List of Titles

American National Standard

ANSI/AAMI BF7:1989/(R)2002

Blood transfusion micro-filters

AAMI Association for the Advancement of Medical Instrumentation

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BF7 Blood Transfusion Micro-Filters

ANSI/AAMI BF7-1989/(R)2002
(revision of ANSI/AAMI BF7-1982)

American National Standard for Blood Transfusion Micro-Filters

Developed by
Association for the Advancement of Medical Instrumentation

Approved 10 November 1989 and reaffirmed 31 January 2002
American National Standards Institute, Inc.

Abstract:

This standard contains labeling requirements, performance requirements, test methods, and terminology for disposable blood transfusion micro-filters for use with adult populations to remove microaggregates from blood or blood products during transfusion.

Association for the Advancement of Medic`al Instrumentation
AAMI Blood Filter Committee Representation

This standard was processed and approved for submittal to ANSI by the AAMI Blood Filter Committee. Committee approval of the standard does not necessarily imply that all committee members voted for its approval. At the time it approved this standard by ballot, the AAMI Blood Filter Committee had the following members:

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Sam Wortham, Pall Biomedical Products Corporation

Note: *Participation by federal agency representatives in the development of this standard does not constitute endorsement by the federal government or any of its agencies.*

Foreword*

This standard was developed by the Blood Filter Committee of the Association for the Advancement of Medical Instrumentation. The objective of this standard is to describe those requirements which will ensure adequate delivery of filtered stored blood and blood components while removing microaggregates without traumatizing blood components. This standard contains referee test methods to be used to ensure that the performance requirements are met.

During the five-year review of this standard, the committee clarified the scope by specifying that it included disposable micro-filters for use with adult populations only. Changes in two glossary terms were made to reflect current usage. These changes constitute the revisions that are reflected in this second edition of the standard.

The concepts incorporated in this document should not be considered inflexible or static. This standard, like any other standard, must be reviewed and updated periodically to assimilate progressive technological developments. To remain relevant, it must be modified as advances are made in technology and new data come forward.

Establishing compliance with this standard may involve the use of hazardous materials, operations, and/or equipment. Therefore, users of this document should establish appropriate safety practices and proceed with caution.

This standard reflects the conscientious efforts of concerned health care professionals, in consultation with medical device manufacturers, to develop a standard for those performance levels that could be reasonably achieved at this time.

Suggestions for improving this standard are invited. Comments and/or suggested revisions should be sent to AAMI, 3330 Washington Boulevard, Suite 400, Arlington, VA 22201-4598.

American National Standard
for
Blood Transfusion Micro-Filters

1. Scope

1.1 General

This standard describes safety and performance requirements for disposable micro-filters used for the removal of microaggregates from blood or blood products during transfusion.

1.2 Inclusions

Included within the scope of this standard are disposable micro-filters for blood and blood-derivative transfusions for adult populations only. These are sometimes also referred to as microaggregate filters.

1.3 Exclusions

Excluded from the scope of this standard are filters used for extracorporeal service and other blood filters not intended for blood transfusion. Also excluded are components of standard infusion sets designed to remove readily visible blood clots only.

Note: *For an explanation of the need for this standard, as well as the rationale for its provisions, see Appendix A.*

2. Applicable Documents

2.1 *United States Pharmacopeia* (XX). Easton, PA: Mack Publishing, 1980.

2.2 ASTM. *Method of Test for Pore Size Characteristics of Membrane Filters for Use with Aerospace Fluids.* (ANSI/ASTM D2499-69). Philadelphia: American Society for Testing and Materials, 1969.

2.3 SAE. *Bubble Point Test Method.* (ARP-901). Warrendale, PA: Society of Automotive Engineers, 1968.

2.4 ASTM. *Particles from Aerospace Fluids: Microscopial Sizing and Counting on Membrane Filters.* (ANSI/ASTM F312-69). Philadelphia: American Society for Testing and Materials, 1969.

2.5 SAE. *Procedure for the Determination of Particulate Contamination of Hydraulic Fluids by the Particle Count Method.* (ARP-598). Warrendale, PA: Society of Automotive Engineers, 1960 (1969).

3. Requirements

3.1 Labeling Requirements

3.1.1 General. The term labeling refers to any printed matter which appears on the device, its accessory items, or its container and to all documentation which accompanies the device. In addition to federal regulations applicable to the labeling of all medical devices, the requirements contained in this section shall apply to devices within the scope of this standard.

3.1.2 Primary Package Labeling. The following information shall appear on that part of the package panel or label that is most likely to be visible under customary conditions of display:

(1) The product name printed prominently, parallel to the base of the package, and in boldface type at least half as large as that used for any trade or brand name thereof;

(2) The product identification or reorder number;

(3) The intended use;

(4) The name and address of the manufacturer and/or distributor;

(5) A statement of sterility and nonpyrogenicity, or non-sterility, of contents;

(6) The following or similar caution: "Federal (USA) law restricts this device to sale by or on the order of a physician," or a revision thereof as prescribed by regulation;

(7) The net contents in number of units; and

(8) The filter manufacturer's or distributor's lot number or other control number which will permit tracing the materials used in the manufacture of the filter.

3.1.3 Information/Instructions for Use. The following shall appear on the package, package label, or in a package insert:

(1) Directions for use;

(2) Direction to discard or destroy the filter after single patient use;

(3) Storage and handling instructions;

(4) Capacity as determined per 4.2.3.3—i.e., the average number and range of units of type-compatible outdated, human whole blood within 7 days of its expiration date, or packed red cells, which can be filtered consecutively at 20 to 22°C to give effluent which satisfies the requirements of 3.2.3.3(2);

(5) Any contraindications including those determined in 3.1.4—i.e., any significant difference (greater

than twice the mean standard error) between the pre- and postfiltration measurements of 3.1.4; and

(6) Residual priming volume in milliliters of saline.

3.1.4 Disclosure Information. Information on removal characteristics (as per 3.2.3.2) and blood constituents shall be obtained by the manufacturer to establish adequacy of design, and shall be available from the manufacturer upon request. Information on blood constituents shall include any significant difference of mean values ("t" test at p = 0.05) between pre- and postfiltration values, and what that difference is, for the blood constituents as follows:

(1) Pre- and postfiltration hematocrits, erythrocyte counts, leukocyte counts, total protein, and supernatant hemoglobin values shall be determined using fresh (less than 48 hours old) human blood filtered when at 10 to 12°C, 20 to 22°C, and 35 to 37°C, and outdated human whole blood within 7 days of its expiration date at 10 to 12°C, 20 to 22°C, and 35 to 37°C, and fresh and outdated packed red cells at 10 to 12°C, 20 to 22°C, and 35 to 37°C.

