List of Titles

American National Standard

ANSI/AAMI RD47:2002
& RD47:2002/A1:2003

Reuse of hemodialyzers

AAMI Association for the Advancement of Medical Instrumentation

The Objectives and Uses of AAMI Standards and Recommended Practices

It is most important that the objectives and potential uses of an AAMI product standard or recommended practice are clearly understood. The objectives of AAMI's technical development program derive from AAMI's overall mission: the advancement of medical instrumentation. Essential to such advancement are (1) a continued increase in the safe and effective application of current technologies to patient care, and (2) the encouragement of new technologies. It is AAMI's view that standards and recommended practices can contribute significantly to the advancement of medical instrumentation, provided that they are drafted with attention to these objectives and provided that arbitrary and restrictive uses are avoided.

A voluntary *standard* for a *medical device* recommends to the manufacturer the information that should be provided with or on the product, basic safety and performance criteria that should be considered in qualifying the device for clinical use, and the measurement techniques that can be used to determine whether the device conforms with the safety and performance criteria and/or to compare the performance characteristics of different products. Some standards emphasize the information that should be provided with the device, including performance characteristics, instructions for use, warnings and precautions, and other data considered important in ensuring the safe and effective use of the device in the clinical environment. Recommending the disclosure of performance characteristics often necessitates the development of specialized test methods to facilitate uniformity in reporting; reaching consensus on these tests can represent a considerable part of committee work. When a drafting committee determines that clinical concerns warrant the establishment of *minimum* safety and performance criteria, referee tests must be provided and the reasons for establishing the criteria must be documented in the rationale.

A *recommended practice* provides guidelines for the use, care, and/or processing of a medical device or system. A recommended practice does not address device performance *per se*, but rather procedures and practices that will help ensure that a device is used safely and effectively and that its performance will be maintained.

Although a device standard is primarily directed to the manufacturer, it may also be of value to the potential purchaser or user of the device as a fume of reference for device evaluation. Similarly, even though a recommended practice is usually oriented towards health care professionals, it may be useful to the manufacturer in better understanding the environment in which a medical device will be used. Also, some recommended practices, while not addressing device performance criteria, provide guidelines to industrial personnel on such subjects as sterilization processing, methods of collecting data to establish safety and efficacy, human engineering, and other processing or evaluation techniques; such guidelines may be useful to health care professionals in understanding industrial practices.

In determining whether an AAMI standard or recommended practice is relevant to the specific needs of a potential user of the document, several important concepts must be recognized:

All AAMI standards and recommended practices are *voluntary* (unless, of course, they are adopted by government regulatory or procurement authorities). The application of a standard or recommended practice is solely within the discretion and professional judgment of the user of the document.

Each AAMI standard or recommended practice reflects the collective expertise of a committee of health care professionals and industrial representatives, whose work has been reviewed nationally (and sometimes internationally). As such, the consensus recommendations embodied in a standard or recommended practice are intended to respond to clinical needs and, ultimately, to help ensure patient safety. A standard or recommended practice is limited, however, in the sense that it responds generally to perceived risks and conditions that may not always be relevant to specific situations. A standard or recommended practice is an important *reference* in responsible decision-making, but it should never *replace* responsible decisionmaking.

Despite periodic review and revision (at least once every five years), a standard or recommended practice is necessarily a static document applied to a dynamic technology. Therefore, a standards user must carefully review the reasons why the document was initially developed and the specific rationale for each of its provisions. This review will reveal whether the document remains relevant to the specific needs of the user.

Particular care should be taken in applying a product standard to existing devices and equipment, and in applying a recommended practice to current procedures and practices. While observed or potential risks with existing equipment typically form the basis for the safety and performance criteria defined in a standard, professional judgment must be used in applying these criteria to existing equipment. No single source of information will serve to identify a particular product as "unsafe". A voluntary standard can be used as one resource, but the ultimate decision as to product safety and efficacy must take into account the specifics of its utilization and, of course, cost-benefit considerations. Similarly, a recommended practice should be analyzed in the context of the specific needs and resources of the individual institution or firm. Again, the rationale accompanying each AAMI standard and recommended practice is an excellent guide to the reasoning and data underlying its provision.

In summary, a standard or recommended practice is truly useful only when it is used in conjunction with other sources of information and policy guidance and in the context of professional experience and judgment.

INTERPRETATIONS OF AAMI STANDARDS AND RECOMMENDED PRACTICES

Requests for interpretations of AAMI standards and recommended practices must be made in writing, to the Manager for Technical Development. An official interpretation must be approved by letter ballot of the originating committee and subsequently reviewed and approved by the AAMI Standards Board. The interpretation will become official and representation of the Association only upon exhaustion of any appeals and upon publication of notice of interpretation in the "Standards Monitor" section of the *AAMI News*. The Association for the Advancement of Medical Instrumentation disclaims responsibility for any characterization or explanation of a standard or recommended practice which has not been developed and communicated in accordance with this procedure and which is not published, by appropriate notice, as an *official interpretation* in the *AAMI News*.

AAMI Recommended Practice

ANSI/AAMI RD47:2002
& RD47:2002/A1:2003
(Consolidated text;
Revision of ANSI/AAMI RD47:1993)

Reuse of hemodialyzers

Corrected copy

Developed by
Association for the Advancement of Medical Instrumentation

Approved 7 November 2002 (recommended practice) and 21 March 2003 (amendment) by
American National Standards Institute, Inc.

Abstract: This recommended practice is addressed to the physician responsible for reprocessing hemodialyzers. It covers personnel and patient considerations, records, equipment, physical plant and environmental safety, reprocessing material, patient identification and hemodialyzer labeling, reprocessing and storage procedures, disposition of rejected dialyzers, preparation for subsequent use, patient monitoring, and quality assurance and quality control. This document does not endorse either single use or reuse of dialyzers.

Keywords: blood, dialysis, labeling, medical equipment, packaging, personnel, records, reprocessing, reuse, test

List of Titles

AAMI Recommended Practice

This Association for the Advancement of Medical Instrumentation (AAMI) recommended practice implies a consensus of those substantially concerned with its scope and provisions. The existence of an AAMI recommended practice does not in any respect preclude anyone, whether they have approved the recommended practice or not, from manufacturing, marketing, purchasing, or using products, processes, or procedures not conforming to the recommended practice. AAMI recommended practices are subject to periodic review, and users are cautioned to obtain the latest editions.

CAUTION NOTICE: This AAMI recommended practice may be revised or withdrawn at any time. AAMI procedures require that action be taken to reaffirm, revise, or withdraw this recommended practice no later than five years from the date of publication. Interested parties may obtain current information on all AAMI documents by calling or writing AAMI.

All AAMI standards, recommended practices, technical information reports, and other types of technical documents developed by AAMI are *voluntary*, and their application is solely within the discretion and professional judgment of the user of the document. Occasionally, voluntary technical documents are adopted by government regulatory agencies or procurement authorities, in which case the adopting agency is responsible for enforcement of its rules and regulations.

Published by

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

Printed in the United States of America

ISBN 1–57020–181–1

List of Titles

Contents

List of Titles

Committee representation

Association for the Advancement of Medical Instrumentation

Renal Disease and Detoxification Committee

This recommended practice was developed by the AAMI Renal Disease and Detoxification Committee. Committee approval of the recommended practice does not necessarily imply that all committee members voted for its approval.

At the time this document was published, the **AAMI Renal Disease and Detoxification Committee** had the following members:

Cochairs:
LeRoy J. Fischbach
Richard A. Ward, PhD

Members:
G. Steven Acres, MD, Carolina Regional Nephrology Associates
Matthew J. Arduino, DrPH, U.S. Centers for Disease Control and Prevention
D. Michael Blankenship, MD, Texarkana Kidney Disease & Hypertension Center
Danilo B. Concepcion, CHT, CCHT, St. Joseph Hospital Renal Center
R. Barry Deeter, RN, MSN, University of Utah Dialysis Program
Robert Dudek, U.S. Filter
Mark David Einziger, MS, Church & Dwight Co Inc.
Martin S. Favero, PhD, Johnson & Johnson
LeRoy J. Fischbach, Minntech Corporation
Gema Gonzalez, U.S. Food and Drug Administration, CDRH/ODE
Anders G. Hultsten, Gambro Lundia AB
Bertrand L. Jaber, MD, New England Medical Center
Jerome C. James III, PhD, Aksys Limited
James M. Kaar, Baxter Healthcare Corporation
Rodney S. Kenley, MS, American Association of Kidney Patients
Nathan W. Levin, MD, Renal Research Institute LLC
Douglas A. Luehmann, DaVita, Inc.
Bruce H. Merriman, Central Florida Kidney Centers
Patricia Peterson, RN, CNN, Medisystems Services Corporation
John A. Rickert, Osmonics Medical Systems
Mark M. Rolston, Renal Care Group
James D. Stewardson, Brighton, CO
Scott N. Walker, Fresenius USA
Richard A. Ward, PhD, Kidney Disease Program, University of Louisville

Alternates:
Robert J. Chambers, Gambro BCT Inc.
Christine Colon, Baxter Healthcare Corporation
Conor Curtin, Fresenius Medical Care NA Dialysis Products Division
Russell Dimmitt, AS, Renal Care Group Inc.
Barbara I. McCool, U.S. Food and Drug Administration, CDRH/ODE
Gregory Montgomery, U.S. Filter

The committee wishes to thank the **AAMI Hemodialyzer Reuse Task Group** for its work to develop the initial drafts of this document.

Chair:	Nathan W. Levin, MD
Members:	Matthew J. Arduino, DrPH, U.S. Centers for Disease Control and Prevention
	D. Michael Blankenship, MD, Texarkana Kidney Disease & Hypertension Center
	Robert Donald Borcicky, Jr., Renal Care Group Inc.
	R. Barry Deeter, RN, MSN, University of Utah Dialysis Program
	Martin S. Favero, PhD, Johnson & Johnson
	LeRoy J. Fischbach, Minntech Corporation
	Jerome C. James III, PhD, Aksys Limited
	Nathan W. Levin, MD, Renal Research Institute LLC
	Miriam C. Provost, U.S. Food and Drug Administration, CDRH/ODE
	John A. Rickert, Osmonics Medical Systems
	Scott N. Walker, Fresenius USA
	Robert L. Wilkinson, Baxter Healthcare Corporation
	Paul D. Wise, EE, Hattiesburg Clinic Dialysis Unit
Alternates:	Christine Colon, Baxter Healthcare Corporation
	James M. Kaar, Baxter Healthcare Corporation
	Brooks E. Rogers, Fresenius Medical Care NA Dialysis Products Division

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

Foreword

This recommended practice was developed by the AAMI Renal Disease and Detoxification Committee based on initial drafting work of its Hemodialyzer Reuse Task Group. The committee's objective is to acknowledge the widespread practice of hemodialyzer reprocessing, without endorsement or criticism; to indicate risks associated with hemodialyzer reprocessing; and to provide recommendations for optimal hemodialyzer reprocessing as a service to patients, physicians, and facilities.

This recommended practice reflects the conscientious efforts of health care professionals, patients, and medical device manufacturers to develop recommendations for optimal hemodialyzer reprocessing procedures. These recommendations are not meant to be construed as universally applicable in all circumstances. This document is intended to guide physicians in charge of hemodialyzer reprocessing, particularly the directors of dialysis facilities, in initiating a new hemodialyzer reprocessing program or evaluating an existing program against present-day technology and accepted practices.

This recommended practice should be considered flexible and dynamic. As technology advances and new data is brought forward, this recommended practice will be reviewed and, if necessary, revised. Within the context of this recommended practice, "shall" indicates requirements strictly to be followed to conform to the standard. "Should" indicates, that either among several possibilities one approach is recommended as particularly suitable without mentioning or excluding others, or that a certain course of action is preferred but not necessarily required, or that (in the negative form) a certain possibility or course of action should be avoided but is not prohibited. "May" indicates a course of action is permissible within the limits of the standard. "Can" is used as a statement of possibility and capability. Finally, "must" is used only to describe "unavoidable" situations, including those mandated by the government regulation.

The use of phrases such as "have been shown," "an established procedure," or "demonstrated success," or others of similar words signifies that the basis for the process may be found in a manufacturer's labeling, medical or scientific literature, standards or publications from authoritative agencies, or clearly documented, scientifically sound studies performed locally.

These guidelines were developed by professionals and are not designed for regulatory applications, but have been put into service as such.

The concepts incorporated in this recommended practice should not be considered inflexible or static. The recommendations presented here should be reviewed and updated periodically to assimilate technological developments.

The rationale for this recommended practice (annex A) not only contains explanations of the need for the provisions of the recommended practice, but also gives proposed revisions that were not included in this recommended practice and the reasons for those exclusions. The reader is encouraged to review carefully the rationale for each section to better understand the recommended practice itself and the state of the art in reprocessing hemodialyzers.

AAMI standards and guidelines are based on the national consensus of physicians, engineers, other health care professionals, government representatives, patients, and industry. This consensus has traditionally focused on technology design, performance, and testing—areas in which the AAMI membership has considerable knowledge and experience. During the development of this document, several interest groups requested detailed requirements for informed patient consent with respect to the reuse of hemodialyzers. It is not clear whether informed patient consent requirements can or should be developed by a consensus of the groups mentioned. It may be more appropriate for informed patient consent requirements to be developed by physicians, patients, and their representatives. This document does not go as far as the patients' representatives requested on that subject, although it does go farther than previous documents of this type. The extent to which AAMI or any standards organization should develop informed patient consent requirements can be determined as this guideline is evaluated during its use.

This printing integrates American National Standard ANSI/AAMI RD47:2002 and Amendment 1 to that standard (ANSI/AAMI RD47:2002/A1:2003) into one document.

Suggestions for improving this recommended practice are invited. Comments and suggested revisions should be sent to AAMI, Attn: Standards Department, 1110 N. Glebe Road, Suite 220, Arlington, VA 22201-4795.

NOTE—This foreword does not contain provisions of the American National Standard ANSI/AAMI RD47:2002, *Reuse of hemodialyzers*, and its amendment.

Introduction: Need for this AAMI recommended practice

In June 1980, the Bureau of Medical Devices of the U.S. Food and Drug Administration (FDA), now the Center for Devices and Radiological Health (CDRH), transmitted to AAMI the final report of an FDA-sponsored study, "An Investigation of the Risks and Hazards Associated with Hemodialysis Devices," that was undertaken to recommend ways of controlling these risks and hazards. This information was compiled to assist the medical community and to provide data to support the development of recommended practices.

Since 1980, the reported incidence of hemodialyzer reuse has risen dramatically, from an estimated 16 % of patients in 1980 to an estimated 80 % of clinics in 2001 (Tokars, et al., 2001). This increase may be attributed, in part, to the increasing pressure of federal measures to contain the costs of health care implemented by the prospective reimbursement regulations initiated on 1 August 1983.

Although good results have been demonstrated by the practitioner experienced in hemodialyzer reprocessing, the widespread application of this technique in the absence of detailed consensus guidelines has created greater opportunities for the nonexpert practitioner to use inadequate methods. Moreover, cost saving by any procedure that adds risks to the patient if improperly done may cause some patients and health care professionals to suspect that the welfare of the patient may not be the primary concern. These fears may be justified because merely claiming that reuse is safe, without defining details of the process, allows unsafe procedures to appear under the guise of acceptable medical practice. Thus, failure to ensure that reuse is done safely for all patients causes the brush of mistrust to paint all practitioners alike, when, in fact, the multiple use of hemodialyzers may actually improve the quality of care and access to dialysis. Those who are expert in reprocessing hemodialyzers can, therefore, perform a valuable service by developing guidelines for the less-experienced practitioner which will achieve the high quality of care that health care professionals want for their patients. This recommended practice has been written to respond to the concern of patients, health care professionals, and manufacturers that dialyzer reprocessing be conducted safely and effectively.

It was against this background that AAMI convened a consensus-development conference in May 1983 for the purpose of examining the issues surrounding reuse of hemodialyzers and discussing the position of the medical and scientific community on the subject. One recommendation emerging from this conference, in which representatives from many medical and scientific societies participated, was that a nationally developed recommended practice, which was approved by a consensus for the reprocessing of hemodialyzers was desirable and necessary for patient safety and continued clinical efficacy. Another recommendation was that the guidelines be developed under the auspices of AAMI because AAMI could coordinate the development of a national consensus. AAMI subsequently established the Hemodialyzer Reuse Subcommittee of the Renal Disease and Detoxification Committee. The subcommittee's membership includes representatives of manufacturers, patients, health care organizations, government agencies, and health care professionals.

