ISO 11607-2 to show the integrity of the system. In addition, the maintenance of the sterile barrier system through transport and shelf life over 5 years was investigated.

- Mechanical tests were conducted in order to demonstrate that the Heraeus COPAL® exchange G Spacers function as intended and are safe and effective for their intended use.

    - The compressive strength of the COPAL® exchange G spacers were tested in accordance with ISO 14879-1, ISO 7206-4 and ISO 7206-6. The results show that COPAL® exchange G spacers are equivalent to the predicate devices.
    - The cyclic fatigue tests were performed according to ISO 14879-1 and ISO 14242-1:2012. Regarding the cyclic fatigue, the COPAL® exchange G spacers are equivalent compared to the predicate devices.
    - Abrasion tests were performed according to ISO 14243-1:2009 and ISO 14242-1:2012. The results show that COPAL® exchange G spacers are equivalent to the predicate devices.

In summary, the verification and validation testing performed demonstrate that the Heraeus COPAL® exchange G Spacers function as intended and is safe and effective for their intended use and where appropriate were tested and found to be substantially equivalent to the predicate devices.

8. CONCLUSION OF SUBSTANTIAL EQUIVALENCE

The Heraeus COPAL® exchange G Spacers have been shown to be substantially equivalent to the predicate devices. Substantial equivalence has been demonstrated through a comparison of intended use, design and technological characteristics, as well as performance testing. The information provided within this premarket notification supports

substantial equivalence of the subject device to the predicate devices. and demonstrates them to be essentially identical.