(2) Pre- and postfiltration platelet counts and total white blood cell counts shall be determined for fresh blood.

(3) Pre- and postfiltration hematocrit, erythrocyte count, and supernatant hemoglobin shall be determined for frozen, thawed, deglycerolized erythrocytes.

3.2 Performance Requirements

3.2.1 Packaging. The package which contains the device shall meet the following requirements:

(1) Package design, construction, and material shall be adequate to protect the device during customary conditions of storage, handling, and shipping.

(2) Packaging shall permit aseptic removal or provide for maintenance of the sterile fluid pathways.

(3) The opening of the package and the removal of the product from the packaging shall not contribute to the deposition of fibers and foreign matter in the fluid pathways.

3.2.2 Structural Integrity

3.2.2.1 Housing Integrity. The following requirements shall be met:

(1) The filter housing shall be capable of withstanding a static internal gas pressure of 450 millimeters of mercury (8.7 psi, gauge) applied at a minimum rate of 45 millimeters of mercury per second (mmHg/sec) [0.87 psi/sec], without visible evidence of leakage.

(2) When the filter is sold with an attached administration set, then the filter-recipient set coupling shall withstand a static internal gas pressure of 450 mmHg (8.7 psi, gauge) applied at a minimum rate of 45 mmHg/sec (0.87 psi/sec) without visible leakage.

3.2.2.2 Media Integrity. The filter media itself and the media-housing bond shall be capable of withstanding the stress of a pressure drop across the filter of 450 mmHg (8.7 psi, gauge) for a period of 10 minutes.

3.2.3 Filter Performance

3.2.3.1 Filter Cleanliness. The filter shall provide no more than the following effluent particle levels when subjected to the water or other solvent flush test of 4.2.3.1:

(1) 0.90 particle per milliliter of solvent flush larger than 10 micrometers;

(2) 0.35 particle per milliliter of solvent flush larger than 25 micrometers;

(3) 0.65 fiber per milliliter of solvent flush.

3.2.3.2 Removal Characteristics. The filter shall exhibit adequate removal characteristics by compliance with either of the following requirements:

(1) **Simulated Blood Challenge.** The filter, when tested in accordance with the simulated blood suspension test of 4.2.3.2(1), shall remove at least 80 percent of the particles represented by diameters greater than 40 and less than 100 micrometers (µm).

(2) **Particle Challenge.** The filter, when tested in accordance with the latex spherical particle suspension test of 4.2.3.2(2) shall remove at least 80 percent of the number of particles larger than 40 µm in diameter and less than 100 µm.

3.2.3.3 Volume Capacity. The filter shall meet the following requirements:

(1) **Gravity Flow.** Individual units of packed red cells—approximately 250 to 300 cubic centimeters (cc)—or outdated human whole blood (approximately 500 cc) within 7 days of expiration date and having hematocrits of 75 to 85 percent and 35 to 52 percent, respectively, shall pass through the filter at 20 to 22°C under gravity flow within a period no longer than one hour.

(2) **Total Capacity.** The average number and range of units of type-compatible, outdated human whole blood (hematocrit 35 to 52 percent) within 7 days of its expiration date, or packed red cells (hematocrit 75 to 85 percent), which can be filtered consecutively at 20 to 22°C to give effluent which satisfies the removal characteristics requirement of 3.2.3.2, shall be determined and be disclosed in the information/instructions for use (as per 3.1.3(4)). The last unit that may be considered to have passed through the filter must do so at an average flow rate no less than 100 cc per minute on the last filtered unit at a pressure not to exceed 300 mmHg.

3.3 Interface Characteristics

3.3.1 Filters Without Attached Administration Sets

3.3.1.1. The outlet port shall accept insertion of conventional blood administration set spikes. The outlet port shall allow administration set insertion without user contact with the fluid pathway portion of the port. The outlet port shall not permit an insertion depth of the administration set coupler to an extent sufficient to contact the filter medium.

3.3.1.2 The spike shall be designed to provide a seal between the spike and the blood container housing before the spike penetrates the seal of the blood container outlet port to establish a fluid pathway. The spike shall allow insertion without user contact with the spike tip or shaft.

3.3.1.3 The spike shall seal securely enough to ensure retention and avoid leakage under a static internal gas pressure of 450 mmHg (8.7 psi, gauge) applied at a minimum rate of 45 mmHg/sec (0.87 psi/sec).

3.3.1.4 If the filter is designed for use on multiple units of blood, then the spike shall allow removal from the blood container outlet port assembly without damage to the spike or blood container. Reinsertion into subsequent units must meet all the performance requirements for the spike (as per 3.3.1.2, 3.3.1.3, and 3.3.1.5).

3.3.1.5 The spike length shall permit adequate sealing with the blood container outlet port without excessive entry into the container.

3.3.2 Filters With Attached Administration Sets

3.3.2.1 The male needle adapter shall accept conventional hubs for needles and catheters.

3.3.2.2. See interface characteristics described in 3.3.1.2.

3.3.2.3 The spike, outlet port, and male luer (needle) adapter shall provide secure seals at conventional junctions

and shall avoid leakage under a static internal gas pressure of 450 mmHg (8.7 psi, gauge) applied at a minimum rate of 45 mmHg/sec (0.87 psi/sec).

3.3.2.4 See interface characteristics described in 3.3.1.4.

3.3.2.5 See interface characteristics described in 3.3.1.5.

3.4 Material Safety

3.4.1 Toxicity Potential Evaluation. Materials in the fluid pathway shall pass toxicology test procedures.

3.4.2 Sterility. Each filter shall be sterile, unless clearly labeled to the contrary.

3.4.3 Pyrogenicity. Each sterile filter shall be nonpyrogenic.

4. Tests.

This section contains test methods to provide means of verifying the performance of blood transfusion micro-filters. These test methods and procedures are for use in determining compliance with the requirements of Section 3. All instrumentation and measurement equipment shall be appropriate for measuring the test parameter in question and shall conform to laboratory standards whose calibration is traceable to the primary standards at the U.S. National Bureau of Standards. The referee test methods and procedures of this section are not intended for design qualification purposes or for quality control testing; therefore, no confidence limits are specified. A change in design or construction material may, however, be accompanied by the reapplication of the appropriate test methods and procedures to establish continued compliance with the requirements of Section 3.

