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American National Standard

ANSI/AAMI RD17:1994
& ANSI/AAMI RD17:1994/A1:2002

Hemodialyzer blood tubing

AAMI Association for the Advancement of Medical Instrumentation

List of Titles

Association for the Advancement of Medical Instrumentation
1110 N. Glebe Rd., Suite 220
Arlington, VA 22201-4795

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RD17 Hemodialyzer Blood Tubing

Hemodialyzer blood tubing

ANSI/AAMI RD17:1994 & ANSI/AAMI RD17:1994/A1:2002

(Revision of ANSI/AAMI RD17:1984)

Developed by
Association for the Advancement of Medical Instrumentation

Approved 30 August 1994 by
American National Standards Institute, Inc.

Abstract:

This standard establishes minimum safety and performance requirements for tubing segments intended for use in transporting blood from a patient's vascular access device to a hemodialyzer, and tubing segments intended for use in transporting blood to a patient's vascular access device from a hemodialyzer.

Association for the Advancement of Medical Instrumentation

Renal Disease and Detoxification Committee

This standard was developed by the Renal Disease and Detoxification Committee of the Association for the Advancement of Medical Instrumentation. Committee approval of the standard does not necessarily imply that all committee members voted for its approval. At this time, the Renal Disease and Detoxification Committee has the following members:

Cochairmen: Ronald E. Easterling, M.D.
Albert E. Jarvis, Ph.D.

Members:
Allen Alfrey, M.D., VA Medical Center, Denver, CO
Albert Babb, Ph.D., University of Washington, Seattle, WA
David Berkowitz, ECRI
James T. Boag, Colorado Medical
William Burkinshaw, Culligan USA
Louis Cosentino, Ph.D., Renal Systems
Norman Deane, M.D., Manhattan Kidney Center
William J. Dorson, Jr., Ph.D., Arizona State University
Ronald E. Easterling, M.D., American Society for Artificial Internal Organs
Martin S. Favero, Ph.D., Centers for Disease Control, Atlanta, GA
Katie Fox, R.N., American Medical Products
Lois Foxen, R.N., St. Joseph Hospital Renal Center, Orange, CA
Robert Galonsky, SUNY Downstate Medical Center
Frank Gotch, M.D., Ralph K. Davies Medical Center, San Francisco, CA
Albert E. Jarvis, Ph.D., CD Medical
Prakash Keshaviah, Ph.D., Minneapolis Medical Research Center
Murray Klavens, National Association of Patients on Hemodialysis and Transplantation
Lawrence Kobren, Center for Devices and Radiological Health, Food and Drug Administration

Stephen B. Kurtz, M.D., Mayo Clinic, Rochester, MN
William Litchfield, National Kidney Foundation
Douglas Luehmann, Hennepin County Medical Center, Minneapolis, MN
Barry Mason, Hemodialysis, Inc.
Joseph H. Miller, M.D., VA Wadsworth Medical Center, Los Angeles, CA
Edwin A. Pecker, Arts & Science Technology, Inc.
Vincent B. Pizziconi, Ph.D., Arizona State University, Tempe
Marie Reid, Center for Devices and Radiological Health, Food and Drug Administration
Martin Roberts, Ph.D., Organon Teknika
Michael Rzeppa, Plymouth, Ml
John H. Sadler, M.D., University of Maryland Hospital
Thomas K. Sawyer, M.D., Northwest Kidney Center, Seattle, WA
Donald W. Schoendorfer, Ph.D., HemaScience Laboratories
Marshall Smith, Sams
Dean Spatz, Osmonics
Donald Stephens, B-D Drake Willock
James Stewardson, Cobe Laboratories
Douglas L. Vlchek, Hospal Medical Corporation

Alternates:

Lee Bland, Centers for Disease Control, Atlanta
James Dugan, CD Medical
LeRoy J. Fischbach, Renal Systems
Stuart Kaufer, National Association of Patients on Hemodialysis and Transplantation
Vera Kucic, Cobe Laboratories
John Mitchell, Mayo Clinic
Mark A. Paulson, Osmonics
Frans Van Antwerpen, Ph.D., Organon Teknika

Executive Committee Members:

Albert Babb, Ph.D., University of Washington, Seattle
William J. Dorson, Jr., Ph.D., Arizona State University
James Dugan, CD Medical
Ronald E. Easterling, M.D., American Society for Artificial Internal Organs
Prakash Keshaviah, Ph.D., Minneapolis Medical Research Center
Murray Klavens, National Association of Patients on Hemodialysis and Transplantation
Lawrence Kobren, Center for Devices and Radiological Health, Food and Drug Administration
William Litchfield, National Kidney Foundation
Douglas Luehmann, Hennepin County Medical Center, Minneapolis, MN
Vincent B. Pizziconi, Ph.D., Arizona State University, Tempe
Marie Reid, Center for Devices and Radiological Health, Food and Drug Administration
Thomas K. Sawyer, M.D., Northwest Kidney Center, Seattle, WA
James Stewardson, Cobe Laboratories

Acknowledgment: *The contribution of Kenneth D. Serkes, M.D., of Omnis Surgical, former industry cochairman of the committee, is gratefully acknowledged.*

NOTE—Participation by federal agency representatives in the development of this standard does not necessarily constitute endorsement by the federal government or any of its agencies.

