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American National Standard

ANSI/AAMI AT6:1991/(R)1996

Autologous transfusion devices

AAMI Association for the Advancement of Medical Instrumentation

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AT6 Autologous Transfusion Devices

Autologous transfusion devices

ANSI/AAMI AT6-1991
(Revision of ANSI/AAMI AT6-1982)

American National Standard
Autologous transfusion devices

Developed by
Association for the Advancement of Medical Instrumentation

Approved 30 September 1991 by
American National Standards Institute

ABSTRACT:

The objective of this standard is to provide labeling and performance requirements, test methods, and terminology that will help establish a reasonable level of safety and efficacy for autologous transfusion devices.3330 Washington Boulevard, Suite 400 Arlington, VA 22201.

Committee representation

Association for the Advancement of Medical Instrumentation

Autologous Transfusion Committee

This standard was developed by the Autologous Transfusion Committee. Committee approval of this standard does not necessarily imply that all committee members voted for its approval.

The AAMI **Autologous Transfusion Committee** has the following members:

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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 Autologous Transfusion Committee of the Association for the Advancement of Medical Instrumentation.

The first edition of this standard, entitled *Autotransfusion Devices*, was approved as an American National Standard in May 1982. Since all AAMI and American National Standards must be reviewed and, if necessary, updated at least once every five years, a review of the standard was initiated in 1986. This process led to the preparation and issuance of this second edition to the standard, *Autologous transfusion devices*.

The objective of this standard is to provide labeling and performance requirements, test methods, and terminology that will help establish a reasonable level of safety and efficacy for autologous transfusion devices.

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

Suggestions for improving this standard are invited. They should be sent to: Technical Programs, AAMI, 3330 Washington Boulevard, Suite 400, Arlington, VA 22201.

NOTE — This foreword is not part of the American National Standard *Autologous transfusion devices* (ANSI/AAMI AT6-1991).

Autologous transfusion devices

1 Scope

1.1 General

This standard establishes requirements for sterile, disposable systems and associated electromechanical hardware designed to collect and filter or process, or both, extravasated blood for reinfusion into the patient's circulation. Aspects of these systems related to collection, anticoagulation (systemic and regional), storage, processing and filtration, and reinfusion are within the scope of this standard.

1.2 Inclusions

1.2.1 Emergency/trauma devices

Traumatic or spontaneous rupture of blood vessels may result in substantial blood accumulation in the thorax and other body cavities. This blood may be removed for subsequent reinfusion into the patient by the appropriate use of autologous transfusion devices that are variously composed of a suction catheter, tubing, reservoirs, an anticoagulation system, processing or filtration systems (or both), and a reinfusion system. Devices designed for this purpose fall within the scope of this standard.

1.2.2 Intraoperative retrieval devices

Intraoperative retrieval devices are also included within the scope of this standard and may consist of a suction catheter, tubing, reservoirs, an anticoagulation system, processing or filtration systems (or both), and a reinfusion system.

1.2.3 Postoperative devices

These devices are similar to chest drainage systems described in 1.2.1 and are also included within the scope of this standard.

2 Applicable documents

2.1 AMERICAN SOCIETY FOR TESTING AND MATERIALS. *Standard test method for microscopic sizing and counting particles from aerospace fluids on membrane filters.* ASTM F312. Philadelphia: ASTM, 1969 (1980).

2.2 *United States Pharmacopeia.* 22 and NF 17. Easton, PA: Mack Publishing Co., 1990.

2.3 Licensing of limulus amebocyte lysate — use as an alternative for rabbit pyrogen test. *Federal Register*, 13 January 1978, vol 43, p. 1,996.

2.4 Licensing of limulus amebocyte lysate — use as an alternative for rabbit pyrogen test. *Federal Register*, 4 November 1977, vol 42, p. 57,749.

2.5 ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Safe current limits for electromedical apparatus.* ANSI/AAMI ES1 — 1985. Arlington (Vir.): AAMI, 1985. American National Standard. ISBN 0-910275-50-5.

2.6 SOCIETY OF AUTOMOTIVE ENGINEERS. *Procedure for the determination of particulate contamination of hydraulic fluids by the particle count method*. ARP-598. Warrendale, PA: Society of Automotive Engineers, 1960.

3 Requirements

3.1 Labeling requirements

3.1.1 Electromechanical device markings

3.1.1.1 All controls and switches shall be clearly and concisely labeled to identify their function.

3.1.1.2 All variable controls shall have the OFF and ON positions clearly labeled.

3.1.1.3 Labels affixed to the device shall not be degraded by routine handling and disinfection.

3.1.1.4 All controls, displays, and associated markings shall be clearly visible to an operator (with normal vision) seated or standing 1 m in front of the device at a light level of 215 lux (20 footcandles).

3.1.2 Disposable blood contact components

Because of the nature of these components, labeling information is not required on the device itself but may

instead be included on the outer wrap of the package containing the disposable component or as a package insert. This information shall include:

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

a) component name, part number (if applicable), manufacturer, lot number, sterility expiration date, and other information deemed appropriate for intended use;

b) diagrammatic or other instructions needed for proper set-up and use.