Note: *The paragraph numbering of this section corresponds to that of Section 3, except for the first digit. For example, the requirements of 3.2.2 are tested in accordance with the methods of 4.2.2.*

4.1 Labeling

Compliance with the requirements of 3.1.1, 3.1.2, and 3.1.3 can be determined by visual inspection.

4.1.4 Disclosure Information. Hematocrit, erythrocyte count, leukocyte count, total protein, supernatant hemoglobin, and platelet count shall be determined according to one of the standard methods given in the references in Appendix A (Band et al. 1971; Biggs 1976; Davidson & Henry 1974). Measurements shall be made before and after filtration of fresh and outdated packed red cells, fresh human whole blood (preferably less than 24 hours old, but certainly less than 48 hours old), and type-specific, anticoagulated, outdated human whole blood within 7 days of its expiration date. In all cases, measurements shall be made at each of three temperature ranges: 10 to 12°C, 20 to 22°C, and 35 to 37°C. Measurements of each of the above blood constituents shall be made with both fresh and outdated packed red cells and blood, except that platelet counts shall be made with fresh blood only. Filters shall be primed in accordance with the manufacturer's instructions. Filtration shall be at 300 mmHg pressure through 134 centimeters (cm) of 0.118-inch nominal-inside-diameter tubing. Postfiltration measurements shall be made after passage of a single unit of blood (500 cc) and again after the maximum number of units of blood—capable of being filtered in accordance with referee test method 4.2.3.3—have been filtered consecutively through a single filter unit. The test shall be repeated with ten representative filter units and all data shall be utilized. All data shall be analyzed statistically by correlated t-tests with paired observations of mean values ("t" test at $p = 0.05$). A significant difference between pre- and postfiltration measurements shall be one greater than twice the mean standard error of the measurement. All data shall be gathered and available from the manufacturer on request.

The hematocrit, erythrocyte count, and supernatant hemoglobin values shall be determined according to one of the standard methods given in the references in Appendix A (Band et al. 1971; Biggs 1976; Davidson & Henry 1974). Measurements shall be made before and after frozen, thawed, deglycerolized erythrocytes at

each of three temperatures (10 to 12°C, 20 to 22°C, and 35 to 37°C) are passed through the filter. Filters shall first be primed in accordance with the manufacturer's instructions. Filtration shall be at 300 mmHg pressure through 134 cm of 0.118-inch nominal-inside-diameter tubing. Postfiltration measurements shall be made after passage of a single unit and again after passage of the maximum number of units capable of being filtered before flow is obstructed, in accordance with referee test method 4.2.3.3. The test shall be repeated with ten representative filter units and all data shall be analyzed statistically by correlated t-tests with paired observations of mean values ("t" test at p = 0.05). A significant difference between pre- and postfiltration measurements shall be a difference greater than twice the mean standard error of the measurement. Again, all data shall be gathered and available from the manufacturer on request.

4.2 Performance Requirements

4.2.1 Packaging. Compliance with the requirements of 3.2.1 can be determined by visual inspection.

4.2.2 Structural Integrity

4.2.2.1 Housing Integrity

(1) Pressure shall be applied at a minimum of 45 mmHg/sec (0.87 psi/sec, gauge) with nitrogen gas or oil-free compressed air to one port of the test unit with the other port(s) occluded so that a static pressure of 450 mmHg is reached, the unit being immersed neither less than 3 cm nor more than 25 cm under water. Failure shall be indicated by a steady stream of bubbles (defined as 5 or more per sec) rising from bonded sites or the housing itself. The leakage measurement period shall be at least 5 sec in duration, following a premeasurement immersion period of 10 seconds, with pressure maintained at 450 mmHg for the full 15-sec test period. This procedure is equivalent to referee test method 4.3.1.3.

(2) If the filter is provided with an attached administration set, then occlusion shall be at a point distal to the site of mating and the test performed as in 4.2.2.1(1) above, with the additional stipulation that leakage at mating sites shall also constitute failure. This procedure is equivalent to referee test method 4.3.2.3.

4.2.2.2 Media Integrity. A viscous aqueous solution (e.g., using 1000 centipoise methyl cellulose solution) shall be prepared to sufficiently achieve a 450-mmHg pressure drop across the filter for a period of 10 minutes (min). This solution shall be applied to the filter and, following a 10-min period, the filter shall be subjected to a forward bubble point test (Applicable Document 2.3) with oil-free compressed air or nitrogen gas at a differential pressure of 4 cm of water. Passage of 5 visible bubbles or more per second shall constitute failure.

4.2.3 Filter Performance

4.2.3.1 Filter Cleanliness. All operations shall be performed in an operating, certified laminar flow hood equipped with high-efficiency particulate air (HEPA) filters. Install a dummy filter (i.e., a filter housing not containing any filter medium) in a fixture containing a test sample holder, fluid circulation apparatus, and an analysis membrane holder downstream of the test sample holder. The fluid shall be USP Water-for-Injection filtered through a 0.8-µm filter. Wash the test fixture and both sides of a black-gridded 0.8-mm pore-size, blank analysis membrane using this fluid. Install the analysis membrane using smooth-tip forceps, and allow the fluid to flow through the dummy filter sample at a rate of 500 cc/min, or at the maximum pressure drop of 450 mmHg (8.7 psi, gauge), for 5 min. Remove the analysis membrane, place it in a petri disc container with the cover slightly ajar, dry in a laminar flow hood, and count microscopically the particles collected on the membrane surface (as per Applicable Document 2.4 and/or 2.5). Repeat the procedure from the beginning using a test filter sample. The blank count may not exceed 10 percent of the maximum acceptable counts given in 3.2.3.1. Calculate the difference between the test and blank counts for all particles larger than 10 µm in diameter, larger than 25 µm in diameter, and for all fibers. All counts shall be less than or

equal to those given in 3.2.3.1.

4.2.3.2 Removal Characteristics

(1) **Simulated Blood Challenge.** Pooled units of ABO compatible, outdated human whole blood within 7 days of expiration date, or outdated red cells within 7 days of expiration date, shall be considered the test fluid. The hematocrit of the pooled whole blood units shall be 35 to 52 percent and shall be adjusted with physiological serum only if necessary. The hematocrit of the packed red cells shall be 75 to 85 percent without dilution. The test fluid shall be prefiltered, using a mesh with 200-µm openings, in order to remove clots and gross debris that may obscure the aperture of an electronic particle counter. In order to be considered an acceptable test fluid, the simulated blood suspension shall contain 350 to 5000 particles per milliliter of test fluid in the 40- to 100-µm diameter range as determined by the electronic volume sensing procedure described below.