Foreword* 

This standard was developed by the Renal Disease and Detoxification Committee of the Association for the Advancement of Medical Instrumentation, in cooperation with the American Society for Artificial Internal Organs and the Health Industry Manufacturers Association.

The concepts incorporated in this document should not be considered inflexible or static. This standard, like any other, must be modified as advances are made in technology and as new data are brought forward. AAMI standards-development procedures provide for review and, if necessary, updating of all standards at least once every five years.

This standard reflects the conscientious efforts of concerned health care professionals and medical device manufacturers to develop a standard for those performance levels that could be reasonably achieved as of this writing.

Suggestions for improving this standard are invited. Comments and/or suggested revisions should be sent to AAMI, 1901 North Fort Myer Drive, Suite 602, Arlington, VA 22209.

Hemodialyzer Blood Tubing

1 Scope

1.1 General

This standard is intended to provide minimum requirements to ensure safe and effective performance of hemodialysis blood tubing sets.

1.2 Inclusions

This standard includes all tubing segments which are used to transport blood (or fluids) from a patient's vascular access device to a hemodialyzer, as well as all tubing segments that are used to transport blood (or fluids) to a patient's vascular access device from a hemodialyzer. In addition, all components of that tubing, including drip chambers, infusion tubings or ports, clamp occlusion segments, sampling and injection tubing segments or ports, monitor lines or ports, and segments which are used to pump blood, retain or capture air and blood debris, infuse medications or fluids, sample the blood stream, monitor pressures, and make connections to other devices, are included within the scope of this standard.

1.3 Exclusions

Excluded from the scope of this standard are tubings which are integral components of a hemodialyzer or other blood purification device to which the blood tubing set is attached. Also excluded are peritoneal dialysis tubing sets.

NOTE—The rationale for the development of this standard, including a statement of the need for the standard as well as the rationale for the specific provisions of the standard, is provided as the appendix.

2 Normative references

The following documents contain provisions, which, through reference in this text, constitute provisions of this AAMI standard. At the time of publication, the editions indicated were valid. All documents are subject to revision, and parties to agreements based on this AAMI standard are encouraged to investigate the possibility of applying the most recent editions of the documents listed below.

2.1 ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Biological evaluation of medical devices, Part 1:* Guidance on selection of tests. ANSI/AAMI 10993-1:1994. Arlington (Vir.): AAMI, 1994.

2.2 ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Biological evaluation of medical devices, Part 1:* Selection of tests for interactions with blood. ANSI/AAMI/ISO

10993-4:1993. Arlington (Vir.): AAMI, 1994.

2.3 INTERNATIONAL ORGANIZATION FOR STANDARDIZATION. *Extracorporeal blood circuit for haemodialysers, haemofilters, and haemoconcentrators*. ISO 8638. Geneva: ISO, 1989.

2.4 TRIPARTITE SUBCOMMITTEE ON MEDICAL DEVICES. *Tripartite biocompatibility guidance for medical devices*. September, 1986.

2.5 UNITED STATES PHARMACOPEIA. Pyrogen Test. *United States pharmacopeia* (XXII). Easton, PA: Mack Publishing, 1989.

2.6 UNITED STATES PHARMACOPEIA. Bacterial Endotoxins Test. *United States pharmacopeia* (XXII). Easton, PA: Mack Publishing, 1989.

3 Definitions

3.1 "arterial" blood tubing: The extracorporeal blood tubing connecting the blood access device (needle or cannula) to the blood inlet of the hemodialyzer.

3.2 internal diameter (ID): The inner diameter of the crosssection of tubing.

3.3 manufacturer: The party responsible for the quality control of a product.

3.4 metrology program: A program which assures proper accuracy and performance of measurement and control equipment and thereby ensures the validity of test results. This program includes traceability, which refers to the ability to trace the accuracy of standards used for calibration back to recognized standards at the National Institute of Standards and Technology (NIST).

3.5 negative pressure: Subatmospheric pressure

3.6 nominal: The representative value stated by the manufacturer.

3.7 nonpyrogenic: Free of fever-producing materials within the limit of error of test methods for such determinations as per United States Pharmacopeia (USP).

3.8 outer diameter (OD): The outer diameter of the cross-section of tubing.

3.9 roller pump: An extracorporeal device that propels blood through pliable tubing by means of the sequential action of rollers compressing the tubing.

3.10 sterile: Free of living microbial organisms within the limit of error of test methods for such determinations. Accepted as sterile by methods of good manufacturing practices. A demonstration that the likelihood of viable organisms present is $<10^{-6}$.

3.11 "venous" blood tubing: The extracorporeal blood tubing connecting the hemodialyzer blood compartment outlet and the blood access device (needle or cannula).

4 Requirements

4.1 Labeling Requirements

The term "labeling" as used in this standard includes any written material accompanying a hemodialyzer blood tubing set or affixed to its package or container(s).

4.1.1 Device markings

Labeling of the blood tubing set itself is neither required nor practical. Blood tubing sets shall, however, be color-coded. Red shall identify the segment(s) conveying blood from the patient access device to the dialyzer (arterial) and blue shall identify the segment(s) conveying blood from the dialyzer (venous) to the

patient's return access. Blood access ports shall be color-coded. Additionally, if there is no blood access port between 50 and 100 mm of either end of the tubing, a color marking shall appear in this region of the tubing. This marking shall obscure no more than 10 mm of tubing and shall be unremovable and resistant to discoloration under normal operating conditions.