3.1.3 Operator's manual/instructions for use

The manufacturer or supplier shall provide a manual of instructions for operation and use. The manual shall provide instructions for both electromechanical devices and disposable blood contact components and shall be divided into separate sections to ensure that instructions are clearly understood. The manual shall include at a minimum (where applicable), the following information:

a) Detailed instructions on technique of use, including descriptions of the purpose and intended use of the device, the principles of operation, and the assembly of the autologous transfusion system;

b) An enumeration of any known, potential complications that may be associated with device use, for example, such side effects of anticoagulation as citrate toxicity, depression of serum calcium, or a bleeding tendency;

c) A caution or warning notice with the following or similar language: "Caution: The use of reinfused blood from this device may be contraindicated (for example in the presence of sepsis or malignancy). The responsibility for the use of this device in all cases belongs solely to the physician ordering its use";

d) For those components of the autologous transfusion system in direct contact with blood and intended by the manufacturer for single use, the following or similar statement, "Disposable—For Single Use Only";

e) An illustration of device features, including the location of all operating controls, adjustments, and components necessary for operation and on-site servicing of the instrument;

f) Any necessary additional components, identified by name or descriptive terminology and source of supply, required for the safe and effective use of the instrument but not supplied with it;

g) A list of operator-replaceable parts;

h) Specifications and physical planning data such as weight, dimensions, and space requirements;

i) Power requirements, including frequency, voltage, apparent power, branch circuit current, power cord length, and power cord plug;

j) Environmental considerations, such as temperature, relative humidity, and shipment and storage conditions required for proper equipment performance;

k) The following minimum technical information:

1) Aspiration flow capacity and reinfusion flow capacity in terms of peak flow milliliters per minute (ml/min);

2) Storage capacity(ies) of the reservoir, processing, and transfusion vessel(s);

3) Where processing is provided as a device feature, the conditions recommended by the manufacturer for processing, the time taken to process the cells, and the degree of hemolysis caused by the processing;

4) The amount of stroma-free (soluble) hemoglobin expected in the product;

5) The manufacturer's recommendation for dwell-time limits in the reservoir (where applicable) and recommended procedure for anticoagulation to achieve these limits safely, along with the following or similar language: "The safe length of time that blood or blood products may remain in the appliance or plastic disposables is a medical decision and will vary with each case where perioperative salvage is used";

6) Total cell recovery;

7) The contribution of the system itself (equipment) to any change in red cell concentrations expected under normal conditions of use;

l) Recommended safe positive and negative gauge pressures for the system;

m) The following or similar language: "Caution: Actual performance results may vary depending on many in-use variables";

n) Conditions that must be met to prevent air embolization;

o) The following or similar language, "Information concerning the 24-hour survival of fresh autologous blood passed through the device is available upon request."

3.1.4 Service manual

Service information, including a description of those adjustments and repairs that can safely be performed by the user, as well as instructions for the preventive maintenance needed to keep the device in proper operating condition, shall be provided to the user either as a part of the operator's manual, or instructions for use, or in a separate service manual.

3.1.5 Collection container labeling

When collection containers are provided by the manufacturer for use with the system, suitable patient identification labels shall also be provided. Specific patient blood identification is the responsibility of the user.

3.2 Performance requirements

3.2.1 System integrity

The sterile fluid pathway of the device shall be capable of withstanding, without leakage, a positive gauge pressure twice the recommended positive gauge pressure, or a negative gauge pressure twice the recommended negative gauge pressure, or one atmosphere of negative gauge pressure, whichever is smaller in absolute value. In addition, the sterile fluid pathway shall withstand, without leakage, a flow of water twice the maximum aspiration flow capacity and twice the maximum reinfusion flow capacity of the device, as stated in the disclosure information.

3.2.2 Cleanliness

The apparatus shall provide no more than the following effluent particulate levels: 50 particles per ml, for particles larger than 10 μm; 5 particles per ml, for particles larger than 25 μm; and 6.5 fibers per ml.

3.2.3 Regional anticoagulation

Means shall be provided for the delivery of the appropriate ratio of anticoagulant to retrieved whole blood.

3.2.4 Filtration

Means to remove from the circuit such macrodebris and microdebris as clots, bone, fat, bowel contents, and

microaggregates of formed elements shall be provided, either by means integral to the device, or by a generic recommendation or prescription within the operator's manual or instructions for use specified in 3.1.3.

3.2.5 Interface characteristics

3.2.5.1 Material sterility

All components used within the wound and fluid pathway shall be provided sterile by the manufacturer; those intended for use in the sterile field shall be packaged to facilitate sterile presentation.

3.2.5.2 Component conformity

The manufacturer shall assure that all components recommended for use with the device fit together mechanically and that the resulting assembly complies with system integrity requirements (3.2.1).

3.2.6 Material safety requirements

3.2.6.1 Toxicity

Materials used in the fluid pathway shall be shown to be nontoxic.

3.2.6.2 Pyrogenicity

The fluid pathway shall be shown to be nonpyrogenic.

3.2.7 Electrical safety

The autologous transfusion system shall meet the risk current requirements, as applicable, of the American National Standard, *Safe current limits for electromedical apparatus* (Applicable document 2.5).

4 Tests

This section describes all of the inspections, examinations, and tests to be performed to ascertain device conformance with the requirements of Section 3. (Other, equivalent test methods may be used.) Except for the first digit, the paragraph designations in section 4 correspond to those in section 3. For example, the requirement of 3.2.1 is tested according to 4.2.1.

Unless otherwise indicated, all measurements and tests shall be made at the following ambient conditions:

— temperature: 23°C ± 4°C (73°F + 7°F);

— relative humidity: 20 to 80%;

— atmospheric pressure: 725 mmHg, + 50 mmHg, -75 mmHg;

— alternating current (AC) supply frequency: nameplate frequency ± 3%.

The accuracy of instruments used to measure the test conditions and test equipment for testing section 3 requirements shall be verified within 12 months prior to the tests. All such instruments and test equipment shall:

a) be appropriate for measuring the test parameters;

b) have an accuracy of at least one-third the tolerance for the variable being measured;

c) conform to laboratory standards whose calibration, where possible, is traceable to the primary standards of the National Institute of Standards and Technology.

