Designation: F2808 – 23

Standard Test Method for Performing Behind-the-Knee (BTK) Test for Evaluating Skin Irritation Response to Products and Materials That Come Into Repeated or Extended Contact with Skin[1]

This standard is issued under the fixed designation F2808; 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 The behind-the-knee (BTK) method, using the popliteal fossa of human volunteers as a test site, simultaneously evaluates the inherent chemical irritation and the potential for mechanical irritation of substrates and products that are designed to come into repeated or extended close contact with the skin (see validation references (**1-7**)).[2] This is a bilateral test comparing a test material to a reference material with a known safety profile.

1.2 This test method shall be used by qualified health care professionals experienced in good clinical practice (GCP) procedures.

1.3 This test method can be performed using human subjects on either intact or compromised skin. Testing should be performed on intact skin for test substrates or products expected to have contact with normal, intact skin, or for direct comparison to products with a known skin irritation profile. Testing can be performed on compromised skin for test substrates or products that may commonly come into contact with damaged skin (for example, skin with diaper rash, or chapped skin) or skin that is expected to be hydrated.

1.4 Visual scoring of erythema and dryness is performed by a trained skin grader on a predefined scale.

1.5 Prior to use in this test, materials shall undergo overall favorable biocompatibility testing consistent with the approach outlined in protocol Practice F748 or ISO 10993-1:2009. As a part of this series of testing, irritation per Practice F719 or ISO 10993-10 shall be conducted.

1.6 The values stated in inch-pound units are to be regarded as standard. No other units of measurement are included in this standard.

1.7 *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.*

1.8 *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 *ASTM Standards:*[3]

D6355 Test Method for Human Repeat Insult Patch Testing of Medical Gloves

F719 Practice for Testing Materials in Rabbits for Primary Skin Irritation

F748 Practice for Selecting Generic Biological Test Methods for Materials and Devices

2.2 *ISO Standards:*[4]

ISO 10993-1:2009 Biological Evaluation of Medical Devices—Part 1: Evaluation and Testing Within a Risk Management Process

ISO 10993-10 Biological Evaluation of Medical Devices—Part 10: Tests for Irritation and Delayed-type Hypersensitivity

3. Terminology

3.1 *Definitions:*

3.1.1 *chemical irritation, n*—irritation caused by a physiological response to the chemical nature of a material. Such physiological responses may include: oxidation or reduction reactions, dehydration, disruption of the keratin ultra-structure, or direct injury to cellular macromolecules or organelles.

[1] This test method is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devices and is the direct responsibility of Subcommittee F04.16 on Biocompatibility Test Methods.

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

[3] 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.

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

3.1.2 *compromised skin, n*—skin that is treated with repeated application of surgical tape prior to the first sample application.

3.1.3 *edema, n*—observable swelling from abnormal accumulation of fluid in connective tissue.

3.1.4 *erythema, n*—redness of the skin.

3.1.5 *mechanical irritation, n*—irritation caused by movement and friction of products intended to remain in contact with the skin for extended periods of time.

3.1.6 *popliteal fossa, n*—the area at the back of the knee.

3.1.7 *reference material, n*—a material similar in form and composition to the test material. The reference material should have a known safety and irritation profile.

3.1.8 *skin grades, n*—visual assessments of erythema and dryness according to a defined scale (see 10.3).

3.1.9 *test material, n*—any material or product expected to come into contact with skin.

3.1.10 *trained skin grader, n*—personnel who have been trained to reliably recognize erythema and dryness reactions by using reference examples, and by performing side-by-side scoring with an experienced skin grader.

4. Summary of Test Method

4.1 Samples are applied to the back of the knee using an elastic knee band or brace. As the subjects go about their everyday activities, normal movements generate friction between the test sample and the skin at the test site, thereby adding the element of mechanical irritation. Thus, the BTK test protocol evaluates a combination of mechanical irritation and the inherent chemical irritation potential of materials and products that come into contact with the skin.

4.2 This is a randomized, controlled, double blind study in which both the subjects and skin grader are unaware of the treatment assignments. Test and reference materials are applied for 6 h per day, for five days. Skin reactions are graded for erythema and dryness prior to the first sample application (that is, at baseline), each morning prior to subsequent sample applications, and upon the removal of the sample at the end of each period.

4.3 Test materials are applied once each test day to normal, intact skin to evaluate potential reactions to products that normally come into contact with intact skin. To evaluate potential reactions to products that normally come into contact with damaged skin, the skin can be compromised by using tape stripping prior to the first sample application.

5. Significance and Use

5.1 This test method is intended to assess a combination of inherent chemical irritation and mechanical irritation for products and materials expected to come into contact with the skin. It is a comparative approach whereby the potential irritation of a test material is compared to that of a reference material similar in form and composition. The reference material should have a known safety and irritation profile.

6. Interferences and Precautions

6.1 Possible protocol deviations that could interfere with or affect the outcome of the study include the fit of the elastic knee band and the activity level of the subjects. As in any clinical study, adherence to the protocol conditions will offset any potential confounding issues.

6.2 The use of lotions, powders, creams, or skin care products in the skin area at the test sites during the course of the study may impact the study results. In addition, shaving the skin behind the knee, exposing the test sites to tanning or the sun, or swimming or hot tub use during study participation should not be permitted, since these practices and activities may produce low levels of skin irritation in some persons.

6.3 Anti-inflammatory medications may interfere with the normal development of the skin irritation reaction and should not be used during the study.

6.4 Normal showering or bathing cannot be allowed during the sample application of 6 h per day, but can be allowed during the 18 h each day when the test samples are not in place.

6.5 Some persons will experience some degree of skin irritation at the test sites. In addition, some persons may experience slight discomfort from the manner in which the samples are applied (that is, an elastic knee band). In most cases, these effects are anticipated to be reversible when sample application concludes.

7. Apparatus

7.1 An artificial light source, with a 100 W incandescent daylight blue bulb or an alternate light source with a similar coloring rendering index (CRI), is used to illuminate the application areas for erythema grading and an illuminated 10× magnifying lens is used to grade dryness.

8. Reagents and Materials

8.1 Elastic knee bands or braces are used to hold the samples in place.

8.2 Test materials include substrates and products that are designed to come into repeated or extended close contact with the skin. The appropriate reference sample is a similar material or product that has been demonstrated through biocompatibility testing to be a non-irritant.

8.3 If testing is to be conducted on compromised skin, an appropriate surgical tape is required.

9. Hazards

9.1 No specific hazards have been identified for this test protocol. However, if any of the test materials tested should fall under biohazard, then all used test materials should be handled and discarded by the test site staff following biohazard standard operating procedures (SOPs).

10. Calibration and Standardization

10.1 No calibration of specific equipment is required.

10.2 Skin graders shall be trained to recognize the degrees of severity of the irritation reactions described in the grading scales given in Appendix X7.