4.1.2 Unit package labeling

Each blood tubing set shall be accompanied by or contain at least the following:

a) the name and address of the manufacturer;

b) the name of the product and the manufacturer's identification code (e.g., catalog number, trade name, common name, model number);

c) a description sufficient to identify the product;

d) an identifying lot number permitting complete traceability of manufacturing history;

e) the date of sterilization, the month and year, accurate within 30 days;

f) the following statement or similar language: "Caution: Federal law (USA) restricts this device to sale by or on the order of a physician";

g) information as to whether the entire packaged product or the fluid pathway only is provided sterile and nonpyrogenic, and a warning statement that damage to the package or components can render the product nonsterile and unsafe to use.

h) any special conditions for storage and handling;

i) a statement that the manufacturer assures the sterility, nonpyrogenicity, and performance of the device only when the device is undamaged and prepared and used as recommended for single use only;

j) reference to instructions for use, when applicable, for operating procedures;

k) other descriptive information, warnings, and precautions that are deemed appropriate by the manufacturer and that will conveniently fit on the label.

4.1.3 Package insert/instructions for use

At least the following items shall be provided:

a) general descriptive information:

1) a description of the product, including nominal volumes of the blood pathway and nominal dimensions of the blood pathway segments;

2) the internal diameter of the pump segment shall be specified;

3) other information important for satisfactory use, if not available on a package insert;

b) warranty information for first use of the hemodialyzer blood tubing, including:

1) general limits and conditions of the warranty;

2) a statement such as, "The manufacturer assures the purity and performance of this device only when undamaged and prepared as recommended for single use only";

c) recommended procedures for assembly, for preparation for use, and for terminating dialysis;

d) recommended operating procedures;

e) cautions and warnings including, but not necessarily limited to, the following:

1) a warning regarding the potential for air embolism;

2) a warning that the manufacturer assumes no responsibility if the tubing is used with any device other than those designated as compatible with the tubing, along with instructions for determining compatibility. The warning should include instructions for determining if the venous line clamp will occlude effectively and how the relationship of the tubing to air detectors is evaluated;

3) a warning that pump segments can collapse partially at great prepump negative pressures or at reduced blood flow rates;

4) a warning that kinked blood tubing can cause severe hemolysis undetected by monitors. Care should be taken, especially between the blood pump and dialyzer, to see that the tubing is properly aligned and not under stress;

f) any special conditions for storage and handling;

g) the outer diameter (expressed as gauge) of the largest needle that may be safely used at the injection site, and information about the needle puncture procedure;

h) the sterilization method(s) used;

i) a statement that the following information is available to the user upon request:

1) a list of the generic names of device materials (composition) which will come into contact with the blood, if not available on the package insert;

2) recommended hemodialysis systems with which the tubing is compatible, if not described in the package insert.

4.2 Device performance

4.2.1 Requirements for the materials

4.2.1.1 Sterility and nonpyrogenicity

The blood pathway shall be sterile and nonpyrogenic when delivered unopened and undamaged to the user.

4.2.1.2 Material safety

Component materials shall be nontoxic according to appropriate toxicity tests (see 5.2.1.2).

4.2.1.3 Residual ethylene oxide

Residual ethylene oxide, ethylene chlorohydrin, and ethylene glycol shall be no greater than limits proposed by the Food and Drug Administration (FDA) *Federal register*, vol. 43, no. 122, 6/23/78, page 27482.

— Ethylene oxide 25 ppm

— Ethylene chlorohydrin 25 ppm

— Ethylene glycol 250 ppm

If the FDA establishes different standards, these devices shall meet the required FDA standard.

4.2.2 Mechanical integrity

The hemodialyzer blood tubing shall withstand 1.5 times the maximum recommended positive operating pressure and a negative pressure 1.5 times the maximum recommended negative pressure, unless this pressure exceeds a negative pressure of 700 millimeters Mercury (mmHg). In this case, the blood tubing shall withstand a negative pressure of 700 mmHg. In addition, blood tubing sets and connections shall be subject to appropriate testing at the time of manufacture in order to assure mechanical integrity. The product

shall be packaged to minimize damage during shipment.

4.2.3 Physical characteristics

4.2.3.1 Volume

The volume of the blood path of the blood tubing set shall be ± 20% of the manufacturer's stated volume.

4.2.3.2 Filters

Where provided as an integral component of a blood tubing set, blood filters shall readily allow passage of blood cells at flow rates of at least 500 ml/min or as specified by the manufacturer.

4.2.3.3 Access ports

Sites used for injection or sampling via needle and syringe shall be capable of withstanding repeated puncture by at least a 21-gauge (0.8-mm internal diameter) standard needle without leakage and allow disinfection by an iodophor or comparable antiseptic agent. Such sample/injection sites shall have a protective feature to minimize the risk of accidental self-puncture.

4.2.3.4 Flow dynamics construction

Transitions in cross-sectional areas at joints and fittings shall be tapered.

4.2.3.5 Internal diameter of pump segment

The internal diameter of the pump segment shall not vary more than ± 5% of nominal values.