4.1 Compliance with labeling requirements

Compliance with the requirements of 3.1.1 through 3.1.5 can be determined by inspection, except for the

requirements of 3.1.3 (k), for which compliance can be determined by the following tests.

4.1.3 Operators manual/instructions for use

(k) (1) Aspiration and reinfusion flow capacity

Some factors that may influence the results of the (k,1) test are: moderate systemic, total systemic, and regional anticoagulant, continuous reinfusion, intermittent reinfusion, volume of anticoagulation added, diameter of delivery catheter, use of microemboli filter, and selection of blood vessel used.

In view of the number of variables likely to be encountered in a clinical situation, the manufacturer cannot be expected to make precise claims as to the aspiration flow and reinfusion flow capacities of the device under the conditions of use. The manufacturer should, however, test the device under the conditions outlined in the operator's manual, including testing at the maximum recommended pressures and including in the test circuit all components of the system that would normally be in use or recommended for use with the system.

Depending on the manufacturer's specifications, testing models can be devised using stored or fresh whole human blood or fresh whole blood from experimental animals. Any whole human blood used shall have a hemoglobin content of 12g/100 ml ± 2.0g/100 ml. The hematocrit may be adjusted by centrifugation or the addition of a standard 0.9% sodium chloride (NaCl) solution.

Typical conditions reported should include the hematocrit, the anticoagulant and its concentration, and the age and temperature of the blood.

For the aspiration flow capacity measurement only, a synthetic solution with the same viscosity as blood (for example sugar solution or suspension of latex particles) may be used. (See Appendix B for the protocol for obtaining and handling fresh anticoagulated human blood.)

If whole blood from experimental animals is used, it should be collected within the preceding three hours in 500 cc blood donor bags adequately anticoagulated and stored nonrefrigerated until use.

(k) (2) Storage capacities of the reservoir, processing, and transfusion vessels

The manufacturer shall fill each reservoir, processing, and transfusion vessel as appropriate, in turn, with liters of 0.9% NaCl until the container is full. The amount of saline required to fill the container shall equal the storage capacity stated in the operator's manual.

(k) (3) Processing

Some of these requirements can be verified by inspection. Adequacy of processing can be verified by the filtration tests in 4.2.4.

(k) (4) Stroma-free (soluble) hemoglobin

Preprocessing and postprocessing hemoglobin measurements shall be made according to the procedure outlined in 4.1.3(k)(7). The postprocessing test results shall be consistent with the manufacturer's labeled cell-free hemoglobin concentrations.

(k) (5) Dwell time

Dwell time is the time the blood remains in the device prior to reinfusion into the patient, including the time in the reservoir. The test shall be performed in the device configuration recommended in the manufacturer's instructions for use and at the recommended aspiration rates and pressures. The blood shall be processed for the manufacturer's recommended dwell time. Following the reinfusion procedure, the tests in 4.1.3(k)(6) and (7) shall be performed to determine that blood processed according to the dwell-time recommendation of the manufacturer produces suitable red cell product.

(k) (6) Total cell recovery

The protocol of 4.1.3(k)(7) shall be followed. White cell and platelet counts shall be performed before and after the blood's passage through the manufacturer's component or system. Values obtained shall be consistent with those stated in the manufacturer's instructions for use.

(k) (7) Change in red cell concentrations

This requirement provides comparison data on the damage to formed elements of blood under controlled, *in vitro* conditions. Fresh whole human blood, collected in either citrate phosphate dextrose (CPD) or citrate phosphate dextrose with adenine (CPDA-1), shall be used. Whole human blood shall have a hemoglobin content of 12g/100 ml ± 2.0g/100 ml; the hematocrit may be adjusted by centrifugation or the addition of a standard 0.9% NaCl solution.

The autologous transfusion system shall be assembled to include all components of the system normally used during operation or recommended by the manufacturer for use with the device. The blood shall be pooled into an inert, warmed (37°C) plastic container with siliconized surfaces; where no aspiration wand is recommended, the blood shall be infused directly into the device. The blood will be introduced into the autologous transfusion device at the maximum recommended aspiration flow rate and pressure and then will continue along the normal flow path of the system. If a reservoir is included in the system, the blood will be stored in the reservoir for the maximum manufacturer-disclosed dwell time as per 3.1.3(k)(5). The blood will then be collected from the system in a warm (37°C), siliconized, plastic container at the maximum recommended reinfusion rate and pressure. The quantity of blood entering and exiting the system as well as the hematocrit of entering and exiting blood shall be measured and recorded. Total red cell recovery shall be expressed as:

$$\text{Total Red Cell Recovery} = \frac{\text{Hct}_o \times V_o}{\text{Hct}_i \times V_i} \times 100\%$$

where:

— Hct_i= Hematocrit of entering blood;

— Hct_o= Hematocrit of exiting blood;

— V_i= Volume of entering blood;

— V_o= Volume of exiting blood.

The preprocessing and postprocessing hemoglobin levels shall be measured and recorded.

4.2 Compliance with performance requirements

4.2.1 System integrity

For the pressure test, the assembled apparatus shall be sealed at one end and connected to a pressure source at the other. In the portion of the circuit subjected to a positive pressure, the complete system shall be immersed in a clear liquid and the fluid path subjected to an air pressure equal to twice the manufacturer's recommended pressure. Leakage shall be indicated by a steady stream of bubbles or the loss of more than 0.25 cc of air per minute (cc/min); the test period shall be at least one minute in duration. In the portion of the circuit subjected to negative gauge pressures, the fully assembled apparatus shall be filled with a clear liquid and left unsubmerged. A negative gauge pressure equal to twice the manufacturer's recommended pressure or one atmosphere of negative gauge pressure, whichever is smaller in absolute value, shall be applied to the system. Again, a steady stream of bubbles or the collection of 0.25 cc/min of gas in the system will indicate leakage.