In November 1984, an AAMI technology assessment conference was held on the subject of reuse of hemodialyzers. The fourth draft of the recommended practice being written by the AAMI subcommittee was reviewed by those attending the conference. Presentations were also made about the results of a survey of hemodialyzer reprocessing in the United States, water for reprocessing, germicides, statistical analysis, methods of performance testing, reprocessing machines, the perspective of patients, the viewpoint of manufacturers, reprocessing in the home, and the FDA's position on the reprocessing of medical devices. Future revisions of the recommended practice incorporated information gleaned from the conference and comments from other interested parties. In October 1987, the Centers for Medicare & Medicaid Services (CMS), formerly the Health Care Financing Administration (HCFA) adopted the recommended practice as part of their regulations governing Medicare reimbursement. Because the guideline was not constructed as a regulation, many questions arose as surveyors attempted to enforce compliance. The AAMI Hemodialyzer Reuse Subcommittee issued an interpretive guideline in 1991 that clarified the issue of dialyzer performance verification, the most common source of misunderstanding in the previous version. When the reuse document was reviewed in 1993, the interpretation was incorporated. Subsequently, the Centers for Medicare & Medicaid Services adopted the 1993 revisions in a manner similar to their adoption of the 1987 version. Dialyzer manufacturers are now expected to follow the FDA guidance document titled "Guidance for Hemodialyzer Reuse Labeling" (6 October 1995). This guidance requires a manufacturer to label its dialyzers for either single use or multiple use. In cases of labeling a dialyzer for reuse, the FDA guidance document requires that the manufacturer perform certain bench testing using simulated reuse, and then perform a limited clinical trial to support the bench results. Those data are submitted to the FDA and reviewed as part of the 510(k) Premarket Notification for the reusable dialyzer.

In the early 1990s, a statistically significant association was reported between mortality and the use of low-flux dialyzers reprocessed with certain germicides in freestanding clinics (Held, et al., 1994; Feldman, et al., 1996). No cause-and-effect relationship was established in those studies and potentially confounding variables, such as a "center effect" and the adequacy of dialysis, were not evaluated. Indeed, the results of more recent studies (Collins,

et al., 1998; Ebben, et al., 2000; Port, et al., 2001) suggest that factors other than the choice of germicide may have contributed to the differences in outcome.

List of Titles

American National Standard

ANSI/AAMI RD47:2002
& RD47:2002/A1:2003
(consolidated text)

Reuse of hemodialyzers

1 Scope

This recommended practice describes the essential elements of good practice for reprocessing hemodialyzers in order to help ensure device safety and effectiveness. These practices embrace considerations of the device and the patient, as well as attention to equipment, facilities, cleaning and disinfection methods, labeling, preparation for multiple use, and quality control of the reuse process. This document does not endorse either single use or reuse of dialyzers.

Regardless of the labeling recommendations, prescription to reuse remains the sole responsibility of the patient's physicians. This recommended practice, therefore, is addressed to the physician responsible for the hemodialyzer reprocessing program. Users, however, should be aware that dialyzers intended for reuse must be labeled for reuse in accordance with the Food and Drug Administration (FDA) guidance document "Guidance for Hemodialyzer Reuse Labeling" (6 October 1995).

The committee recognizes that such dialyzer characteristics as biocompatibility and clearance of larger molecules may be affected by reuse. Changes in dialyzer performance and biocompatibility vary with the materials of construction and the reuse method employed. Detailed analysis of these factors is beyond the scope of this document. Specific information on the effects of reuse on dialyzer performance and biocompatibility may be obtained from the dialyzer manufacturer and the scientific literature (Cheung, et al., 1999). This recommended practice does not address every risk or benefit that may be associated with reuse.

1.1 Inclusions

This recommended practice is directed to the physician in charge of hemodialyzer reprocessing by either the manual or the automated method. Subjects included within the scope of this recommended practice are recordkeeping, personnel considerations, patient considerations, equipment considerations, physical plant and environmental safety considerations, reprocessing material considerations, patient identification and hemodialyzer labeling, reprocessing and storage procedures, disposition of rejected dialyzers, preparation for subsequent use, patient monitoring, quality assurance, and quality control.

1.2 Exclusions

This recommended practice does not cover the reprocessing of blood tubing sets nor does it address labeling and performance requirements for single-use hemodialyzers.

2 Normative references

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

ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Water treatment equipment for hemodialysis applications.* ANSI/AAMI RD62:2001. Arlington (VA): AAMI, 2001. American National Standard.

CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC). *Recommendations for preventing transmission of infections among hemodialysis patients*. MMWR 50, No. RR-5, 2001.

CODE OF FEDERAL REGULATIONS (CFR). Title 29, Volume 6, Part 1910. Revised as of July 1, 1998.

NATIONAL KIDNEY FOUNDATION. National Kidney Foundation report on dialyzer reuse. Task Force on Reuse of Dialyzers, Council on Dialysis, National Kidney Foundation. *Am J Kidney Dis* 30:859–871, 1997.

OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION (OSHA). Bloodborne Pathogens Standard. OSHA Regulations, 29 CFR, Part 1910.1030, 1991.

OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION (OSHA). Occupational Exposure to Formaldehyde. OSHA Regulations, 29 CFR, Part 1926.1148, 1995.

OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION (OSHA). Hazard Communications. OSHA Regulations, 29 CFR, Part 1910.1200, 1995.

GARNER JS. Guideline for Isolation Precautions in Hospitals. Hospital Infection Control Practices Advisory Committee. *Infection Control and Hospital Epidemiology* 17:53–80, 1996, and *Am J Infection Control* 24:24–52, 1996.

BOLYARD EA, TABLAN OC, WILLIAMS WW, PEARSON ML, SHAPIRO CN, DEITCHMAN SD, and THE HOSPITAL INFECTION CONTROL PRACTICES ADVISORY COMMITTEE. Infection Control in Healthcare Personnel. Guideline for infection control in healthcare personnel, 1998. *Am J of Infection Control* 26:289–354, 1998, and *Infection Control and Hospital Epidemiology* 19:407–463,1998.

3 Definitions

For the purposes of this AAMI recommended practice, the following definitions apply.

3.1 cleaning: Flushing of a solution or solutions through the blood and dialysate compartments or the passage of fluid through the membrane (i.e., reverse ultrafiltration [UF]) to purge the dialyzer of blood and other substances.

3.2 clearance: Measure of net flux of a given solute across the hemodialyzer membrane that is expressed as the number of milliliters of blood completely cleared of a solute per unit of time. For the purpose of this recommended practice, clearance includes clearance because of ultrafiltration. (See also **clearance, open-loop system**.)

3.3 clearance, open-loop system: Clearance determined in a test system in which the solutions perfusing the hemodialyzer are discharged to drain after one passage through the hemodialyzer. The calculation for clearance by this method is as follows:

$$\text{Clearance (mL/min)} = \frac{(C_{Bi} - C_{Bo})Q_{Bi}}{C_{Bi}} + \frac{C_{Bo}Q_{UF}}{C_{Bi}}$$

where

C_{Bi} = concentration of solute in the fluid entering the blood compartment

C_{Bo} = concentration of solute in the fluid leaving the blood compartment

Q_{Bi} = flow rate of fluid entering the blood compartment; and

Q_{UF} = ultrafiltration rate

3.4 dialyzer: See hemodialyzer.

3.5 disinfection: Destruction of pathogenic and other kinds of microorganisms by thermal or chemical means. Disinfection is a less lethal process than sterilization, because it destroys most recognized pathogenic microorganisms but not necessarily all microbial forms. This definition of disinfection is equivalent to low-level disinfection in the Spalding classification.

3.6 endotoxin: Endotoxins are the major component of the outer cell wall of gram-negative bacteria. Endotoxins are lipopolysaccharides, consisting of a polysaccharide chain covalently bound to lipid A. Endotoxins can acutely activate both humoral and cellular host defenses, leading to an acute syndrome characterized by fever, shaking chills, hypotension, multiple organ failure, and even death if allowed to enter the circulation in a sufficient dose. Long-term exposure to low levels of endotoxin has been implicated in a chronic inflammatory response, which may contribute to some of the long-term complications seen in hemodialysis patients. However, the mechanisms of this process remain incompletely understood. (See also **pyrogen**.)

3.7 fiber bundle volume (FBV): Aggregate volume of patent hollow fibers contained within the blood compartment of a hollow-fiber dialyzer. Sometimes, incorrectly used interchangeably with total cell volume (TCV), which includes header volume.

3.8 first-use syndrome: Symptom complex characterized by chest tightness, back pain, dyspnea, angioedema or laryngeal edema, peripheral numbness and tingling, flushing of the skin, pruritis, and nausea and vomiting, occurring within minutes of the initiation of dialysis with a new dialyzer. Although usually mild in nature, in extreme cases the symptoms may progress to respiratory arrest and death. The etiology of first-use syndrome is not completely understood. However, the term usually is considered to include anaphylactoid reactions to residual ethylene oxide in ethylene oxide sterilized dialyzers and anaphylactoid reactions resulting from the induction of

bradykinin release by negatively charged AN69®[1)] membrane. The latter reactions are exacerbated by the presence of ACE inhibitors, which suppress bradykinin degradation. Anaphylactoid reactions, similar to first-use syndrome, have also been reported with reused dialyzers. The risk of these reactions is also increased when ACE inhibitors are present.

3.9 formaldehyde: Formaldehyde (HCHO) solution, USP (nominal concentration 37 % by weight [W/W] or 40 % by volume [W/V]). Generally contains 8 % to 16 % methanol for stabilization. A dilution of 1 part of formaldehyde with 9 parts of water yields 4 % (W/V). Also called formalin. Concentrated formaldehyde stored under adverse conditions can polymerize to form paraformaldehyde, a white precipitate.

3.10 germicide: Agent that kills microorganisms.

3.11 hazard: Situation or condition that could be detrimental to patients or staff members.

3.12 heat disinfection: Physical method of disinfection used in reprocessing some dialyzer types.

3.13 hemodialyzer: Extracorporeal device that changes the chemical composition of the blood by diffusive and convective transfer of substances between the blood and a solution of chemicals through a semipermeable membrane and which functions within clinically acceptable rates of water and solute transport.

3.14 high-level disinfection: Process that kills all vegetative bacterial cells, *Mycobacterium tuberculosis* var. *bovis*, fungi, all small or nonlipid viruses, and, if the contact time is long enough, most bacterial endospores.

3.15 labeling: Display of written, printed, or graphic matter on a dialyzer including all packaging and package inserts.

3.16 lipopolysaccharide (LPS): Major outer membrane component of gram-negative bacteria. Lipopolysaccharides are important antigenic factors and are endotoxins. The general structure is a heteropolysaccharide chain (core polysaccharide and O-specific chain) covalently bound to a glycolipid (lipid A). (See also **endotoxin**.)

3.17 low-level disinfection: Process or procedure that inactivates most vegetative bacteria, except for *Mycobacterium tuberculosis* var. *bovis* and some viruses. See also **disinfection**.

3.18 material safety data sheets (MSDS): Documents that identify, for any chemicals, the degree and type of any hazards and appropriate precautions. Manufacturers are required to provide these documents upon request.

3.19 membrane: Semipermeable material between the blood and dialysate compartments of a hemodialyzer.

3.20 multiple use: Use of a device for more than one procedure, after suitable reprocessing of the device.

3.21 OSHA: Occupational Safety and Health Administration.

3.22 performance: Solute and fluid mass transfer capabilities of a hemodialyzer.

3.23 port, blood: Opening into the blood compartment of a hemodialyzer.

3.24 port, dialysate: Opening into the dialysate compartment of a hemodialyzer.

3.25 ppm: Abbreviation for parts per million.

3.26 preprocessed dialyzer: Dialyzer subjected to reprocessing procedure before first use.

3.27 pyrogen: Fever-producing substance. Note that pyrogens are most often lipopolysaccharides of gram-negative bacterial origin. (See also **endotoxin**.)

3.28 quality assurance (QA): Verification that written policies and procedures have been developed and are being implemented.

3.29 quality control (QC): Determination that the materials, process tests, and performance of the final product meet the designated specifications.

3.30 rebound: Increase in germicide concentration after rinsing to a particular concentration.

[1)] AN69® is a registered trademark of Hospal.

3.31 removal of germicide: Passage of a solution through the blood and dialysate compartments of a hemodialyzer to purge it of the germicide.

3.32 reverse ultrafiltration: Passing of fluids through the membrane from the dialysate compartment to the blood compartment. This action is used to clean the membrane of blood products for the purpose of reuse.

3.33 risk: Event that is considered likely or possible, and that is potentially hazardous but has not yet occurred or resulted in detrimental clinical consequences.

3.34 Standard Precautions: Synthesis of the major features of universal (blood and body fluid) precautions (designed to reduce the risk of transmission of bloodborne pathogens) and body substance isolation (designed to reduce the risk of transmission of pathogens from moist body substances). Standard Precautions apply to (1) blood; (2) all body fluids, secretions, and excretions, except sweat, regardless of whether they contain visible blood; (3) nonintact skin; and (4) mucous membranes. Standard Precautions are designed to reduce the risk of transmission of microorganisms from both recognized and unrecognized sources of infection in health care settings.

3.35 sterile: Free of all microbial life, including highly resistant bacterial spores.

3.36 total cell volume (TCV): Volume of an aqueous liquid to fully prime the blood compartment of a hollow-fiber hemodialyzer. This volume is the sum of the fiber bundle volume and the header volume.

3.37 toxic substance: Substance that, in sufficient amounts, causes harm to an exposed organism.

3.38 transmembrane pressure (TMP): Pressure exerted across the semipermeable membrane, from the blood to the dialysate side of the dialyzer, which can be expressed by the following equation:

$$TMP = (P_{Bi} + P_{Bo})/2 - (P_{Di} + P_{Do})/2 - P_{oncotic}$$

where:

$P_{oncotic}$ = oncotic pressure created by plasma proteins

P_{Bi} = pressure at the arterial (inlet) port of a hemodialyzer blood compartment

P_{Bo} = pressure at the venous (outlet) port of a hemodialyzer blood compartment

P_{Di} = pressure at the inlet port of a hemodialyzer dialysate compartment

P_{Do} = pressure at the outlet port of a hemodialyzer dialysate compartment

3.39 validation or process validation: Establishment of documented evidence providing a high degree of assurance that a given process will consistently yield a result meeting predetermined specifications and quality characteristics.

3.40 ultrafiltration: Transfer of fluid from the blood compartment to the dialysate compartment through the dialysis membrane as a result of a pressure gradient (transmembrane pressure) existing between the blood and dialysate compartments.

3.41 use number: Number of times a hemodialyzer has been used for dialysis treatments with a single patient.

4 Records

All records described in this recommended practice shall meet the requirements for medical records, including completeness, legibility, and security. A place should be provided for the signature or other unique mark of identification of the person completing each step of the reprocessing procedure (i.e., the person performing preventive maintenance procedures, the person[s] investigating complaints, and the person[s] conducting quality assurance [QA] and quality control [QC] activities). Maintaining these records is the responsibility of the medical director.

4.1 Dialyzer reprocessing manual

The dialyzer reprocessing manual should be a compilation of all specifications, policies, training materials, manuals, methodologies, and procedures, that may be integrated into the dialysis facility's policy and procedures manual. The dialyzer reprocessing manual should also contain samples of forms and labels, if appropriate. The operational logs, manuals, and files may be kept separate from the dialyzer reprocessing manual. The dialyzer manufacturer's labeling should be consulted to determine if a specific dialyzer requires special considerations.

4.2 Reprocessing record

Records shall be kept that identify the new dialyzer, the date of each reprocessing step, the person performing the procedure, his or her signature or other identifying mark, and the results of tests of device performance and safety. This information should be recorded in a reprocessing log or the patient's chart, whichever is more convenient. Patients must be permitted to read records pertaining to the reprocessing and reuse of their own dialyzers.

4.3 Equipment maintenance record

Records shall be maintained of the dates of preventive maintenance procedures and the results of scheduled testing in order to ensure the proper functioning of reprocessing equipment, environmental-control equipment, safety equipment, or other equipment.

4.4 Personnel health monitoring records

A file must be kept of the results of medical examinations of personnel that are required by OSHA or other regulatory agencies.