A resistive pulse spectroscopy particle counter shall be used with a 200-µm aperture. The counter shall be calibrated and operated in accordance with the manufacturer's instructions. Size calibration control settings shall be selected such that mean particle volumes for particles with diameters greater than 40 µm and less than 100 µm are determined using at least three channels.

To a beaker used with a stirring device, add 97 milliliters (ml) of Isoton (or equivalent) filtered through a 0.8-µm pore-size filter. While stirring continuously at 30 to 40 revolutions per minute, add 0.75 ml of Zap-Isoton or equivalent lysing solution. Mix the simulated blood suspension (while at 20 to 22°C) using a gentle, end-to-end rotation and swirling motion. Withdraw a 3.0-ml aliquot of the unfiltered simulated blood suspension using a volumetric pipette, and deliver it at a slow, uniform rate into the continuously stirred solution of Isoton and Zap-Isoton which serves to lyse the blood cells. Initiate particle counting in the manometer mode 15 to 30 sec after adding the 3.0-ml aliquot once the mixture becomes transparent. The resulting count may be used to calculate the prefiltration mean number of particles and to determine if the requirements for an acceptable test fluid are met.

Withdraw one unit (approximately 500 cc) of the simulated blood suspension and pass it, at 20 to 22°C, through a micro-filter test sample at a flow rate of no less than 100 ml/min and a pressure not to exceed 300 mmHg applied at a minimum rate of 60 mmHg/sec (1.16 psi/sec). Within 10 min after completing filtration, perform the electronic volume sensing procedure (described above) using a 3.0-ml aliquot of the filtered simulated blood suspension. Two additional 3.0-m aliquots should be taken from the same filtered unit, and results from all three counts for the 40- to 100-µm diameter size range should be averaged to calculate the postfiltration mean number of particles.

Postfiltration counts of 34 or fewer are within experimental error and may be discarded. A final 3.0-ml aliquot is taken from the unfiltered simulated blood suspension and, if the requirements for the acceptable test fluids are met, this count is averaged with the initial count to calculate the prefiltration mean number of particles for the 40- to 100-µm size range. If the requirements for an acceptable test fluid are not met for either the initial or final aliquots, then the entire procedure shall be repeated.

The removal efficiency shall be calculated, using all readings only in the 40- to 100-µm size range, for each test sample by subtracting the postfiltration mean from the prefiltration mean number of particles, dividing the difference by the prefiltration mean number of particles, and multiplying by 100 to obtain a percentage. The test procedure shall be performed with a total of ten micro-filter test samples. The average filtration removal efficiency of all ten test samples must be at least 80 percent, with the filtration removal efficiency of any individual test filter being at least 50 percent, in order to meet this performance requirement.

(2) **Particle Challenge.** An influent suspension shall be prepared from serial dilutions of a stock suspension (using vigorous agitation). The stock suspension shall contain 1 ml of latex spheres (with a nominal diameter of 45 µm) injected into a l-liter bag of a 7 percent sodium chloride (NaCl) solution. The suspension shall be carefully mixed before proceeding further. Mixing may be

accomplished by rapidly pressing down with the fingers of each hand at locations about an inch from the ends of the bag; each end of the bag may be impacted alternately, about twice each second, for one minute. A 10-ml aliquot of the stock suspension shall be diluted in 1 liter of the 7 percent NaCl solution which will be used as the influent suspension. A l-liter, well-mixed influent suspension shall be prepared (as just described) for each micro-filter test sample. In order to be considered an acceptable test fluid, a milliliter of the influent suspension shall contain approximately ten spheres larger than 45 µm (± 5 µm) in diameter as determined by optical microscopic count.

Prior to the collection of spheres in any of the test sequences, a blank determination shall be made. An analytical filter holder shall be assembled on a l-liter filtering flask, using a 0.8-µm pore-size, 47-millimeter (mm) diameter, analytical disc filter. The disc filter and the filter funnel shall be pre-rinsed with filtered water, the disc inserted onto the funnel base using flat forceps, the funnel section clamped into place, and the holder inserted into a filter flask provided with a vacuum source. Purified Water (USP) filtered through a 0.8-mm filter shall be used as the blank influent; 100 ml of influent shall be introduced into the funnel. The vacuum shall be applied, and released when 10 ml remain in the funnel. The walls of the funnel shall then be washed using a solvent dispenser with approximately 20 ml of additional filtered water, and the vacuum applied until all the liquid is drawn through the disc filter. The vacuum shall then be turned off and the clamp and funnel section of the filter holder removed. The disc filter shall be carefully removed using flat forceps and placed in a petri disc container. The slide cover shall be placed slightly ajar to permit complete drying of the disc filter. The analysis funnel shall be rinsed with filtered water in preparation for the next test and stored in a laminar flow hood or other clean location. The disc filter shall be scanned microscopically at a total magnification of 40 to 50X; the blank shall be found to contain no spheres.

The blank procedure shall be repeated, this time substituting a 100-ml aliquot of the influent suspension for the filtered Purified Water (USP) in order to obtain an influent count. A pre-rinsed analytical filter holder shall be assembled on a l-liter filtering flask, using a 0.8-µm pore-size, 47-mm diameter, analytical disc filter (as described earlier). The disc filter and the filter funnel shall be pre-rinsed with filtered water, the disc inserted onto the funnel base using flat forceps, the funnel section clamped into place, and the holder inserted into a filter flask provided with a vacuum source. A well-mixed 100-ml aliquot of the influent suspension shall be introduced into the funnel. A vacuum shall be applied, and released when 10 ml remain in the funnel. The walls of the funnel shall then be washed using a solvent dispenser with approximately 20 ml of additional filtered water, and the vacuum applied until all of the liquid is drawn through the disc filter. The vacuum shall then be turned off and the clamp and the funnel section of the filter holder removed. The analysis funnel shall be rinsed with filtered water in preparation for the next test and, until then, stored in a laminar flow hood or other clean location. The disc filter shall be carefully removed using flat forceps and placed in a petri disc container. The slide cover shall be placed slightly ajar to allow the disc filter to dry completely. The number of latex spheres on the disc filter shall be counted microscopically at a total magnification of about 40 to 50X and, with the aid of a stage micrometer, an image splitter shall be adjusted to a 42-µm shear. (The image splitter may be adjusted to within ± 2 µm; it shall be set to encompass the lower limit of the nominal diameter range of the influent particle suspension.)

