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Standard Guide for Cell Culture Growth Assessment of Single-Use Material[1]

This standard is issued under the fixed designation E3231; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This guide outlines best practices to consider when setting up a representative leachable test method to detect if a material is compatible with cell culture media or manufacturing processes. This guide does not replace or supersede cell growth tests like USP <87>, USP <88> (plastic/elastomeric materials), or ISO 10993 (medical device materials), that are used in assessing biological reactivity in humans. Polymeric materials that have passed these tests have been found to leach compounds under normal process conditions that can inhibit cell culture growth for some cell lines. See Refs (**1-5**).[2] Test methods that are representative of the manufacturing conditions will help identify materials that are appropriate for use during manufacturing.

1.2 This guide may be relevant to biopharmaceutical manufacturing, cell-based therapeutics, vaccines, cell-based diagnostics, and other areas.

1.3 The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

1.4 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety, health, and environmental practices and determine the applicability of regulatory limitations prior to use.*

1.5 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 *USP Documents:*[3]
USP <87> Biological Reactivity Tests, In Vitro
USP <88> Biological Reactivity Tests, In Vivo

2.2 *ISO Documents:*[4]
ISO 10993 Biological Evaluation of Medical Devices

3. Terminology

3.1 *Definitions:*

3.1.1 *bis(2,4-di-tert-butylphenyl)-phosphate (bDtBPP), n*—leachable compound known to inhibit cell growth (CAS # 69284-93-1).

3.1.2 *dimethyl sulfoxide (DMSO), n*—(CH3)2SO (CAS # 67-68-5).

3.1.3 *test articles, n*—the material being tested.

3.1.4 *test media, n*—cell culture media that has been used to extract potential leachables from the test articles.

3.1.5 *the gray (Gy), n*—the SI unit for absorbed radiation dose, and defined as the absorption of one joule of energy, in the form of ionizing radiation, per kilogram of matter, that is one gray = 1 J/kg.

4. Summary of Guide

4.1 This guide outlines best practices to assess compatibility of polymeric materials with animal cell cultures used in the manufacture and processing of vaccine, gene, cell and protein therapies reliant on cell-based processes. The best practices may be used to reveal compatibility issues in a cell culture system that includes the cell culture medium, the cell line and the polymeric test articles that are under evaluation.

4.2 The guide starts with an overview of typical cell culture compatibility studies and then outlines best practices for each aspect of the study.

[1] This guide is under the jurisdiction of ASTM Committee E55 on Manufacture of Pharmaceutical and Biopharmaceutical Products and is the direct responsibility of Subcommittee E55.04 on General Biopharmaceutical Standards.

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[2] The boldface numbers in parentheses refer to a list of references at the end of this standard.

[3] Available from U.S. Pharmacopeial Convention (USP), 12601 Twinbrook Pkwy., Rockville, MD 20852-1790, http://www.usp.org.

[4] Available from International Organization for Standardization (ISO), ISO Central Secretariat, BIBC II, Chemin de Blandonnet 8, CP 401, 1214 Vernier, Geneva, Switzerland, http://www.iso.org.

5. Significance and Use

5.1 A risk-based approach must be used to determine the cell lines, test articles, and materials used for testing. An evaluation of relevant factors should be made to determine if a test article is representative of the intended use.

5.2 Cell culture compatibility should be assessed if the material is in direct contact with cell culture medium regardless of duration of contact. Test articles can be of a single material or assembled from a multitude of materials.

5.3 Two perspectives to single-use material cell culture compatibility assessments are the supplier and the end user perspectives. It is understood that the supplier may have better access to single-use materials and material manufacturing processes, while having limited access to representative cell lines. Supplier assessment of materials are best tested using cell lines available that have shown known material sensitivity. The end users may have more limited access to materials but access to more representative cell lines and processes. Therefore assessment of compatibility of material with a specific cell line in a process is best evaluated by the end user.

5.4 This guide outlines best practices to establish test procedures. Appendix X1 outlines an example test procedure for a commercially available CHO cell line.

6. Cell Culture Compatibility Testing Overview

6.1 Fig. 1 highlights the main stages of organizing cell culture compatibility testing. Key aspects are highlighted in the figure and detailed best practices for each stage are covered in the subsequent sections. Appendix X1 shows an example of what a test could look like using an industrially available media and cell line.

