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Standard Terminology Relating to Tissue Engineered Medical Products[1]

This standard is issued under the fixed designation F 2312; 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 terminology defines basic terms and presents the relationships of the scientific fields related to Tissue Engineered Medical Products (TEMPs). Committee F04 has defined these terms for the specific purpose of unifying the language used in standards for TEMPs.

1.2 The terms and relationships defined here are limited to TEMPs. They do not apply to any medical products of human origin regulated by the U.S. Food and Drug Administration under 21 CFR Parts 16 and 1270 and 21 CFR Parts 207, 807, and 1271.

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

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 and health practices and determine the applicability of regulatory limitations prior to use.*

2. Referenced Documents

2.1 *ASTM Standards:* [2]

F 2027 Guide for Characterization and Testing of Substrate Materials for Tissue-Engineered Medical Products

F 2311 Guide for Classification of Therapeutic Skin Substitutes

2.2 *Government Documents:*[3]

21 CFR Parts 16 and 1270, Human Tissues, Intended for Transplantation (July 29, 1997)

21 CFR Parts 207, 807, and 1271, Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing (January 19, 2001)

3. Significance and Use

3.1 The need for standards regarding TEMPs has also prompted a need for definitions. This terminology sets forth definitions of the most commonly used terms and specifies the relationship among the sciences and components applied in tissue engineering to develop TEMPs. Use of these terms and an understanding of these relationships will unify the ASTM TEMPs standards with a common language such that the users of these standards can understand and interpret the standards more precisely. Terms specific to a TEMP standard will also be defined within the respective standard as appropriate.

3.2 *Defining Terms*—Terms are defined with a broad scope to encompass these new products known as TEMPs. For instance, the definition for somatic cell therapy as stated in the "Guidance for Human Somatic Cell Therapy and Gene Therapy" (**5**)[4] is recognized in this terminology. However, for the purposes of TEMPs that contain cells, we have added the definition of "cell" which is much broader and not limited to the use of living cells.

3.3 *Clinical Effects of TEMPs*—The users of this terminology should note that terms used regarding the clinical effects of TEMPs, for instance, "modify or modification" of the patient's condition, may also be interpreted to "enhance, augment, transform, alter, improve, or supplement." Similarly, "repair" may also serve to mean "restore."

3.4 The diagram in Fig. 1 shows the relationships of components of TEMPs and of the fields of science (for example, technologies and principles) used in tissue engineering to create TEMPs. Certain TEMPs may be tissue engineered or produced *in vitro* by using specific components and sciences to create an off-the-shelf TEMP for the users. Other TEMPs may by design require the users to place the components inside the patient, (that is, *in vivo*) to rely upon the patient's regenerative potential to achieve the product's primary intended purpose. The expectation of a TEMP used for therapeutic clinical applications is to have a therapeutic effect, specifically to repair, modify or regenerate the recipient's cells, tissues, and organs or their structure and function. Such a TEMP may be used for human and non-human applications. In

[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 F04.41 on Classification and Terminology for TEMPs.

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[2] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For Annual Book of ASTM Standards volume information, refer to the standard's Document Summary page on the ASTM website.

[3] Available from U.S. Government Printing Office Superintendent of Documents, 732 N. Capitol St., NW, Mail Stop: SDE, Washington, DC 20401.