4.5 Complaint investigation record

Records shall be kept of all complaints by patients and staff members about failures of preprocessed and reprocessed dialyzers or possible adverse reactions to any dialyzers; the results of a comprehensive investigation of these alleged problems; and, if appropriate, the corrective actions taken. The records should be reviewed periodically for trends of adverse reactions. Compliance with the FDA's Medical Device User Reporting procedures should be considered.

4.6 Quality assurance and quality control record

A record shall be kept of the date and results of QA and QC evaluations and the person or persons conducting the evaluations.

5 Personnel qualifications and training

5.1 Qualifications

Personnel shall possess adequate education, training, or experience to understand and perform procedures outlined by the individual dialysis facility relevant to the facility's multiple-use program. New personnel range in knowledge from those with no medical background who are fully trained by the facility, to licensed practitioners with extensive medical background. Education should be geared to meet the needs of this wide range of personnel.

5.2 Training

5.2.1 Curriculum

The dialysis facility's physician or director shall establish a training course for the persons performing hemodialyzer reprocessing. A written document should give details about the curriculum and, in particular, address the potential risks to patients and staff members of not following correct procedures. The curriculum should include at least the following information:

a) the facility's specific reprocessing procedure, including a rationale for each step;

b) basic documentation requirements of the program;

c) the operation and maintenance of the facility's specific equipment for reprocessing hemodialyzers and, if appropriate, the dialysis systems and components;

d) microbiology with respect to aseptic technique, the collection and handling of samples, and personnel safety precautions for infectious hazards;

e) the risks and hazards of multiple use of hemodialyzers;

f) the consequences of not performing tasks properly;

g) the risks and hazards associated with toxic substances used in reprocessing hemodialyzers, proper handling of these substances, and procedures for handling spills and proper disposal of toxic substances;

h) the use and location of protective eyewear, respirators, masks, and special clothing;

i) emergency procedures as required by the facility; and

j) the principles of dialysis, emphasizing the characteristics of the hemodialyzer and the effect of reuse on these characteristics.

5.2.2 Documentation

Each person performing procedures for the multiple use of dialyzers should have successfully completed the dialysis facility's training course relevant to that person's task and demonstrated competence in the area covered by his or her training. Successful completion of training should be certified by the medical director or his or her designated representative and recorded in the trainee's personnel file along with verification of the trainee having received the instruction. Retraining is necessary when new procedures are undertaken. Annual review of competence is required with appropriate retraining if deficiencies are found.

6 Patient considerations

6.1 Medical issues

An order to reprocess hemodialyzers shall be made by a physician knowledgeable about reprocessing and its medical and economic implications. Because the current human immunodeficiency virus (HIV), hepatitis B, or hepatitis C status of a patient cannot be known with certainty, all staff potentially exposed to the patient's blood shall observe Standard Precautions. Dialyzers should not be reprocessed from patients who have tested positive with hepatitis B surface antigens. Precautions for all infectious hazards should be emphasized and included in the reprocessing procedures. Written procedures should stipulate whether and how reprocessing will be done for patients who have shown sensitivity to materials used in the reprocessing of hemodialyzers.

6.2 Informed consent

The Centers for Medicare & Medicaid Services (CMS) *Conditions for Coverage of Suppliers of End-Stage Renal Disease (ESRD) Services* states that all patients in a dialysis facility will be fully informed regarding reuse of dialyzers. Printed material such as brochures describing the facility's services should contain a statement about dialyzer reprocessing if reuse is performed. National renal organizations may have additional materials available.

7 Equipment

Each piece of equipment used for reprocessing shall be appropriately designed, constructed, and tested to perform its intended task. Types of reprocessing systems vary from sophisticated microprocessor-controlled systems to hand-operated valving systems. Satisfactory operation of manual and automated systems shall be ensured by appropriate functional tests. Strict QC and QA shall be maintained for any type of dialyzer reprocessing equipment. Additionally, complete documentation of system function, operating procedures, potential system failures, and dialyzer-reuse criteria shall be included in the dialyzer reprocessing manual, known to the operator, and available for review.

7.1 Water systems

The system providing water for reprocessing shall meet all of the requirements for pressure and flow rate for operating the reprocessing equipment under minimal and peak load conditions. Product water used for rinsing, cleaning, filling, and diluting the germicide shall be shown to comply with the chemical and microbiological quality requirements specified in the current version of ANSI/AAMI RD62. Water bacteriology monitoring shall be carried out where the dialyzer is connected to the reuse system or as close as possible to that point.

7.2 Reprocessing systems

7.2.1 Utility requirements

The quality, pressure, flow rate, and temperature of the water used for reprocessing should be specified in the dialyzer reprocessing manual, established before the initiation of a reprocessing program, and maintained thereafter. The manufacturer or designer's recommendations for the water supply should be followed. Provision should also be made for adequate drains, ventilation, and electrical power.

7.2.2 Process control testing

7.2.2.1 Dialyzer test methods (11.3) shall be established before clinical use of the reprocessed dialyzers. Verification of tests should be repeated after each significant change in the reprocessing system. For automated systems, adherence to the manufacturer's instructions can verify the tests. For manual systems, confirmation of the accuracy of total cell volume (TCV) measurement and the membrane integrity test can verify the tests.

7.2.2.2 The test for the concentration of germicide or chemical shall be established before clinical use of the reprocessed dialyzers (11.4.1.6 and 12.3.2). For systems using heat disinfection, verifiable evidence shall be available before the next use that dialyzers have been exposed to the appropriate temperature for the time required.

If chemicals are used to enhance heat disinfection, both a presence test and a verification of time and temperature shall be performed.

7.2.3 Maintenance

Written maintenance procedures and a schedule of preventive maintenance activities designed to minimize equipment malfunctions should be established. In the case of purchased reprocessing equipment or safety equipment, the recommendations of the vendor should be followed unless documented experience supports alternative approaches. If the manufacturer's recommendations are not available, reuse equipment and safety equipment should be inspected on a semiannual basis. A record shall be kept of preventive maintenance activities (see 4.3), accompanied by the signature of the person performing the maintenance.

7.2.4 Repairs

If the reprocessing system fails to function as expected, qualified personnel should investigate and repair the problem. The reprocessing system function testing should be repeated after repairs of automated equipment and, if appropriate, after repairs of manual equipment before either the dialyzer is reprocessed or the reprocessed dialyzer is used for clinical dialysis.

8 Physical plant and environmental safety considerations

8.1 Reprocessing area and ventilation

The reprocessing area should be designed to suit the operation carried out and maintain acceptable ambient concentrations of harmful substances (see Table 1). The area should be kept clean and sanitary. It may be part of the dialysis treatment area, as long as equipment used is properly designed and vented to meet the requirements for environmental safety (see 8.5).

Table 1—OSHA environmental exposure limits (29 CFR 1910, 1 July 1998), except as indicated

Substance/material	**Limits (PEL)**[a)]
Acetic acid	10 ppm TWA[b)]
Chlorine dioxide (syn: chlorine oxide)	0.1 ppm TWA
Citric acid	None developed
Formaldehyde	0.75 ppm TWA 2 ppm STEL[c)] (15 min) 0.5 ppm action level
Glutaraldehyde	0.2 ppm ceiling NIOSH/OSHA
Hydrogen peroxide	1 ppm TWA
Peracetic acid	None developed
Phenol	5 ppm TWA

ppm = parts per million

[a)]PEL (permissible exposure limit) represents the limit of what employees can be exposed to; PELs can be TWAs or STELs.

[b)]TWA (time-weighted average) represents the limit of what an employee can be exposed to in an eight-hour period.

[c)]STEL (short-term exposure limit) represents the limit of what an employee can be exposed to in any 15-minute time period.

8.2 Storage area

Reprocessing materials, hemodialyzers awaiting reprocessing, and reprocessed hemodialyzers should be stored so as to minimize deterioration, contamination, or breakage. New, used, and reprocessed dialyzers should be segregated to make clear the status of each group of dialyzers. Environmental contamination of the storage area should be controlled and monitored, if the personnel determine those actions to be necessary. Storage areas for new dialyzers and reprocessing materials should be designed to facilitate rotation of stock and cleaning. Storage arrangements should also take into account fire safety considerations, OSHA regulations, and other appropriate regulations.

8.3 Laboratory area

Tests that do not require special facilities, such as certain tests for germicide levels, may be done in the reprocessing or dialysis treatment area, whichever is appropriate.

8.4 Personnel protection

Personnel shall wear durable gloves and protective clothing when handling the dialyzer during initiation and termination of dialysis and during the reprocessing procedure. Standard Precautions shall be observed. Personnel shall wear eye protection when performing steps that may result in spills or splashes of substances of known or suspected toxicity. These agents shall be handled only in areas with adequate ventilation, washing facilities, eye-wash stations, appropriate respirators, and spill control materials. When personnel are handling concentrated toxic substances, they shall wear aprons impervious to these substances.

8.5 Environmental safety

The dialysis facility shall have written procedures for safe storage and handling of chemicals used in reprocessing (see National Institute for Occupational Safety and Health [NIOSH]/OSHA, 1980; Sax, 1979; material safety data sheets [MSDS]). Vapors from reprocessing materials must be maintained below potentially toxic levels (see Table 1).

9 Reprocessing supplies

9.1 Specifications and testing

Each reprocessing material should meet a written specification. The fulfillment of that requirement may be determined by certification by the product's supplier that the product meets necessary specifications, labeling for its intended purpose, or by testing procedures by trained personnel, as appropriate. The requirement may also be complied with by purchasing a specific grade as specified by the process, such as USP citric acid. When the user performs testing, he or she should maintain a log of the date of test, the identifying number (lot number) of the batch, the person performing any testing, and the test results. Over the past few years, bleach (sodium hypochlorite) manufacturers have begun selling household bleach in many new formulas. The concentration of sodium hypochlorite has gone from 5.25 % to 6.15 % in many cases. The CDC has not changed its recommendations for diluting the bleach to take into account these percentage changes. However, manufacturers of bleach have also begun using additives such as fragrances and scents in their products commercially marketed in grocery stores. When bleach is purchased from a commercial outlet, the labeled concentration should be between 5.25 % and 6.15 %, and the formula should not contain fragrances or scents.

9.2 Inventory control

Reprocessing supplies should be used on a first-in, first-out basis, and outdated supplies should be identified and discarded.

10 Hemodialyzer labeling

Each reprocessed hemodialyzer shall be used for only one patient. Therefore, the labeling shall uniquely identify the patient who is using the dialyzer. The dialyzer should also be labeled with other information essential to proper reuse procedure.

10.1 Time of labeling

Each hemodialyzer shall be labeled before or at the first use of the device, and the label shall be updated after each use (see 10.3).

10.2 Label composition

Markings should be resistant to normal reprocessing and dialysis procedures. The dialyzer labeling should not obscure the manufacturer's model number, lot number, or indicators of the direction of blood or dialysate flow or other pertinent information unless provision is made for recording this information on the label. The label on hemodialyzers with transparent casings should permit the blood path to be readily inspected.

10.3 Information recorded

The dialyzer shall be labeled with the patient's name, the number of previous uses, and the date of the last reprocessing. Dialyzers of patients with similar last names should have a warning to the user to take extra care in ensuring that the name or other identifying information on the label corresponds to that of the patient. If there is sufficient room, the dialyzer may also be labeled with the results of tests, the signature or other unique means of identifying the person performing the various steps in the reprocessing procedure, and the reference values for performance parameters. If this information appears on the label, a permanent record should also be kept (see 4.2).

Electronic records are acceptable. If records are electronic, the test results should be available to the user. Home dialysis patients are exempted from the recommendation that the patient's name appear on the label, unless the dialyzers are taken to a dialysis facility for reprocessing.

11 Reprocessing

The multiple use of a dialyzer begins with the labeling of the new dialyzer (see section 10) and then continues with the reprocessing procedures described in this section. Preparation of the reprocessed dialyzer for the next dialysis is described in section 12. The cycle is repeated after the next use of the dialyzer until the dialyzer does not meet the criteria for continued use. A systems diagram of these procedures is given in annex B (normative). The results of the tests and the signature or other unique means of identifying the person performing each step should be maintained in a permanent record (see 4.2). Completion of all reprocessing steps, tests, and inspections should be documented in the reprocessing record, accompanied by the signature or other unique means of identification of the person completing them. When appropriate for the reprocessing procedure in use, all dialyzer manufacturer's instructions regarding reuse should be carefully followed.

11.1 Transportation and handling

Persons handling used dialyzers during transportation shall do so in a clean and sanitary manner maintaining Standard Precautions until the dialyzer is disinfected both internally and externally. To inhibit bacterial growth, dialyzers that cannot be reprocessed within 2 hours should be refrigerated and not allowed to freeze. Other transportation and handling issues (such as prolonged delays in reprocessing) not described in this recommended practice shall be validated and documented by the responsible party.

11.2 Rinsing/cleaning

11.2.1 Many facilities preclean dialyzers. This process is typically accomplished with an apparatus developed by users and is intended to remove gross deposits of blood and products before rinsing and cleaning with a reprocessing machine or device. When precleaning is done, it is necessary to include it as part of the reprocessing procedures. All applicable requirements for design and maintenance of equipment included in this document should be adhered to for precleaning of equipment. The maximum pressures for the dialyzer, or other limits set by the manufacturer, should also be adhered to.

11.2.2 Dialyzer reprocessing should be initiated in sufficient time to produce a reprocessed device that meets the requirements of section 11.3. Each dialysis facility should establish its time limits. Staff involved in handling, transporting, or storing of dialyzers locally or at remote locations shall follow Standard Precautions to prevent exposure to the operator and contamination of the physical environment.

11.2.3 Precleaning the dialyzer (rinsing and cleaning) shall be done with a fluid or fluids made with water that meets the specification of the current version of ANSI/AAMI RD62, *Water treatment equipment for hemodialysis applications*.

11.2.4 Diluted solutions of hydrogen peroxide, sodium hypochlorite, peracetic acid, or other chemicals may be used as cleaning agents for the blood compartment, provided that the cleaning agent has been shown to be reduced to safe levels by subsequent flushing and has no significant adverse effects on the structural integrity and performance of the dialyzer.

Each chemical shall be rinsed from the dialyzer before the next chemical is added, unless mixing is known to be safe and effective for reprocessing. For example, a cleaning agent, such as sodium hypochlorite, shall be rinsed from the dialyzer before adding formaldehyde in order to avoid noxious fumes and degradation of disinfectant. Combining sodium hypochlorite and peracetic acid may produce hydrochloric acid vapors, which are harmful if inhaled.

11.3 Performance measurements

The performance characteristics of dialyzers may change following reprocessing. The ultrafiltration coefficient may increase or decrease. Clearances of small or large molecular weight solutes may also increase or decrease depending on the chemicals, methods, and dialyzer membrane used. The dialyzer labeling and medical literature should be consulted for information related to changes in *in vitro* and *in vivo* performance.

11.3.1 Performance test after each use

A direct or indirect measure of the *in vitro* clearance of a small molecule such as sodium or urea shall be used as the actual rejection criterion. If clearance is used, a 10 % loss is acceptable. Total cell volume (TCV) may be used for hollow-fiber dialyzers. The acceptable TCV is at least 80 % of the original TCV. The dialyzer prescription should take into account the 10 % loss in clearance (20 % loss in TCV) that may occur with dialyzer reuse. Whenever possible, dialyzers should be preprocessed to establish the original TCV. If it is not possible to preprocess the dialyzer to obtain a baseline total cell volume, other methods such as "volume averaging of the lot" should be used.

11.3.2 Ultrafiltration

In vitro ultrafiltration coefficients should not be used to predict *in vivo* results. If the expected weight loss is not achieved with the reprocessed dialyzer, the reprocessing method and all other weight removal variables should be reevaluated.

11.3.3 Blood path integrity test

A membrane integrity test such as an air pressure leak test shall be done between uses.

11.4 Germicide

The rinsed and cleaned dialyzer shall be treated by a process that prevents adverse effects caused by microbial contamination. The blood and dialysate compartments of the dialyzer shall be sterilized or subjected to high-level disinfection because an inadequate germicidal process may result in infection in the patient. Low-level disinfection is sufficient for the exterior of the device. The user shall consult the dialyzer labeling for contraindications or warnings regarding methods and applicability of specific germicidal processes or chemicals.

