April 26, 2019

XVIVO Perfusion, Inc.
Jaya Tiwari
Clinical Research Program Manager
3666 S. Inca Street
Englewood, Colorado 80110

Re: P180014
Trade/Device Name: XPS™ with STEEN Solution™ Perfusate
Product Code: PHO
Filed: May 11, 2018
Amended: August 7, 2018, January 28 and March 21, 2019

Dear Jaya Tiwari:

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 XPS™ with STEEN Solution™ Perfusate. This device is indicated for use in flushing and temporary continuous normothermic machine perfusion of initially unacceptable excised donor lungs during which time the ex vivo function of the lungs can be reassessed for transplantation. We are pleased to inform you that the PMA is approved. You may continue commercial distribution of the device upon receipt of this letter. 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). 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 two (2) years after manufacture for the STEEN Solution™ Perfusate and the XVIVO Disposable Lung Circuit™ and at four (4) years post-manufacture for the XVIVO Organ Chamber™ and the XVIVO Disposable Lung Cannula Set ™. This is to advise you that the protocols you used to establish this expiration dating are considered approved protocols 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. Each report, identified as a "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.

PMA Post-Approval Studies:

1. ***NOVEL/NOVEL Extension Continuation Long-Term Post Approval Study of NOVEL and NOVEL Extension Subjects:***

   The NOVEL/NOVEL Extension Continuation Long-Term PAS is a two-arm observational study intended to evaluate long-term outcomes of the NOVEL trial patients. The study population includes all NOVEL and NOVEL Extension patients, including both arms of the study, who consent to participation. The primary effectiveness endpoint is Bronchiolitis Obliterans Syndrome (BOS)-free survival through 5 years after transplantation. The follow-up period for all patients is through 5 years. You are required to have set up this PAS, have collected additional follow up-data on at least 40% of your NOVEL/NOVEL Extension study population for this PAS, and have submitted the initial interim PAS report to FDA within 6 months of PMA approval. By the 1-year interim report, you are required to provide follow-up data on at least 90% of study subjects. You are required to submit a final report to FDA when all patients reach 5-year follow-up, and to have 5-year follow-up data for at least 90% of study subjects.

2. ***Long-Term Evaluation Post-Approval Study of the XPS™ System with STEEN Solution™ Perfusate:***

   The Long-Term Evaluation PAS of the XPS™ System with STEEN Solution™ Perfusate is a prospective, single arm, multi-center study of all comers using the XPS™ System with STEEN Solution™. The study's objectives are to 1) confirm 12-month patient survival data and assess long term performance (i.e., 5 years post-transplantation), 2) assess the effect of the new transplantability criteria (i.e., including the Adaptive Eligibility Criteria introduced in 2014) on lung utilization; and 3) assess real world use of the device with current lung allocation rules. The study will collect data on

all donor lungs that are preserved on the XPS™ system and all patients who receive XPS™-treated lungs for 5 years following initiation of the PAS, and includes follow-up for 5 years post-transplantation. The primary endpoint for the study is a composite of 12-month survival and incidence of Primary Graft Dysfunction (PGD) Grade 3 at 72 hours post-transplantation, and these data will be compared to data from the United Network Organ Sharing (UNOS) Scientific Registry of Transplant Recipients (SRTR) registry. The study also assesses, among other things, the incidence of BOS at 1-5 years post-transplantation, Quality of Life at 1-5 years post-transplantation, and patient survival at 1-5 years post-transplantation. The basic elements of this study were agreed upon via interactive review on April 26, 2019 (see email of April 26, 2019).

You will be allowed to continue marketing your device per the approval of HDE120003 for up to 6 months following PMA approval, while the PAS study is being initiated. Within 6 months of PMA approval, you are required to initiate your study, i.e. your FDA-approved PAS clinical protocol and Statistical Analysis Plan should be in place. Following study initiation, all donor lungs that are preserved on the XPS™ system and all patients who receive XPS™-treated lungs (i.e., all-comers) should be captured in the PAS for the next 5 years. You are required to submit interim PAS reports to FDA as described above. The first interim report should be submitted 6 months after PMA approval. You are required to submit a final report to FDA when all patients reach 5-year follow-up and have 5-year follow-up data on all enrolled study subjects.

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).

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes complete protocols of your post-approval studies described above. You must also obtain approval of your PAS protocol within 120 days of the date of this letter. Your PMA supplements should be clearly labeled as a "PMA Post-Approval Study Protocol" as noted above and submitted to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

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 Gema Gonzalez at 301-796-6519 or Gema.Gonzalez@fda.hhs.gov.

Sincerely,

Joyce M. Whang -S

for
Benjamin R. Fisher, Ph.D.
Director
Division of Reproductive, Gastro-Renal,
and Urological Devices
Office of Device Evaluation
Center for Devices and Radiological Health