May 31, 2019

Miriam C. Provost, Ph.D.
Vice President of US Regulatory and FDA Relations
TransMedics, Inc.
200 Minuteman Road, Suite 302
Andover, MA 01810

Re: P160013/S002
Trade/Device Name: Organ Care System (OCS™) Lung System
Product Code: QBA, PHO
Filed: August 14, 2018
Amended: September 27, 2018, March 1, 2019

Dear Miriam C. Provost:

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) supplement for the Organ Care System (OCS™) Lung System for expanding the indication for use to include preservation of donor lung pairs initially deemed unacceptable for procurement and transplantation based on the limitations of cold static preservation. The TransMedics Organ Care System (OCS™) Lung is a portable normothermic organ perfusion, ventilation and monitoring medical device indicated for preservation of standard criteria donor lung pairs and for preservation of donor lung pairs initially deemed unacceptable for procurement and transplantation based on the limitations of cold static preservation. The device allows for ex vivo assessment of donor lungs prior to transplantation. We are pleased to inform you that the PMA supplement 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 24 months. 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 in order 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. Separate PAS Progress Reports must be submitted for each study every six (6) months during the first two (2) years of the study and annually thereafter, unless otherwise specified by FDA. Two (2) copies of each report, identified as "EXPAND Continuation PAS" or "OCS Lung PAS: Donor Lungs Initially Deemed Unacceptable (DLIDU)" in accordance with how the study is identified below and bearing the applicable PMA reference number, should be submitted to the address below.

1. EXPAND Continuation PAS (OCS-LUN-122018 Rev 2.0 dated May 24, 2019):

The EXPAND Continuation PAS is a single-arm, prospective, observational study designed to evaluate long-term outcomes in EXPAND Trial patients. All 79 US and OUS EXPAND patients will be approached to provide informed consent to be followed for up to 5 years post transplantation. Only patients who provide written informed consent will be enrolled in this PAS. The primary effectiveness endpoint is BOS-free survival through 5 years after transplantation. Other endpoints include 5-year survival and 5-year freedom from BOS.

Continued approval of the PMA is based, in part, on your completion of the EXPAND Continuation PAS. You are required to do the following:

- Enroll (i.e., re-consent) your first study subject by October 31, 2019
- Complete subject enrollment by December 31, 2019
- Complete the 5-year study and submit a Final Report to the Agency by February 23, 2022

2. OCS Lung PAS: Donor Lungs Initially Deemed Unacceptable (DLIDU) (OCS-LUN-PAS01 Rev 2.0 dated May 29, 2019)

The post-approval study is a prospective, single-arm, multi-center, observational study designed to evaluate the short- and long-term safety and effectiveness of the OCS Lung System for donor lungs initially deemed unacceptable for procurement and transplantation based on limitations of cold static storage. Data will be collected through the Organ Care System (OCS™) Lung Thoracic Organ Perfusion (TOP) Registry for Donor Lungs, which is an all-comers registry designed to evaluate the use of the OCS device in the real-world setting. The TOP Registry collects data on all donor lungs that are preserved on the OCS system and all patients who receive OCS-preserved lungs in the United States. Data will be collected through the United Network of Organ Sharing (UNOS) Registry. Data that are not routinely collected in UNOS, but required for the PAS will also be collected, with source document verification.

This PAS will enroll all patients who are transplanted with OCS-preserved donor lungs that are initially deemed unacceptable. The Primary Analysis Population (PAP) will be comprised of the first 266 patients who meet the recipient eligibility criteria for the Donor Lungs Initially Deemed Unacceptable Primary Analysis Population and are transplanted with donor lungs from a donor who meets the donor eligibility criteria for the Donor Lungs Initially Deemed Unacceptable Primary Analysis Population, according to adjudication by the Clinical Events Committee (CEC). The full PAS cohort will consist of the PAP and all other enrolled patients who are transplanted with OCS-preserved donor lungs initially deemed unacceptable but do not meet the PAP criteria. Study enrollment will end when all 266 patients who meet the PAP criteria have been enrolled.