11.4.1 Interior (blood/dialysate compartment)

11.4.1.1 Germicidal process

Chemical germicides or other procedures used for disinfecting of hemodialyzers shall have been shown to accomplish at least high-level disinfection when tested in dialyzers artificially contaminated with appropriate microorganisms. If formaldehyde is used as the sole germicidal agent, the CDC recommends that a concentration of 4 % (W/V) be used in both the blood and dialysate compartments with a minimum contact time of 24 hours at a temperature of at least 20 °C; lower concentrations or shorter contact times are appropriate if equivalent results can be demonstrated under other conditions. Formaldehyde used for reprocessing dialyzers should not be cloudy. Concentrated formaldehyde stored under adverse conditions can polymerize to form paraformaldehyde, a white precipitate. Formaldehyde should be of *United States Pharmacopoeia* (USP) or better quality. When other germicides are used, the manufacturer's instructions should be followed. If the germicide has an expiration date from the manufacturer, staff members should be sure that the chemical is not outdated. Some germicides have recommendations for maximum storage time after dilution or activation and before usage. If this is the case, the expiration date of the prepared germicide solution should be marked on the outside of the germicide solution container, and that date should be checked at the beginning of each day, before reprocessing begins. If other germicides such as heat and citric acid are used, it is necessary to ensure that the correct time, temperature, and concentration are being used. If the temperature of the disinfection process is elevated, appropriate recording means shall be employed to ensure that this criterion has been met. If maximum storage temperature limitations exist, records should be maintained to document this criterion. The disinfection process shall not adversely affect the integrity of the dialyzer. Germicides shall be rinsed from the dialyzer to below known toxic levels within a rinse-out period established for the particular germicide (see 12.4). To prevent injury, staff members shall take care not to mix reactive materials such as sodium hypochlorite and formaldehyde.

11.4.1.2 Dialyzer header cleaning and disinfection

The cleaning and disinfection of the header space should be done only when necessary and only before the dialyzer is reprocessed. The manufacturer's instructions should be followed. Header caps and O-rings shall be kept with their respective dialyzers.

If the header space is cleaned, it shall be done in a manner to prevent infection and damage to the dialyzer. If the header cap is removed to clean the header space, cleaning shall be done with water meeting the requirements of the current version of ANSI/AAMI RD62, *Water treatment equipment for hemodialysis applications.*[2] If instruments or other materials (e.g., header caps and 4x4 gauze pads) are used, they should be shown not to cause damage to the end of the dialyzer and shall be new or cleaned and disinfected between uses. Once the O-ring and the header cap are cleaned and before they are reassembled at the end of the dialyzer, they should be disinfected. The disinfectant shall not be rinsed and shall be allowed to remain on the dialyzer components as they are reassembled. This procedure is done before reprocessing the dialyzer. Overtightening the header caps may cause damage to the cap, and undertightening the cap may cause blood leaks. If any cracking of the header occurs, the process should be evaluated.

If the header space is cleaned with the header cap in place, it is necessary to ensure that the end of the fiber bundle is not damaged. If water is used, it shall meet the requirements of the current version of ANSI/AAMI RD62, *Water treatment equipment for hemodialysis applications*. If an instrument such as a tie wrap is used, it should be made of soft plastic or other material that will not damage the end of the fiber bundle and be disinfected between uses.

If automated equipment is used, the manufacturer's instruction for use shall be followed.

[2] The CDC recommends that only a stream of RO water be used to rinse clots from the headers of the dialyzer.

11.4.1.3 Chemical germicide diluent

The water used to prepare the germicide solution shall meet the requirements of the current version of ANSI/AAMI RD62, *Water treatment equipment for hemodialysis applications*.

11.4.1.4 Chemical germicidal procedure

If applicable, the hemodialyzer shall be filled with the germicide solution until the concentration in the hemodialyzer is at least 90 % of the prescribed concentration. The ports of chemically disinfected dialyzers shall be disinfected and then capped with new or disinfected caps. The caps may be disinfected with dilute bleach, with the chemical used for disinfecting the hemodialyzer, or with any other germicide approved by the FDA as a disinfectant that does not adversely affect the materials of the dialyzer.

11.4.1.5 Water quality monitoring

The water used to rinse and clean dialyzers and dilute the germicide should be tested for bacterial contamination and pyrogens according to the requirements of the current version of ANSI/AAMI RD62, *Water treatment equipment for hemodialysis applications*, before a reprocessing program is undertaken. Once dialysis with the reprocessed hemodialyzers has begun, testing for bacterial contamination should be frequent (e.g., weekly). Less frequent testing, but not less than monthly, may be appropriate if there is a documented history of at least 3 months of results consistently below the levels allowed in the current version of ANSI/AAMI RD62, *Water treatment equipment for hemodialysis applications*.

11.4.1.6 Chemical germicide concentration

Reprocessing systems in which each batch of germicide is manually prepared, each batch of germicide shall be tested before use to verify the proper concentration of the germicide. This requirement does not apply in cases in which each dialyzer is tested for concentration before setup. When the germicide is diluted on-line, its concentration in the hemodialyzer immediately after reprocessing should be checked at least monthly for each reprocessing system. When the germicide is partially or fully diluted by the user, it is of great importance that the solution be thoroughly mixed.

11.4.2 Exterior

The outside of the dialyzer should be soaked or wiped clean of visible blood and other foreign material. For chemically disinfected dialyzers, a low-level germicide that is compatible with the dialyzer's materials of construction should be used for this purpose. Sodium hypochlorite at a concentration of 0.05 % is usually suitable. Certain commercial low-level disinfectants may cause some plastics used for dialyzers to crack after repeated or prolonged exposure.

11.5 Inspection

The hemodialyzer shall be examined after reprocessing to ensure that the external surface is clean, the dialyzer is not damaged, and the rinsing of blood has been satisfactorily completed. The dialyzer should also be aesthetically acceptable in appearance to patients and staff.

11.5.1 The dialyzer jacket should be free of visible blood or other foreign material.

11.5.2 There shall be no leaks or cracks in the dialyzer jacket or the blood or dialysate ports.

11.5.3 No more than a few dark, clotted fibers should be evident on inspection of the exterior of the hollow fibers.

11.5.4 The headers of hollow-fiber dialyzers should be free of all but small peripheral clots or other deposits.

11.5.5 Blood and dialysate ports shall be capped without evidence of leakage.

11.5.6 The label shall be properly filled out and legible.

11.6 Disposition of rejected dialyzers

Reprocessed dialyzers that have been rejected for failure to meet performance, inspection, or other release criteria should either be immediately discarded or further reprocessed and subjected to the performance requirements of 11.3, 11.4, and 11.5. If the dialyzer is to be further reprocessed, rather than discarded, it shall be labeled as rejected and stored in a quarantine area to preclude use until requirements are met.

11.7 Storage

Reprocessed dialyzers that meet the performance and inspection criteria for multiple use should be stored according to the provisions of 8.2. Prolonged storage (greater than 1 month) should be documented to be safe and effective.

Dialyzers that have exceeded the facility's maximum storage time shall be reprocessed or discarded. The dialyzer and disinfectant labeling should be consulted regarding proper storage conditions.

12 Preparation for dialysis and testing for chemical germicides and potentially toxic residues

A written procedure that has been shown to be effective shall be followed.

12.1 Visual inspection

The dialyzer should be inspected before it is prepared for use. Completion of this inspection should be recorded in the reprocessing record (see 4.2), along with the signature or other unique means of identifying the person completing the inspection. The inspection should include the following:

a) The reprocessed dialyzer shall be legibly labeled with the information recommended in 10.3.

b) There should be no indication of structural damage or tampering with the dialyzer.

c) The ports of the dialyzer should be properly capped.

d) The presence of germicide in the dialysate and blood compartments, including headers, should be confirmed, and there should be no evidence of leakage from the ports or other portions of the dialyzer.

e) The duration and conditions of storage should be appropriate for the agent or method used to sterilize or disinfect the dialyzer; and

f) The cosmetic appearance of the dialyzer should be aesthetically acceptable to the staff and the patient.

12.2 Verification of patient identification

Except in the case of home dialysis, two persons should check that the first and last names on the dialyzer and any other appropriate identifying information correspond to the identifying information on the patient's permanent record. If possible, one of the persons checking identification should be the patient. Completion of this step shall be recorded, along with the signature or other unique means of identifying the person verifying patient identification.

NOTE—This step may be done later in the procedure but shall precede initiation of dialysis.

12.3 Verification of germicidal contact

The contact time of the germicide or disinfection procedure shall comply with the facility's protocol and the manufacturer's recommendations. The presence of chemical germicide in each hemodialyzer shall be ensured through either direct testing or an on-line process and procedural control. If other disinfection (e.g., heat) procedures are used, there shall be methods to ensure that each hemodialyzer has been properly subjected to the disinfection process. A record shall be kept indicating that the dialyzer has undergone the appropriate storage time, and the record shall be appropriately verified.

12.3.1 Presence test of each hemodialyzer

Certain germicide manufacturers require testing for the presence of germicide in each hemodialyzer before the rinsing step. These instructions should be followed.

12.3.2 Process control and sampling

In the absence of the requirement in 12.3.1, the presence of germicide may be ensured by a direct presence test of each hemodialyzer or the use of process control and sampling of the dialyzer for germicide. Sections 12.3.2.1 and 12.3.2.2 provide examples of what can be used to comply with this requirement.

12.3.2.1 Process control

a) Use hemodialyzer germicide filling equipment with on-line automatic monitors during the germicide dilution and hemodialyzer filling process; or

b) Use an indicator substance (e.g., FD&C Blue #1), which has been added to the germicide, and that reliably indicates the presence of germicide. If blue dye is used, it should be added to the germicide concentrate before dilution, not to the fully diluted solution. Note that use of dye may be inappropriate with certain germicides such as peracetic acid.

12.3.2.2 Sampling for process validation

a) Sample at least one hemodialyzer per patient shift per reuse system with a direct presence test (do not use a Schiff test for formaldehyde for this purpose because it will detect the presence of inadequate concentrations of formaldehyde). Samples should be taken immediately after the dialyzers have been reprocessed.

b) For germicide prepared in batches, sample at least one hemodialyzer from each batch with a direct presence test. Samples should be taken immediately after the dialyzers have been reprocessed.

c) Sampling and testing are to be accomplished before patients use any hemodialyzers processed on this shift.

NOTE—The requirements of this section are fulfilled if every dialyzer is subjected to post-storage/pre-priming direct presence testing.

12.4 Priming the dialyzer and rinsing the germicide

If the manufacturer's instructions so require, a germicide presence test shall be performed before the germicide is rinsed from the dialyzer. The dialyzer shall be rinsed and primed according to a written procedure that has been documented to produce a reduction in the concentration of germicide to an acceptable level and result in a physiological solution in the blood and dialysate compartments. The dialyzer manufacturer's instructions should be considered in developing these procedures.

12.4.1 Testing for residual germicide

Residual germicide shall be measured by a test of appropriate sensitivity according to a written procedure to ensure that the germicide level is below the maximum recommended residual concentration. In the case of formaldehyde, the recommended maximum level is 3 ppm. Completion of this step shall be documented, along with the signature or other unique means of identifying the person performing the test. A written policy should establish the maximum allowable time between rinsing the germicide from the dialyzer and beginning dialysis. Certain germicides have been demonstrated to disperse into solid components or less rapidly exchangeable compartments of the hemodialyzer. The priming, removal, and residual testing process should be reinstituted after a delay sufficient to bring concentrations of germicide above the recommended level (rebound). Additional rinsing should be performed to yield a germicide level below the maximum recommended concentration before initiating of dialysis. A rinse procedure should be defined and documented step by step, and all personnel should be familiar with and follow it. If heat disinfection is used, the dialyzer should be cool to the touch before it is primed with saline.

12.5 Written procedure for tests for germicide or other residues

There shall be a written procedure for all tests employed in preparing the dialyzer for use, including mention of each test's sensitivity. The germicide manufacturer's instructions for use should be consulted in determining the maximum residual level. The physician in charge of the reuse program shall approve any alterations in the procedures.

13 Monitoring

13.1 Dialysis

The clinical course of the patient should be observed and recorded during each dialysis to identify possible complications caused by new or reprocessed dialyzers. Dialyzer failures should be recorded and systematically evaluated. Home dialysis patients and their assistants should be instructed in the appropriate observation, recording requirements, and reporting procedures.

13.2 Symptoms

13.2.1 Fever and chills

Patients' temperatures should be measured and recorded at least before and after dialysis with new and reprocessed dialyzers. A temperature of over 37.8 °C or 100 °F, taken orally, or chills should be reported to the physician. Any patient with an unexplained fever and/or chills should be evaluated for the possibility of a pre-existing infection (e.g., access site). The dialysis procedure should also be evaluated to rule out the use of contaminated water, errors in treatment delivery, or incorrect dialyzer reprocessing.

13.2.2 Other symptoms

Other unexplained symptoms such as pain in the blood-access arm at the onset of dialysis should be evaluated by the physician and consideration given to the possibility that the symptom may be attributed to residual disinfectant in the new or reprocessed dialyzer or contamination of the water treatment equipment. Suspected reactions to the

residual germicide should prompt reevaluation of the rinsing procedure and a test for residual germicide (see 12.4.1).

13.2.3 Recording

Any significant events such as the occurrence of symptoms listed in 13.2.1 and 13.2.2 should be recorded on an incident report form which would include the results of any evaluations conducted by the physician and others, and the event should be considered for reporting to the manufacturer(s) in accordance with the FDA's Medical Device User Reporting procedures. The resolution of actual or suspected problems caused by reprocessed dialyzers should be indicated. This form should be kept in the complaint investigation record file (see 4.5).

13.3 Dialyzer failures

Dialyzer blood leaks should be recorded in a log kept in the complaint investigation record file (see 4.5). If there is excessive deviation from the expected performance, testing should be repeated (see 11.3.1) and appropriate adjustments made in the reprocessing procedure.

13.4 Clinical results

Monitoring of relevant patient results is recommended to ensure that all parameters relating to hemodialyzer clearance are being met. Specifically, examination of urea reduction ratio (URR) or Kt/V over time is necessary. The failure of these results to meet the expectations of the dialysis prescription should be investigated. Deterioration of a patient's clinical condition or variability of routine dialysis procedures (heparinization, ultrafiltration, erythropoieten requirement) requires investigation of all practices, including reuse. Reports of investigations should be filed in the complaint log.

14 Quality assurance

It is the responsibility of all staff members to critically scrutinize all materials, practices, operations, and outcomes. Criteria that serve as the scale for evaluation may be drawn from local experience and practice relative to the specific activity under review, consensus documents such as AAMI guidelines or standards, aggregated regional or national data, or other accepted norms. The criteria chosen as the internal standards of a facility shall be documented in its policy and/or procedure manual. Process review should be part of the activity of the individual carrying out the process, and oversight of that review by another qualified member of the staff or a group of staff members should affirm, modify, or repeat these observations to confirm or improve the process. Clinical outcomes serve as the most important indicator of quality of all dialysis treatment practices including reuse. Final oversight is the responsibility of the medical director. See Table 2 for a summary of the audit schedule.

Table 2—Quality assurance audit schedule

	Daily	Weekly	Monthly	Quarterly	Semi-annually	Annually
Patient information policy (14.3)						x
Equipment manuals and procedures (14.4)						x
Equipment maintenance and repair policies (14.4)						x
Environmental safety (8.1)						x
Environmental safety (8.2)				x		
Environmental safety (8.4)				x		
Reprocessing supplies (9)					x	
Water treatment* (11.4.1.5)			x			
Hemodialyzer labeling (10)				x		
Reprocessing procedures** (14.8)			x		x	
Procedures for preparation for dialysis (14.9)				x		

* More frequent monitoring may be required initially as described in 11.4.1.5.

** These functions may allow for the less frequent review period indicated according to the circumstances specified in their respective sections.

14.1 Records

A record of review, comments, trend analysis, and conclusions arising from QA practices will serve as a foundation for future review and as documentation to external evaluation.

14.2 Schedule of quality assurance activities

Problems in a particular aspect of operations should be reviewed and tracked until a solution is in place and demonstrated to be effective. High-volume tasks that are recognized as hazardous should have frequent (weekly or daily) oversight. Practices with little potential for harm may need critical scrutiny on only a quarterly or annual basis. The medical director is responsible for scheduling review, endorsing findings, and, when appropriate, implementing changes.

14.3 Patient considerations

Personnel should audit at least annually compliance with the facility's policy to inform patients of the facility's reuse practices.

