



March 22, 2018

TransMedics, Inc
% Miriam Provost, PhD
Vice President of US Regulatory and FDA Relations
TransMedics, Inc.
200 Minuteman Road
Suite 302
Andover, Massachusetts 01810

Re: P160013

Trade/Device Name: Organ Care System (OCS™) Lung System

Filed: May 23, 2016

Amended: May 23, 2016, September 22, 2016, October 20, 2016, December 6, 2016, July 12, 2017, August 4, 2017, August 17, 2017, August 22, 2017, September 12, 2017, November 15, 2017, February 20, 2018, February 26, 2018

Product Code: QBA

Dear Miriam 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) for the Organ Care System (OCS™) Lung System. The TransMedics® Organ Care System (OCS™) Lung System is a portable organ perfusion, ventilation, and monitoring medical device indicated for the preservation of standard criteria donor lungs in a near physiologic, ventilated, and perfused state for double lung transplantation. 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.

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 the Lung Perfusion Set and the OCS™ Lung Solution 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. Two copies of 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. This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final 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. For more information on these requirements, please see the UDI website, <http://www.fda.gov/udi>.

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 an "ODE Lead PMA Post-Approval Study Report" or "OSB Lead PMA Post-Approval Study Report" in accordance with how the study is identified below and bearing the applicable PMA reference number, should be submitted to the address below.

1. ODE Lead PMA Post-Approval Study – INSPIRE Continuation PAS (Revision 1.0, dated January 9, 2018):

The INSPIRE Continuation PAS is a two-arm observational study intended to evaluate long-term outcomes of the INSPIRE Trial patients. The study population will include all U.S. INSPIRE patients and all OUS INSPIRE patients who consent to participation. The primary effectiveness endpoint is BOS-free survival through 5 years after transplantation. The follow-up period for all patients will be up to 5 years. Interim PAS reports will be submitted to FDA at 6, 12, 24, and 36 months after PMA approval. A final report will be submitted to FDA when all patients complete their 5-year follow-up.

2. OSB Lead PMA Post-Approval Study – OCS Lung Thoracic Organ Perfusion (TOP) PAS Registry (Revision 1.0, dated March 4, 2018):

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. This all-comers registry is designed to evaluate the use of the OCS device in the real-world setting. As such, the PAS will collect data on all donor lungs that are preserved on the OCS system and all patients who receive OCS-treated lungs. The only exception is the transplantation of OCS-treated marginal lungs that are tracked in the EXPAND II trial. 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.

Five hundred (500) patients who are transplanted with OCS-perfused lungs at 30 sites in the United States will be followed for 5 years post-transplantation. The primary endpoint is patient and graft survival at 12 months. The co-secondary endpoints are total ischemic time and incidence of PGD3 within 72 hours. Additional study endpoints include: PGD3 at 72 hours; 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 respiratory failure, bronchial anastomotic complications, and pulmonary-related infection; patient survival at 30 days; patient survival through initial hospital stay (if longer than 30 days); Kaplan-Meier estimates for patient survival 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; re-transplantation at months 12, 24, 36, 48, and 60; and freedom from re-transplantation and mortality 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 Primary Analysis Population will be comprised of the first 289 patients who meet the approved indication for use according to adjudication by the Clinical Events Committee (CEC). The following hypothesis tests will be conducted in the Primary Analysis Population when all 289 patients have completed 1 year of follow-up. For the primary endpoint, this study will test the hypothesis that 1-year patient and graft survival in the PAS is greater than 79%. For the co-secondary endpoints, data from the PAS (OCS treatment group) will be compared to historical control data from the INSPIRE study for the following: to test the hypothesis that mean total ischemic time is lower in the OCS versus historical control groups; and to test the hypothesis that incidence of PGD3 within 72 hours is lower in the OCS versus historical control groups. The full PAS cohort of 500 patients will continue to be followed for 5 years, for evaluation of all study endpoints using descriptive analyses.

You are required to provide reports to FDA every six months for the first two years after device approval, and annually thereafter until study completion. In addition, interim reports will be submitted for analyses of 1-year and 5-year follow-up in the Primary Analysis Population. 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 study initiation until submission of the 1-year Primary Analysis Report; in the 1-year Primary Analysis Report; and in the Final PAS Report. PAS summary data will be posted on the PAS webpage as follows: information

on study progress from each interim report limited to: number of sites enrolled; number of patients enrolled; baseline characteristics (such as age, race/ethnicity, etc); results from the 1-Year Primary Analysis Report (1-year follow-up data in the Primary Analysis Population); and results from the final PAS Report (5-year follow-up in 500 patients).

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.

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes the agreed upon complete protocol for the new enrollment post-approval study described above, including the electronic Case Report Forms (eCRFs). Subject enrollment in the PAS may not begin until agreement has been reached on the finalized eCRFs. Your PMA supplement should be clearly labeled as an "OSB Lead PMA Post-Approval Study Protocol" as noted above and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing. Please include a brief cover letter stating that the only changes to the PAS protocol are in the eCRFs and that no changes were made to other parts of the protocol.

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>).

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, 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>.

In accordance with the recall requirements specified in 21 CFR 806.10, 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 copies 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 in 6 copies, 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
PMA 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 Andrew Fu, PhD at 301-796-5881 or Andrew.Fu@fda.hhs.gov.

Sincerely,

Randall G. Brockman -S

for

William H. Maisel, MD, MPH
Director
Office of Device Evaluation
Center for Devices and Radiological Health