Designation: F 2311 – 06

Standard Guide for Classification of Therapeutic Skin Substitutes[1]

This standard is issued under the fixed designation F 2311; 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 defines terminology and provides a system of classification for products that can be substituted for human or animal skin grafts (or grafts of the dermal or epidermal component tissues of skin) in medical and surgical therapies. This guide is intended to include (or be expandable to) possible future tissue engineered skin technology that could provide novel or superior therapeutic properties to those of natural skin grafts.

1.2 As much as possible, terminology is based on medical dictionary definitions.

1.3 Substitutes for skin grafts are classified by clinical utility only; the classification is independent of the technology used to make a skin substitute, its components, or whether the sources of components include human or animal tissue or other biological or non-biological materials.

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 requirements prior to use.*

2. Terminology

2.1 *Definitions:*

2.1.1 *skin*, *n*—the outer integument or covering of the body, consisting of the dermis and the epidermis, and resting upon the subcutaneous tissues. **Dorland's**

2.1.2 *tissue*, *n*—an aggregation of similarly specialized cells united in the performance of a particular function. **Dorland's**[2]

2.1.3 *Skin Lesions:*

2.1.3.1 *full-thickness skin wound, n*—a skin wound with the loss of epidermis, and all of the dermis or at least the depth of dermis that includes most or all sources of epidermal cells from epidermal adnexae (glands and follicles).

2.1.3.2 *lesion, n*—any pathological or traumatic discontinuity of tissue or loss of function of a part. In this guide, "skin lesion" is intended to encompass skin wounds and skin ulcers. **Dorland's**

2.1.3.3 *open wound, n*—a wound that communicates with the atmosphere by direct exposure. **Dorland's**

2.1.3.4 *partial thickness skin wound, n*—a skin wound with the loss of the epidermis and part of the dermis, but retaining a layer of viable dermal tissue that includes the sources of epidermal cells from which the wound can heal spontaneously by epidermal tissue regeneration.

2.1.3.5 *ulcer, n*—a local defect, or excavation of the surface of an organ or tissue, which is produced by the sloughing of inflammatory necrotic tissue. **Dorland's**

2.1.3.6 *wound, n*—an injury or damage, usually restricted to those caused by physical means with disruption of the normal continuity of structures. Called also injury and trauma. **Dorland's**

2.1.4 *Skin Wound Physiology:*

2.1.4.1 *granulations, n*—granulation tissue.

2.1.4.2 *granulation tissue, n*—the newly formed vascular tissue normally produced in the healing of wounds of soft tissue and ultimately forming the cicatrix [scar]; it consists of small, translucent, red, nodular masses or granulations that have a velvety appearance. **Dorland's**

2.1.4.3 *scar, n*—fibrous tissue replacing normal tissues destroyed by injury or disease. **Stedman's**[3]

2.1.4.4 *wound contraction, n*—the shrinkage and spontaneous closure of open skin wounds. **Dorland's**

2.1.4.5 *wound contracture, n*—a condition of fixed high resistance to passive stretch of muscle, skin or joints resulting from fibrosis and scarring of the skin or the tissues supporting the muscles or the joints, or both. (This definition is a modification of Dorland's definition of contracture, "a condition of fixed high resistance to passive stretch of muscle, resulting from fibrosis of the tissues supporting the muscles or the joints, or disorders of the muscle fibers," because that definition does not address fibrosis and scarring in skin.)

2.1.4.6 *wound inflammation, n*—a localized protective response elicited by injury or destruction of tissues, which serves to destroy, dilute, or wall off (sequester) both the injurious agent and the injured tissue. It is characterized in the acute form by the classical signs of pain (dolor), heat (calor) redness

[1] This guide is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Devices and Materials and is the direct responsibility of Subcommittee F04.41 on Classification and Terminology for TEMPs.

Current edition approved May 1, 2006. Published May 2006. Originally approved in 2003. Last previous edition approved in 2003 as F 2311 – 03

[2] Dorland, WAN, *Dorland's Illustrated Medical Dictionary*, 29th Ed., W. B. Saunders Company, Philadelphia, 2000.

[3] Stedman, T. L., *Stedman's Medical Dictionary*, 27th Ed., Lippincott Williams & Wilkins, Philadelphia, 2000.

(rubor), swelling (tumor), and loss of function (functio laesa). Histologically, it involves a complex series of events, including dilation of arterioles, capillaries, and venules, with increased permeability and blood flow; exudation of fluids, including plasma proteins; and leukocytic migration into the inflammatory focus. **Dorland's**

2.1.5 *Skin Wound Closure and Healing:*

2.1.5.1 *heal, v*—to restore wounded parts or to make healthy. **Dorland's**

2.1.5.2 *healing, n*—the restoration of integrity to injured tissue. **Dorland's**

2.1.5.3 *Discussion*—In the surgical wound closure, an important distinction is made according to whether the surgeon expects the healing to be accomplished by granulation tissue. This distinction is made because in the normal physiology of wound healing, granulation tissue matures into scar with wound contracture, which is an undesirable outcome (see 4.1.2). Wound closure "by approximating the wound edges or performing a skin autograft" is called "healing by first intention," and wound closure by "allowing spontaneous healing from the edges" is called "healing by second intention."