14.4 Equipment

Designated staff members should audit written procedures and manuals for relevance at least annually and whenever adverse findings could be attributed to equipment failure. Designated staff should also audit maintenance and repair policies at least annually.

14.5 Physical plant and environmental safety considerations

Designated staff members should audit the provisions of 8.1 at least annually. The provisions of 8.2 and 8.4 should be audited quarterly.

14.6 Reprocessing supplies

Designated staff members should audit the provisions of section 9 at least semiannually.

14.7 Hemodialyzer labeling

Designated staff members should audit the provisions of section 10.

14.8 Reprocessing

Initially, designated staff members should audit the written procedures for the various steps in this process and verify implementation at least monthly. Subsequently, semiannual audits may be sufficient if there is a documented history of favorable results. Trend analysis should be performed.

14.9 Preparation for dialysis

At least quarterly, designated personnel should audit the written procedures and verify their implementation. At least quarterly, designated staff members should verify the tests for the presence of germicide and the test for residual germicide by using positive and negative control solutions, on those products that are not specifically intended for use in dialyzer reuse germicide indicator tests and which have not been cleared by the FDA.

Annex A
(informative)

Rationale for the development and provisions of this recommended practice

A.1 Scope

The practice of reusing dialyzers has been performed in the United States since the 1960s. Until the mid-1990s, even dialyzers labeled by manufacturers for single use were reused. Reuse was an accepted practice performed by approximately 80 % of dialysis facilities. As an understanding grew of the effects of reuse on dialyzer performance, it became apparent that the dialysis community needed to be better informed.

In light of the widespread practice of reuse and its potential effect on patient care, the Food and Drug Administration (FDA) determined that manufacturers' labeling must reflect the actual commercial marketing and clinical use of hemodialyzers.

Labeling requirements for multiple-use dialyzers are covered in the FDA's "Guidance for Hemodialyzer Reuse Labeling," of 6 October 1995. Dialyzers labeled for multiple use must include instructions for their safe and effective reuse. Manufacturers are expected to recommend at least one method of reuse for dialyzers labeled for multiple use. *In vitro* performance data at various flow rates for K_{UF} as well as clearance of urea, creatinine, and vitamin B_{12}/inulin must be provided at the 0, 1st, 5th, and 15th reuse. *In vivo* performance data at various flow rates for K_{UF} as well as clearance of urea (spKt/V – URR), albumin, and β_2 microglobulin (high flux only) must also be provided.

Instructions for adequately cleaning, rinsing, and testing the dialyzer as well as instructions for preparation before use (priming) must be included in the labeling (package insert). Warnings must be included against the use of any reprocessing agents or processes known to adversely affect the manufacturer's dialyzer.

Initially, blood tubing sets reprocessed as a unit with the hemodialyzer were included within the scope of this recommended practice to accommodate such reprocessing methods. The committee subsequently decided to exclude blood tubing sets because it believed that insufficient data exist on the practice of blood tubing reuse. In making this decision, the committee did not take a position either for or against the reprocessing of tubing sets. The Centers for Medicare & Medicaid Services (CMS) Conditions for Coverage of Suppliers of End-Stage Renal Disease (ESRD) Services limits the reuse of blood tubing to those tubing sets for which the manufacturer has developed a specific reprocessing protocol which has been accepted by the FDA. Further information on the reprocessing of blood tubing can be found in AAMI TIR6:1990, *Reuse of hemodialyzer blood tubing*.

Labeling and performance requirements for new hemodialyzers are covered by ANSI/AAMI RD16, *Hemodialyzers*.

A.2 Normative references

For the purposes of this recommended practice, the references cited in section 2 apply.

A.3 Definitions

For the purposes of this recommended practice, the definitions given in section 3 apply.

A.3.13 Hemodialyzer: Initially, the FDA used the water permeability to classify dialyzers into Class II (Conventional, K_{UF} < 8 mL/h/mmHg) or Class III (High Permeability, K_{UF} > 8 mL/h/mmHg). However, the dialysis community has most commonly used the terms "high flux," "low flux," and "high efficiency." In 1997, the HEMO Study defined low-flux dialyzers as having "a mean clearance of β_2 microglobulin < 10 mL/min during the first use" and high-flux dialyzers as having "an ultrafiltration coefficient (K_{UF}) > 14 mL/h/mmHg and a mean β_2 microglobulin clearance of > 20 mL/min during the first use or over the lifetime of the dialyzer model with a given reprocessing method." High efficiency refers to dialyzers that can remove relatively large amounts of low molecular weight solutes. Currently the FDA still uses water permeability to differentiate between high-flux and conventional dialyzers. A high-flux dialyzer will have a K_{UF} of > 8 mL/h/mmHg, whereas a conventional dialyzer will have a K_{UF} of < 8 mL/h/mmHg.

In 1997, AdvaMed (formerly HIMA) filed a request with the FDA on behalf of all dialyzer manufacturers to reclassify high-flux dialyzers from Class III into Class II. This request was accepted and all dialyzers, hemofilters, and hemoconcentrators are now Class II. This device classification has no effect on the user. It identifies the risk category and marketing clearance scheme for the manufacturers.

A.3.16 Lipopolysaccharide (LPS): is not destroyed by low-temperature chemical disinfection procedures commonly used with dialyzer reuse, but may be destroyed by exposure to temperatures of 95 °C and 1.5 % citric acid for 20 hours (McAllister, Arduino, Bland, 1994).

A.4 Records

Documentation is essential to a safe, effective hemodialyzer reprocessing program. The overall dialyzer reuse procedure documentation includes reference materials, procedures, and policies, some of which may be distributed in the facility for operating purposes. The other records serve to document aspects of the reuse procedure for each dialyzer, along with QC and QA measures, so that a complete history of the reprocessing of each dialyzer and QC/QA procedures exists. The committee felt that when the useful life of a dialyzer is over and no notable events have occurred, the reprocessing records for that dialyzer need not be kept. Allowance is made for keeping the reprocessing record data in the reprocessing log, the patient's chart, or a combination of the two, because both of them are traceable, permanent records, and it may be inconvenient to record all of the information in one location. The committee decided not to include a specific recommendation for a checklist for initiating dialysis because, although a checklist is a convenient way to ensure that the procedure is followed, the same purpose can be served by completing the recommended documentation for preparing the reprocessed dialyzer for dialysis (see 12.1, 12.2, and 12.4.1).

A.4.1 Dialyzer reprocessing manual

The committee rejected a proposal to include a statement that the dialyzer reprocessing manual should not recommend or describe any methods for which the dialyzer or disinfectant manufacturer has indicated a contraindication.

A.5 Personnel qualifications and training

The committee rejected a proposal to include curricula covering the entire range of technical activities related to dialysis. The committee felt that more limited training is appropriate as a minimum for personnel who are not involved in other aspects of dialysis. A proposal to recommend that training could be less extensive for personnel with relevant previous training also was not rejected because certification of training (see 5.2.2) renders the recommendation superfluous.

A.6 Patient considerations

A.6.1 Medical issues

The committee's primary objective was not to recommend medical indications for reprocessing or evaluate the medical or economic implications of reprocessing but to provide recommendations for safe reuse practice.

At the time of this writing, the Centers for Disease Control and Prevention (CDC) does not object to reprocessing and reusing dialyzers from patients with hepatitis C or patients with known HIV infection because of the low viral burden and transmission efficiencies. The committee recommends, however, that standard precautions be used in the reprocessing of all dialyzers. These precautions include the use of gowns, masks, and gloves. Each facility should be aware of the hazards of infection and set policies accordingly.

A.6.2 Informed consent

The committee decided, upon legal advice, that it is not appropriate for an AAMI recommended practice to suggest elements of informed consent, although this section originally contained them. The committee considered the following arguments about this issue. Those who believe that specific informed consent for the use of reprocessed hemodialyzers ought to be required maintain that greater patient participation in the therapeutic process need not impair the physician's ability to deliver quality care. Rather, they say, involvement ensures that quality care will remain the primary impetus of decisions to reuse. Those who do not agree with informed consent specifically for multiple use of hemodialyzers point out that specific consent is not required for the other aspects of dialysis therapy and could be counterproductive because of the confusion that could be created by personal preferences for, as examples, length of dialysis, choice of blood flow, fluid removal rate, and the like. They argue that multiple use of hemodialyzers can properly be implied in the consent for hemodialysis therapy as are other therapy parameters. Those backing this view also assert that for most patients honest, trusting interaction with their personal physicians is a sufficient guarantee of quality, and imposing a dictatorial relationship may lead patients to seek recourse through legal means.

The topic of physician-patient relationships is important in view of the concerns of some patients about the adequacy and safety of reprocessing procedures and the possibility that financial savings from the multiple use of hemodialyzers might contribute to the economic benefit of others rather than to the improvement of the quality of care. The committee also considered the question of the patient's right to freely choose not to participate in a hemodialyzer reprocessing program. Consensus could not be reached on this issue because of the underlying conflict between individual self-determination and financial constraints imposed by society (Rettig, 1982).

Some patients have expressed fear of increased risk, anger over presumed profits, and frustration surrounding consent issues. Establishing QA practices such as those recommended here and sharing information with patients,

educating them, responding to questions, and eliminating any impression of secrecy are encouraged as effective solutions to these problems.

The fact that most of dialysis facilities reprocess hemodialyzers and the long history of this technique support the conclusion that multiple use of hemodialyzers is customary medical practice. Courts might find that consent for dialyzer reprocessing per se is not required, but this issue has not yet been adjudicated.

The National Kidney Foundation's position paper and the American Association of Kidney Patients recommend that patient consent for dialyzer reuse be obtained.

A.7 Equipment

Validation of dialyzer performance and of the concentration of germicide was initially recommended after the repair of automated equipment to guard against possible faulty functioning of this complex apparatus. The recommendation was tempered by the words "if appropriate" for manual systems because replacing hoses, valves, and the like in those simple systems will not affect performance. The recommendation was subsequently changed to include testing the function of the reprocessing system because the committee judged that demonstrating proper functioning of the system is an adequate QC measure.

An earlier recommendation that the system prevent cross-contamination of water used for reprocessing and water used for dialysis was based on an episode in which water containing formaldehyde was introduced into water used for dialysis. The committee decided to delete this recommendation because the mishap was not attributable to a reprocessing system (the formaldehyde was put into the water system for dialysis to disinfect that system) and because it may be desirable to use the same source for the water used for dialysis as the water used for reprocessing hemodialyzers in order to achieve the recommended water quality.

It is particularly important that all water that comes into contact with the fluid pathways for blood or dialysate be of recommended quality because the blood side of the dialyzer might take up endotoxin that could be released into the circulation during the subsequent dialysis.

A.8 Physical plant and environmental safety considerations

A proposal that the reprocessing area be supplied with HEPA-filtered air, a laminar flow station, and positive pressure to surrounding areas was rejected. Such measures to control bacterial contamination were deemed inappropriate for reprocessing because the exposure of the dialyzer to bacterial contamination is limited to making connections comparable to setting up the device for dialysis. Another proposal that the reprocessing area be negatively pressurized to control odors was rejected because the committee agreed that other methods can achieve odor control. The committee also determined that it was not necessary to recommend facility design, because a number of configurations have been shown to be satisfactory, including use of automated equipment in the dialysis treatment area.

The statement about personnel health monitoring was included in response to a comment referring to the CFR (Chapter 29, Part 1910.20), which addresses access to employee exposure and medical records. The committee is unaware of any state department of public health that requires personnel health monitoring in this area, but the states themselves are another possible source of information on this question.

A.9 Reprocessing supplies

A.9.1 Specifications and testing

Testing of all incoming materials had been proposed. In recognition of the fact that most medical supplies are certified by the vendor and not tested by the user, the committee decided to recommend that supplies need not be tested by the facility doing hemodialyzer reprocessing if they are marketed for hemodialyzer reprocessing.

A.9.2 Inventory control

The committee suggested that supplies should be used on a first-in, first-out basis to avoid deterioration over time in storage.

A.10 Hemodialyzer labeling

A.10.1 Time of labeling

The committee recognized the importance of identifying the patient who will be exclusively using the dialyzer and required the dialyzer to be labeled at the time of first use.

A.10.2 Label composition

The committee initially recommended using indelible ink to label the dialyzer but changed the recommendation to any method resistant to normal reprocessing and use procedures; other satisfactory materials exist, and requiring indelible ink might preclude some techniques, such as bar coding.

A.10.3 Information recorded

A proposal that the label contain all of the recommended information was rejected because space is limited on the label, and such extensive labeling is unnecessary. Displaying the number of previous uses on the label is recommended so that this information is readily available. Displaying the date of the last reprocessing facilitates verification that sufficient time has elapsed since the introduction of the germicide to achieve sterilization or disinfection.

Home dialysis patients are exempted from the recommendation that the patient's name appear on the label, unless the dialyzers are taken to a dialysis facility for reprocessing. It is the intent of the committee to make certain that the correct dialyzer is used on the patient. Requiring special labeling for home patients would normally not be necessary, unless the dialyzer was being transported outside the home, because only one patient would have access to the dialyzer.

A.11 Reprocessing

A.11.1 Transportation and handling

It was recommended at first that only disinfected caps be used to occlude the ports of the dialyzer. This recommendation was modified to include caps from the same dialyzer maintained in a clean condition, because experience indicates that this method is acceptable. The committee later decided that this recommendation is adequately addressed by the general statement about handling the hemodialyzer in a clean and sanitary manner.

During the 2002 revision of this recommended practice, the committee recognized that the refrigeration temperature of the dialyzers stored for extended periods of time was not specified. It was decided to recommend that dialyzers not reprocessed within 2 hours should be refrigerated and not allowed to freeze. The committee believed that this was sufficient to retard bacterial growth.

A suggestion was also made that unprocessed dialyzers be stored in bags until they were reprocessed to minimize the risk of cross-contamination between dialyzers. This method would accomplish the requirements in this section; other methods have also been successfully used.

A.11.2 Rinsing/cleaning

A.11.2.1 The committee considered stipulating a period of time after dialysis within which reprocessing should begin. Consensus was not reached on the period of time, and the committee decided that meeting performance guidelines is the goal of such a specification. Aqueous liquids rather than gases such as air are the preferred fluid for rinsing and cleaning (Bass, et al., 1973).

A.11.2.2 A proposal that only treated water or physiological saline be used was not at first accepted, because some safe and effective techniques use untreated water or nonphysiological concentrations of solute in the rinsing solution. The committee thought that the important goals were meeting the recommendations for satisfactory performance (see 11.3) and ensuring the presence of a physiological solution in the dialyzer before starting dialysis (see 12.4). After further comment and review, the committee endorsed as a reasonable safeguard the use of water meeting AAMI bacteriological standards (AAMI, 1982) or having a maximum level of bacterial LPS of 1 ng/mL. In 2001, the committee created a separate standard, ANSI/AAMI RD62, *Water treatment equipment for hemodialysis application*s, which is now referenced throughout this document.

Originally, the chemical quality of the water was not specified because of lack of consensus on this issue. Although the committee agreed that high-quality water is not necessary to protect the patient from chemical contamination, it recognized that data exist suggesting that reprocessing with water of reverse osmosis quality yields more reuses (F. Gotch, personal communication). ANSI/AAMI RD62, *Water treatment equipment for hemodialysis applications*, now contains chemical standards for water for dialyzer reuse.

The committee had included a recommendation that any device that interfaces between the blood compartment and the permanent equipment should be cleaned and disinfected between each hemodialyzer reprocessed. The recommendation was deleted because permanent equipment sometimes makes a direct connection with the hemodialyzer and because data demonstrating the need for the recommendation is lacking.

A.11.3 Performance measurements

As dialysis facilities have attempted to rigidly comply with the 1986 edition of this recommended practice after its adoption by the Centers for Medicare & Medicaid Services (formerly HCFA), some personnel have misunderstood or expressed concern about the "validation" for indirect measures such as TCV as indicators of performance of reprocessed dialyzers. *In vitro* clearances require special measures and may expose the hemodialyzer to additional risks. *In vivo* clearances are subject to multiple confounding variables. In view of these misunderstandings and concerns, the emphasis of this requirement has been changed. The essential function of the hemodialyzer is mass transfer adequate to provide the prescribed care to the patient. Change in TCV has been documented in the medical literature (Deane and Bemis, 1981) as an indirect measurement having a close relationship to the retained mass transfer of small molecules by the hemodialyzer, and may be used for the routine test of residual dialyzer performance. An integral component of the ongoing verification of the proper performance of the hemodialyzer is the monitoring requirement of section 13.

