September 28, 2021

TransMedics, Inc.
Thalia Charles
Director, Regulatory Affairs
200 Minuteman Road, Suite 302
Andover, Massachusetts 01810

Re: P200031
Trade/Device Name: Organ Care System (OCS™) Liver
Product Code: QQK
Filed: June 30, 2020
Amended: February 11, 2021

Dear Thalia Charles:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Organ Care System (OCS™) Liver. The TransMedics® Organ Care System (OCS™) Liver is a portable extracorporeal liver perfusion and monitoring system indicated for preservation and monitoring of hemodynamics and metabolic function which allows for ex-vivo assessment of liver allografts from donors after brain death (DBD) or liver allografts from donors after circulatory death (DCD) ≤55 years old and with ≤30 mins of warm ischemic time, macrosteatosis ≤15%, in a near-physiologic, normothermic and functioning state intended for a potential transplant recipient. We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below. Although this letter refers to your product as a device, please be aware that some approved products may instead be combination products. The Premarket Approval Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm identifies combination product submissions.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at one year for the OCS Liver Perfusion Set and three years for the OCS Liver Bile Salts. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

Continued approval of the PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. This report, identified as "Annual Report" and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

In addition to the above, and to provide continued reasonable assurance of the safety and effectiveness of the PMA device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below.

**1. OCS Liver PROTECT Continuation PAS (Protocol Number OCS-LVR-01-PAS, Rev. 1.0, dated September 14, 2021):**

The OCS Liver PROTECT Continuation PAS is an observational study designed to evaluate long-term outcomes in the PROTECT trial cohort. The 300 patients who were randomized to the OCS and control (cold storage) arms in the PROTECT trial will be followed up to 2 years post-transplant. The primary effectiveness endpoint is liver graft survival at 24 months post-transplant. The other study endpoint is patient survival at 24 months post-transplant.

You must meet the following timelines for the PROTECT Continuation PAS:

- Complete 2-year follow-up on all PAS participants by November 30, 2021
- Submit a Final Report by February 28, 2022

**2. OCS Liver PROTECT CAP Continuation PAS (Protocol Number OCS-LVR-02-PAS, Rev. 1.0, dated September 14, 2021):**

The OCS Liver PROTECT CAP Continuation PAS is an observational study designed to evaluate long-term outcomes in the PROTECT CAP cohort. Seventy-four subjects who were transplanted with OCS-preserved livers in the CAP study will be followed through 2 years post-transplant. The primary effectiveness endpoint is liver graft survival at 24 months post-transplant. The other study endpoint is patient survival at 24 months post-transplant.

You must meet the following timelines for the PROTECT CAP Continuation PAS:

- Complete 2-year follow-up on all PAS participants by March 31, 2023
- Submit a Final Report by June 30, 2023

**3. OCS Liver Perfusion (OLP) New Enrollment PAS (Protocol Number OCSLIVER-01-PAS, Rev. 1.0, dated September 16, 2021):**

The OLP registry is a multi-center, single-arm, observational study designed to evaluate the short- and long-term safety and effectiveness of the OCS Liver System for DBD and DCD donor livers preserved on OCS according to the approved indication. To evaluate real-world use of the device, the OLP registry will include all liver transplant centers in the U.S. that will commercially use the OCS Liver System, with a minimum of 15 sites enrolled.

The PAS will enroll the initial 160 sequential adult primary liver transplant recipients who are transplanted with an OCS-perfused DBD or DCD donor liver according to the approved indication. If the initial 160 recipients do not include at least 60 DCD donor liver transplants, the OLP registry will continue to enroll only DCD donor liver recipients until 60 DCD recipients have been enrolled. This is to ensure adequate assessment of device performance in DCD donor livers. PAS participants will be followed for 2 years post-transplantation and all analyses will be stratified by DBD and DCD donor populations.