Alternatively, a microscope equipped with an ocular reticle calibrated with a micrometer may be used at 100X magnification. Illumination shall be adjusted to obtain the greatest sphere definition. The plate shall be scanned, counting latex spheres greater than 42 µm, that is, all cases where the split image of a sphere overlaps on the image splitter. In order to be considered an acceptable test fluid, a milliliter of the influent suspension shall contain approximately ten spheres larger than 45 µm (± 5 µm) in diameter as determined by optical microscopic count.

In order to obtain an effluent determination, the remaining 900 ml of the influent suspension shall be carefully mixed and passed through a micro-filter test sample, followed by l-liter of 7 percent NaCl solution. A pre-rinsed analytical filter holder shall be assembled on a 1-liter filtering flask, using an 0.8-µm pore-size, 47-mm diameter, analytical disc filter. The disc filter and the filter funnel shall be pre-rinsed with filtered

water, the disc inserted onto the funnel base using flat forceps, the funnel section clamped into place, and the holder inserted into a filter flask provided with a vacuum source. The well-mixed 900 ml left over from the influent suspension used in the influent determination above shall be passed through a micro-filter test sample and into the funnel. This shall be followed by l-liter of a 7 percent NaCl solution. A vacuum shall be applied until all the liquid is drawn through the disc filter, then turned off, and the clamp and funnel section of the filter holder removed. The disc filter shall be carefully removed using flat forceps and placed in a petri disc container. The slide cover shall be placed slightly ajar so the disc filter can completely dry. The number of latex spheres on the disc filter shall be counted microscopically at a total magnification of about 40 to 50X and, with the aid of a stage micrometer, an image splitter shall be adjusted to a 42-µm shear. (The image splitter may be adjusted to within ± 2 µm; it shall be set to encompass the lower limit of the nominal diameter range of the influent particle suspension.)

Alternatively, a microscope equipped with an ocular reticle calibrated with a micrometer may be used at 100X magnification. Illumination shall be adjusted to obtain the greatest sphere definition. The plate shall be scanned, counting latex spheres greater than 42 µm (all cases where the split image of a sphere overlaps on the image splitter).

The removal efficiency shall be calculated for each test sample by subtracting the number of latex spheres in the effluent from the number of latex spheres in the influent suspension, dividing the difference by the number of latex particles in the influent, and multiplying by 100 to obtain a percentage. The test procedure shall be performed with one micro-filter test sample, and a filtration removal efficiency of at least 80 percent is necessary to satisfy the performance requirement.

4.2.3.3 Volume Capacity

(1) **Gravity Flow.** In order to provide uniformity, a standard blood infusion set containing 0.118-inch nominal-inside-diameter tubing shall be used except where the micro-filter is intended to be sold with an infusion set attached. In either case, approximately 120 cm of tubing shall be used and a 1 to 1.5 inch 16 gauge needle shall be placed at the end of the infusion set. Filters shall be primed in accordance with the manufacturer's instructions. Gravity flow testing shall be performed at 20 to 22°C using individual units of packed red cells having a hematocrit of 75 to 85 percent, or outdated human whole blood having a hematocrit of 35 to 52 percent, within 7 days of their expiration dates, the filter being inserted directly into the blood or packed red cell container. The midpoint of the container shall be positioned 134 cm above the end of the needle. A waste receptacle shall be positioned below the needle, the tubing clamp shall be opened, and the tubing unkinked at the point of compression. Timing shall begin when flow from the needle is fully established, and an entire unit (approximately 500 cc for whole blood and 250 to 300 cc for packed red cells) must pass through the test filter within one hour. A total of ten test filters shall undergo the above test and eight of them must pass the test in order to meet the requirements of 3.2.3.3(1).

(2) **Total Capacity.** For each micro-filter test sample passing the gravity flow test, the filter and attached administration set shall be carefully disconnected from the blood unit without disconnecting the infusion set or losing the prime. Also remove the 16 gauge needle. The filter spike shall be inserted into individual units of type-compatible, outdated human whole blood having a hematocrit of 35 to 52 percent, or packed red cells having a hematocrit of 75 to 85 percent without dilution, within 7 days of expiration date and at 20 to 22°C. The blood bag unit shall be suspended from a suitable stand and placed in a standard blood pressure cuff. The tubing set clamp shall be opened and the initial effluent allowed to drain into a waste receptacle while unkinking the tubing. The flow shall then be directed into a 500-ml or 1000-ml graduated cylinder. Pressure shall be applied at a minimum rate of 60 mmHg/sec (1.16 psi/sec) sufficient to maintain an average flow rate of about 100 ml/min; however, 300 mmHg shall not be exceeded on the pressure cuff.

This test sequence shall be repeated with as many consecutive units of type-compatible blood as possible

until a flow rate of at least 100 ml/min can no longer be maintained below or at 300 mmHg. Referee test method 4.2.3.2(1), the simulated blood challenge, shall then be applied using a 3.0-ml aliquot taken from the final filtered effluent within 10 min after completing the capacity test. The volume capacity of the filter shall be defined as the lesser of the two values: (a) the number of complete units filtered before the flow rate decreases to an average of less than 100 cc/min on the last unit filtered, or (b) the number of complete units filtered before the removal characteristics requirement is not met. The simulated blood challenge shall be repeated with ten representative filter samples and the average and range, rather than only the minimum, shall be reported.

4.3 Interface Characteristics

4.3.1 Filters Without Attached Administration Sets

4.3.1.1 Insert the spikes of representative samples of conventional administration sets into filter outlet ports according to the manufacturer's instructions. Determine whether (1) the administration set spike seals on the filter outlet port, (2) the spikes are easy to insert, and (3) the junction is made without user contact with the spike or the fluid pathway portion of the outlet port. Determine by observation, mechanical measurement, or radiographic technique that the depth of insertion of the administration set coupler does not allow contact with the filter medium.

4.3.1.2 Place empty blood containers in suitable restraints. Using the units assembled in 4.3.1.1, insert the filter spikes into the empty containers according to the manufacturer's instructions. Determine whether (1) the spike seals on the container's outlet port prior to seal puncture, (2) there is ease of insertion, and no contact with the container, (3) there is ease of seal puncture, and (4) the junction is made without user contact with the spike or container shaft.

