DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

APPROVAL ORDER FOR HDE SUPPLEMENT, REQUESTING AN EXEMPTION FROM PROFIT PROHIBITION AND AN ADN

Vericel Corporation **February 18, 2016**
Attention: Deborah Ladenheim, PhD
Sr. Regulatory Strategy Consultant
64 Sydney Street
Cambridge, MA 02139

Re: BH990200.34
Epicel® (cultured epidermal autografts)
Filed: December 7, 2016
Amended: February 10, 2016 and February 16, 2016

Dear Dr. Ladenheim:

The Center for Biologics Evaluation and Research (CBER) of the Food and Drug Administration (FDA) has reviewed your Special Labeling Supplement to the above humanitarian device exemption (HDE), which requests, in accordance with 613(b) of the Food and Drug Administration Safety and Innovation Act (FDASIA), a determination that your humanitarian use device (HUD) meets the conditions of either subclause (I) or (II) under section 520(m)(6)(A)(i) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended by the FDASIA, so that your device may be sold for an amount that exceeds the costs of research and development, fabrication, and distribution of the device (i.e., for profit). Your original HDE for this device was approved prior to the enactment of FDASIA, on October 25, 2007. Based upon the information submitted, the HDE supplement is approved subject to the conditions described in the approval order for your original HDE, and you may begin selling your device, indicated for treatment of patients who have deep dermal or full thickness burns comprising a total body surface area greater than or equal to 30%, for profit upon receipt of this letter. You may continue selling your device for profit as long as the number of devices distributed in any calendar year does not exceed the annual distribution number (ADN). The ADN for this device has been determined to be 360,400.

You must immediately notify the agency by submitting an HDE report (21 CFR 814.126) whenever the number of devices shipped or sold in a year exceeds the ADN. FDA may also inspect the records relating to the number of your devices distributed during any calendar year. See section 520(m)(6)(B) of the FD&C Act. If you notify the FDA that the ADN has been exceeded, or if FDA discovers through an inspection that the ADN has been exceeded, then you are prohibited to sell your device for profit for the remainder of the year. See section 520(m)(6)(D) of the FD&C Act. If additional information arises regarding the ADN for your device, you may submit an HDE supplement (21 CFR 814.108) requesting that FDA modify the ADN based upon this additional information. See section 520(m)(6)(C) of the FD&C Act.

For additional information on the ADN, please see the "Guidance for HDE Holders, Institutional Review Boards (IRBs), Clinical Investigators, and FDA Staff - Humanitarian Device Exemption (HDE) Regulation: Questions and Answers" at: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm110194.htm. You may also contact PMA/HDE Staff at (301) 796-5640.

This device is indicated and labeled for use in pediatric patients or in a pediatric subpopulation and is permitted by FDA to be sold for profit in accordance with section 520(m)(6)(A)(i)(1) of the FD&C Act, and therefore will be subject to annual review by the agency's Pediatric Advisory Committee (PAC). As stated in section 520(m)(8) of the FD&C Act, the PAC annually reviews all HUDs described in section 520(m)(6)(A)(i)(1) of the FD&C Act, which are HUDs approved under an HDE that are intended for the treatment or diagnosis of a disease or condition that occurs in pediatric patients or in a pediatric subpopulation, and such device is labeled for use in pediatric patients or in a pediatric subpopulation in which the disease or condition occurs, and that are exempt from the profit prohibition, in accordance with section 520(m)(6) of the FD&C Act. See section 520(m)(8) of the FD&C Act.

The PAC reviews these devices to ensure that the HDE remains appropriate for the pediatric populations for which it is approved, in accordance with 520(m)(2) of the FD&C Act. The requirements under section 520(m)(2) of the FD&C Act include that (1) the target population of the device is fewer than 4,000 individuals in the United States; (2) the device would not be available to a person with the disease or condition without the HDE and there is no comparable device available to treat or diagnose such disease or condition; and (3) the device does not expose patients to an unreasonable risk or significant risk of illness or injury and the probable benefit to health from the use of the device outweighs risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. The PAC will also conduct periodic review of adverse events for this device.

Failure to comply with the conditions of approval as described in the approval order for the original HDE or any post-approval requirement constitutes a ground for withdrawal of approval of an HDE.

You are reminded that as soon as possible and before commercial distribution of your device you must submit an amendment to this HDE with copies of all approved labeling in final form. The labeling will not routinely be reviewed by FDA staff when HDE supplement 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.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and reference the above HDE number to facilitate processing. One of those three copies may be an electronic copy (eCopy), in an electronic format that FDA can process, review and archive (general information: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/P

remarketSubmissions/ucm134508.htm; clinical and statistical data: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm136377.htm).

Food and Drug Administration
Center for Biologics Evaluation and Research
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Silver Spring, MD 20993-0002

If you have questions concerning this approval order, please contact Ron Chamrin, at (240) 402-8269.

Sincerely yours,

Celia M. Witten, PhD, MD
Director
Office of Cellular, Tissue, and Gene Therapies
Center for Biologics Evaluation and Research