The primary endpoint is patient and graft survival at 1 year. The safety endpoint is liver graft survival at 6 months. Additional clinical endpoints include: incidence of ischemic, non-anastomotic biliary complications through 1-year; incidence of non-ischemic, anastomotic biliary complications through 6 months; Kaplan-Meier estimates for patient survival at 1- and 2-years; and Kaplan-Meier estimates for graft survival at 6 months, 1- and 2-years.

In addition to the patient outcomes listed above, the following data will be collected: OCS Liver perfusion parameters (hepatic artery flow and pressure, portal vein flow and pressure, perfusate temperature, perfusate hematocrit, and perfusate venous saturation); lactate levels; pH value at beginning and end of OCS perfusion; total bile volume at end of OCS perfusion; incidence of and clinical reasons for donor liver turndown following OCS perfusion; incidence of and reasons for conversion to cold storage after initiation of OCS perfusion; device malfunctions that are routinely obtained from customer complaints and MDRs; and the donor liver utilization rate.

The primary analysis population will be comprised of the first 160 sequential patients who meet the approved indication for use according to adjudication by the Clinical Events Committee (CEC). For the primary endpoint, this study will test the hypothesis that 1-year patient and graft survival in the PAS is greater than a performance goal of 83.5%. This study will also test the hypothesis that 6-month graft survival is greater than a performance goal of 85.5%. The full PAS cohort will continue to be followed for 2 years, for evaluation of all study endpoints using descriptive analyses.
From the time of study protocol approval, you must meet the following timelines for the OLP New Enrollment PAS:

- First patient enrolled within 6 months
- 20% of patients enrolled within 15 months
- 50% of patients enrolled within 21 months

- 100% of patients enrolled within 33 months
- Submission of Final Report 3 months after study completion (i.e., last enrolled patient completes 2-year follow-up)

In addition, you must submit separate periodic reports on the progress of the OLP New Enrollment PAS as follows:

- PAS Progress Reports every 6 months until subject enrollment has been completed, and annually thereafter.
- If any enrollment milestones are not met, you must begin submitting quarterly enrollment status reports (i.e., every 3 months), in addition to your periodic (6-months) PAS Progress Reports, until FDA notifies you otherwise.

For the first two condition of approval studies, you must submit separate PAS Progress Reports for each study, every 6 months till the date of the submission of Final Report specified in this letter.
Each PAS report should be submitted to the address below identified as a "PMA Post-Approval Study Report" in accordance with how the study is identified above and bearing the applicable PMA reference number.

Be advised that failure to comply with any post-approval requirement, including the initiation, enrollment, reporting, and completion requirements outlined above, constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c) and 814.46(a)(2).

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.46(a)(3)-(4).

Be advised that protocol information, interim and final results will be published on the Post Approval Study Webpage https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm.
In addition, results from any post approval study should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (https://www.fda.gov/media/71327/download).

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final Unique Device Identification (UDI) rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR 830 Subpart E). Additionally, 21 CFR 814.84 (b)(4) requires PMA annual reports submitted after September 24, 2014, to identify each device identifier currently in use for the subject device, and the device identifiers for devices that have been discontinued since the previous periodic report. It is not necessary to identify any device identifier discontinued prior to December 23, 2013. Combination Products may also be subject to UDI requirements (see 21 CFR 801.30). For more information on these requirements, please see the UDI

website, https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-udi-system.

Before making any change affecting the safety or effectiveness of the PMA device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" https://www.fda.gov/media/81431/download.

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52 for devices or post-marketing safety reporting (21 CFR 4, Subpart B) for combination products, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems and on combination product post-marketing safety reporting is available at (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products).

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the post-marketing safety reporting requirements (21 CFR 4, Subpart B) for combination products, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/industry-guidance-recalls.

CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet Home Page located at https://www.fda.gov/medical-devices/device-approvals-denials-and-clearances/pma-approvals. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for

review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with a copy of all final labeling. Final labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final labeling is identical to the labeling approved in draft form. If the final labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Bridget Wildt at 301-796-0244 x0244 or Bridget.Wildt@fda.hhs.gov.

Sincerely,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Office Director
OHT3: Office of GastroRenal, ObGyn,
General Hospital and Urology Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health