4.3.1.3 Using the units assembled in 4.3.1.2, close the clamps on the fluid delivery tubes. Gradually apply a static air pressure of 450 mmHg (8.7 psi, gauge) at a minimum rate of 45 mmHg/sec (0.87 psi/sec) through a second port on the container (or the "Y" type administration set). Immerse the entire assembly neither less than 3 cm nor more than 25 cm under a clear liquid (e.g., water) and look for leaks in the blood container/spike junction and the outlet port/administration set junction. The leakage measurement period shall be at least 5 sec in duration, following a premeasurement immersion period of 10 sec, with pressure maintained at 450 mmHg for the full 15-sec test period. All junctions shall remain intact and allow no leakage; leakage would be indicated by a steady stream of visible bubbles (defined as 5 or more per sec). This procedure is equivalent to referee test method 4.2.2.1.

4.3.1.4 Using the units assembled in referee test method 4.3.1.2, remove the filter spikes from the empty blood containers. Observe that (1) the spike is easily removed from the container, (2) there is no damage to the spike or to the container, and (3) removal can be accomplished without contact with the spike or the container outlet port. Insert the filter spikes into additional blood containers filled with any test fluid, observing parameters (1), (2), (3), and (4) of referee test method 4.3.1.2. Repeat this step until the number of insertions corresponds to the volume capacity as determined by referee test method 4.2.3.3, observing all the parameters for insertion and removal.

4.3.1.5 Using the units assembled in 4.3.1.4, open the clamps on the tubing delivering the fluid and observe that a fluid pathway is established from the container through the filter and the administration set. Observe the residual volume of fluid remaining in the blood container. Determine by measurement that this residual volume is less than 10 ml.

4.3.2 Filters With Attached Administration Sets

4.3.2.1 Attach a representative number of samples of conventionally hubbed needles and catheters into the administration set needle adapters of an equal number of filters. Observe the ease of attachment or lack thereof.

4.3.2.2 Place empty blood containers in suitable restraints. Using the units assembled in referee test method 4.3.2.1, insert the filter spikes into the empty containers according to the manufacturer's instructions. Observe parameters (1), (2), (3), and (4) of referee test method 4.3.1.2.

4.3.2.3 Using the units assembled in referee test method 4.3.2.2., occlude the needle or catheter. Follow referee test method 4.3.1.3, and, in addition, look for leaks in the needle/ administration set junction.

4.3.2.4 Using the units assembled in 4.3.2.2, follow referee test method 4.3.1.4.

4.3.2.5 Using those units assembled in 4.3.2.2, remove the occlusion from the needle or catheter and follow referee test method 4.3.1.5.

4.4 Material Safety

4.4.1 Toxicity Potential Evaluation. Either the *in vivo* biological testing procedures or the *in vitro* procedures described below shall be passed. These tests shall be applied only in the initial qualification of materials to be used in the manufacture of blood filters.

(1) ***In Vitro* Evaluation of Components.** Each component of the filter which will come into contact with blood shall be thoroughly rinsed in Purified Water (USP) and Reagent Grade Normal Hexane, or cleaned by procedures used in the manufacture of the device. The materials shall be air dried between rinses. The following test procedure shall be followed:

(a) Procure a viable culture of L929 mouse fibroblasts.

(b) Establish a monolayer in petri dishes using Eagle's medium with Earles salts containing 10 percent fetal calf serum.

(c) Prepare agar overlayer by adding equal amounts of 2 percent melted agar to 2X Eagle's medium. To this, add 2 percent calf serum and 1 percent of a 0.01 percent solution of microfiltered neutral red. Adjust the pH to 7.2 with sodium bicarbonate.

(d) Decant fluid medium from established monolayer and wash the cells twice with phosphate buffered saline (pH 7.0).

(e) Dispense the agar medium over the monolayer when the temperature approaches 37°C in a quantity to provide approximately 3 mm coverage over the cells.

(f) Implant a sample of each component of the filter which will come in contact with blood, along with negative and positive controls.

(g) Incubate for 24 hours at 37°C in 6 percent carbon dioxide.

(h) Read the size of zone and percentage of cells that have been lysed within the zone.

Any material that produces a zone of lysis, irrespective of the size of the clear zone below the sample, should be disqualified from further consideration as a blood-path component of the filter, unless it can be shown by other testing procedures (such as those described by (2) or (3) below) that it would not compromise the safety of the device. Determination of cell lysis shall be made by using an optical microscope.

(2) ***In Vitro* Evaluation of the Filter.** (This test may be omitted if the testing procedure in (1) above does not produce a zone of lysis.) Three representative samples of the sterile filter shall be filled with physiological saline and three others with vegetable oil (sesame or cottonseed). Two of the saline and two of the vegetable oil solvent-filled filters shall be extracted in an oven at 50°C for 24 hours and the others in an oven at 37°C for 72 hours. Prepare discs (6.25 mm) of filterpaper (pretested for suitability) by punching #7 paper with a standard paper punch. Saturate individual discs with the oil

and saline extracts and subject both to a cytotoxicity assay as described in (1) above.

(3) ***In Vivo* Evaluation of the Filter.** Using the saline and oil extracts prepared under (2) above, conduct intracutaneous, intravenous, and intraperitoneal studies in the manner described below.

(a) *Intracutaneous Irritation.* Restrain two rabbits in the dorsal recumbant position and depilate the abdominal skin. Using a colored pencil or pen, divide the skin into eight segments, four on each side of the median line. Inject intradermally 0.3 ml of each extract together with its solvent control (pretested for suitability) so that each rabbit receives an intradermal injection of saline and of oil in addition to injections of each of the three saline and each of the three oil extracts. Ten to twenty minutes following the last intradermal injection, infuse each rabbit with 1 ml per kilogram of a 1 percent solution of Trypan Blue in 0.9 percent saline. Include a positive control (e.g., procaine hydrochloride). Examine and score the injection sites at 1/2, 1, and 3 hours using the scoring system outlined in Table 1.

Table 1

Scoring Intracutaneous Irritation Injections

Color	*Score*
No color	0
Faint but discernible blue color	2
Distinct blue color throughout	4
Deep blue color throughout	
Ischemic central area surrounded by blue halo	16

Next, calculate the threshold irritant concentration according to the ratings derived from injection site scores as shown in Table 2.

Table 2

Calculating the Threshold Irritant Concentration*

Maximum Average Score	*Rating*
0	Non-irritating
1-3	Mildly irritating
4-7	Moderately irritating
8 or greater	Markedly irritating

*The Threshold Irritant Concentration (TIC) refers to that concentration, expressed as a percentage, which produces no more than a mild irritation.