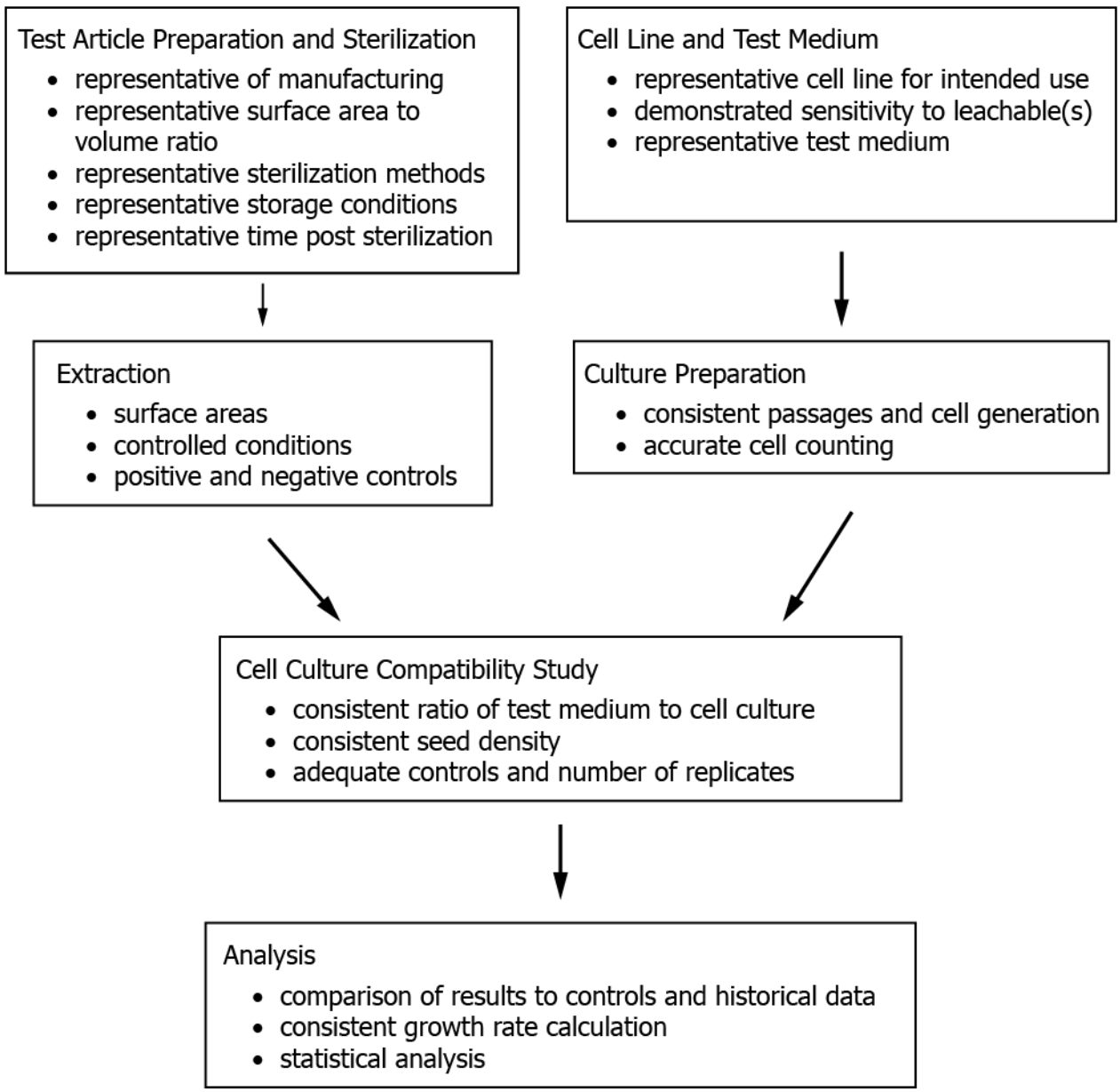

FIG. 1 Cell Culture Compatibility Testing Design: Key Considerations for Success