List of Titles

American National Standard

ANSI/AAMI RD47:1993

# Reuse of hemodialyzers

AAMI Association for the Advancement of Medical Instrumentation

List of Titles

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



## Copyright and Permissions

# RD47 Reuse of Hemodialyzers

American National Standard

ANSI/AAMI RD47—1993
(Revision of AAMI ROH—1986)

**Reuse of hemodialyzers**

Developed by
**Association for the Advancement of Medical Instrumentation**

Approved 3 May 1993 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.

**Association for the Advancement of Medical Instrumentation**

**AAMI Renal Disease and Detoxification Committee**

**AAMI Hemodialyzer Reuse Subcommittee**

This recommended practice was revised by the Hemodialyzer Reuse Subcommittee of the Renal Disease and Detoxification Committee. Committee approval of the standard does not necessarily imply that all committee members voted for its approval.

At this time, the **Renal Disease and Detoxification Committee** has the following members:

*Cochairpersons:* John H. Sadler, MD
James D. Stewardson

*Members:*
Roy A. Ackerman, PhD, Astre Corporate Group
Kathleen Althier, NANT
David A. Berkowitz, ECRI
D. Michael Blankenship MD, Texarkana Kidney Disease Center, Texarkana, AK
James T. Boag, Consultant, Seattle, WA
Spencer Colburn, HCFA
R. Barry Deeter, University of Utah Dialysis Program
William Dorson, Jr., PhD, ASAIO
Paul Duke, Mesa Medical, Inc.
Martin S. Favero, PhD, Centers for Disease Control
Lois Foxen, RN, St. Joseph Hospital, Orange, CA
Robert Galonsky, Downstate Medical Center, Brooklyn, NY
George Harper, American Association of Kidney Patients
Albert Jarvis, PhD, Lakeland, FL
Nathan W. Levin, MD, Beth Israel Medical Center, New York, NY

Douglas A. Luehmann, Minntech Corporation/Renal Systems
James McCarthy, MD, Mayo Clinic, Rochester, MN
C.W. Miller, West Suburban Kidney Center, Oak Park, IL
David Ogden, MD, University of Arizona Health Science Center
Marie Reid, FDA Center for Devices and Radiological Health
John H. Sadler, MD, University of Maryland Hospital
Tom K. Sawyer, MD, Northwest Kidney Center, Seattle, WA
Gary Schwab, University of Rochester Medical Center, Rochester, NY
James D. Stewardson, Cobe Labs, Inc.
Larry C. Taylor, Baxter Healthcare Corporation
Douglas L. Vlchek, Dialysis Management, Inc.
Scott N. Walker, Fresenius/Seratronics
Richard A. Ward, PhD, University of Louisville School of Medicine
Duane G. Wombolt, MD, Renal Physicians Association

*Alternates:*
Maryann S. Allen, ECRI
Lee A. Bland, Centers for Disease Control
Vera K. Buffaloe, Cobe Labs, Inc.
Norman Deane, MD, Renal Physicians Association
Christopher Fedele, Baxter Healthcare Corporation
Leroy J. Fischbach, Minntech Corporation, Renal Systems
Donald R. Hamilton, FDA/Center for Disease and Radiological Health
Ben J. Lipps, PhD, Fresenius/Seratronics
Vincent B. Pizziconi, ASAIO
Joseph Sala, NANT
Lou Sand, American Association of Kidney Patients

At this time, the **Hemodialyzer Reuse Subcommittee** has the following members:

*Cochairpersons:*
Paul D. Duke
Nathan W. Levin, MD

*Members:*
Kathleen Altier, NANT
D. Michael Blankenship, MD, Texarkana Kidney Disease Center, Texarkana, AK
James T. Boag, Consultant, Seattle, WA
Sally Burrows-Hudson, RN, End Stage Renal Disease Network, Sausalito, CA
Spencer Colburn, HCFA
R. Barry Deeter, University of Utah Dialysis Program
Paul D. Duke, Mesa Medical, Inc.
President, American Nephrology Nurses Association
Martin S. Favero, PhD, Centers for Disease Control
Leroy J. Fischbach, Minntech Corporation/Renal Systems
Lois Foxen, RN, St. Joseph Hospital, Sausalito, CA
Susan K. Hansen, Organon Teknika Co., Durham, NC
George Harper, American Association of Kidney Patients
Albert Jarvis, PhD, Lakeland, FL
Nathan W. Levin, Beth Israel Medical Center, New York, NY
Edmund G. Lowrie, MD, National Medical Care, Inc.
C.W. Miller, West Suburban Kidney Center, Oak Park, IL
Neil Otchin, MD, Virginia Central Office
Vincent B. Pizziconi, ASAIO
Marie Reid, FDA Center for Devices & Radiological Health