A score of 3 or lower is acceptable for a test substance and 1 or lower is acceptable for a solvent control. In a second pair of rabbits, complete the same series of intradermal injections as described above, but do not infuse with Trypan Blue. Score the degree of erythema after 24 hours using the scheme in Table 3; a score of zero or 1 is acceptable for either a test substance or a solvent control.

Table 3

Scoring Degree of Erythema after 24 Hours

Erythema	*Score*
No erythema	0
Barely perceptible erythema	1
Well-defined erythema	2
Moderate erythema	3
Severe erythema	4

(b) *Intravenous Toxicity.* The saline extract prepared under 3.4.1(2) shall be used to establish whether there is a measurable level of systemic toxicity following the intravenous injection of the extract (Applicable Document 2.1, Biological Tests—Plastics).

(c) *Intraperitoneal Toxicity.* The oil extract shall be used to establish whether there is a measurable level of systemic toxicity following the intraperitoneal injection of the extract (Applicable Document 2.1, Biological Tests—Plastics).

4.4.2 Sterility. The test shall be conducted as for parenteral devices as stated in Applicable Document 2.1.

4.4.3 Pyrogenicity. The test shall be conducted as for pyrogen testing using either the method described in Applicable Document 2.1 or an equivalent limulus amebocyte lysate test.

5. Glossary

Fiber. A particle longer than 100 µm with a length-to-width ratio of greater than 10:1, regardless of composition.

Fresh Blood. Blood which is utilized usually within 24 hours, but in no case more than 48 hours, after collection.

Indated Blood. Blood which has been preserved and stored at 4°C for a clinically acceptable period, which is based on its useful shelf-life. Currently, blood may be stored up to 21 days in CPD (citrate phosphate dextrose) anticoagulant and up to 35 days in CPD adenine, or up to 42 days in AS-1 (adsol) or AS-3 (Neutricel) and still be considered indated.

Inspection. As used in this standard, inspection is defined as examination (e.g., visual, auditory) and/or investigation, without the use of special laboratory appliances or procedures.

Latex Spheres. While alternate materials may be qualified, the work upon which the test method included in this standard is based utilized commercially available latex spheres, with a nominal diameter of 45 µm.

Outdated Whole Blood. Blood which has been preserved and stored at 4°C but not used within a clinically acceptable period. A hematocrit of 35 to 52 percent without dilution with saline, but permitting dilution with serum if necessary, is specified throughout this standard.

Packed Red Cells. Blood from which the plasma has been removed and which has a hematocrit of 75 to 85 percent without dilution (i.e., without either saline or serum or other diluent).

Particle Size. The maximum dimension of the particle, which for a sphere is the diameter.

Simulated Blood for Challenge Test. A suspension prepared as described in 4.2.3.2(1).

Appendix A*
Rationale for the Development and Provisions of This Standard

A1. Introduction.

This appendix provides the rationale for the initiation of a standards-development effort on blood transfusion micro-filters, as well as the rationale for each of the specific requirements of the standard. It also reflects, as nearly as possible, committee deliberations which resulted in the requirements of Section 3 and the test methodologies of Section 4.

A2. Need for This Standard.

Blood transfusion micro-filters, designed to remove microaggregates from blood and blood products during transfusion, are used routinely and frequently in many situations where blood replacement is a necessary part of medical therapy.

Excessively large pore size may allow potentially harmful microaggregates (particles) to enter the patient's vascular system and possibly cause harmful alteration in brain and lung function. In addition, inadequate filter surface area may cause excessive flow resistance or premature clogging of the filter that may result in inadequate blood delivery to the patient.

Therefore, work was initiated to define minimum safety and performance requirements for these devices, together with appropriate test methodologies, which would both address current clinical needs and allow for design innovation.

A3. Rationale for the Specific Provisions of This Standard

A3.1 Labeling Requirements

A3.1.1 General. There are two factors which control the label content of a medical device. Firstly, there are the requirements defined in Part 820, Chapter 1, Title 21, of the *Code of Federal Regulations—Good Manufacturing Practice for Medical Devices*—specifically sections 820.120, 820.121, and 820.130. These regulations establish requirements for proper handling, legibility, expiration dates, and many other aspects of labeling pertaining to good manufacturing practices. Secondly, Part 801, Chapter 1, Title 21, of the *Code of Federal Regulations,* and Section 502 of the Federal Food, Drug and Cosmetic Act (as amended in October 1976) specifically state what constitutes proper labeling and misbranding for a drug or device. These two sets of requirements comprise the federal regulations referred to in 3.1.1 of this standard. All labeling pertaining to blood transfusion micro-filters is controlled by these regulations and must comply with them. They are included in this voluntary standard for informational purposes and for completeness.

However, this standard requires other important labeling information concerning the use, safety, and expected performance of the device. Therefore, specialized labeling requirements, particular to blood transfusion micro-filters, were developed and are included in 3.1.2, 3.1.3, and 3.1.4 of this standard.

A3.1.2 Primary Package Labeling. These requirements are intended to furnish the physician with reliable information concerning those parameters that ordinarily must be taken into account during a procedure.

A3.1.3 Information/Instructions for Use. These requirements assure that adequate information about the expected performance of the device is provided when the device is supplied to the user. The committee also considered specifying that the maximum period of time during which any single filter may be employed be the same as the period of ambient use recommended for blood and blood products, but the committee concluded that this stipulation is beyond the scope of this standard.

A3.1.4 Disclosure Information. For safety, the physician and others in the patient care system should be aware of any effects of filtration on normal blood constituents. While filtration of fresh blood has not been indicated in medical practice, the great fragility of constituents of fresh blood represents the most stressful clinical situation that may be encountered and any detrimental effects should be noted. Filtration of stored blood under high pressure infusion represents the most likely clinical situation and should therefore also be

investigated. Standard test methods are cited as references, for guidance only, since several equivalent protocols are available and users may prefer to exercise their own judgment (Band et al. 1971; Biggs 1976; Davidson & Henry 1974).

For safety, the physician and others in the patient care system should be aware of any effects of filtration on blood components used in transfusion therapy. However, disclosure information on certain blood components, such as platelet concentrates, was considered beyond the scope of this standard because of currently limited clinical use.

A3.2 Performance Requirements

A3.2.1 Packaging. These requirements consider both the outer and inner packaging and address the risk of loss of sterility and contamination. The outer package protects the filter from mechanical abuse, and the inner package (including protective end caps, if any) prevents loss of integrity which could lead to a loss of sterility. Consideration was also given to static resistivity and decay of packaging materials, but requirements have not been included in the standard because these factors were not considered hazards. In addition, functional requirements were addressed rather than packaging material specifications.