The test period shall be at least one minute in duration. In circumstances where the preceding test method cannot be applied, owing to the variations of an individual manufacturer's design, the manufacturer must provide an equivalent test method.

For the water flow test, the system to be tested shall be set up in the configuration recommended in the manufacturer's instructions for use. A steady stream of water at twice the manufacturer's stated maximum aspiration flow capacity and twice the maximum reinfusion capacity shall be applied. No leakage of water should be evident.

4.2.2 Cleanliness

All operations shall be performed in an operating, certified, laminar flow hood equipped with high-efficiency particulate air (HEPA) filters. The test apparatus shall include all devices supplied by the manufacturer, filled to their maximum operating volume (which shall be stated) and operated according to standard operating procedures. Test fluid shall be introduced into the system by gravity and assistance from any associated normally operating electromechanical apparatus, if required, until the device is full and the effluent tested. The fluid shall be USP-grade Water for Injection filtered through a 0.8 µm filter.

The test fixture (filter holder and attachments) and both sides of a black-gridded, 0.8 µm pore, blank-analysis membrane are washed with the fluid. The test membrane will be placed in a petri dish container with the cover slightly ajar and dried in a laminar flow hood. The control count of particles collected on the membrane surface are counted microscopically (see Applicable documents 2.1 and/or 2.6). Then this particle counting procedure is repeated from the beginning (including washing the test fixture and membrane with filtered water) using the test apparatus. The test membrane will be placed at the effluent port, and the total volume of the system will be drained through the test membrane by gravity. A vacuum may be used to assist in filtration through the test membrane. After the analysis membrane is removed, placed in a petri dish container with the cover slightly ajar, and dried in a laminar flow hood, the particles collected on the membrane surface are counted microscopically (see Applicable documents 2.1 and/or 2.6). The particle/fiber counts for all particles larger than 10 µm in diameter, for those larger than 25 µm in diameter, and for all fibers is calculated as:

$$\text{Particle/Fiber Count} = \frac{\text{Count}_{\text{test}} - \text{Count}_{\text{control}}}{\text{Total Test Fluid Volume}}$$

All particle and fiber counts shall be less than or equal to those given in 3.2.2.

4.2.3 Regional anticoagulation

When heparin is the anticoagulant and the system does not incorporate processing apparatus, an activated clotting time test shall be used to verify adequate anticoagulation. Heparin removal shall be determined by thrombin time tests or another standard heparin assay. For systems incorporating processing features and using citrate anticoagulant, adequate anticoagulation shall be determined by a standard whole blood clotting-time test. Verification of citrate removal is not normally required, since citrate metabolizes so quickly that the likelihood of toxic effect is remote, except during the anheptic phase in a patient that is undergoing liver transplantation, or where the patient has substantially impaired liver function. For this reason, verification of citrate removal should be available upon demand from the manufacturer.

4.2.4 Filtration

Pooled units of ABO-compatible, human whole blood or human red cells outdated within seven days of expiration date will be considered the test fluid. The hematocrit of the pooled units shall be 35% to 52% and shall be adjusted with physiological saline if necessary. The test fluid shall be prefiltered through a mesh with 170 µm openings, in order to remove clots and gross debris that may obscure an electronic particle

counter's aperture. To be an acceptable test fluid, the simulated blood suspension must contain 350 to 5,000 particles per ml of test fluid in the 40- to 100-µm range as determined by the following electronic volume sensing procedure.

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 so that the mean particle volumes for particles with diameters greater than 40 and less than 100 µm are determined on at least three channels.

To a beaker having a stirring device, 97 ml of Isoton, filtered through a 0.8 µm pore disc filter, is added. As the Isoton is being stirred continuously at 30 to 40 rpm, 0.75 ml of Zap-Isoton is added. The simulated blood suspension is then mixed at room temperature (20 to 22°C) with a gentle, end-to-end rotation and swirling motion. A 3.0-ml aliquot of the unfiltered, simulated blood suspension is withdrawn via a volumetric pipette and delivered at a slow, uniform rate into the continuously stirred solution of Isoton and Zap-Isoton. Particle counting in the manometer mode is initiated 15 to 30 seconds after the 3.0-ml aliquot is added, when the mixture becomes transparent. The resulting count may be used to calculate the prefilteration mean number of particles and to determine that the acceptable test fluid requirements have been met.

Next, one unit (approximately 500 cc) of the simulated blood suspension is withdrawn and passed at room temperature (20 to 22°C) through a microfilter test sample at a flow rate of not less than 100 ml/min and a pressure not exceeding 300 mmHg, applied at a minimum rate of 60 mmHg per second (1.16 psi/sec). Within 10 minutes of the completion of filtration, the above-mentioned electronic counting procedure is performed on the 3.0-ml aliquot of the filtered, simulated blood suspension. Two additional 3.0-ml aliquots are taken from the same filtered unit, and from all three counts of particles in the 40- to 100-µm range are averaged to calculate the postfiltration mean number of particles. Postfiltration counts of 34 or fewer particles 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 acceptable test fluid requirements are met, this count is averaged with the initial count to calculate the prefiltration mean number of particles in the 40- to 100-µm range. If these requirements 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 in the 40- to 100-µm range for each test sample, by subtracting the postfiltration mean number of particles from the prefiltration mean, dividing the quotient 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 10 microfilter test samples. The average filtration removal efficiency of all 10 must be at least 80 percent, and the filtration removal efficiency of any individual test filter must be at least 50% to meet this performance requirement.

4.2.5 Interface characteristics

4.2.5.1 Material sterility

Compliance with this requirement can be determined by the appropriate sterility tests of the U.S. Pharmacopeia (Applicable document 2.2) and by visual inspection.

