September 20, 2021

Energy Delivery Solutions
William Ehringer, Ph.D.
CEO
3315 Industrial Parkway
Jeffersonville, IN 47130

Re: K201789
Trade/Device Name: CT-STOR
Regulation Number: 21 CFR§ 876.5885
Regulation Name: Tissue Culture Media for Human Ex Vivo Tissue and Cell Culture Processing Applications
Regulatory Class: II
Product Code: NDS
Dated: August 19, 2021
Received: August 20, 2021

Dear William Ehringer:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies.

You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Glenn B. Bell, Ph.D.
Director
DHT3A: Division of Renal, Gastrointestinal,
Obesity and Transplant Devices
OHT3: Office of GastroRenal, ObGyn,
General Hospital and Urology Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*

K201789

Device Name

CT-STOR

Indications for Use *(Describe)*

CT-STOR is a liquid culture media intended for *ex vivo* cell and tissue processing applications

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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5. 510(k) Summary

Owner's Name: Energy Delivery Solutions

Address: 3315 Industrial Parkway
Jeffersonville, IN 47130

Phone Number: (812) 920-0596

Contact Person: William Ehringer, PhD, Kristyn Smith, or Caitlin Stanton
Energy Delivery Solutions

Classification Name: Media, Culture, ex vivo, Tissue and Cell

Date of Preparation: September 11, 2021

Device Name: CT-STOR

Common Name: Culture Media

Regulation Name: Tissue culture media for human ex vivo tissue and cell culture processing applications.

Regulatory Class: II

Product Code: NDS

Regulation Number: 21 CFR 876.5885

Panel: Gastroenterology/Urology

Legally Marketed Device for Substantial Equivalence Comparison:

CT-STOR is substantially equivalent to the currently marketed device:

- AIM-V® Medium, Invitrogen Corporation; 510(k) K022086 (Invitrogen Corporation)

Device Description

CT-STOR is a tissue culture media intended for human *ex vivo* tissue and cell culture processing applications. AIM-V® is the predicate device and is also a tissue culture media intended for human *ex vivo* tissue and cell culture processing applications. CT-STOR and AIM-V® are composed of chemically defined nutrient materials in solution (with or without supplements) that are essential

for the survival and development of tissue or cells of human or other animal origin. These nutrients are provided in liquid form for use in supporting the growth or maintenance of human tissue and cells.

Intended Use

CT-STOR is a liquid tissue culture media product intended for *ex vivo* tissue and cell culture processing applications.

Principles of Operation and Technological Characteristics

CT-STOR is a serum-free medium developed in 2016 to support cells and tissues for *ex vivo* preservation. CT-STOR is substantially equivalent to AIM-V®, which is a serum-free medium developed in 1987 in collaboration with Dr. Steven Rosenberg (National Cancer Institute) to support adoptive immunotherapy (lymphokine-activated killer (LAK) cells) clinical trials that were being conducted by Dr. Rosenberg and collaborating investigators. Tissue culture media products for human *ex vivo* tissue and cell culture applications have been explored and tested as described in peer-reviewed literature.

The formula for CT-STOR has remained the same since it was first manufactured with only a few minor alterations to composition. CT-STOR is prepared from a formulation of Dulbecco's Modified Eagle Medium (DMEM), adenosine-5'-triphosphate (ATP), purified soy phosphatidylcholine, 2,3-Dioleoyloxy-propyl-trimethylammoniumchloride (DOTAP) and ascorbic acid (Vitamin C). Each of the components of CT-STOR play a significant role in *ex vivo* maintenance of cells and tissues.

The central role of ATP in cell and tissue viability and maintenance has been studied since the discovery of ATP in 1929 [Khakh B., 2009]. Slight changes in intracellular ATP can play a significant role in cell function or dysfunction, and thus cellular control of intracellular ATP is critical [Khakh B., 2009]. When cells or tissues are removed from the body, there is a disruption in cell ATP production due to hypoxia [Kim J., 2014]. Addition of ATP to cell and tissue culture media results in trophic signaling and also in helping maintain intracellular ATP levels [Burnstock, G., 2016]. CT-STOR contains micromolar quantities of ATP that are protected and encapsulated in lipid vesicles, which has been shown to increase growth factor expression and decrease inflammatory markers [Castro, A., 2019].

The role of lipids in cell maintenance is three fold. First, lipids play a structural role in cellular membranes [Whitford W., 2004]. A small cell may contain 10^9 phospholipids in the cell membrane, which if not supplemented in some form will lead to cell death [Alberts B., 2002]. Lipid supplementation to culture media has typically occurred by the addition of serum albumin, which acts as a carrier for lipids [Whitford W., 2004]. In serum-free media, the lipids can come from various sources, such as adding a media supplement (e.g. ExCyte, Millipore), or by adding liposomes, lipid dispersions, or micro-emulsions [Savonniere S., 1996]. Secondly, lipids act as an energy store. For example, a phosphatidylcholine with two palmitic fatty acids yields 258 ATP molecules [Bhagavan, N., 2002]. In some cells, such as cardiomyocytes, the preferred energy source is by beta-oxidation of fatty acids, specifically oleic acid [Lopaschuk, G., 2010]. Third,

lipids play a significant role in cell transport and signal transduction. Lipids are the important in endosomes, golgi vesicles, and vacuoles, as well as in several kinases.

Ascorbic acid plays a significant role in cell and tissue viability during isolation [Shaghaghi, H., 2015]. As a powerful anti-oxidant, ascorbic acid acts as a reactive oxygen species (ROS) scavenger during hypoxia [Guauquil, V., 2004]. When ROS levels in cell and tissue culture media are increased significant destruction of cell membranes, proteins, DNA and RNA does occur. Thus, addition of ascorbic acid to culture media can decrease ROS-induced cell damage.

Conclusion

CT-STOR and AIM-V® Medium are used for human *ex vivo* tissue and cell culture processing applications and have the same principles of operation, technical characteristics, efficacy (generic cellular growth and maintenance) and safety (consistent in chemical content and formulation, biocompatibility with cells, and purity). Their efficacy in supporting survival, growth, development, and maintenance of human cells or tissue culture systems has been well established in scientific publications included in this submission. Both CT-STOR and AIM-V® are manufactured in accordance with QSR requirements and are labelled as aseptically processed. Thus, CT-STOR is substantially equivalent to the legally marketed device intended for the human *ex vivo* tissue and cell culture processing applications.

Indications for Use
CT-STOR is a liquid culture media intended for *ex vivo* cell and tissue processing applications.

Summary of Non-Clinical Testing

CT-STOR has been tested on human dermal fibroblasts (HDFa) cells when demonstrating performance testing for CT-STOR stability (i.e. validation). Primary HDFa cells were purchased from American Type Culture Collection (ATCC, *PCS-201-012, Primary Dermal Fibroblast; Normal, Human, Adult (HDFa)*, Manassas, VA) and plated at 10,000 cells per well on a 24-well plate. Cells were allowed to proliferate in complete growth media for 24 hours (ATCC, PCS-201-030, Fibroblast basal medium with added Fibroblast Growth Kit-Serum-free, PCS-201-040). After 24 hours, cells were switched to either control media (PCS-201-030, Fibroblast basal medium) or test media (CT-STOR, Energy Delivery Solutions, Jeffersonville, IN). HDFa cells were allowed to proliferate for 48 hours with the respective test media. After 48 hours cell proliferation was assessed and seeding comparisons defined (see below table).

CT-STOR Days Aged	**Seeding Comparison (%)** ***Acceptable Limit: > 75%***
8	95.09%
128	173.43%