A3.2.2 Structural Integrity

A3.2.2.1 Housing Integrity. Blood filters are intended for use in situations which could require rapid transfusion of large volumes of blood; housing or coupling failures requiring filter replacement prior to functional exhaustion consume valuable time and compromise function and sterility. A pressure of 450 mmHg was considered adequate for a leak test (as opposed to a burst test) because this is one and one-half times the typical use pressure. In addition, 45 mmHg/sec is approximately one and one-half times the maximum pressure that can be applied by manually inflating a conventional blood bag pressure cuff. It was also noted that an air test is more stringent than a liquid test and that 450 mmHg is seldom exceeded in practice.

A3.2.2.2 Media Integrity. Rupture of the filter medium could not only cause functional failure, but also permit dumping of large amounts of collected debris into a patient's circulatory system. A flow fatigue test is an indication of the ability of the filter medium, and medium/housing bond(s), to withstand the stresses of pressurization while partially occluded.

A3.2.3 Filter Performance

A.3.2.3.1 Filter Cleanliness. Testing is necessary to assure that the filter media itself neither migrates nor contains significant debris which could be infused as a nonbiodegradable aggregate into the patient, thereby subverting the primary objective of preventing the passage of debris into the patient. Microscopic counting allows quantification of the number and identification of the nature of particles and fibers. The particle count levels are empirical. They are considered stringent, but attainable by manufacturers. Stringent sizing standards are indicated because physiologic particles are distensible, while the manufacturing debris from filters is assumed to be essentially nondistensible. Therefore, equating equal passage for rigid filter material and distensible physiological particles is not valid. Water is suggested as the flush fluid because it is a physiological fluid that can be readily standardized and is commonly used in microscopic counting.

A3.2.3.2 Removal Characteristics. This requirement acts to assure efficacy of the product. Passage of blood cell aggregates into patients has been indicated as a significant potential hazard to the integrity of the vascular system, especially the pulmonary system (Connell & Swank 1973; Jenevein & Weiss 1964; Moseley & Doty 1970a & b; Reul, Jr. et al. 1973; Reul, Jr. et al. 1974). For each manufacturer's filter, the physician must have knowledge of the removal effectiveness of the filter in order to ensure that the patient receiving massive transfusion is not further compromised.

Alternate protocols are specified due to a division of committee opinion as to whether the referee test method should utilize a simulated blood suspension. Those in favor of using a simulated blood suspension

argued that the most critical properties of the aggregates to be removed have not been established (i.e., size, shape); therefore, the test fluid should utilize blood cell aggregates even though processing may alter their properties. Those opposed argued that blood cell aggregates have been shown to lose adhesiveness and increase in size on storage; this being the case, the test fluid should utilize rigid particles (rather than deformable aggregates) to provide a more stringent test while simultaneously producing a standardized material capable of yielding reproducible results. Considering the methodological limitations inherent in testing microaggregate filters (Eisert & Eckert 1979), both protocols were incorporated as alternatives in order to encompass both viewpoints. Both protocols gave the same relative rankings of filtration efficiency for blood micro-filters, although the actual value of the removal ratings varied from one test method to the other. The size range of 40- to 100-µm diameter was chosen to distinguish micro-filters from standard infusion sets. This is a minimum range that is not intended to discourage the filtration of particles smaller than 40 µm or larger than 100 µm. A removal rating of 80 percent was considered a minimum value that would not discriminate against innovative products.

A3.2.3.3 Volume Capacity. For safety, especially in emergency situations, the physician and others in the patient care system should be aware of the blood flow rate and total volume of blood which can be effectively processed with each manufacturer's filter. Multiple determinations are necessary since debris in stored blood, and even pooled blood or simulated blood suspensions, varies widely in magnitude and composition from one sample to another. (For example, blood pooling changes coagulation characteristics and does not necessarily yield the mean of the individual parameters.) In this way, filter capacity is determined in the same manner in which blood is actually administered. A one-hour maximum delivery time for a single unit was considered to be the limit beyond which practical utility of the filter could not ordinarily be assured.

A3.3 Interface Characteristics

A3.3.1 Filters Without Attached Administration Sets. The spike requirements derive from a need for functionality and interchangeability with blood containers from different manufacturers. If the spike cannot be readily interfaced with different blood containers, without risk of separation or leakage under conditions of pressure infusion, there is a potential risk to the patient. The spike length must be adequate to provide seal puncture, but excessive length results in unnecessary blood loss and increases the possibility of container puncture. The function of the spike is to establish a fluid pathway; therefore, flow should not be affected through interface or by cores resulting from seal penetration. Risk of touch contamination while interfacing the filter with blood containers should be held to a minimum through proper design. Requirements for the outlet port address a need for functionality and interchangeability with administration sets from different manufacturers. Again, if the outlet port cannot be readily interfaced with different administration sets, without risk of separation or leakage under pressure infusion, there is a potential risk to the patient. The outlet port must be capable of receiving conventional sets, but excessive insertion depth could damage the filter medium, thereby possibly compromising performance requirements. Risk of touch contamination should be minimized here as well. It is hoped that blood containers will be standardized in the future, so as to help ensure compatibility between spikes and containers.

A3.3.2 Filters With Attached Administration Sets. For patient safety, it is important to ensure that the male needle adapter can be readily interfaced with conventional needles and catheters from different manufacturers without risk of separation or leakage under conditions of pressure infusion. It is hoped that needles and catheters will be standardized in the future.

A3.4 Material Safety. The materials comprising the "fluid pathway" should be evaluated to assure minimum toxicity. Biological testing procedures of significant value in the evaluation of materials intended for use in blood filtration are presented as an alternative to the more general procedures appearing in official compendia (Guess et al. 1965; Hoppe et al. 1950). Plastic components are pre-rinsed prior to testing to rule out handling as a source of toxic response.

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Annotations from BF7.pdf

Page 4

Annotation 1; Label: AAMI; Date: 10/06/2000 4:11:10 PM
*This Foreword is not a part of the American National Standard for Blood Transfusion Micro-Filters, ANSI/AAMI BF7—1989.

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Annotation 1; Label: AAMI; Date: 10/06/2000 4:33:20 PM
*The Threshold Irritant Concentration (TIC) refers to that concentration, expressed as a percentage, which produces no more than a mild irritation.

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Annotation 1; Label: AAMI; Date: 10/06/2000 4:35:45 PM
*This Appendix is not a part of the American National Standard for Blood Transfusion Micro-Filters. ANSI/AAM1 BF7-1989.