healing by first intention, n—healing in which union or restoration of continuity occurs directly without intervention of granulations. **Dorland's**

healing by second intention, n—union by closure of a wound with granulations which form from the base and both sides toward the surface of the wound. **Dorland's**

2.1.5.4 *tissue regeneration, n*—healing in which lost tissue is replaced by proliferation of cells, which reconstruct the normal architecture. **medweb**[4]

2.1.5.5 *tissue repair, n*—healing in which lost tissue is replaced by a fibrous scar, which is produced from granulation tissue. **medweb**

2.1.5.6 *wound closure, n*—the provision of an epithelial cover over a wound. It can be accomplished by approximating wound edges, performing a skin [auto]graft, or allowing spontaneous healing from the edges. **Churchill's**[5]

2.1.6 *Therapies for Skin Wounds and Ulcers*:

2.1.6.1 *maintenance therapy, n*—therapy of chronically ill patients that is aimed at keeping the pathology at its present level and preventing exacerbation.

2.1.6.2 *skin allograft therapy, n*—the treatment of skin wound or skin ulcer by the temporary topical application of skin allograft(s).

2.1.6.3 *skin replacement surgery, n*—surgery that permanently replaces lost skin with healthy skin.

2.1.7 *Biomaterials and Grafts:*

2.1.7.1 *allograft, n*—a graft of tissue between individuals of the same species but of disparate genotype. Called also allogeneic graft and homograft. **Dorland's**

2.1.7.2 *autograft, n*—a graft of tissue derived from another site in or on the body of the organism receiving it. **Dorland's**

2.1.7.3 *biomaterial, n*—any substance (other than a drug), synthetic or natural, that can be used as a system or part of a system that treats, augments, or replaces any tissue, organ, or function of the body. **Dorland's**

2.1.7.4 *dermal autograft, n*—a skin [autograft] from which epidermis and subcutaneous fat have been removed; used instead of fascia[6] in various plastic [surgery] procedures. **Dorland's**

2.1.7.5 *dressing, n*—any of various materials utilized for covering and protecting a wound. **Dorland's**

2.1.7.6 *engraftment, n*—incorporation of grafted tissue into the body of the host. **Dorland's**

2.1.7.7 *epidermal autograft, n*—an autograft consisting primarily of epidermal tissue, including keratinocyte stem cells, but with little dermal tissue.[7]

2.1.7.8 *full thickness skin autograft, n*—a skin [auto]graft consisting of the epidermis and the full thickness of the dermis. **Dorland's**

2.1.7.9 *graft, n*—any tissue or organ for implantation or transplantation. **Dorland's**

2.1.7.10 *graft take, n*—engraftment.

2.1.7.11 *skin substitute, n*—a biomaterial, engineered tissue, or combination of biomaterials and cells or tissues that can be substituted for a skin allograft, a skin autograft, an epidermal autograft, or a dermal autograft in a clinical procedure.

2.1.7.12 *split thickness skin autograft, n*—a skin [auto]graft consisting of the epidermis and a portion of dermis. **Dorland's**

2.1.7.13 *xenograft, n*—a graft of tissue transplanted between animals of different species. Called also heterograft, heterologous graft and heteroplastic graft.[8] **Dorland's**

2.1.7.14 *xenotransplantation, n*—any procedure that involves the transplantation, implantation, or infusion into a human recipient of either (*a*) live cells, tissues, or organs from a nonhuman animal source, or (*b*) human body fluids, cells, tissues or organs that have had *ex vivo* contact with live nonhuman animal cells, tissues or organs.[9]

[4] Hiley, P., and Barber, P. C., *General Pathology (Pathology Foundation Course)*, Chapter 3, Healing and Repair, Department of Pathology, University of Birmingham, U.K., http://medweb.bham.ac.uk/http/depts/path/Teaching/foundat/repair/healing.html.

[5] *Churchill's Illustrated Medical Dictionary*, Churchill Livingstone, New York, 1989.

[6] "a sheet or band of fibrous tissue such as lies deep to the skin …" (**Dorland's**).

[7] For practical details, see Fang, P., Engrav, L. H., Gibran, N. S., Horani, S., Kiriluk, D. B., Cole, J. K., Fleckman, P., Heimbach, D. M., Gauer, G. J., Matsumura, H., Warner, P., "Dermatome steeing for autografts to cover Integra®," *J Burn Care Rehabil*, 23, 2002, pp. 327-332; and Kagan, R. J., Invited editorial *J Burn Care Rehibil*, 23, 2002, pp. 326.

[8] Note that the United States Public Health Service (USPHS) and the United States Food and Drug Administration define "Xenotransplantation" more broadly as "any procedure that involves the transplantation, implantation, or infusion into a human recipient of either (*a*) live cells, tissues, or organs from a nonhuman animal source, or (*b*) human body fluids, cells, tissues, or organs that have had *ex vivo* contact with live nonhuman animal cells, tissues or organs." Because this guide is intended to classify skin substitutes by clinical equivalency, and not by composition, the dictionary definition is used, for this guide only. It should be understood that an allograft or autograft substitute may include animal components which cause it to be also a xenotransplant by the Food and Drug Administration definition.

[9] Guidance for Industry, Source Animal, Product, Preclinical, and Clinical Issues Concerning the Use of Xenotransplantation Products in Humans, U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research (CBER), April 2003.