4.2.3.6 Connectors to the hemodialyzer

The connector to the hemodialyzer shall meet the specifications of 2.3[1)], or shall be compatible with the hemodialyzer blood port and meet the same performance specifications.

4.2.3.7 Connectors to the blood access device

This connection shall meet the specifications of 2.3. A male Luer-lock fitting is specified because it is compatible with blood access devices.

4.2.3.8 Compliance of tubing

The tubing shall be capable of being occlusively clamped by functional clamps of the devices listed in 4.1.3(i)(2).

4.2.3.9 Clamps supplied as part of the blood tubing set

Clamps that are supplied as part of the blood tubing set shall completely occlude the tubing segment for which they are designed and shall be capable of remaining closed under normal operating conditions.

5 Tests

This section contains referee test methods for verifying the performance of hemodialyzer blood tubing sets. Other test methodologies may be used if the test facility establishes that the results obtained are equivalent to those that would be obtained if the methods of this standard were used.

The tests shall adequately address factors contributing to measurement error, such as outgassing of test fluids; uncontrolled temperature variation; degradation of test substances with heat, light, and time; system contamination by foreign materials, algae, bacteria; and parameter stabilization times. All instruments for measuring physical quantities, including length, mass, volume, flow rate, concentration, and pressure, shall be regularly maintained and calibrated in accordance with an ongoing metrology program traceable to the calibration standards of the National Institute of Standards and Technology (NIST).

The test methods and procedures are intended for initial product qualification, for periodic revalidation of stated product claims, and for determining compliance with section 4 of this standard. They are not intended to be used in routine quality assurance inspection.

The paragraph numbers below correspond, except for the first digit, with those of section 4.

5.1 Labeling requirements

5.1.1 Device markings

Compliance with the requirements of 4.1.1 can be verified by visual inspection.

5.1.2 Unit package labeling

Compliance with the requirements of 4.1.2 can be verified by visual inspection.

5.1.3 Package insert/instructions for use

Compliance with the requirements of 4.1.3 can be verified by inspection.

5.2 Tests for device performance

5.2.1 Requirements for the materials

5.2.1.1 Sterility and nonpyrogenicity

Each manufacturer is required by the FDA to comply with device Good Manufacturing Practice (GMP) regulations as they apply to sterility assurance. Sterile Device GMP guidelines are available from the Center for Devices and Radiological Health (CDRH). Compliance with GMP regulations involves appropriate process qualification and controls, the appropriate use of biological indicators, and final product sterility testing (or parametric release testing as approved by the CDRH for individual manufacturers' sterilization processes).

The release of products labeled nonpyrogenic normally entails testing each batch for pyrogenicity in accordance with either the USP rabbit test or the alternate Limulus amebocyte lysate (LAL) test (2.5 and 2.6); however, parametric release is also an alternative, provided that approval is obtained from CDRH. The USP rabbit test and the LAL test are considered the referee tests for pyrogenicity.

5.2.1.2 Material safety

All materials of composition of the blood or dialysate compartments shall pass appropriate toxicity tests. Suggested tests for determining safety, reflecting state-of-the-art test procedures, are outlined in 2.1, 2.2, and 2.4.

5.2.1.3 Residual ethylene oxide

Residual ethylene oxide, ethylene chlorohydrin, and ethylene glycol shall be no greater than limits proposed by the FDA *Federal register*, vol. 43, no. 122, 6/23/78, page 27482.

— Ethylene oxide 25 ppm

— Ethylene chlorohydrin 25 ppm

— Ethylene glycol 250 ppm

If the FDA establishes different standards, these devices shall meet the required FDA standard.

5.2.2 Test method for mechanical integrity

In preparation for this test, any injection port(s) in the blood tubing shall be punctured as specified in 4.2.3.3, and an occluded needle shall be left in the puncture site while the tubing is subjected to simulated

dialysis.

Simulated dialysis shall be carried out by recirculating blood or fluid of equivalent viscosity, at 37 ± 1.5°C, through the blood tubing, using the manufacturer's recommended blood pump, maximum recommended blood flow rate, and maximum recommended pressure. The fluid shall then be immediately drained from the blood tubing. Without delay, the connector for the hemodialyzer shall be joined by a connector meeting the specifications of the blood port of the hemodialyzer to a piece of tubing that has been clamped. The other end of the blood tubing shall be attached by a suitable connection to a pressurizing pump equipped with a pressure gauge (figure 1). Any side lines, such as those intended for monitoring or infusion, shall be closed by applying the clamps provided with the blood tubing. The blood tubing shall then be immersed in water at 37°C and pressurized with air to 1.5 times the maximum operating pressure recommended by the manufacturer. There shall be no evidence of leakage for a period of 10 minutes following pressurization. A steady stream of bubbles arising from any point in the blood tubing is evidence of unsatisfactory performance.

Any portion of the blood tubing and its connectors that may be subjected to subatmospheric pressure during dialysis shall also be subjected to a negative pressure test immediately following the positive pressure test. The system shown in figure 1 shall also be used for this test, with two exceptions: (1) the blood tubing shall be filled with adequately deaerated water at 37°C; and (2) a clamp shall be applied to isolate the portion of the blood tubing that can be subjected to subatmospheric pressure. The tubing shall then be dried off and suspended in air. A negative pressure 1.5 times the manufacturer's recommended negative pressure shall be applied for 10 minutes, unless this pressure is greater than 700 mmHg below atmospheric pressure at sea level. In the latter case, a pressure of 700 mmHg below atmospheric pressure at sea level shall be applied. An unsatisfactory test result is indicated by the appearance of bubbles in the blood tubing.