4.2.5.2 Component conformity

Compliance with this requirement can be determined by inspection and by the tests in 4.2.1.

4.2.6 Material safety requirements

4.2.6.1 Toxicity

Material in the fluid pathway shall be consistent with U.S. Pharmacopeia toxicity test criteria. (Applicable document 2.2)

4.2.6.2 Pyrogenicity

Pyrogen testing shall be performed in accordance with the U.S. Pharmacopeia rabbit tests or the Limulus amebocyte lysate test (Applicable documents 2.3 and 2.4, respectively).

4.2.7 Electrical safety

Tests to determine compliance with this requirement can be found in the applicable sections of the American National Standard, *Safe current limits for electromedical apparatus* (Applicable document 2.5).

5 Glossary

dwell time: The period of time the blood remains in the device before it is reinfused. The time the blood is in contact with the device from beginning to end.

processing: The period of time during which the device is in contact with blood (that is from collection through reinfusion).

storage: The period of time that the blood may be stored, either in the device reservoir or in a separate storage container, before it is no longer considered suitable for reinfusion.

total cell recovery: The percentage change in cell volume from preprocessing to postprocessing:

$$\text{Total Red Cell Recovery} = \frac{Hct_o \times V_o}{hct_i \times V_i} \times 100\%$$

where:

— Hct_i= Hematocrit of entering blood;

— Hct_o= Hematocrit of exiting blood;

— V_i= Volume of entering blood;

— V_o= Volume of exiting blood.

Appendix A

Rationale for the development and provisions of this standard

A.1 Introduction

Autologous transfusion refers to the harvest, storage, and reinfusion of the blood products of the same patient. There are several clinically distinct situations where autologous transfusion may be desirable, useful, or life saving, especially when homologous blood products are not immediately available. Such types of clinical autologous transfusion include:

a) elective preoperative harvest and storage;

b) elective perioperative harvest, storage, and reinfusion during slow, moderate bleeding;

c) emergency perioperative harvest, storage, and reinfusion during massive exsanguination into a body cavity, with or without extracorporeal oxygenation; and

d) perioperative harvest of useful blood products derived from the patient, either from a body cavity or from an extracorporeal circuit, during which specific products can be purified and concentrated prior to reinfusion into the patient.

The instrumentation required for each of these functions is distinctly different. Thus, the AAMI Autologous Transfusion Committee encountered difficulty in attempting to encompass all four applications within one standard. At the same time, the Food and Drug Administration's Bureau of Medical Devices (now the Center for Devices and Radiological Health) encouraged the committee to write a standard encompassing all instruments designed for autologous transfusion.

A.1.1 Elective preoperative storage

The technique of elective preoperative storage is attractive, as it permits the patient to contribute to his or her own care and can potentially expand the number of blood donors. If this blood is not required by the donor, it can be released to supplement regular blood bank stocks, provided it is tested and approved as donor blood.

A.1.2 Elective perioperative salvage during slow, moderate bleeding

Devices to collect, store, and reinfuse blood from a patient bleeding slowly (for example less than 500 cc/per hour) have a limited storage capacity. Since the collected blood has been affected by prolonged contact with an internal body surface, it may not clot, and obviously, under these circumstances, additional anticoagulant may not be required to prevent clotting in the external circuit. Patients using such a device will most probably have a near-normal clotting profile, and the slow, sustained bleeding may be treated without recourse to blood bank products. The blood so harvested may contain intrinsic and extrinsic factors activated by contact with a nonendothelialized surface and tissue thromboplastin. Some of these activated factors may be neutralized by hypothesized antiactivated-factor antibodies in the shed blood. Any remaining activated proteins would, it is hoped, be cleared by the reticuloendothelial system after patient infusion, thus preventing disseminated intravascular coagulopathy.

A.1.3 Massive harvest of shed whole blood (with patient heparinized or without systemic anticoagulation)

The patients who may benefit from autologous transfusion devices are those undergoing open-heart surgery or those subject to trauma to the heart or a major blood vessel. The blood loss rate would range from 1 to 1,000 cc/min, with the device being designed to reinfuse harvested blood as rapidly as it is collected.

There is some difference between fully heparinized (3 mg/kg) patients and those patients with an intact clotting mechanism. Normal hemostasis depends on active platelets, vasoconstriction, and clotting proteins. In the absence of heparin, contact of the blood with air, plastic surfaces, and tissue thrombnoplastin will activate the clotting proteins and result in the deposion of fibrin (clot) in the apparatus or in the patient's blood vessels immediately upon reinfusion. This process can be inhibited by mixing the harvested blood with anticoagulant as soon as it is harvested.

Blood harvested by suction from an open wound is contaminated, too, with air, tissue thromboplastin, bone chips, fat, and other materials foreign to the circulation. Air can be removed by venting the reservoir and is usually not a problem in the autologous transfusion device used in conjunction with an extracorporeal oxygenator. However, contamination with air does become a problem when air pressure is used to hasten the infusion of blood into the patient via a direct air-blood interface. The use of an autologous transfusion device involving such a pressurized interface is more dangerous in the absence of an extracorporeal oxygenator, because the air traps inherent in the oxygenator are lacking. This increased risk suggests, besides the use of a trained operator (for example, perfusionist, nurse anesthetist, or RN), the need for some additional safety features:

a) use of a separate infusion mechanism;

b) use of a bubble-detecting sensor to stop the infusion pump when bubbles are detected in the infusion line;

c) a valve system to prevent air infusion.

User experience and awareness is the final protection against air embolization from devices.

NOTE—This appendix is not part of the American National Standard, Autologous transfusion devices (ANSI/AAMI AT6-1991).

