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Designation: ~~F719 – 81 (Reapproved 2012)~~ F719 – 20

Standard Practice for Testing ~~Biomaterials~~Materials in Rabbits for Primary Skin Irritation[1]

This standard is issued under the fixed designation F719; 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 practice covers a procedure by which the irritancy of a ~~biomaterial~~material may be assessed through contact with abraded and intact skin of rabbits.

1.2 The results of this practice depend upon the effectiveness with which contact between the skin and the test material is established and maintained. Because of the operator technique included in performing this test, it is important that the test be performed by personnel with appropriate training.

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 may involve hazardous materials, operations, and equipment. 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~~ safety, health, and ~~health~~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.*

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2. Referenced Documents

2.1 *ASTM Standards:*[2]

F619 Practice for Extraction of Medical Plastics

ASTM F719-20
https://standards.iteh.ai/catalog/standards/sist/6b987859-5eed-4450-be73-59150ca9a503/astm-f719-20

3. Summary of Practice

3.1 Exposure of skin to the test material is accomplished by means of a patch test technique employing two intact and two abraded sites on the back of each of ~~six albino rabbits.~~ three albino rabbits per test article. The skin is clipped free of hair one day prior to testing. The test substance is applied using 0.5 mL for liquids, 0.5 g for solids or semisolids, and a 2.5 by 2.5-cm square patch for films. After application, each test site is covered with a 2.5 by 2.5-cm gauze flat, and the entire trunk is occluded with a polyethylene sleeve. After 24 h, the sleeve, flat, and test material are removed, and test sites are evaluated for erythema and edema.

4. Significance and Use

4.1 Materials that are to be in contact with the skin should not cause irritation to the skin. Since it is probably the substances leached from a material that cause the irritation, this practice provides for direct material-skin contact testing or for skin exposure to the liquid extract of the test material. The rationale for this rabbit test is that it is a comparatively quick and ~~inexpensive~~sensitive method which, through use over the years, has become a generally accepted method. Additionally, the albino rabbit allows for easy visualization of erythema and edema, which are the cardinal signs of skin irritation.

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[1] This practice 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] 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.

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5. Materials and Manufacture

5.1 *Young New Zealand Albino Rabbits,* Healthy young adult albino rabbits of either sex, weighing not less than 2 kg, shall be used. Animal care shall be in accordance with the "Guide for Care and Use of Laboratory Animals";[3]

5.2 *Gauze Flats,* 2.5 by ~~2.5-cm,~~2.5-cm;

5.3 *Polyethylene Sleeves,* extra ~~clear, and~~clear;

5.4 *Adhesive Tape,* ½-in. width.

6. Test Specimen

6.1 The test specimen may be one of three forms:

6.1.1 Test 0.5 mL of ~~liquids or saline~~ liquids, saline, or vegetable oil extract liquids obtained in accordance with Practice F619.

6.1.2 Test 0.5 g of solids or semisolids.

6.1.3 Test films 2.5 by 2.5 cm.

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ASTM F719-20
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[3] National Research Council, "Guide for the Care and Use of Laboratory Animals," Washington, DC, *National Academy Press*, 2011.

NOTE 1—A vehicle control for liquids is required because of the potential for false positives due to skin temperature changes when handling rabbits. Positive controls may be used to validate the test method. The use of ~~5 % procaine HCl~~ 2.5 % sodium lauryl sulfate (SLS) as a positive control is suggested. For the positive control to be valid, the Primary Irritation Index should be ≥2.0 indicating moderate to severe irritation response (Table 2).[4]

6.2 The pH of the solutions should be measured and reported, if appropriate.

7. Procedure

7.1 *Preparation of Test Animals:*

7.1.1 Twenty-four hours before the test, clip the hair from the backs of the animals so as to expose two test areas on each side of the spine, which are 10 cm apart.

7.1.2 To obtain more effective contact between the skin and the test substance, it may be necessary to use a non-irritating depilatory agent. This test method may be used to ensure that the depilatory agent is non-irritating.

7.1.3 Test sites may be designated as two on each side of the spine. Alternatively, the area may be divided into quadrants with test and control substances applied to each quadrant.

7.2 *Test Procedure:*

7.2.1 Wipe the exposed area of the back with alcohol.

7.2.2 As an option for materials that may be applied to contact breached or compromised skin, half the sites may be abraded while the other half remain intact. Using a sterile blade, abrade two of the four sites by moving the blade at right angles to the cutting surface in a scraping motion to create a denuded area of skin. Alternatively, make four epidermal incisions (which penetrate the stratum corneum but not the dermis), with two perpendicular to the other two.

7.2.3 Place the appropriate amount of the test material, as described in 6.1, on one intact and one abraded or incised site. Place the control material on the other abraded and intact sites.

7.2.4 Immediately occlude the sites by placing gauze flats on the test and control sites. Secure the patches with adhesive tape.

7.2.5 Tightly wrap the animal's trunk with a clear polyethylene sleeve.

7.3 *Test Site Examination and Scoring:*

7.3.1 Remove the polyethylene sleeve, gauze flats, test and control materials, and any excess test or control liquids 24 h after applying the test and control substances. ~~Use alcohol~~ Gently wipe the area with gauze to remove excess liquids. Use of diluted alcohol or other solutions for removing excess ~~liquids.~~liquids shall be justified, as they may irritate the skin.

7.3.2 Using the criteria of Table 1, score test sites for erythema and edema 1 h after removal.

7.3.3 Rescore test sites for erythema and edema in accordance with Table 1 at 24 and 48 h after removal . Take care to distinguish test site erythema from minor skin temperature changes.

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NOTE 2—~~There is a possibility of infection associated with skin abrasion. Since infection would cause the same symptoms (erythema and edema) as would primary irritation, it is essential to ensure that the reaction is not due to~~To account for any severe reaction not addressed in Table 1~~infection. Any reaction at the control sites could be an indication of infection. If infection is suspected, the test should be repeated with a new animal, and the test substance cultured.~~, if there is more than slight eschar formation or necrosis observed at site, the site should be assigned a score of 4 for both erythema and edema (regardless of actual score). The scores should be discussed in the test report.

TABLE 1 Scoring Criteria for Test Reactions

Reaction	Description	Score
Erythema (ER)	Erythema and Eschar	
	No erythema	0
	Very slight erythema (barely perceptible)	1
	Well-defined erythema (pale red in color)	2
	~~Moderate to severe erythema (red and area well defined)~~	~~3~~
	Moderate erythema (red and area well defined)	3
	Severe erythema (beet redness to slight eschar formation)	4
Edema (ED)	Edema Formation	
	No edema	0
	Very slight (barely perceptible)	1
	Slight edema (edges of area well defined by definite raising)	2
	Moderate edema (edges raised approximately 1 mm)	3
	Severe edema (raised more than 1 mm and extending beyond the area of exposure)	4

[4] ~~H. H. Draize,~~Lee, C.H. and ~~Appraisal of the Safety of Chemicals in Foods, Drugs,~~Maibach, H.I., "The sodium lauryl sulfate model: an overview," ~~*and Cosmetics,*~~*Contact Dermatitis, 33,* ~~1965, p. 46.~~pp. 1-7, 1995.