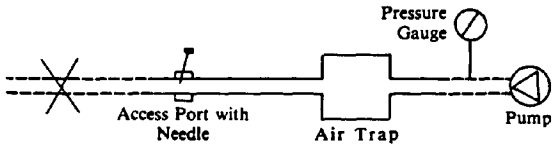

Figure 1—Test system for determining mechanical integrity of the hemodialyzer blood tubing

The requirement for appropriate mechanical integrity tests at the time of manufacture shall be determined by inspection.

5.2.3 Physical characteristics

5.2.3.1 Volume

Volumes shall be determined from volumetric measurements of representative samples. The volume of bubble traps shall be assumed to be 75% of the total volume of the bubble trap.

5.2.3.2 Filters

During simulated diaysis, the pressure is monitored on either side of the filter to assure compliance (see 5.2.2).

5.2.3.3 Access ports

Access ports should be punctured and simulated dialysis carried out to assure that the access ports seal against pressure. Other requirements are determined by inspection.

5.2.3.4 Flow dynamics construction

Compliance with 4.2.3.4 can be determined by inspection.

5.2.3.5 Internal diameter of pump segment

The internal diameter of the pump segment shall be determined by measuring the fluid volume of the segment and calculating the internal diameter from the equation:

$$ID = 2(V/\pi L)^{0.5}$$

where

V = volume of the segment

L = length of the segment

5.2.3.6 Connectors to the hemodialyzer

Compliance with 4.2.3.6 can be verified by inspection.

5.2.3.7 Connectors to the blood access device

Compliance with 4.2.3.7 can be verified by inspection.

5.2.3.8 Compliance of tubing

Compliance with 4.2.3.8 can be verified by pressure tests in 5.2.3.9.

5.2.3.9 Clamps supplied as part of the blood tubing set

Clamps supplied with the blood tubing shall be applied to the tubing segment for which they are designed. In the case of clamps designed for the blood path, appropriate tubing shall be used on the fitting meeting the specifications of the dialyzer blood port, and this tubing shall be clamped with the clamp designed for the blood path. The blood tubing shall then be pressurized with air to 1.5 times the maximum recommended pressure by the manufacturer and immersed in water at 37°C for 10 minutes, with no evidence of leakage. A steady stream of bubbles is evidence of unsatisfactory performance.

Annex A
(informative)

Rationale for the development and provisions of this standard

A.1 Introduction

This standard specifically addresses extracorporeal blood tubing devices for hemodialyzers. Included within the scope of the standard are those blood tubing devices intended for use in conventional and in single-needle dialysis procedures. The standard does not cover blood access devices or separate tubing for connecting associated devices to the blood tubing because of the unique characteristics of these devices and the differences in labeling and packaging.

The products addressed by this standard include hemodialysis blood tubing as defined in the scope of this document and as cited in the *Federal register,* 46(15):25042-25053, January 23, 1981 (proposed rules) notice, "Medical devices, classification of gastroenterology-urology devices, proposed rules: 21 CFR 876.5820, hemodialysis system and accessories." This notice proposed that blood tubing sets for hemodialyzers be classified for regulatory purposes into Class II.

As defined in the Medical Device Amendments of 1976 of the U.S. Food, Drug, and Cosmetic Act, Class II designates those devices that are, or possibly will be, subject to the requirements of a performance standard promulgated in accordance with Section 514 of the Act, as amended. A device is placed in Class II if the Food and Drug Administration (FDA) decides that general controls alone are insufficient to provide reasonable assurance of its safety and effectiveness and that there is sufficient information to establish a performance standard to provide such assurance. In the *Federal register,* 48(227):53012-53029, November

23, 1983 (final rules), the FDA published a final rule classifying hemodialyzer blood tubing as Class II.

The need for a blood tubing standard was recognized by the AAMI Renal Disease and Detoxication Committee in 1969. Development of a standard was postponed until the National Institutes of Health report "Evaluation of hemodialyzers and membranes" (NIH, 1977) was published and the FDA contract study, "Investigation of the risks and hazards associated with hemodialysis devices" concluded in 1980 (Keshaviah, 1980). At about the same time, the FDA Gastroenterology-Urology Device Advisory Panel recommended that the establishment of a performance standard for hemodialyzer blood tubing be designated a high priority. The AAMI standard is the culmination of efforts by the committee to develop such a standard, based on the data gathered in the NIH and FDA studies. This standard was placed under review in 1992 and this revision in 1994 reflects the committee's assessment of progress since the original standard.

A.2 Need for the standard

Blood tubings for hemodialyzers are the extracorporeal conduits for the blood of the patient to and from the hemodialyzer. A faulty device can cause serious adverse effects, such as patient blood loss, air embolism, infection, or injury to the operator of the hemodialyzer circuit. The committee therefore determined that a voluntary standard was needed to promote adequate labeling of these devices, uniform testing and reporting of device characteristics, and acceptable toxicity, as well as to provide reasonable assurance of safety and effectiveness. Moreover, as mentioned above, the FDA has classified hemodialyzer blood tubings as Class II devices.

