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Standard Terminology Relating to Microphysiological Systems[1]

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1. Scope

1.1 This terminology defines basic terms and presents the relationships of the scientific fields related to microphysiological systems (MPS). Committee F04 has defined these terms for the specific purpose of unifying the language used in standards for MPS.

1.2 The terms and nomenclature presented in this standard are for the specific purpose of unifying the language used in MPS standards and are not intended for labeling of regulated medical products.

1.3 *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.*

1.4 *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 *ISO Standards:*[2]

ISO 22442-1:2020 Medical Devices Utilizing Animal Tissues and Their Derivatives

ISO/TS 21560:2020 General Requirements of Tissue-Engineered Medical Products

3. Terminology

biomarker, *n*—a characteristic that is evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention. It is a portmanteau of "biological marker" and is sometimes referred to as a signature molecule.

biosensor, *n*—devices that use specific biochemical reactions and/or molecular recognition to detect the presence and/or the concentration of an analyte. Biosensors consist of three parts: a component that recognizes the analyte and produces a signal, a signal transducer, and a detector/reader device.

body-on-a-chip, *n*—interconnected organ mimics with continuous or recirculating flow, with organ sizes and flow determined by a physiologically based pharmacokinetic (PBPK) model. It can consist of human and/or animal cells and contains all organs with some listed explicitly and others grouped as "other tissues" integrated within a non-biological platform.

disease-on-a-chip, *n*—an *in vitro* model system with the desired genetic background disease, environmental factors, inducible symptoms, and/or interaction between disease-relevant cell types under physiological conditions. These systems incorporate or mimic a specific disease stage in organ(s) or tissues integrated within a non-biological platform.

disorganized 2D system, *n*—a cellular monolayer over a surface which lacks the anatomy of *in vivo* tissues and need not possess the physiological functions of in vivo tissues.

disorganized 3D system, *n*—a multilayered cellular system that substantially lacks the ordered histoarchitecture of the *in vivo* organ or tissue and need not possess the physiological function of *in vivo* tissue.

functional microphysiological system, *n*—a microphysiological system that reproduces electrical, mechanical, and/or barrier function without necessarily reproducing the anatomy. Can be 2D, 3D, or hybrid 3D model systems with functional characteristics of living.

human-on-a-chip, *n*—a subset of body-on-a-chip which consists of various human organ mimics using continuous or recirculating flow. Human-on-a-chip can include patient derived, stem cell derived, or primary cells/tissues integrated within a non-biological platform.

hybrid 3D systems, *n*—where a monolayered cellular system is integrated with a MEMs device or devices to provide a multilayered construct that enables the establishment of mechanical, electrical, and/or barrier functions that give at least one output similar to that of an *in vivo* output.

[1] This terminology is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devices and is the direct responsibility of Subcommittee F04.43 on Cells and Tissue Engineered Constructs for TEMPs.

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[2] Available from American National Standards Institute (ANSI), 25 W. 43rd St., 4th Floor, New York, NY 10036, http://www.ansi.org.

micro-electro mechanical systems (MEMs), *n*—miniature integrated devices or systems that combine mechanical and electrical components ranging in size from a few micrometers to a millimeter. They must have elements of defined mechanical functionality, whether or not these elements can move. They can have the ability to sense, control, and actuate on the microscale, and may generate effects on an associated microphysiological system.

microfluidics, *n*—the engineering or use of devices that apply fluid flow to channels generally smaller than 1 mm but not smaller than 0.1 μm, in at least one dimension.

microphysiological systems, *n*—fit-for-purpose devices, containing one or more engineered organ(s), organ substructures, and/or functional organ unit(s) in a controllable microenvironment. An MPS represents one or more aspects of the organ or organ system's dynamics, functionality, and/or (patho)physiological response such as responding to biologic, mechanical, electromagnetic (light and/or radiation), or pharmaceutical stimuli *in vivo*. Ideally, an MPS has the capacity to be monitored under real time. MPS platforms may comprise mono-cultures, co-cultures of multiple cell types, maintenance of explants derived from tissues/organs, and/or inclusion of organoid cell formations.

multi-organ microphysiological systems, *n*—combinations of two or more living engineered organ mimics that directly or indirectly share fluids or have other direct or indirect connections, such as pneumatic, mechanical, or electrical, that emulate systemic organ interactions.

organized 2D system, *n*—a monolayered cellular system that is arranged or arranges into a structure or structures that possess physiological functions.

organized 3D system, *n*—a multilayered cellular system that is arranged or arranges into a structure that retains aspects of the anatomy and function of *in vivo* tissue.

organ mimic, *n*—a subset of microphysiological systems that recapitulates one or more aspects of an organ's or organs' *in vivo* dynamics, functionality, structure, and/or (patho)physiological response(s).

DISCUSSION—An organ mimic can be an organ-on-a-chip or an organoid. An organ-on-a-chip cannot be an organoid.

organoid, *n*—an *in vitro*, self-assembled, 3D micro-tissue or organ developed from stem cells that recapitulates tissue or organ micro-anatomy and functionality of *in vivo* tissues or organs.

organ-on-a-chip, *n*—a subset of microphysiological systems that replicates one or more aspects of an organ's *in vivo* dynamics, functionality, structure, and/or (patho)physiological response(s) of multiple cell types integrated within a non-biological platform.

physiologically based pharmacokinetic (PBPK) model, *n*—a mathematical model that simulates the concentration of a drug or chemical over time in cells, tissue(s), and blood, by taking into account the route(s) of exposure, rate of the drug's absorption into the body, distribution in tissues, metabolism, and excretion (ADME) on the basis of interplay between organ function and physicochemical and biochemical parameters.

preserved anatomy, *n*—the condition when an *in vitro* system mimics selected aspects of *in vivo* anatomy, but may not mimic *in vivo* functionality.

preserved functionality, *n*—the condition when an *in vitro* system mimics selected aspects of *in vivo* functionality, but may not mimic *in vivo* anatomy.

subject-on-a-chip, *n*—a subset of human-on-a-chip with cells or tissues and genetics derived from a single individual integrated within a non-biological platform. The system can include environmental factors and interaction between disease-relevant cell types under physiological conditions.

tissue, *n*—an aggregation of similarly specialized cells and an extracellular matrix united in the performance of particular functions

tissue-on-a-chip, *n*—a subset of microphysiological systems that contains a single modeled living tissue type integrated within a non-biological platform.

4. Keywords

4.1 alternatives to animal models; biomedical research; body-on-a-chip; disease models; drug development; drug discovery; drug screen; drug studies; drug validation; ex vivo testing; in vitro/ex vivo drug screening system; in vitro/ex vivo physiology study system; in vitro testing; microphysiological model; microphysiological systems; multi-organs on a chip; organ-on-a-chip; organs-on-chips; pathophysiology studies; patient-specific testing; pharmacology testing; physiology studies; precision medicine; regenerative medicine; tissue-on-a-chip; toxicology