A.11.3.1 Performance test after each use

Clearance, a measure of the solute transport of the hemodialyzer, should be maintained within acceptable limits to ensure that dialysis is adequate to prevent uremic complications. Because of the established clinical importance of lower molecular weight clearance (Lowrie, et al., 1981), the committee decided that the urea clearance should be the recommended criterion for rejecting a dialyzer. The alternative of sodium clearance was included because sodium and urea clearances are similar, and measuring the former may be more easily accomplished. In developing the first edition of this recommended practice, published in 1986, the committee adopted ± 10 % of the initial value as the maximum acceptable change in the urea or sodium clearance of a reused dialyzer. The basis for this decision was the belief that a ± 10 % change in urea clearance would not result in a clinically significant change in a patient's predialysis blood urea nitrogen (BUN) concentration. Subsequently, it has been recognized that predialysis BUN is a poor marker of dialysis adequacy and that a 10 % decrease in urea clearance could lead to inadequate dialysis if the dialysis prescription was marginal. Therefore, in the 2002 revision of this recommended practice, the committee added a caveat that a ± 10 % change in urea or sodium clearance was acceptable as long as the patient's prescription took into account the possibility of a 10 % decrease in urea clearance.

The committee recognized that the clearance of larger molecules is largely membrane limited (Collins and Ramirez, 1979; Dorson, et al., 1983) as opposed to the clearance of small molecules, which is largely flow-rate limited. Larger molecule clearances will therefore be disproportionately decreased by loss of membrane area or increased membrane resistance caused protein coating of the membrane, as compared with clearances of small molecules (Pizziconi, 1985). In 1986, when this recommended practice was initially developed, the committee considered, but ultimately decided against, a proposal to include vitamin B_{12} clearance as a criterion for rejection. It decided not to include vitamin B_{12} clearance as a rejection criterion because of (a) uncertainty about the significance of protein coating of the membrane in reprocessed hemodialyzers (Gotch, 1985), (b) lack of evidence supporting the clinical relevance of vitamin B_{12} clearance when the change in clearance is within that observed with reprocessed dialyzers, and (c) extensive experience demonstrating the safety of either monitoring urea clearance or using an appropriate indirect test for the urea clearance (Deane and Bemis, 1981). By the time of the 2002 revision of RD47, it had become widely accepted that solutes much larger than vitamin B_{12} were involved in some of the long-term complications of end-stage renal disease. Further, the committee recognized that the clearance of larger molecules may be affected by the type of reuse cycle used, especially the cleaning agent. Specifically, failure to use a cleaning agent such as bleach that effectively strips adsorbed protein from the membrane may lead to a significant decrease in the clearance of large molecules by high-flux dialyzers, even though the clearance of urea and the TCV are maintained in an acceptable range (Westhuyzen, et al., 1992; Ouseph, et al., 1997; Leypoldt, et al., 1998; Cheung, et al., 1999). Using bleach with some high-flux dialyzers may actually increase the clearance of large molecules, and possibly albumin, through mechanisms that are not completely understood (Diaz, et al., 1993; Kaplan, et al., 1995; Murthy, et al., 1998; Cheung, et al., 1999). These effects appear to be membrane dependent (Westhuyzen, et al., 1992; Murthy, et al., 1998; Cheung, et al., 1999). The committee is unaware of any practical test method for routine monitoring of large molecule clearance, and users are advised to consult the manufacturer's literature for more information on the effects of different reuse practices on the performance of specific membranes.

Although direct clearance measurements could be used to demonstrate compliance with the ± 10 % change in urea clearance, determining the urea clearance for each dialyzer reprocessed is impractical. Several dialysis machines now allow noninvasive, automated on-line measurement of the ionic clearance of a dialyzer. Because the ionic clearance has been shown to correlate closely with urea clearance (Steil, et al., 1993; Lindsay, et al., 2001), this technique can be used to follow directly the clearance of a reused dialyzer. There are also indirect tests that reflect the mass transfer characteristics of a dialyzer, which may be used in lieu of clearance measurements. A change in the residual TCV of hollow-fiber hemodialyzers is the most widely used indirect test for changes in small molecule clearance. This method has been shown to be a good index to monitor the solute transport capacity of the reprocessed hollow-fiber hemodialyzer (Gotch, 1985). The volume of a hollow-fiber hemodialyzer (TCV) is readily measured in the clinical setting. When methods of reprocessing are used that do not cause a significant change in the permeability or geometry of the membrane, a loss of TCV of 20 % corresponds to a loss of urea clearance of less than 10 % (Gotch, January 1984). Volume change is recommended as a QC test only for hollow-fiber

hemodialyzers because other hemodialyzer geometries do not have the relatively noncompliant blood compartment necessary for the validity of this measurement in predicting solute transport.

The question of the appropriate volume to use as the reference TCV has been asked many times. The answer is not quite as clear as it might seem. Each hemodialyzer manufacturer supplies information regarding the total blood volume. However, the techniques used by hemodialyzer manufacturers are often quite different from those employed during hemodialyzer reuse and may yield somewhat different results. For example, several manufacturers measure the volume using kerosene, a liquid that does not "wet" the membrane. The TCV of dialyzers can vary from the values used to develop the original manufacturer's literature, from lot to lot, and from hemodialyzer to hemodialyzer within a lot. In general, these variations are of little consequence in providing the proper transport properties designed into the hemodialyzer. When the hollow-fiber diameter decreases, the internal volume and surface area also decrease. Although it might appear that this would cause lower urea clearance, it does not. The shorter diffusion distances of the smaller fiber diameter cause an increase in urea transport rate, offsetting the loss in surface area. Following similar scientific principles, when individual fibers become plugged as the hemodialyzer is repeatedly used, the surface area associated with those plugged fibers is lost to solute transport and overall clearance decreases. This loss in transport is not linear because the (now) higher velocity in the remaining fibers causes an increase in the diffusion rate inside each fiber. This is the reason that a 20 % loss in surface area only yields about a 10 % loss in urea clearance. Therefore, what is important in the reuse setting is the loss in TCV relative to the original volume of the hemodialyzer.

The committee recommended that, whenever possible, the user measure the original volume of each hemodialyzer before the first patient use and record that value as the reference TCV (reprocessing volume) for all subsequent reprocessings. The committee also recognized that obtaining this measurement is not always practical. In the absence of a preprocessing volume measurement for an individual hemodialyzer, the user should use the calculated average preprocessing volume for that hemodialyzer model. The average preprocessing volume can be determined by averaging the preprocessing volume of approximately 10 dialyzers (or 20 % of the monthly usage of dialyzers, whichever is less) for each hemodialyzer model. This figure should be rechecked monthly. Substantial changes in average preprocessing volume should be investigated.

Initially, a change in the *in vitro* ultrafiltration coefficient of the hemodialyzer (K_{UF}) or its inverse, the membrane hydraulic resistance (R_m), was proposed as an alternative to a change in TCV as an indirect measure of a change in solute clearance (Pizziconi, 1985). However, this method was never validated in a clinical setting, and at the time of the 2002 revision of this recommended practice, it was considered to have no utility as a QC measure for contemporary hemodialyzers.

The committee recognized that other factors can influence the effective clearance of toxins during the dialysis session or can influence interpretation of the results. These factors include the following:

a) fistula recirculation;

b) accurate blood and dialysate flow rates;

c) accurate time of dialysis;

d) compliance with dietary limitations;

e) selection of appropriate hemodialyzer type and blood and dialysate flow rates;

f) membrane surface coating that may affect higher molecular weight toxins;

g) variations in the original clearance of the hemodialyzer; and

h) variations in the clearance of the hemodialyzer caused by reuse;

Users should be aware that the HEMO Study (Cheung, et al., 1999) identified reductions as well as increases in the clearance of β_2 microglobulin with the use of certain combinations of dialyzers, cleaning agents, and reuse germicides.

Of particular concern to this committee were any variations in hemodialyzer functions related to reuse procedures. Although cases have been documented (Delmez, et al., 1989), they are rare, especially when compared to the frequency of other factors listed above. For this reason, the committee strongly felt that the monitoring requirements of section 13 are of great importance to use in conjunction with the individual hemodialyzer measurements recommended in 11.3.

A.11.3.2 Ultrafiltration

Ultrafiltration rate (UFR) is the flow rate of fluid that passes through the membrane under a given pressure gradient at a given temperature. It is the product of the ultrafiltration coefficient of the hemodialyzer (K_{UF}) and the

transmembrane pressure. The K_{UF}, and thus the UFR at a given transmembrane pressure, may be affected by changes in the intrinsic permeability of the membrane, the surface area of the membrane, and the presence of hydraulically resistive deposits on the membrane. Cleaning agents such as sodium hypochlorite may affect the intrinsic water permeability of many types of dialysis membranes (Cheung, et al., 1999).

In vitro K_{UF} is not recommended to predict *in vivo* ultrafiltration performance because the former overestimates the latter (Gotch, January 1984; Wineman, 1984) in hollow-fiber hemodialyzers. This difference occurs in part because of the additional hydraulic resistance of the formed elements and proteins in blood. Additionally, thrombus-occluding hollow fibers may be highly permeable to water, and ultrafiltration may occur from either water passage through the occluding thrombus or retrograde flow from the unoccluded end of the fiber. These factors give a higher ultrafiltration coefficient during aqueous perfusion *in vitro*, whereas *in vivo* ultrafiltration across clotted fibers results in hemoconcentration of blood in clotted fibers to the point where osmotic pressure and hydraulic pressure drop to equal the transmembrane pressure, thus decreasing the ultrafiltration coefficient in the occluded fiber to zero. Similar data are not available for other types of dialyzers, but because clotting also occurs in those devices, the committee decided that *in vitro* K_{UF} should not be recommended to predict *in vivo* ultrafiltration performance in those devices as well.

The committee recognized that surface deposits can significantly affect ultrafiltration (Pizziconi, personal communication, August 1984). This subject is not included in the recommended practice because of the controversy surrounding the clinical significance of protein deposits on the membrane (see A.11.3.1) and the lack of evidence for a significant decrease of *in vitro* K_{UF} using present-day reprocessing techniques (Gotch, January 1984; Wineman, 1984).

The committee also recognized that *in vitro* K_{UF} measurements in hollow-fiber dialyzers can be used to estimate *in vivo* ultrafiltration if they are corrected for the percentage change in priming volume to reflect the amount of clotting and the normal *in vitro*-to-*in vivo* drop caused by the ultrafiltration of blood rather than protein-free solution. The committee decided not to include this information in the recommended practice because of the lack of consensus on the utility of this approach.

Measurement of *in vitro* ultrafiltration is temperature dependent. *In vitro* aqueous K_{UF} will change approximately 2 % per °C. Thus, care should be taken to know the actual temperature at which the measurement is made. If the measurement temperature is not 37 °C, the appropriate temperature compensation algorithm should be used to correct the reading to 37 °C (see Pizziconi [1983] for an appropriate algorithm).

A.11.3.3 Blood path integrity test

The 1986 edition of this recommended practice did not include a blood path integrity test. Because of on recommendations by the Centers for Disease Control and Prevention (CDC), the committee agreed to add such a test to the second edition of the recommended practice. This test is based on the observation that only a small amount of air leaks through wetted membranes, resulting in a pressure drop of less than 10 % of the test pressure. A maximum allowable pressure drop is not given because of variations among test systems and dialyzers.

A.11.4 Germicide

Until 1996, chemical germicides used in the health care setting were regulated by two government agencies: the Environmental Protection Agency (EPA) and the FDA. Chemical germicides formulated as disinfectants or sterilants were regulated and registered by the Disinfectants Branch, Antimicrobials Division, EPA. The authority for this responsibility comes under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The EPA required manufacturers of chemical germicides formulated as sanitizers, general disinfectants, or disinfecting or sterilizing (sporicide) products to test formulations by using specific protocols for microbicidal activity, stability, and toxicity to humans. If a germicidal chemical was advertised and marketed for use on a specific medical device (e.g., a hemodialysis machine or flexible fiberoptic endoscope), then the germicide came under the additional regulatory control of the FDA, Center for Devices and Radiological Health, which is the federal agency that regulates medical devices. Under the authority of the 1976 Medical Device Amendment to the Food, Drug, and Cosmetic Act, a germicide that was marketed for use on a specific medical device is itself considered a medical device in a regulatory sense, and the manufacturer was required, in addition to EPA registration, to contact the FDA and submit a Premarket Notification—510(k)—before legally marketing the product.

In the early 1990s, the FDA began actively regulating all liquid chemical germicides with health care indications. To avoid the potential problem of regulating the same product under multiple classes, the FDA decided to regulate liquid chemical germicides as a separate type of medical device; therefore, it determined that they were unclassified devices. In an effort to ease the burden of this dual regulation, a memorandum of understanding (MOU) was signed between the FDA and the EPA, that gave the FDA primary responsibility for premarket efficacy data review of liquid chemical sterilants and high-level disinfectants and gave the EPA primary responsibility for premarket efficacy data review of general purpose disinfectants.

Additionally, the FDA adapted the basic terminology and classification scheme described by Spaulding (1971) to categorize medical devices, and the four levels of processing as proposed by the CDC: sterilization, high-level disinfection, intermediate-level disinfection, and low-level disinfection (Favero and Bond, 2000). Also, the FDA regulatory authority over a particular instrument or medical device dictates that the manufacturer is obligated to provide the user with adequate instructions for the "safe and effective'' use of that instrument or device. Those instructions must include methods to clean and disinfect or sterilize the item if it is marketed as a reusable medical device. The FDA regulates chemical germicides formulated as antiseptics, preservatives, or drugs that are used on or in the human body or as preparations to be used to inhibit or kill microorganisms on the skin. However, the method used to regulate and assess potency for these formulations is significantly different from the methods used for sterilants and disinfectants. The FDA has an advisory panel that reviews nonprescription antimicrobial drug products. Manufacturers of such formulations voluntarily submit data to the panel, which in turn categorizes the products for their intended use (e.g., health care personnel hand washes, patient preoperative preparations, surgical hand scrubs).

A.11.4.1 Interior (blood/dialysate compartment)

A.11.4.1.1 Germicidal process

The following discussion of germicidal agents is limited to the use of high-level germicides for reprocessing dialyzers. sterilization is an appropriate option, if feasible, because sterilization has a greater potential for killing microorganisms.

Over the years, many techniques and germicides have been employed in dialyzer reuse programs, ranging from simple refrigeration to the use of quaternary ammonium compounds (which are very low-level germicides) to formaldehyde concentrations of 1 % to 6 %, glutaraldehyde solutions, solutions containing peracetic acid as the active ingredient, and, more recently, heat disinfection with and without the use of citric acid.

The reason, in part, for using formaldehyde at concentrations that are less than the sterilization cycle concentration (i.e., 8 % for 12 hours at 20 °C) is that the challenge of microorganisms is not normally composed of bacterial spores. After the hemodialyzer is removed from a patient, there are two main points at which a microbiologic risk can occur: when water is used to rinse and clean the dialyzer, and when water is used to prepare the chemical germicide used for disinfection. In each case, the water is usually treated in the dialysis center itself for purposes of preparing dialysis fluids. The water that is produced is not sterile and does contain water bacteria.

Gram-negative bacteria contain LPS, or bacterial endotoxins, which cause pyrogen reactions in dialyzing patients if the endotoxins are introduced into the bloodstream. Outbreaks of pyrogenic reactions during dialysis have ceased when steps were taken to reduce the colony count in the dialysate when it was counted at the end of dialysis, to fewer than 2000 per mL. The maximum allowable colony count in the water used for dialysis was estimated to be 200 per mL (ANSI/AAMI RD5:1982). The committee initially recommended this limit for the water used to dilute the germicide used for reprocessing hemodialyzers as a reasonable bioburden to be controlled by the germicidal procedure. Subsequently, it decided to add the alternative of a maximum bacterial LPS concentration of 1 ng per mL for the water used to dilute the germicide because the association of reprocessed hemodialyzers with pyrogenic reactions has been defined by the LAL test rather than by culture (Petersen, et al., 1981), and because the LAL test detects both viable and nonviable bacterial contamination. The committee acknowledged the evidence for cross-reactions between certain LAL tests and cellulosic materials (Pearson, et al., 1984) and the concern about the reproducibility of LAL tests. There is no evidence that cross-reactions apply to reprocessed hemodialyzers, and, even so, patient safety would not be compromised because acceptable reprocessed hemodialyzers would be mistakenly discarded rather than excessively contaminated hemodialyzers used. The committee also recognized that the LAL test is the test specified by the *United States Pharmacopoeia* (USP) for detecting bacterial endotoxin in water. Furthermore, the committee believes that reliable, reproducible LAL tests are readily available.