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

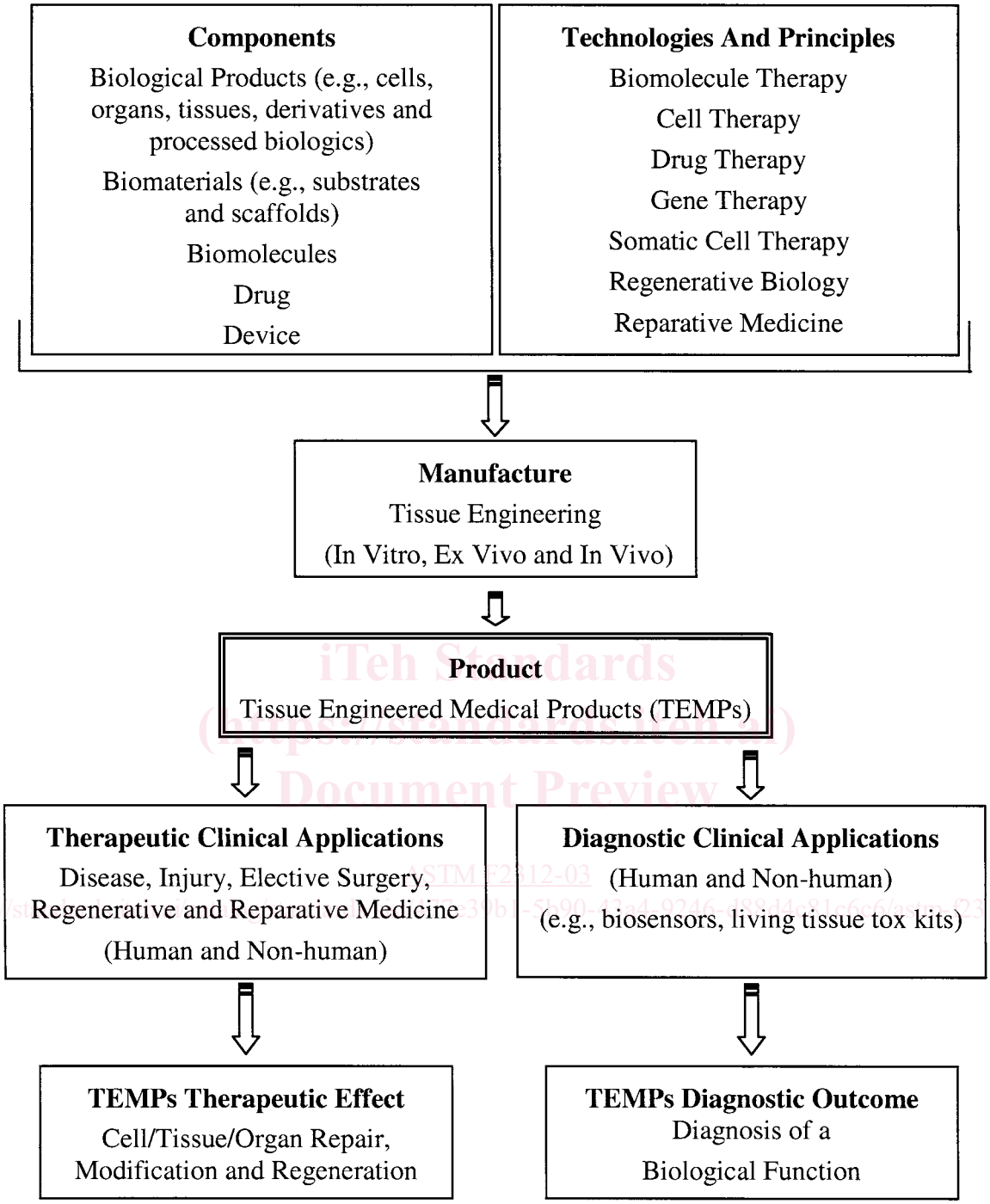

FIG. 1 Relationships of the Fields of Tissue Engineering to Tissue Engineered Medical Products

other applications, a TEMP may be used in diagnostic clinical applications, or both, to achieve an investigative outcome of the function of the cells, tissues, and organs.

4. Terminology

biological product, *n*—"any virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsphenamine or its derivatives (or any trivalent organic arsenic compound) applicable to the prevention, treatment, or cure of diseases or injuries of man." **(6)**. The term analogous product is interpreted to encompass somatic cell and gene therapy **(15)**. A biological product may be used as a component of a TEMP. For the purposes of TEMPs, these biological products may be of any origin (that is, organism), tissue type, developmental stage, and may be living, non-living, and genetically or otherwise modified.

biomaterial, *n*—"material intended to interface with biological systems to treat, augment, replace or evaluate any tissue, organ or function of the body," **(1)**. Biomaterials in their raw

or virgin form are known as substrates (Guide F 2027). Biomaterial substrates may be natural materials (Guide F 2027), synthetic or combinations thereof. When biomaterial substrates are assembled into a construction they are often referred to as scaffolds. A biomaterial (substrate and scaffold) may be used as a component of a TEMP.

