



Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

August 12, 2014

Mary Pohl
Product Specialist, Transplantation
XVIVO Perfusion, Inc.
3666 S Inca Street
Englewood, CO 80110

Re: H120003
HUD Number: 08-0194
XVIVO Perfusion System (XPS™) with STEEN Solution™ Perfusate
Filed: July 10, 2012
Amended: November 15, 2012, June 5, October 18, and November 15, 2013, January 8
and 23, February 20, and June 20 and 25, 2014
Procode: PHO

Dear Ms. Pohl,

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your humanitarian device exemption (HDE) application for the XPS™ System with STEEN Solution™ Perfusate. This device is indicated for the 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 your HDE is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below.

The sale, distribution, and use of this device are limited to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) under the authority of section 515(d)(1)(B)(ii) of the FD&C Act. In addition, in order to ensure the safe use of the device, FDA has further restricted the device within the meaning of section 520(e) of the FD&C Act under the authority of section 515(d)(1)(B)(ii) of the FD&C Act insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the FD&C Act.

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 this HDE is contingent upon the submission of periodic reports, required under 21 CFR 814.126, at intervals of one year (unless otherwise specified) from the date of

approval of the original HDE. Two (2) copies of this report, identified as "Annual Report" and bearing the applicable HDE 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 814.126.

In addition to the above, an HDE holder is required to maintain records of the names and addresses of the facilities to which the HUD has been shipped, correspondence with reviewing institutional review boards (IRBs), as well as any other information requested by a reviewing IRB or FDA.

In addition to the Annual Report requirements, you must provide the following data in post-approval study reports (PAS). Two (2) copies of this report, identified as "HDE Post-Approval Study Report" and bearing the applicable HDE reference number, should be submitted to the address below.

Long-Term Evaluation Study for XPS™ System with STEEN Solution™ Perfusate: You have agreed to conduct a study as follows: the purpose of the study is to evaluate the longer-term safety and to collect quality of life data for patients who were transplanted with an *Ex Vivo* Lung Perfusion (EVLP) treated lung. This will be a prospective, multicenter, two-arm study with a total of 252 patients consisting of both a premarket cohort and newly enrolled patients. The treatment arm will consist of 126 patients who receive EVLP treated lungs that were initially considered unacceptable, and the comparator arm will consist of 126 patients who are transplanted with standard lungs that were preserved with cold storage method. The study will enroll patients in six to 20 clinical centers in the United States. The study participants will be followed for three years after transplantation. Data at the two and three year time points will be collected through the United Network of Organ Sharing (UNOS) Registry. The primary endpoint is the non-inferiority of the three-year survival rate of the EVLP group, as compared to the comparator group. The secondary endpoints include the quality of life (i.e., functional status, physical capability, and employment status), episodes of rejection as described by the UNOS registry, and lung function measured by Forced Expiratory Volume (FEV1) at two and three years post-transplantation. Other safety outcomes to be collected will include bronchiolitis obliterans syndrome, hospitalization for rejection or infection, bronchial strictures, graft failure and death at two and three years post-transplantation. Additionally, EVLP transplant suitability will be analyzed by summarizing (with confidence intervals) the data collected on lungs undergoing the EVLP procedure by viable/not viable for transplant.

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 HDE.

Within 30 days of your receipt of this letter, you must submit an HDE supplement that includes a complete study protocol of your post-approval study. Your HDE supplement should be clearly labeled as a "Post-Approval Study Protocol" and submitted in triplicate to the address below. Please reference the HDE number above to facilitate processing. Please be advised that the results from these studies should be included in the labeling as these data become available. Any

updated labeling must be submitted to FDA in the form of an HDE Supplement.

FDA would like to remind you that you should submit separate PAS Progress Reports every six (6) months during the first two (2) years of the study and annually thereafter. The reports should clearly be identified as Post-Approval Study Report. Two (2) copies for each study, identified as "HDE Post-Approval Study Report" and bearing the applicable HDE reference number, should be submitted to the address below. For more information on post-approval studies, see the FDA guidance for how to handle PAS imposed as condition of approval.

www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm#2

Before making any change affecting the safety or effectiveness of the device, you must submit an HDE supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39 except a request for a new indication for use of for a humanitarian use device (HUD). A request for a new indication for use for an HUD shall comply with the requirements set forth in 21 CFR 814.110 which includes obtaining a new designation of HUD status for the new indication for use and submission of an original HDE application in accordance with §814.104. The application for the new indication for use may incorporate by reference any information or data previously submitted to the agency.

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 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 www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm.

This device may not be sold for an amount that exceeds the costs of research and development,

fabrication, and distribution of the device. See section 520(m)(3) of the Federal Food, Drug, and Cosmetic Act.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of an HDE. 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.

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 HDE by making available a summary of the safety and probable benefit of the device upon which the approval was based. The information can be found on the FDA CDRH Internet HomePage located at <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/HDEApprovals/ucm161827.htm>. Written requests for this information can also be made to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the HDE 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 requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the FD&C Act.

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

Any information to be submitted to FDA regarding this HDE should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above HDE number to facilitate processing:

U.S. Food and Drug Administration
Center for Devices and Radiological Health
HDE 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 Ms. Gema Gonzalez at (301) 796-6519.

Sincerely yours,

Christy L. Foreman -A

Christy Foreman
Director
Office of Device Evaluation
Center for Devices and Radiological Health
Food and Drug Administration