This standard is intended to be used by manufacturers as a guide for design qualification. While the committee's principal concern was to ensure adequate, safe treatment of the patient, other considerations have influenced the requirements addressing theoretical hazards or remote, mild risks.

The committee has attempted to set standards that are consistent, whenever possible, with financial constraints and user convenience. Specific requirements have been set whenever the committee could identify a clear need for the requirement and could define a feasible referee test. Requirements of a more general nature or requirements for disclosure upon request were written when the need for a requirement was unclear, adequate performance criteria could not be defined, or an appropriate test was not available.

A.3 Definitions

A.4 Rationale for the specific provisions of this standard

This section contains the rationale for each of the requirements of section 4 of the standard. The paragraph numbers below correspond to those of section 4.

A.4.1 Labeling requirements

Currently, there are two federal regulations that control the label content of a medical device: (1) Part 820, Chapter 1, Title 21, of the *Code of federal regulations*, "Good manufacturing practices for medical devices," specifically sections 820.120, 820.121, and 820.130 which establish requirements for proper handling, legibility, and other aspects of labeling as they pertain to good manufacturing practices; and (2) part 801, chapter 1, title 21, of the Code of federal regulations and section 502 of the U.S. Food, Drug, and Cosmetic Act (as amended in October 1976) which specifically state what constitutes proper labeling and misbranding of a drug or device.

All labeling pertaining to hemodialyzer blood tubing is controlled by these regulations and must comply with them. While this standard reiterates some of these federal labeling requirements, it also sets forth additional significant labeling criteria, specific to hemodialyzer blood tubing, which the committee considered necessary in order to help assure proper use of the device. Section 4.1 of the standard is divided into requirements for information that should be displayed on the unit package and requirements for other information which may be provided in separate literature accompanying the device, when provision of this

information on the package itself is deemed impractical or superfluous. No requirements are given for a device label, since such a label is not feasible for hemodialyzer blood tubing (although 4.1.1 does address color coding).

Reuse of nominally disposable hemodialyzer blood tubing is not a widespread practice currently, though it was done more broadly in the past. *Reuse of hemodialyzer blood tubing* (AAMI TIR6—1990) addresses this practice. There is little published about reuse of blood tubing, thus the customary basis for establishing a new practice is not available. In 1989, the U.S. Congress provided that blood tubing could not be reused except by procedures registered with the FDA by the first of the year. Only one such method qualified, and that one, for arterial tubing only, is included in the TIR. Some experts believe that the lack of publications is due to the simplicity and freedom from trouble of reuse of blood tubing. There is no effort underway at present to establish other procedures for hemodialyzer blood tubing reuse. Any method would have to meet the FDA guidance and demonstrate that the blood tubing can be effectively cleaned and sterilized, and remain safe and effective for its intended use.

All hemodialyzer blood tubings are prepared with a sterile and nonpyrogenic blood path. The exteriors of the blood tubings might or might not be sterile. An indication of whether the exterior of the hemodialyzer blood tubing is sterile is necessary, so that contamination of a sterile field can be avoided.

The committee considered requiring an expiration date, but determined that there are insufficient data to support its establishment. Instead, the committee judged that information on the date of sterilization should be provided, in plain language, on the unit package and shipping container, to facilitate inventory control by the user and to prevent inadvertent use of blood tubing sets considered by the user to be unacceptably "old."

The committee then heard arguments stating that requiring the date of sterilization could result in considerable additional expense. It was decided that only the month and year of manufacture need be disclosed, because: this date is encoded in the lot number required by federal regulations to be displayed on the unit package and shipping container; changing the lot number so that the date of manufacture appears in plain language is much less expensive to implement than providing the date of sterilization; the date of manufacture is almost always within three months of the date of sterilization; and using this earlier date will further decrease the risk of using hemodialyzer blood tubing which the user would consider unacceptably "old."

The committee finally decided that disclosure of month and year of sterilization should be required, especially in view of another consideration—most European countries require this information and thus this requirement is already being met for foreign markets. Furthermore, month and year of sterilization is a labeling requirement in the International Organization for Standardization (ISO) document, *Extracorporeal blood circuit for haemodialysers, haemofilters and haemoconcentrators* (see 2.3). The date of sterilization is required for the device markings only if the blood pathway is sterile outside the unit container; this avoids confusion about the sterility of a device for which the unit container maintains the sterility on the blood pathway.

A requirement for disclosure of the nominal force needed for occlusion of the blood pump segment was considered and ultimately rejected because the clinically relevant parameter is the dimensional adjustment of the blood pump.

A proposal to eliminate identification of the various characteristics of the blood tubing set was not accepted by the committee, in view of the importance of this information, especially to the inexpert operator. The alternative of providing this information on the package insert was permitted in order to avoid unnecessary costs in the production of the package insert/instructions for use.

The committee felt that the method of sterilization and a list of generic names of materials coming into contact with blood should be included to help the clinician evaluate possible adverse reactions to the device and to help in avoiding the use of a device containing materials to which a patient is known to be allergic.

Given the rarity of these reactions, allowance was made for listing more than one method of sterilization, when the same device might be sterilized by different methods.