A.1.4 Controlled harvest, purification, concentration, and reinfusion of components

Devices developed for use in the blood bank can be used in both the operating room and the critical care area to perform their specified functions of fractioning blood into red cells, white cells, platelets, and plasma. Such devices can also be used to perform selective concentration, purification, and reinfusion into the patient. Depending on the circuits employed, the considerations of A1.3 may or may not apply.

The AAMI Autologous Transfusion Committee has attempted to identify the different clinical situations that may require autologous transfusion. The committee was aware of the difficulty of assembling a clear and concise standard that did not interfere with the practice of medicine. The label requirement specifies that the device be limited to use under a physician's prescription and exemplifies this difficulty. Although the outcome following the use of such a device is determined by the status of the patient, the rate of bleeding, the adequacy of anticoagulation, and excellence of the surgery, the standard can be directed only to areas separate from these variables. That is, the effect of the autologous transfusion device on formed elements, proteins, and other blood constituents is added to the effects of contact with air, tissues, and plastic surfaces; when a physician decides to use autologous transfusion, the standard can provide some information on the latter, additional effects that might be expected from the passage of harvested blood through the circuit.

A.1.5 Individual components versus total systems

This standard addresses devices, systems, and components sold by a manufacturer or supplier as a total system or recommended by a manufacturer or supplier for use together. Very often, a user of an autologous transfusion system will buy individual components from a variety of manufacturers and suppliers and assemble the total system in the field. These cases cannot, of course, be addressed by the system performance requirements of the standard. However, a component manufacturer can assure that those components sold separately conform to any requirements of the standard that are specific to such individual components, rather than to the standard's system requirements.

If a manufacturer or supplier recommends or otherwise indicates that certain components can be used in conjunction with the components of other manufacturers or suppliers, it is that company's responsibility to assure that, in such a case, the resulting system will meet the system integrity requirements of this standard. Manufacturers or suppliers making no claims about the efficacy of their components in combination with components of other manufacturers or suppliers cannot, of course, be responsible for system integrity.

A.2 Need for the standard

Since autologous transfusion was first demonstrated by Blundell in 1818, innumerable patients have received infusions of their own blood under all types of circumstances ranging from primitive condition to present-day cardiac surgery. Before blood banks were developed to their present standard of excellence, autologous transfusion was used when the blood in the patient's abdomen was the only blood available. This was particularly true in cases of ruptured ectopic pregnancy; many such cases were reported between the first and second world wars.

Battle casualties in Vietnam prompted Dr. Gerald Klebanoff, then a colonel in the U.S. Air Force, to investigate the equipment necessary for rapid reinfusion of blood to the patient. The device he produced is occasionally used as the only available means to increase the oxygen-carrying capacity of a patient's blood, because the device is more efficient than other devices. Because of the device's tremendous capacity, it can be used in patients who would otherwise probably succumb to the effects of shock and multiple-organ failure.

All autologous transfusion devices have in common the contact of blood with an abnormal environment, the use of anticoagulants, purification (filtration), washing, and reinfusion. Since there are hazards associated with and inherent in all types of these devices, they should be included in a standard addressing these hazards. Massive reinfusion devices will be at a disadvantage in avoiding hazards, because of the patient population on which they are used, and because massive reinfusion requires the processing of one or more circulating blood volumes, a procedure that will amplify any deleterious effect on the blood, its proteins, and formed elements. Moreover, because autologous transfusion devices constitute extracorporeal blood circuits to a greater or lesser degree, performance standards for these devices should take into account those aspects of extracorporeal circuits pertinent to both cardiac surgery and non-cardiac surgery, regardless of the intended use or application of these devices.

A.3 Rationale for the specific requirements of the standard

A.3.1 Labeling requirements

Two factors control the label content of medical devices. First, the regulations defined in Good Manufacturing Practices for Medical Devices (CFR Title 21) specifically sections 820.120, 820. 121, and 820.130, establish requirements for proper handling, legibility, and many other aspects of labeling pertaining to good manufacturing practices. Second, part 801, chapter 1, title 21, of the same code and section 501 of the US Food, Drug and Cosmetic Act (as amended in 1976) specifically state what constitutes proper and improper labeling of medical devices. In addition to the information required by federal regulations, certain critical facts (see 3.1.3) must appear on a label to assure the device is used correctly and moreover, that the user can make an informed and appropriate choice for the specific application when in need of an autologous transfusion device.

A.3.1.1 Electromechanical device markings

Device markings must clearly indicate the function of both the electrical switches and the valves in the fluid path. The need for such labeling increases with the complexity of the system and is inversely proportional to the amount of training the operator receives and the frequency with which the instrument is used by that operator. Regardless, certain minimum labeling requirements must be met.

A.3.1.2 Disposable blood contact components

Although the committee acknowledged the need for certain information to be immediately available at the time of use, members realized the impracticality of requiring device markings on disposable products and so allowed the option-albeit less preferred-of consigning markings to the outer wrap or a package insert.

A.3.1.3 Operator's manual or instructions for use

An operator's manual is required so that the user will have a clear description of the purpose and principles of operation of the instrument, together with information about its capabilities and the types of situations for which it was designed.

Although some hazards accompanying the use of a device may be due to the surgical procedure, the patient's underlying disease state, or both, rather than to the extracorporeal manipulation of the blood, the committee felt it was still important for the operator's manual to enumerate these potential complications so that users will be aware of them.

In addition, certain technical specifications necessary for the user's evaluation of the device for its intended purpose are required in 3.1.3(k); the rationale for these specifications follows. In general, descriptions of the test protocols are not required in the labeling, although manufacturers may choose to include them and are encouraged to cite, on the labeling, the test used.