biomolecule, *n*—a biologically active peptide, protein, carbohydrate, vitamin, lipid, or nucleic acid produced by and purified from naturally occurring or recombinant organisms, tissues or cell lines or synthetic analogs of such molecules. A biomolecule may be used as a component of a TEMP.

biomolecule therapy, *n*—the use of biomolecules to repair, modify, or regenerate the recipient's cells, tissues, or organs or their structure and function, or both. Biomolecule therapy technologies can be applied in tissue engineering to generate TEMPs.

cell, *n*—"the smallest structural unit of an organism that is capable of independent functioning, consisting of one or more nuclei, cytoplasm, and various organelles, all surrounded by a semipermeable cell membrane" **(8)**. Cells are highly variable and specialized in both structure and function, though all must at some stage synthesize proteins and nucleic acids, use energy, and reproduce. A cell or cells may be of any origin (that is, organism), tissue type, developmental stage, and may be living, non-living, and genetically or otherwise modified. Cells may be used as a component of a TEMP.

cell therapy, *n*—the administration of cells (any kind and form) to repair, modify or regenerate the recipient's cells, tissues, and organs or their structure and function, or both. Cell therapy technologies can be applied in tissue engineering to generate TEMPs.

combination product, *n*—as defined in 21 CFR § 3.2(e), the term combination product includes: (*1*) A product comprised of two or more regulated components, that is, drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity; (*2*) Two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products; (*3*) A drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, for example, to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or (*4*) Any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect." Furthermore, "many somatic cell products administered to patients will be combinations of a biological product and a device or of a drug, a biological product, and a device." **(9)**. The term "combination product" may apply to TEMPs.

device, *n*—"an instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar or related article... intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals,... which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes." Devices are "intended to affect the structure or any function of the body." (Section 201(h)(1) **(10)**). Device Criteria: "A liquid, powder, or other similar formulation intended only to serve as a component, part or accessory to a device with a primary mode of action that is physical in nature" **(11)**. A device may be used as a component of a TEMP.

drug, *n*—"articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals." Drugs are "intended to affect the structure or any function of the body of man or other animals." (Section 201(g)(1) **(10)**). Drug Criteria: "A liquid, powder, tablet or other similar formulation that achieves its primary intended purpose through chemical action within or on the body, or by being metabolized" **(11)**. A drug may be used as a component of a TEMP.

drug therapy, *n*—is the delivery of drug(s) that stimulate a specific physiologic (metabolic) response. Drug therapy technologies can be applied in tissue engineering to generate TEMPs.

extracellular matrix, *n*—"(ECM), any material produced by cells and excreted to the extracellular space within the tissues. It takes the form of both ground substance and fibers and is composed chiefly of fibrous elements, proteins involved in cell adhesion, and glycosaminoglycans and other space-filling molecules. It serves as a scaffolding holding tissues together and its form and composition help determine tissue characteristics." **(14)** Extracellular matrix, a biological material or tissue derivative, may be used as a component of a TEMP.

genetic material, *n*—is nucleic acid (either deoxyribonucleic acid or ribonucleic acid). Genetic material is also known as DNA, RNA, genetic element, gene, factor, allele, operon, structural gene, regulator gene, operator gene, gene complement, genome, genetic code, codon, anticodon, messenger RNA (mRNA), transfer RNA (tRNA), ribosomal extrachromosomal genetic element, plasmagene, plasmid, transposon, gene mutation, gene sequence, exon, intron (modified version, **(12)**). Genetic material may be used as a component of a TEMP.

gene therapy, *n*—"is a medical intervention based on modification of the genetic material of living cells. Cells may be modified *ex vivo* for subsequent administration or may be altered *in vivo* by gene therapy products given directly to the subject. When the genetic manipulation is performed *ex vivo* on cells that are then administered to the patient, this is also a type of somatic cell therapy. The genetic manipulation may be intended to prevent, treat, cure, diagnose, or mitigate