Class II Special Controls Guidance Document: Tissue Culture Media for Human *ex vivo* Tissue and Cell Culture Processing Applications; Final Guidance for Industry and FDA Reviewers

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U.S. Department Of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Gastroenterology and Renal Devices Branch
Division of Reproductive, Abdominal and Radiological Devices
Office of Device Evaluation

Preface

Public Comment

Comments and suggestions may be submitted at any time for Agency consideration to Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. When submitting comments, please refer to the exact title of this guidance document. Comments may not be acted upon by the Agency until the document is next revised or updated.

For questions regarding the use or interpretation of this guidance contact Miriam C. Provost, Ph.D. at (301) 594-1220 or by email mxp@cdrh.fda.gov.

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This document is intended to provide guidance. It represents the Agency's current thinking on the above. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute and regulations.

INTRODUCTION

This guidance is based on 1) current scientific knowledge, 2) clinical experience, 3) previous submissions by manufacturers to the FDA, 4) the Safe Medical Devices Act of 1990, 5) the FDA Modernization Act of 1997 and FDA regulations in the Code of Federal Regulations (CFR). As advances are made in science and medicine, and as changes occur in implementation of congressional legislation, these review criteria will be re-evaluated and revised as necessary.

This document is an adjunct to the CFR and other FDA guidance documents for the preparation and review of 510(k) submissions. It does not supersede those publications, but provides additional clarification on what is necessary before the FDA can clear a device for marketing. In general, the submission must provide evidence that the device is substantially equivalent to a predicate device legally marketed in the United States.

The Least Burdensome Approach

The issues identified in this guidance document represent those that we believe need to be addressed before your device can be approved/cleared for marketing. In developing the guidance, we carefully considered the relevant statutory criteria for Agency decision-making. We also considered the burden that may be incurred in your attempt to comply with the guidance and address the issues we have identified. We believe that we have considered the least burdensome approach to resolving the issues presented in the guidance document. If, however, you believe that information is being requested that is not relevant to the regulatory decision for your pending application or that there is a less burdensome way to address the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving

Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html

This document addresses tissue culture media solutions designed for human *ex vivo* tissue and cell culture processing applications. It does not address solutions for flushing, transport and preservations of whole organs, including the kidney, liver, pancreas, heart and lung. It does not address solutions for preservation of the cornea, nor does it address the preservation of specific tissues (e.g., bone, cartilage, bone marrow, etc.) or specific cells (including pancreatic islet cells). Media or supplements containing biologic or cellular components are outside the scope of this document.

As part of the classification process for this device, the following Risks to Health associated with the use of the device were identified:

1. Toxicity to cells or tissues that come in contact with the device;
2. Transfer of bacteria, pyrogens or other adventitious agents from the device to the cells or tissues that come in contact with it;
3. Inadequate support of tissues and cells;
4. Transfer of chemical impurities from the device to the cells or tissues that come in contact with it;

This guidance document includes special controls identified to address these risks.

I. DEVICE DESCRIPTION

A complete description of the solution should be provided. The description should address each of the following issues:

A. A complete description of the base media and a list of all additives or supplements that could possibly be included to customize the TCM

- The anticipated ranges of each additive.

- The description of each component must include its purity (e.g., USP grade).

If components are not USP grade, provide adequate justification to demonstrate that the chemicals possess sufficient purity for use in this product.

B. A general explanation of the purpose of each chemical component, (e.g., prevention of swelling, metabolic support.)

C. The identity of all packaging materials. The manufacturer should identify a legally marketed predicate devices that uses the material for a similar intended

use (i.e., blood and tissue contacting) or should provide biocompatibility test data on the packaging materials, as outlined in CDRH Blue Book memorandum G95-1.

II. PERFORMANCE TESTING

A. Evidence should be submitted to demonstrate the lack of toxicity and the performance of the TCM for maintenance of cell function. Data from the literature may be supplied in lieu of testing, provided the literature data adequately represents the base media and its possible variants. Focus especially on evidence that supports the safety of any component or additive that has cytotoxic effect.

B. Include the results of stability testing that supports the labeled shelf life and analyses for chemical identity, sterility, and particulate levels. At a minimum, there should be stability testing for the base media. However, if certain additives are prone to degradation or precipitation, stability testing should also be performed on solutions with concentrations of these components at a maximum, as a worst case.

III. STERILITY AND ENDOTOXIN TESTING

A. Provide a description of the sterilization method (or manufacturing process, if aseptically filled) along with the sterility assurance level. Consult CDRH Blue Book memorandum, K90-1, "510(k) Sterility Review Guidance 2/12/90" for a description of the sterilization information that should be submitted. The 510(k) submission must contain the results of sterility testing for at least one batch of product.

B. Provide data to demonstrate that the solution is sterile, non-pyrogenic, and if applicable, free of adventitious agents.

IV. LABELING

The labeling must include the prescription use statement found in 21 CFR 801.109(b)(1).