The description of the nominal volume is required, since these data help the user determine the effect of the blood tubing on the blood volume of the patient as well as the best way to rinse the tubing. Providing these data in package inserts rather than in the package insert/instructions for use is an option in recognition of the frequent changes that occur in such products.

A list of the devices with which the blood tubing is compatible is required because of a case where blood tubing was not occlusively clamped by the clamp of an air detector device, resulting in air embolism of the patient. The committee did not think it reasonable to limit use of the blood tubing to only those devices designated by the manufacturer; therefore, the manufacturer must warn the user about attaching tubing to equipment other than that stated to be compatible with the tubing.

A proposed requirement for disclosure of information about hydrophobic-membrane transducer protectors did not become part of this standard as they are not an integral part of currently available blood tubing sets.

Transducer isolators of the compliant, impermeable membrane type can constitute an integral part of currently available blood tubing sets. No special requirements were deemed necessary for these devices.

The requirement for specifying the largest needle that can be safely used to puncture the tubing injection port is intended to minimize the possibility of leakage from the injection port, which can cause significant blood loss or infection. The warning regarding air embolism is essential for blood tubing designed for use with blood pumps since sizable negative pressures can be generated between the blood access device and the blood pump. This is always the case when the access device is a needle in an arterialized vein; air embolism can also occur when the blood access device is a cannula or catheter. In the rare situation in which the motive force of the blood flow through the tubing is arterial pressure, air embolism is also possible under certain circumstances when the blood flow is interrupted. The committee did not accept a proposal for a warning about extractable plasticizers, such as di-2-ethylhexyl phthalate (DEHP) from PVC tubing, since a standard cannot be established for these substances due to lack of evidence for clinical toxicity despite extensive use of PVC plastics in blood transfusion and medical devices including tubing for blood tubing.

The results of a spallation test must be made available to the user on request. This is supported by one study of silicone deposits in the tissue of patients using silicone pumping segments, which attributed their liver disease to a reaction to these deposits (Leong et al., 1982). The committee was also concerned about a report of experimental activation of macrophages not only by particles of silicone, but also by particles of polyvinylchloride tubing (Bommer et al., 1983), which is widely used in the United States.

There is no evidence of significant spallation from PVC pump segments and no evidence of human injury associated with PVC particles from blood tubing. For this reason, the committee did not think it reasonable to include spallation testing in the document.

In recommending labeling criteria, the committee recognized that the user has the ultimate responsibility for prudent application of the device within the terms of the information provided on the manufacturer's labeling.

A.4.2 Device performance

A.4.2.1 Requirements for the materials

These requirements are necessary to ensure the safe use of the device.

A.4.2.1.1 Sterility and nonpyrogenicity

No specific tests for sterility assurance are specified, since each manufacturer is required by the FDA to comply with Good Manufacturing Practices (GMPs) as they apply to sterility claims. Compliance with these

regulations involves appropriate process qualification and controls, appropriate use of biological indicators, and final product sterility testing (or parametric release as approved by FDA for each manufacturer). Furthermore, specifying a particular referee test for determining sterility is of little value, since the nature of this microbiological contamination is such that a test can only expose a heavy contamination level.

The release of a product labeled nonpyrogenic normally entails testing each batch of product for pyrogenicity, using either the USP Rabbit Test or the alternate LAL Test; however, parametric release is also an alternative, provided that approval is received from FDA. The USP Rabbit Test and the LAL Test are considered the referee tests for nonpyrogenicity.

A.4.2.1.2 Material safety

Initially, the committee considered requiring recirculation of 500 ml of an aqueous-based and an oil-based eluate, at 37°C, through the tubing, as proposed by the ISO committee. But when normative references 2.1, 2.2, and 2.4 became available, the AAMI committee decided to make reference to them rather than to require specific tests, which would be either superfluous or incomplete.

A.4.2.1.3 Residual ethylene oxide

Ethylene oxide (EO) and residues of its reaction products, which can remain in a hemodialyzer after sterilization, are potentially toxic. FDA proposed regulation limiting maximum residual EO and residual ethylene chlorohydrin and ethylene glycol is accepted by the committee without additions or modifications.

A.4.2.2 Mechanical integrity

The committee felt that the blood tubing and its connections should withstand a pressure higher than the maximum operating pressure as a safety measure against leaks. An arbitrary standard of 1.5 times the maximum operating pressure was suggested. This value exceeded the 1-fold increase recommended by the ISO committee. The ISO standard (ISO 8638:1989; see 2.3) was accepted for positive pressure tests, in the absence of data supporting a higher requirement. A maximum negative pressure of 700 mmHg was selected for negative pressure tests, because this is the most negative pressure that can be readily achieved in the test system. The connection to the hemodialyzer can be included, since these connections are standardized (see 4.2.3.6).

In addition, testing is required on each tubing set at the time of manufacture to ensure mechanical integrity. These tests are less stringent and, therefore, are not specified.

Proper packaging is required to avoid damage due to stresses during shipment.

A.4.2.3 Physical characteristics

A.4.2.3.1 Volume

The committee recognized that variation among blood tubing sets should be minimized. The level was set at ± 20% because this can be achieved and because the volume of the blood tubing set is relatively small. The committee first proposed calculating the volume from nominal dimensions; the test was changed to a volumetric test in view of the inaccuracies of calculated values.