Patients who are transplanted with OCS-preserved donor lungs initially deemed unacceptable at 30 U.S. sites will be followed for 5 years post-transplantation. The primary endpoint is patient and graft survival at 12 months post double-lung transplant. The secondary endpoints are incidence of PGD3 at 72 hours post-transplantation, donor lung utilization rate, and the incidence of PGD3 within the initial 72 hours post-transplantation. Additional study endpoints include: total ischemia and cross-clamp times for the first and second transplanted lungs; lung graft-related serious adverse events through 30 days post-transplant or initial hospital stay (whichever is longer) including bronchial anastomotic complications and pulmonary-related infection; patient survival (simple proportion) at 30 days, through initial hospital stay (if longer than 30 days), and at months 6, 12, 24, 36, 48, and 60; patient survival (Kaplan-Meier estimates) at months 1, 6, 12, 24, 36, 48, and 60; BOS-free survival at months 12, 24, 36, 48, and 60; freedom from BOS at months 12, 24, 36, 48, and 60; incidence of BOS at months 12, 24, 36, 48, and 60; and incidence of re-transplantation (graft failure) at months 12, 24, 36, 48, and 60.

In addition to the patient outcomes listed above, data will be collected on donor lung turn down and conversion to cold storage following OCS instrumentation. Data related to the OCS device will also be collected, including preservation and ventilation parameter trends (i.e., pulmonary artery pressure, peak airway pressure, and vascular resistance), lung oxygenation capacity, and device malfunctions.

The study will test the hypothesis that 1-year patient and graft survival (primary endpoint) in the PAP is greater than 78%. All other endpoints in the PAP and the full PAS cohort will be analyzed using descriptive analyses.

Independent third-party audits will be conducted bi-annually for the first 36 months after study initiation and annually thereafter. Audit reports will be submitted by the independent auditor to the FDA including any corrective action plans that are required to address the audit findings. A data safety monitoring board, steering committee, and CEC will provide additional data monitoring and study oversight for the duration of the study.

As stated above, you are required to provide interim reports to FDA every six months for the first two years after device approval, and annually thereafter until study completion. In addition, an interim report will be submitted for analysis of 1-year follow-up data in the PAP. Submission of the Final Report will include analyses of 5-year follow-up data in the PAP and 5-year follow-up data in the full PAS cohort. All interim reports will include the UNOS ID and CEC-adjudicated indicator for inclusion in the Primary Analysis Population for each patient enrolled to date, cumulatively. In addition, complete line-item patient-level data will be submitted as follows: every 2 years from the date of PMA approval until submission of the 1-year PAP Analysis Report; in the 1-year PAP Analysis Report; and in the 5-year Final Report. PAS summary data will be posted on the PAS webpage as follows: information on study progress from each interim report including number of sites enrolled, number of patients enrolled, and baseline characteristics (such as age, race/ethnicity, etc.); results from the 1-Year PAP Analysis Report; and results from the 5-Year Final Report.

Continued approval of the PMA is based, in part, on your completion of the OCS™ Lung PAS: Donor Lungs Initially Deemed Unacceptable. You are required to do the following:

- Enroll your first study subject no later than October 31, 2019
- Enroll at least 34 subjects by June 30, 2020
- Enroll at least 65 subjects by December 31, 2020
- Enroll at least 106 subjects by June 3, 2021
- Enroll at least 156 subjects by December 31, 2021
- Enroll at least 211 subjects by June 30, 2022
- Complete enrollment of the Primary Analysis Population (n=266) by January 31, 2023
- Submit 1-Year PAP Analysis Report to the Agency by June 30, 2024
- Submit 5-Year Final Report on Analyses of PAP and the full PAS cohort by June 30, 2028

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

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.

Be advised that protocol information, interim and final results will be published on the Post Approval Study Webpage http://www.fda.gov/devicepostapproval.

In addition, the 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" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm).

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, http://www.fda.gov/udi.

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" http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm.

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 postmarketing 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm and on combination product postmarketing safety reporting is available at (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm).

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the postmarketing 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 http://www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm.

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 HomePage located at http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm. 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 Jessica K. Nguyen, Ph.D. at (301) 796-6277 or Jessica.Nguyen@fda.hhs.gov.

Sincerely,

Benjamin R. Fisher -S

Benjamin R. Fisher, Ph.D.
Director
OHT3: Office of GastroRenal, ObGyn,
General Hospital and Urology Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health