Another group of water bacteria that can constitute a hazard in a dialysis center, is the nontuberculous mycobacteria. They are acid-fast water bacteria and, much like the gram-negative bacteria, survive and are capable of excellent growth in all water, including reverse osmosis and deionized water. Nontuberculous mycobacteria do not contain lipopolysaccharide, and their presence in dialysis fluids would not tend to pose a serious pyrogenic risk to a dialyzing patient. But unlike the gram-negative bacteria, they are considerably resistant to chemical germicides (Carson, et al., 1978). For example, they are between 10 and 100 times more resistant to free chlorine than are *Pseudomonas aeruginosa* and other common gram-negative water bacteria. Some strains of nontuberculous mycobacteria studied can survive a 60 minute exposure to 2 % alkaline glutaraldehyde. By comparison, *Pseudomonas aeruginosa* at a concentration of 10^6 per mL would be inactivated within a matter of minutes. Using 8 % formaldehyde, some strains of nontuberculous mycobacteria have survived up to 6 hours of contact at room temperature; if the challenge had been *Pseudomonas aeruginosa*, the kill rate would have been so fast that it could not have been measured.

The source of nontuberculous mycobacteria in an outbreak of disease among patients dialyzed at a center in Louisiana appeared to be the water used in processing dialyzers. Laboratory studies conducted by the CDC have demonstrated that the nontuberculous mycobacteria associated with the water systems in the Louisiana center can

readily survive 2 % formaldehyde after 24 hours of exposure; in other instances, some strains survived for up to 96 hours. Obviously, those rates do not constitute high-level disinfection. Further laboratory studies have shown that if the concentration of formaldehyde is increased to 4 %, none of the strains of nontuberculous mycobacteria found in the water systems of the dialysis center or, for that matter, any of the strains that the CDC has stockpiled including some extraordinarily resistant strains, survive beyond 24 hours. In another more recent outbreak of mycobacteria infections in a dialysis clinic in California (Lowry, et al., 1990), the CDC also showed incomplete kill of mycobacteria in manually reprocessed high-flux dialyzers using 2.5 % Renalin.

From a conservative standpoint, one should assume that nontuberculous mycobacteria may be part of the microbiologic flora of water used for rinsing and cleaning dialyzers and for preparing aqueous chemical germicides for disinfection and sterilization. Given this assumption, a dialysis center is faced with two alternatives. It could rely entirely on aseptic techniques throughout the reprocessing procedure, use sterile rinse water and sterile germicides (membrane-filter sterilized), and employ strict QC. Most dialysis centers in this country do not have the capability to undertake such a closed-system and complex approach.

The second option would be either to use 4 % instead of 2 % formaldehyde or to use other chemical germicides at concentrations sufficient to produce sterility or high-level disinfection. Although good QC and QA practices and adherence to protocols would have to be maintained, this approach is much simpler. Moreover, a scientific basis apparently exists for considering 4 % formaldehyde at a 24-hour exposure as at least a high-level germicide process. All laboratory data acquired so far shows that 24 hours of exposure with 4 % formaldehyde at room temperature (20 °C) inactivates high levels of all strains of nontuberculous mycobacteria that have been tested; many of the test strains are among the most resistant in the CDC collection.

When 4 % formaldehyde is used, both the dialysate and the blood compartments shall be filled with this concentration to prevent its reduction as a consequence of diffusion of formaldehyde from one compartment to another or of dilution by residual rinse water retained on and in the dialyzer membranes. Dilution can be prevented by passing at least three volumes of 4 % formaldehyde through each compartment before sealing the dialyzer for storage. The committee decided to specify an effluent within 10 % of the original concentration to avoid a design standard that might not be appropriate in the future.

The committee limited the recommendation for 4 % formaldehyde to processes that use formaldehyde as the sole germicide, because it is possible that combinations of germicides might give a satisfactory result with less than 4 % formaldehyde. Concentrations of formaldehyde lower than 4 % and a contact time shorter than 24 hours are permitted if adequate disinfection can be demonstrated, because intermediate conditions have not been tested and might, on further evaluation, prove satisfactory.

The committee is aware of published information regarding the use of 1 % formaldehyde with dialyzers stored at 40 °C for 24 hours (Hakim, et al., 1985). Many dialysis facilities have adopted this procedure without resulting difficulties and it seems to be an acceptable alternative to 4 % formaldehyde at 20 °C.

The committee is also aware of published information regarding the use of 1.5 % USP citric acid elevated to a temperature of 95 °C for 20 hours (Levin, et al., 1995). If that process is to be used, the user should consult the published data to ensure that citric acid is being applied appropriately and there is no negative effect on the dialyzer performance or integrity.

Unfortunately, no realistic procedure exists whereby a dialysis center can monitor the effectiveness of the disinfection procedure. Such sophisticated microbiologic tests cannot be performed in dialysis centers, because the tests require the use of specialized equipment and highly trained microbiologists. Instead, a center should adhere rigidly to established protocols for QC and QA. Tests for total bacteria and endotoxin in the water used to make up the germicide should be conducted at least monthly. If there are problems in maintaining water quality at the level established by ANSI/AAMI RD62:2001, *Water treatment equipment for hemodialysis applications*, the testing may need to be performed more frequently. Testing the germicide's final-use concentration should be a part of the center's QC program as well as verifying that each dialyzer was filled with germicide.

The committee considered a functional reverse osmosis unit and 2 % formaldehyde disinfection, but decided not to rely on this option because the CDC believes that reverse osmosis water might not be adequate to control contamination by nontuberculous mycobacteria, that there is a substantial chance that these highly resistant organisms may be in the source water, and that monitoring the water for nontuberculous mycobacteria is not clinically feasible.

The committee considered a recommendation that the chemical quality of the water used to dilute the germicide should be the same as the water used to make the dialysate. This recommendation was deleted because of the lack of consensus on this issue, as noted earlier (see A.7). Water quality standards for dialysis and for dialyzer reprocessing were made the same in 2001 (see current version of ANSI/AAMI RD62, *Water treatment equipment for hemodialysis applications*).

Potency testing of each batch of germicide is specifically recommended for batches of manually prepared germicides regardless of whether they are used with a manual or an automated system. Germicide solutions that are diluted on-line by automated machines are to be checked for concentration at least monthly. Other requirements for verification of germicide presence are contained in section 12.

The CMS requires (42 CFR 405.2150) that dialyzers not be subjected to multiple germicide solutions because of possible combined actions of the germicides on the hemodialyzer membrane. That requirement does not apply to the original sterilization process or chemical cleaning agents that the hemodialyzer might be exposed to for short periods during the cleaning process for reuse. Certain members of the committee felt that the requirement was unnecessary if each hemodialyzer is subjected to an air pressure leak test as part of the reuse process.

A.11.4.1.2 Dialyzer header cleaning and disinfection

The practice of header removal to remove clotted material has increased over the years. Many dialyzers do not have removable headers, but there are enough dialyzers with removable headers that the practice should be fully addressed. If the headers cannot be removed, other methods are used to remove this clotted material. Those methods should also be addressed. Removing the header allows the user to remove the clotted material from the end of the fiber bundle and the O-ring header assembly. The method of removal of the clotted material has been of concern. Some facilities use running water (AAMI quality) to remove the clotted material, whereas others use 4x4s or instruments to scrape away the clotted material. The main concerns of using 4x4s or instruments to scrape away the clotted material are (1) infection, (2) plugging of fibers, and (3) damage to the end of the fiber bundle.

In the past, removing the headers was associated with reported incidents of bacterial and pyrogenic reactions in patients (Flaherty, et al., 1993). The patient reactions no longer occurred when the headers were disinfected by dipping the O-ring, header, and end of the dialyzer into the appropriate disinfectant. The research on this problem pointed to a double-fault failure system: 1) the bacteria seemed to be coming from a contaminated water source, and 2) the bacteria were not killed by the normal disinfection process. Dipping the dialyzer corrected that situation.

Another concern is that rags, 4x4s, or instruments that are used to clean the clotted material would re-infect the end of the dialyzer. This concern can be removed by using new rags or 4x4s for each dialyzer. When instruments are used, they can be disinfected between treatments.

Plugging of fibers has also been a concern. Because the dialyzer is cleaned and tested after the header cleaning, any plugged fibers would be detected and corrected before they became a problem.

There is also a possibility that, if instruments are used, they could damage the end of the fiber bundle. The user should make certain that no damage occurs.

Several concerns are raised when the headers are not removed and the user attempts to clear the header space of clots. These concerns include infection and damage to the end of the fiber bundle. A multitude of items are used to clean the header space, including water sprays, paper clips, tie wraps, and the like. With water sprays, the possibility of contaminated water always exists. Other items that are inserted can damage the end of the fiber bundle. If the item inserted into the dialyzer is not disinfected between uses, it can cause bacterial transmission; however, the dialyzer is usually disinfected after the header space is cleaned.

Automated header cleaning devices are commercially available.

A.11.4.2 Exterior

Low-level germicides satisfactorily clean the exterior of the device to a degree comparable what a new dialyzer receives. For example, 1:100 dilution of household bleach will achieve the concentration of sodium hypochlorite specified in 11.4.2.

A.11.5 Inspection

The committee considered a recommendation not to accept hemodialyzers with visible clots because venous filters are not used for all hemodialyzer circuits, leading to the risk of embolization to the patient if a clot were to break loose. The committee decided to reject this proposal because the allowable clots are required to be small and in stagnant areas that are present during the first use of the hemodialyzer and because there is no evidence of embolization from reprocessed hemodialyzers that meet this criterion.

A proposal that the number of dark, clotted fibers evident upon external inspection be limited to five was not accepted because a considerably larger number may be clotted without significant adverse effect on performance and because some authorities do not agree that this criterion is essential to an aesthetically pleasing appearance. A recommendation that hemodialyzers with a pink or brownish tint not be acceptable was also deleted because this condition is difficult to define and because glutaraldehyde disinfection results in a slight tan color of the membranes

that has not been shown to impair the safety or performance of the hemodialyzer. The committee recognized that the patient should be included in the aesthetic evaluation of the hemodialyzer.

A.11.6 Disposition of rejected dialyzers

No additional rationale was provided.

A.11.7 Storage

The committee acknowledged that the selection of 1 month as the maximum storage period permitted without validation was arbitrary. The committee was, however, unaware of any adverse effects of storage for up to 1 month and, therefore, felt that this period of time was reasonable.

A.12 Preparation for dialysis and testing for chemical germicides and potentially toxic residues

The committee considered methods other than direct testing of the germicide as a process control in each hemodialyzer. It noted that some automated systems add sodium chloride to the germicide and monitor conductivity. Brilliant Blue (FD&C Blue #1) added to the germicide has also been used to confirm the presence of germicide by visual inspection. There is toxicological data supporting the safety of this method (E. Lowrie, personal communication, 30 December 1984).

For the 1986 edition of this recommended practice, the committee recommended testing each hemodialyzer for the presence of germicide just before rinsing and priming. The committee noted in 1986 that certain germicide manufacturers recommended this procedure, and that their recommendation should be followed. If each hemodialyzer was not tested for the presence of germicide, then a combination of process control and sampling was considered to be adequate. By conducting the test before any dialyzer in a batch were used, all dialyzers from the batch could be quarantined or released at the same time.

The committee recognized that a residual level of less than 3 ppm for formaldehyde is the guideline for reuse in the State of California (California Code of Regulations, Title 22 §75207). This level apparently was chosen to coincide with the sensitivity of tests that detect formaldehyde. The committee decided to recommend a maximum residual level of formaldehyde of 5 ppm for the following reasons (Gotch, 1983).

a) Anti-N-like antibody formation, the only established chronic toxicity caused by formaldehyde in reused dialyzers, does not occur below a residual formaldehyde level of 10 ppm (Howell and Perkins, 1972; White, et al.,1977; Crosson, et al.,1976). Subsequently, at least two published studies (Vanholder, et al., 1988; Ng, et al., 1995) report anti-N-like antibodies in 10 % to 11 % of patients treated with reused dialyzers when the residual formaldehyde level was less than 2 ppm to 3 ppm.

b) The maximum daily dose of formaldehyde from dialysis is less than the California OSHA daily limit, which is based on a five day week, whereas dialysis patients usually dialyze three or fewer times a week (Gotch, 1984a).

c) There is no evidence of toxicity from the long-term use of methenamine by mouth for urinary tract infections at doses that release considerably more formaldehyde to the patient than comes from reused dialyzers.

d) Although tests are commercially available to test for formaldehyde at levels of 1 ppm, residual formaldehyde levels lower than 5 ppm increase the time required to prepare the dialyzer for dialysis.

When the committee revised RD47 in 2002, it decided that there was sufficient information available to indicate that the residual level of formaldehyde should be reduced to less than 3 ppm. The testing technology for residual formaldehyde had also improved, and it was feasible to easily test to less than 3 ppm.

The committee considered establishing maximum residual levels for germicides other than formaldehyde. Because these newer germicides are all cleared by the FDA and could have different allowable levels of residuals even for the same generic type of germicide, the committee determined that it is best to recommend that the manufacturer's instructions for use be followed. The committee noted that toxicology studies are favorable for some of these agents, and the FDA reviews labeling information for them, which includes the maximum residual level.

When checking for the presence or concentration of the germicide in the hemodialyzer, do not place anything into the blood or dialysate ports of the device (e.g., test strip or syringe) to withdraw the sample. Doing so may damage the fibers of the dialyzer and lead to blood leaks during dialysis. If a germicide test strip or kit is being used, the instructions provided by the manufacturer should be followed.

A.12.1 Visual inspection

No additional rationale was necessary.

A.12.2 Verification of patient identification

No additional rationale was necessary.

A.12.3 Verification of germicidal contact

No additional rationale was necessary.

A.12.4 Priming the dialyzer and rinsing the germicide

No additional rationale was necessary.

A.12.4.1 Testing for residual germicide

During the 2002 review of RD47, the committee decided that sufficient evidence was available to require the reduction of the residual level of formaldehyde from 5 ppm to 3 ppm. This evidence, along with the availability of test methods capable of making this determination, led the committee to make this reduction.

A number of procedural steps have been identified that, if not followed, may cause residual germicide to remain in the hemodialyzer following rinsing. The following list of instructions, though not all inclusive, should be carefully considered when developing a facility's rinsing procedure.

a) Air bubbles in the fibers can cause individual fibers to become blocked. Be sure that the arterial line is fully primed before you connect it to the hemodialyzer. If you are using peracetic acid-type germicide, be sure you flush the blood side before beginning dialysate flow.

b) Air trapped in the dialysate side of the hemodialyzer may cause germicide to also remain trapped in portions of the hemodialyzer. Rotate the hemodialyzer during the rinsing process. This action normally will release the trapped air and allow the germicide to be fully rinsed.

c) Germicide may back up into the heparin or monitor lines. Be sure that the heparin line is clamped and that fluid is not forced into the monitor lines.

d) Germicide may back up into the saline bag during the rinsing procedure. Be sure that your procedure accounts for all situations that may force fluid from the dialysis circuit back into the saline bag.

e) Take care to avoid a false negative residual disinfection test, which can happen if you sample too quickly after a quantity of saline has been infused.

f) Discard the prime solution when beginning blood flow to the hemodialyzer. Do not connect the venous line to the venous needle until blood has reached the venous blood line.

A.13 Monitoring

A.13.1 Dialysis

No additional rationale was provided.

A.13.2 Symptoms

Evaluation by a physician is required to determine whether symptoms might constitute an adverse reaction to the reprocessed dialyzer because symptoms during dialysis are commonly the result of other factors, such as infections not attributable to dialysis, and to hypovolemia.

First-use syndrome is a symptom complex characterized by nervousness, chest pain, back pain, palpitations, pruritus, and other usually mild symptoms, occurring minutes following the initiation of dialysis with a new dialyzer. The syndrome is defined by some authorities to include the anaphylactoid reaction occurring usually immediately after the initiation of dialysis in some patients using dialyzers sterilized with ethylene oxide. In addition to first-use syndrome, serious reactions have been reported in patients taking ACE inhibitors and dialyzed on certain synthetic membranes. This reaction is now known to involve increased bradykinin release accompanied by suppression of bradykinin degradation.