A.3.1.3(k)(1) Aspiration and reinfusion flow capacities

Knowledge of these factors enables the user to select a device on the basis of its intended use. Different clinical uses may warrant different aspiration and reinfusion flow capacities. The committee concluded that setting minimum and maximum aspiration and reinfusion flow rates would be neither possible nor meaningful, since the rates depend on so many variables. Aspiration and reinfusion capacities depend on time, as well as on the system configuration being used. Since setting specific rates would limit a device's potential for use in certain applications, the committee preferred to specify test methods and the methods for reporting test results. This gives the user a basis for comparing devices and extrapolating the performance of a specific device in possible use situations.

A.3.1.3(k)(2) Storage capacities of the reservoir, processing, and transfusion vessels

Storage capacity also may influence the device chosen for a particular use. Therefore, it is important that the user be aware of device capacities relative to each of the several containers that might be a part of the system configuration, including reservoirs, processing, and transfusion vessels.

A.3.1.3(k)(3) Processing

Many of the problems in reinfusing diluted "whole" blood back into the patient can be avoided if the red cells are processed or "washed" and only the clean, concentrated, processed red cells reinfused back into the patient. The addition of this purification step, however, increases the dwell time and reduces the rate at which the blood can be reinfused. The manufacturer should, therefore, inform the user of the recommended steps necessary for adequate processing and the effect of the procedure on dwell time, degree of hemolysis, and reinfusion rate.

A.3.1.3(k)(4) Stroma-free (soluble) hemoglobin

Users have shown great interest in knowing the maximum level of stroma-free hemoglobin due to concerns about hemolysis and impairment of renal function. It is important to be able to indicate the maximum concentration that this may be found in the blood product.

A.3.1.3(k)(5) Dwell time

The maximum utilization of an autologous transfusion system requires knowledge of the dwell time for the particular device being used.

A.3.1.3(k)(6) Total cell recovery

White cells may be depleted, as shown by the white cell count, in several ways. Harvest stresses can cause cell rupture, and reinfusion of the white cell contents may promote digestion of the endothelial linings in the lungs and other tissues; also, some plastic surfaces (for example, dialysis membranes) can cause the activation of the C5-A component of complement. This agent produces white cell aggregation, which may be manifest in the test as reduced white cell count. As such aggregates can block the pulmonary vasculature on reinfusion, pulmonary artery pressures may increase. Thus, *in vitro* tests inform the user of the contribution by apparatus of the autologous transfusion system to white cell and platelet reduction.

Platelets usually aggregate in the presence of air or in an abnormal environment. Since loss of platelets is anticipated as a consequence of blood passage through the device, it would be useful to have more precise knowledge of the transdevice cell recovery.

A.3.1.3(k)(7) Change in red cell concentrations

Red cell concentration is an important value, since excessive cell destruction by the device may increase complications and reduce system effectiveness. The committee attempted to formulate the test so that the equipment itself would be tested for its effect on red cell concentration. Given that the manipulation of blood in an extracorporeal circuit will necessarily involve some red cell destruction, the committee's objective was to determine only the contribution of the equipment to this destruction.

Red cells best perform oxygen transport and carbon dioxide excretion as intact cells, and the primary use of autologous transfusion is the maintenance of this oxygen-carrying capacity. Some cells will be destroyed during harvest, but that percentage is not addressed here. The manufacturer should be able to state that, used as directed, the hemolysis of red cells caused by the system is less than 10% over hemolysis caused by the total aspiration, storage, purification, and reinfusion process.

Finally, the rationale for the information requirements of 3.1.3(n) and (o) is provided here.

A.3.1.3(n) Air embolization

The committee felt that air embolization should be addressed because it is a significant hazard, especially when blood is infused under pressure. The manufacturer should inform the user of the procedures to be followed with a given device to prevent this hazard. These recommendations may consist of continuous monitoring by a trained operator or the description of a monitoring device integral to the equipment.

A.3.1.3(o) 24-hour survival of fresh autologous blood

Although the user may need to know the 24-hour survival percentage of fresh autologous blood, and this information should therefore be available, the committee felt that a particular percentage survival rate should not be based on existing requirements for banked red blood cells. In some situations, it might be more desirable to use autologous blood, with a lower percentage of survival, than banked blood, with a higher percentage of red blood cell survival.

A.3.1.4 Service manual

A circuit diagram is desirable for the more complex devices, for both the electrical system and the fluid path. Printed circuits on the hardware greatly facilitate device assembly and use.

A.3.1.5 Collection container labeling

The committee felt that manufacturers providing collection containers for use with their systems should also provide the user with appropriate patient identification labels to minimize the hazard of improper labeling or improper reuse of the blood.

A.3.2 Performance requirements

A.3.2.1 System integrity

These requirements assure the user that the device has the integrity to withstand twice the anticipated normal-use pressure gradient and twice the normal-use flow rate. Since in emergency situations, pressures and flow rates much higher than normal may be used, the committee thought it reasonable to require that the device retain its integrity under these circumstances.

A.3.2.2 Cleanliness

This section was included to provide guidance on the number of nonbiodegradable particles that instrument use may introduce into the patient's circulation and that may contribute to the overall blockage of the pulmonary vasculature. It is important to minimize this number since these nonbiodegradable particles can lodge in capillaries and traumatize vital organs. The limits established for autologous transfusion devices are derived from those established for blood transfusion microfilters (AAMI 1982). The limits in the blood filter standard were empirical counts but are believed to be attainable and were broadened for autologous transfusion devices because these devices are often used in emergency, lifesaving procedures. The consensus of the committee was that the benefits of the use of the device in such situations outweigh any potential risk associated with higher levels of particulates.