A.4.2.3.2 Filters

Passage of blood through filters prevents excessive pressure increases or total occlusion of the system.

A.4.2.3.3 Access ports

A hemorrhage has sometimes occurred when injection ports were punctured with needles that make an opening too large for self-sealing. Since needles of at least 21 gauge are required to remove blood without hemolysis, an injection port must withstand repeated puncture by a 21-gauge needle (0.8 mm internal diameter). The committee recognizes the desirability of a blood port that can withstand larger needles. If

development will allow that, it is not excluded. The requirement for antisepsis is necessary to prevent infection. The requirement for a protective means to minimize accidental self-puncture is intended to help prevent inoculation of the user with potentially contaminated blood.

A.4.2.3.4 Flow dynamics construction

This requirement is intended to help minimize hemolysis and avoid generation of turbulence and high pressure.

A.4.2.3.5 Internal diameter of pump segment

Tight quality control of the internal diameter of the pump segment is necessary to ensure reasonable accuracy of the blood flow rate, which has an important impact on the clearance of the dialyzer. The limits chosen have been demonstrated to be feasible. The committee noted, however, that the permitted ± 5% variance from nominal values means a ± 20 to ± 30 ml/min change in blood flow which could be of clinical significance if dialyses are being carefully done.

A.4.2.3.6 Connectors to the hemodialyzer

Inadequate connections with the tubing connecting the device to the patient blood access port can cause hemorrhage or air embolism. In some cases, users have connected a device to blood tubing that does not fit the blood port, with subsequent injury to the patient. In other cases, blood tubing has been modified by the user because of intentional incompatibility, introduced by manufacturers, between the dialysate tubing and the blood ports of the hemodialyzer. This practice also creates the possibility of an inadequate connection. The ISO committee has proposed that the blood ports and the blood access device connections be standardized and that the blood tubing connectors be standardized accordingly. The European representatives to the ISO committee are unanimous in supporting these requirements. The AAMI committee agreed that the ISO standard connections should be adopted.

A.4.2.3.7 Connectors to the blood access device

The committee felt that the ISO standard should be adopted, when finalized. In the meantime, a male Luer-lock-like fitting is specified because it is compatible with blood access devices.

A.4.2.3.8 Compliance of tubing

Tubing clamps on hemodialysis systems are designed to prevent air embolism. It is essential, therefore, that the tubing be occlusively clamped by such devices.

The committee also considered a requirement for durometer and memory of the tubing that would minimize both irreversible kinks which can occur while the tubing is in the package and kinks when the tubing is set up for dialysis. There are valid concerns about avoiding kinks due to flimsy material, particularly for blood tubing that must be splinted or taped into position. It was found, however, that kinks that develop during storage are highly dependent on environmental conditions and that there was no available test for selecting tubing that resists kinking. Therefore, the committee decided to defer the incorporation of a durometer/memory requirement for the time being.

A.4.2.3.9 Clamps supplied as part of the blood tubing set

Failure of clamps on monitor or infusion tubings can result in hemorrhage or air embolism. Instances of this hazard have been observed by members of the committee. Even though clamps designed to clamp the blood path are not applied during dialysis, failure during priming or disconnection of the tubing when dialysis has been interrupted can lead to leaks. This can result in loss of blood or other fluids in the blood tubing, the introduction of air into the tubing, and/or bacterial contamination of the tubing. A requirement that it should be possible to open such clamps with one hand was rejected, since, at the present time, reliability and convenience of operation tend to be mutually exclusive.

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Annex B
(informative)

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Annotations from RD17.pdf

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Annotation 1; Label: AAMI; Date: 09/28/2000 2:59:59 PM
*This foreword does not contain provisions of the American National Standard, Hemodialyzer blood tubing (ANSI/AAMI RD17—1994).

Amendment 1 to
ANSI/AAMI RD17:1994, *Hemodialyzer blood tubing*

2 Normative references

Add normative reference 2.7 as follows:

2.7 Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices, Part 7: Ethylene oxide sterilization residuals*. ANSI/AAMI/ISO 10993-7:1995. Arlington (Vir.): AAMI, 1995. American National Standard.

4.2.1.3 Residual ethylene oxide

Replace the entire section with the following text:

4.2.1.3 Residual ethylene oxide and ethylene chlorohydrin

The limit for ethylene oxide (EO) and ethylene chlorohydrin (ECH) residuals for each hemodialysis device shall be set according to normative reference 2.7, section 4.3.2, *Prolonged exposure limit* (presently 2 mg/day and 60 mg/month), adjusted for the average number of hemodialysis procedures per month for a dialysis patient, not to exceed 5 mg per device.

5.2.1.3 Residual ethylene oxide

Replace the entire section with the following text:

5.2.1.3 Residual ethylene oxide and ethylene chlorohydrin

Methodology for determining EO and ECH residuals is included in normative reference 2.7

A.4.2.1.3 Residual ethylene oxide

Replace the entire section with the following text:

A.4.2.1.3 Residual ethylene oxide and ethylene chlorohydrin

EO and ECH residues, which can remain in blood tubing after sterilization, are potentially toxic.

Developed by
Association for the Advancement of Medical Instrumentation

Approved 29 April 2002 by
American National Standards Institute