A.13.3 Dialyzer failures

This section sets up conditions under which some of the tests given in section 11 should be conducted. The option of adjusting the algorithm for UFR refers to a significant change of UFR without a significant change of clearance.

A.13.4 Clinical results

Critical assessment of chemistries and the delivered dose of dialysis (Kt/V or urea reduction ratio), as is done monthly, provides a clear trend line to assess treatment. This scrutiny of the patient's treatment and course is the primary confirmation that hemodialyzer performance anticipated from TCV or other indirect estimation is accurate and adequate. The overall effectiveness of the entire treatment, not only the clearance of the dialyzers, is measured. No other measure of the effectiveness of new or reused dialyzers is as clear or relevant. Trend lines developed from this data characterize the quality of therapy. Other professional assessments of patient well-being should be considered. If the practitioner has concerns for "middle molecules" or other clinical parameters, these factors should also be part of the assessment of the delivered therapy.

There are many reasons for an apparent reduction in the mass transfer of urea, other than decreased hemodialyzer clearance as a result of inadequate reprocessing (such as recirculation, decreased dialysis time or blood flow rate, or an inappropriate dialysis prescription). To document adequate mass transfer, one may find parallel measurements of pre- and post-creatinines helpful. When problems develop with any patient or group of patients, monitoring intensity should be increased, and other methods should be used to analyze the problem and define corrective action.

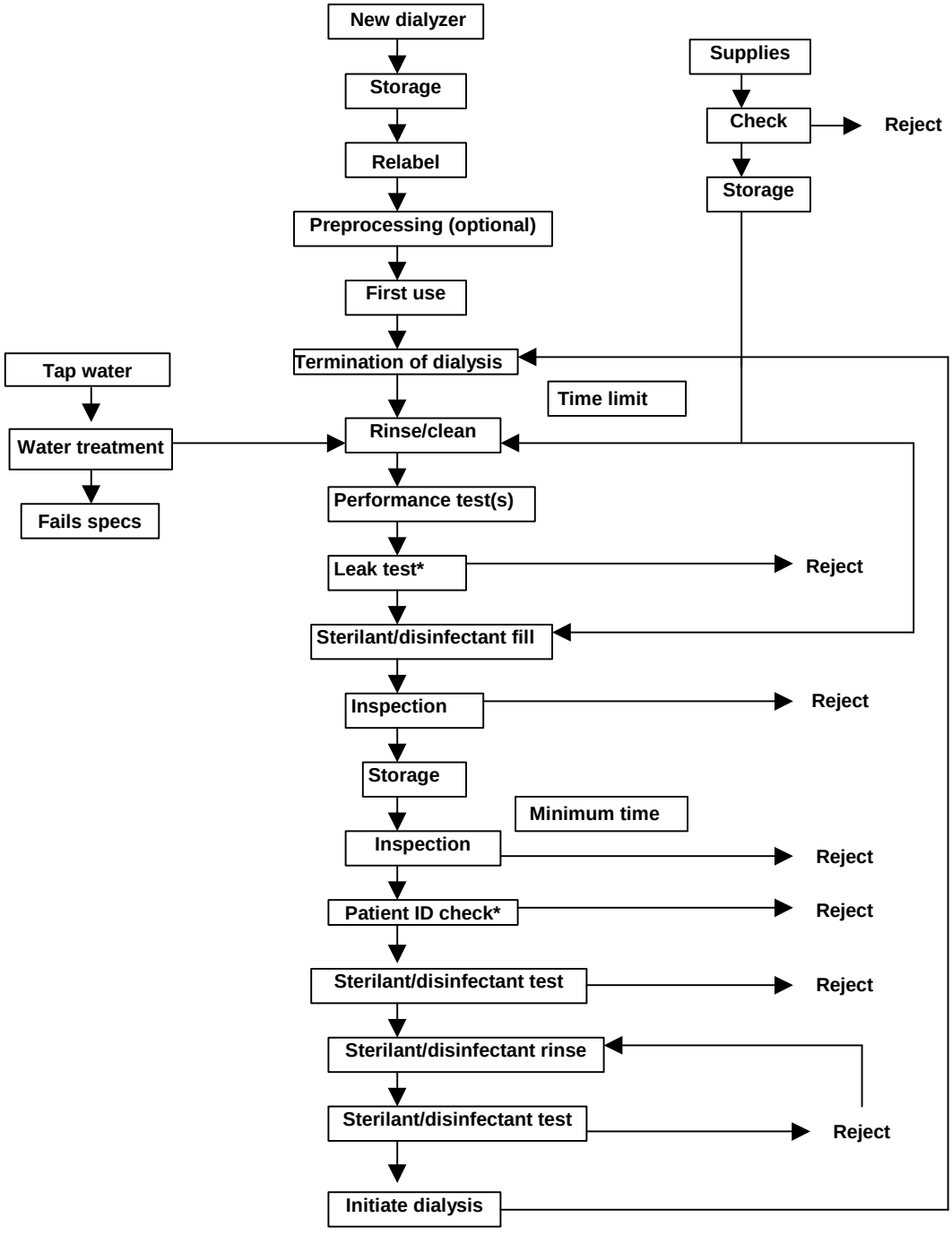
Techniques to compare survival among facilities and for individual facilities against national and regional standard mortality rates are an important instrument for a facility to use in self assessment (Wolfe, et al.,1992). The committee recommends periodic review of this outcome measure.

A.14 Quality assurance

The FDA's 1987 compliance policy guide (7124.16) advises reuse practitioners to establish the following: (a) adequate device cleaning and sterilization; (b) the lack of adverse effects on device quality or physical characteristics; and (c) certainty that the device remains safe, reliable, and effective for its intended use. The committee believes that compliance with those recommendations necessitates use of regularly examined reprocessing procedures that are based on methods of demonstrated effectiveness and are carried out under conditions safe to the patient and the personnel.

Annex B
(normative)

Systems diagram for reprocessing dialyzers



* This step may be done later but shall precede initiation of dialysis.

Annex C
(informative)

Bibliography

ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Hemodialysis systems.* ANSI/AAMI RD5:1982. Arlington (VA): AAMI, 1982.

ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Hemodialyzers.* ANSI/AAMI RD16:1996. Arlington (VA): AAMI, 1996. American National Standard.

ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Reuse of hemodialyzer blood tubing*. AAMI TIR6:1990. Arlington (VA): AAMI, 1990.

BASS OE, et al. Detrimental effects of air rinsing on dialysis membranes. *Trans Am Soc Artif Internal Organs*, 10: 466–470, 1973.

CARSON LA, et al. Growth characteristics of atypical mycobacteria in water and their comparative resistance to germicides. *Appl. Environ. Microbiol.* 36(6):839–846, 1978.

CHEUNG AK, AGADOA LY, DAUGRIDAS JT, et al. Effects of hemodialyzer reuse on clearances of urea and β_2 microglobulin. The Hemodialysis (HEMO) Study Group. *J Am Soc Nephrol.* 10(1):117—27, Jan. 1999.

COLLINS AJ, MA JZ, CONSTANTINI EG, and EVERSON SE. Dialysis unit and patient characteristics associated with reuse practices and mortality: 1989–1993. *J Am Soc Nephrol* 9:2108–2117, 1998.

COLLINS MC, and RAMIREZ WF. Mass transport through polymeric membranes. *J Phys Chem*, 83(17):2294–2301, 1979.

CROSSON JT, MOULDS J, COMTY CM, and POLESKY HF. A clinical study of anti-NDP in the sera of patients in a large repetitive hemodialysis program. *Kidney Int* 10:463, 1976.

DEANE N, and BEMIS JA. Multiple Use of Hemodialyzers (a report to the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases). Contract no. N01-AM-9-2214. New York: Manhattan Kidney Center, June 1981.

DELMEZ JA, WEERTS CA, HASAMEAR PD, and WINDUS DW. Severe dialyzer dysfunction undetectable by standard reprocessing validation tests. *Kidney Int* 36:478-484, 1989.

DIAZ RJ, WASHBURN S, CAUBLE L, SISKIND MS, and VAN WYCK D. The effect of dialyzer reprocessing on performance and β_2-microglobulin removal using polysulfone membranes. *Am J Kidney Dis* 21:405–410, 1993.

DORSON, et al. Technical considerations in multiple use of hemodialyzers. In: *Proceedings of the National Workshop on Reuse of Consumables in Hemodialysis*. Washington, DC: Kidney Disease Coalition, 1983, pp. 11–39.

EBBEN JP, DALLESKA F, MA JZ, EVERSON SE, CONSTANTINI EG, and COLLINS AJ. Impact of disease severity and hematocrit level on reuse-associated mortality. *Am J Kidney Dis* 35:244–249, 2000.

FELDMAN HI, KINOSIAN M, BILKER WB, et al. Effect of dialyzer reuse on survival of patients treated with hemodialysis. *JAMA* 276:620–625, 1996.

FISCHBACH LJ. *Dialyzer Reprocessing Guideline*. Minneapolis (MN): Renal Systems, 1982.

FLAHERTY JP, GARCIA-HOUCHINS S, CHUDY R, and ARNOW PM. An outbreak of gram-negative bacteremia traced to contaminated O-rings in reprocessed dialyzers. *Ann Intern Med* 119:1072–1078, 1993.

GORST DW, RICHES RA, and RENTON PH. Formaldehyde induced anti-N: A possible cause of renal graft failure. *J Clin Path*, 30:956–959, 1977.

GOTCH FA, and KEEN ML. Formaldehyde kinetics in reused dialyzers. *Trans Amer Soc Artif Internal Organs*, 29:396, 1983.

GOTCH FA. Dialyzer transport properties and germicide elution. In: *Proceedings, Seminar on Reuse of Hemodialyzers and Automated and Manual Methods.* New York: National Nephrology Foundation, 1984.

GOTCH FA. The kinetics of sterilant removal from hollow-fiber hemodialyzers. In: *Reuse of Disposable Medical Devices in the 1980s*. Washington, DC: Institute for Health Policy Analysis, Georgetown University Medical Center, March 1984a.

GOTCH FA. Quality control tests for validation of dialyzer performance. In: *Hemodialyzer Reuse: Issues and Solutions*. TAR #10. Arlington (VA): Association for the Advancement of Medical Instrumentation, 1985.

HAKIM RM, FRIEDRICH RA, and LOWRIE EG. Formaldehyde kinetics and bacteriology in dialyzers. *Kidney Int* 28:936–943, 1985.

HELD PJ, WOLFE RA, GAYLIN DS, et al. Analysis of the association of dialyzer reuse practices and patient outcomes. *Am J Kidney Dis* 23:692–708, 1994.

HOWELL D, and PERKINS HA. Anti-N-like antibodies in the sera of patients undergoing chronic hemodialysis. *Vox Sang*, 23:291, 1972.

KAPLAN AA, HALLEY SE, LAPKIN RA, and GRAEBER CW. Dialysate protein losses with bleach processed polysulfone dialyzers. *Kidney Int* 48:510–516, 1995.

LEVIN NW, PARNELL SL, PRINCE HN, et al. The use of heated citric acid for dialyzer reprocessing. *J Am Soc Nephrol*, 6(6):1578–1585, 1995.

LEYPOLDT JK, CHEUNG AK, and DEETER RB. Effect of hemodialyzer reuse: Dissociation between clearances of small and large solutes. *Am J Kidney Dis* 32:295–301, 1998.

LINDSAY RM, BENE B, GOUX N, HEIDENHEIM AP, LANDGREN C, and STERNBY J. Relationship between effective ionic dialysance and in vivo urea clearance during hemodialysis. *Am J Kidney Dis* 38:565–574, 2001.

LOWRIE EG, LAIRD NM, PARKER TF, and SARGENT JA. Effect of the hemodialysis prescription of patient morbidity: Report from the National Cooperative Dialysis Study. *New Engl J Med* 305(20):1176–1181, 1985.

LOWRY PW, BECK-SAGUE CM, et al. Mycobacterium chelonae infections among patients receiving high-flux dialysis in a hemodialysis clinic in California. *Journal of Infectious Diseases* 161:85–90, 1990.

MCALLISTER SK, ARDUINO M, and BLAND L. Low temperature depyrogenation of endotoxin in fluids for use in hemodialysis. Proceedings of the General Meeting of the American Society for Microbiology, May 23–27, 1994, Las Vegas, NV.

MURTHY BVR, SUNDARAM S, JABER BL, et al. Effect of formaldehyde/bleach reprocessing on in vivo performances of high-efficiency cellulose and high-flux polysulfone dialyzers. *J Am Soc Nephrol* 9:464–472, 1998.

NG YY, CHOW MP, WU SC, LYOU JY, HARRIS DC, and HUANG TP. Anti-N_{form} antibody in hemodialysis patients. *Am J Nephrol* 15:374–378, 1995.

OUSEPH R, SMITH BP, and WARD RA. Maintaining blood compartment volumes in dialyzers reprocessed with peracetic acid maintains Kt/V but not β_2-microglobulin removal. *Am J Kidney Dis* 30:501–506, 1997.

PEARSON FJ, et al. Characterization of *limulus* amebocyte lysate-reactive material from hollow fiber dialyzers. *Appl Environ Microbiol* 48:1189–1196, 1984.

PETERSEN NJ, CARSON LA, and FAVERO MS. Bacterial endotoxin in new and reused hemodialyzers: A potential cause of endotoxemia. *Trans Am Soc Artif Internal Organs* 27: 155–159, 1981.

PIZZICONI, VB. Performance and integrity testing of reprocessed dialyzers: A QC update. In *Hemodialyzer Reuse: Issues and Solutions*. TAR #10. Arlington (VA): Association for the Advancement of Medical Instrumentation, 1985.

PORT FK, WOLFE RA, HULBERT-SHEARON TE, Held PJ, et al. Mortality risk by hemodialyzer reuse practice and dialyzer membrane characteristics: Results from the USRDS dialysis morbidity and mortality study. *Am J Kidney Dis* 37:276–286, 2001.

RETTIG R. The ESRD social contract and the politics of reuse. In SADLER JH, ed., *Proceedings of the National Workshop on Reuse of Consumables in Hemodialysis*. Washington, DC: Kidney Disease Coalition, 1982.

SAX NI. *Dangerous Properties of Industrial Materials*, 5th ed. New York: Van Nostrand Reinhold, 1979.

SPALDING EH. Chemical disinfection and antiseptics in the hospital. *J Hosp Res* 9:5–31.

STEIL H, KAUFMAN AM, MORRIS AT, LEVIN NW, and POLASCHEGG HD. *In vivo* verification of an automatic noninvasive system for real time Kt evaluation. *ASAIO J* 39:M348–M352, 1993.

TOKARS JI, MILLER ER, ALTER MJ, and ARDUINO MJ. National surveillance of dialysis associated diseases in the United States, 1997. *Seminars in Dialysis* 2000:13:75–85, 2000.

TOKARS JI, MILLER ER, ALTER MJ, and ARDUINO MJ. National surveillance of dialysis associated diseases in the United States, 2001. National Center for Infectious Diseases Centers for Disease Control and Prevention Public Health Service. Atlanta, GA: Department of Health and Human Services.

VANHOLDER R, NOENS L, DE SMET R, and RINGOIR S. Development of anti-N-like antibodies during formaldehyde reuse in spite of adequate predialysis rinsing. *Am J Kidney Dis* 11:477–480, 1988.

WELBEL SF, SCHOENDORF K, BLAND LA, et al. An outbreak of gram-negative bloodstream infections in chronic hemodialysis patients. *Am J Nephrol* 15(1):1–4, 1995.

WESTHUYZEN J, FOREMEN K, BATTISTUTTA D, SALTISSI D, and FLEMING SJ. Effect of dialyzer reprocessing with Renalin on serum β-2-microglobulin and complement activation in hemodialysis patients. *Am J Nephrol* 12:29–36, 1992.

WHITE WL, MILLER GE, and KAEHNY WD. Formaldehyde in the pathogenesis hemodialysis-related anti-N antibodies. *Transfusion* 17:443, 1997.

WINEMAN J. Comparison of automated reprocessing devices. In: *Proceedings, Seminars on Reuse of Hemodialyzers and Automated and Manual Method*s. New York: National Kidney Foundation, Jan. 1984.

WOLFE RA, GAYLIN DS, PORT FK, HELD PJ, and WOOD CL. Using USRDS generated mortality tables to compare local ESRD mortality rates to national rates. *Kidney Int* 42:991–996, 1992.