A.3.2.3 Regional anticoagulation

In some instances, systemic anticoagulation of the patient is not undertaken. When used to harvest blood from such a patient, therefore, the device must provide for the adequate regional anticoagulation of the harvested whole blood. The choice of an anticoagulant is left to the physician in charge. It is generally accepted, however, that activated clotting times greater than 480 seconds are desirable. The American Association of Blood Banks has determined, and the committee concurred, that a ratio of seven parts of blood to one part of CPD will achieve the desired clotting time. However, when heparin is the anticoagulant, the necessary ratio is determined by variables peculiar to each instance, so that it was impossible for the committee to set a specific ratio. Nevertheless, the autologous transfusion device should be able to deliver the anticoagulant at appropriate ratios throughout the range of aspiration and reinfusion flow rates typically associated with the expected uses of the device. The manufacturer is expected to state the ranges of anticoagulant amount, as well as the type of anticoagulant to be used, if it will affect system performance.

A.3.2.4 Filtration

The harvested blood may contain debris from the wound or aggregates of various blood constituents. Blood harvested from such a variety of sites cannot be standardized, nor can it be assumed to behave in the manner of fresh whole blood harvested from healthy volunteer donors. The use of filters is a medical decision, but because of the potential for extraneous debris, the incorporation of a filter is desirable. Manufacturers can either recommend a filter or describe the exclusion characteristics of the filter system incorporated into their autologous transfusion devices. In fact, certain processing procedures may accomplish the same objective and can be cited by a manufacturer as the method of addressing this requirement.

A.3.2.5 Interface characteristics

A.3.2.5.1 Material sterility

To expedite emergency use, components to be used by the surgeon in the field must be sterile inside and out and when presented, must be suitable for immediate use. This requirement also applies to chest tube drains and other devices connected to the system. Autologous transfusion devices are used almost exclusively with patients who may develop multiple-organ failure for reasons other than autologous transfusion. Once the decision is made to autotransfuse a patient, the user must be especially cautious that reinfusion of organisms from the wound does not complicate the postoperative course. Thus, the user must be assured the device does not contribute to systemic infection; the standard requires the application of a sterilization process designed to destroy or eliminate all viable microbial forms in those parts of the device that are in contact with the blood. In general, industrial sterilization is a statistically based process in which a systems approach to the control of various process determinants provides maximum assurance of consistent production of sterile products. These determinants include knowledge of the presterilization microbial content of the product, the validation of sterilization equipment, the certification of the sterilization cycle, and appropriate tests with biological indicators or dosimeters.

A.3.2.5.2 Component conformity

No accessories recommended by the manufacturer for use with a device should degrade the performance of the device as a whole system relative to any of the performance requirements of this standard.

A.3.2.6 Material safety requirements

A.3.2.6.1 Toxicity

As an extracorporeal circuit, materials can impart plasticizers and other components into the blood. Because the dwell time is generally relatively short, it should be sufficient to establish that toxic contributions from the blood contact surfaces are no greater than those from commercially available homologous blood bags.

A.3.2.6.2 Pyrogenicity

Components used in blood contact must be shown not to release any materials that could elevate patient temperature. A temperature elevation caused by pyrogens may lead to the inappropriate use of antibiotics and will increase the patient's oxygen consumption. Since failure or potential failure in oxygen delivery was the initial reason for the medical decision to autotransfuse, federally mandated tests must be used to ensure that pyrogenic substances are not present.

A.3.2.7 Electrical Safety

The rationale for the current limits of risk accepted in various categories of electromedical equipment is provided in a statement developed for the American National Standard, *Safe Current Limits For Electromedical Apparatus*. The committee initially judged that the "chassis risk" elements of the safe current limits standard would be the principal provisions applicable to autologous transfusion devices. However, the design and intended use of autologous transfusion devices vary, and thus the expected degree of patient contact varies. Therefore, the committee decided to reference the "applicable requirements" of the baseline standard for the current limits of risk, to permit manufacturers of autologous transfusion devices to determine the specific applicability of the safe current limits standard to their particular systems.

A.4 References

ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Blood transfusion micro-filters*. ANSI/AAMI BF7—1989. Arlington (Vir.): AAMI, 1982. American National Standard. ISBN 0-910275-93-9.

Good manufacturing practices for medical devices: General. Code of Federal Regulations. Title 21, chapter 1, part 820.

Appendix B

Protocol for procuring and handling fresh anticoagulated human blood

B.1 Polled human blood: donors

Individuals accepted as blood donors must pass the standards prescribed by the American Association of Blood Banks. All should be healthy and free from acute respiratory disease and should not have taken medication, particularly aspirin, within the preceding two weeks.

Because of the requirement of having the blood drawn, not refrigerated, and used within three hours, donors will have to be processed one to two days in advance of phlebotomy.

B.2 Processing

Samples of blood will be taken from the donors and will be grouped for ABO, typed for Rh, tested for hepatitis B Surface antigen (HBsA), anti-human immunodeficiency virus (HIV), anti-hepatitis B core antibody (HBcAb), and alanine amino transferase (ALT), and screened with a direct and indirect anti-human globulin test (Coombs) and with some type of VDRL or other syphilis test.

The potential donors must be ABO and Rh compatible. HBsAg, anti-HIV, anti-HBcAb, and ALT testing protects the experimenters from exposure to viral agents. The direct and indirect anti-human globulin tests should be negative to prevent both interdonor reactions and shortened survival of the red blood cells due to globulin coating.

B.3 Donations

Some 450 ± 50 ml of blood will be removed from each donor, collected in 500cc blood donor bags, and appropriately anticoagulated.

NOTE — This appendix is not a part of the American National Standard, *Autologous transfusion devices*

(ANSI/AAMI AT6-1991).