John H. Sadler, MD, University of Maryland Hospital
Tom K. Sawyer, MD, Northwest Kidney Center, Seattle, WA
Larry C. Taylor, Baxter Healthcare Corporation
Douglas L. Vlchek, Dialysis Management, Inc.
Scott N. Walker, Fresenius/Seratronics
Duane G. Wombolt, MD, Renal Physicians Association

*Alternates:* Lee A. Bland, Centers for Disease Control
Conor Curtain, National Medical Care
Norman Deane, MD, Renal Physicians Association
William Dorson, Jr., PhD, ASAIO
Christopher Fedele, Baxter Healthcare Corporation
Donald R. Hamilton, FDA Center for Devices & Radiological Health
Ben J. Lipps, PhD, Fresenius/Seratronics
Lou Sand, American Association of Kidney Patients
Luke Schmieder, Mesa Medical, Inc.

*Acknowledgment*

The contribution of Lawrence Kobren of the Health Care Financing Administration, who participated greatly in the development of this recommended practice, is gratefully acknowledged.

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

**Foreword**

This recommended practice was developed by the Hemodialyzer Reuse Subcommittee of the AAMI Renal Disease and Detoxification Committee. 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.

The recommended practice reflects the conscientious efforts of health care professionals, patients, and medical device manufacturers to develop recommendations for optimal hemodialyzer reprocessing facilities and procedures. It is not intended that these recommendations be construed as universally applicable in all circumstances. The document is intended to guide the physician in charge of hemodialyzer reprocessing in initiating a new hemodialyzer reprocessing program or in evaluating an existing program against present-day technology and accepted practices. The term "should" as used in this document reflects the committee's intent to define goals, not requirements, for procedures and facilities. The term "shall" as used here denotes procedures that the committee particularly wished to emphasize or that are required by regulating authorities.

The use of phrases such as "have been shown," "an established procedure," "demonstrated success," or 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.

The committee decided to exclude reuse of blood tubing from this recommended practice because a consensus on this issue could not be reached. This omission does not reflect a judgment on the merits of reusing blood tubing. More information on blood tubing reuse can be found in the AAMI Technical Information Report, *Reuse of hemodialyzer blood tubing* (TIR6-1989).

These guidelines were developed by professionals and are not designed for regulatory applications, but have been put into service as such. They are intended to supplement those regulations and laws, which, while not

enumerated here, should be integral to any program for ensuring the safety and effectiveness of reprocessed hemodialyzers.

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

Department of Health & Human Services-funded epidemiologic studies have shown, in early analyses, a statistically significant association between some reuse practices and reduced survival. No overall negative association with reused dialyzers was found. Other variables in dialysis treatment may be more important in determining survival. Nonetheless, such observations powerfully emphasize the importance of following the reuse practice recommended here and the manufacturer's instructions.

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 these 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 this subject, although it does go further 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.

Suggestions for improving this recommended practice are invited and should be sent to: AAMI, 3330 Washington Boulevard, Suite 400, Arlington, VA 22201-4598.

NOTE—This foreword does not contain provisions of the American National Standard, *Reuse of hemodialyzers* ANSI/AAMI RD47 - 1993) but does provide important information about its development and intended use.

## Reuse of hemodialyzers

### 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," undertaken to recommend ways of controlling these risks and hazards. This information was compiled to assist the medical community and/or to provide data to support the development of standards.

On the subject of reuse, the study found that: "At the present time such standards (for reuse) cannot be proposed for two reasons: First, in the absence of definitive studies, such as the one contemplated by the National Institutes of Health (NIH), the necessary criteria to establish standards cannot be formulated. Second, at the present time, manufacturers label dialyzers as being intended for single use only. Unless these issues are resolved, standards related to reuse are not relevant."

Since 1980, however, the reported incidence of hemodialyzer reuse has risen dramatically, from an

estimated 16 percent of patients in 1980 to an estimated 73 percent of patients in 1989, (Alter, et al., 1991). 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.

While 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 inexpert 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 physicians to suspect that the welfare of the patient may not be the primary concern. 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, these fears may be justified. 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/or access to dialysis. Those who are expert in reprocessing hemodialyzers can therefore perform a valuable service by developing guidelines for the less experienced practitioner that will achieve the high quality of care physicians want for their patients. This recommended practice has been written to respond to the concern of patients, physicians, and manufacturers that dialyzer reprocessing be conducted safely and effectively.

It was against this background that AAMI convened a consensus-development conference in May of 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 and approved consensus recommended practice 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 since 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, 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 Health Care Financing Administration (HCFA) adopted the recommended practice as part of its 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. The 1991 interpretation is reflected in this revision of the recommended practice.

## **1** Scope

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

The committee agrees with CDRH that the manufacturer's responsibility is limited to providing safe,

effective devices with appropriate recommendations for the first use of the device (unless the manufacturer labels it for multiple use) and that subsequent uses of such devices are the sole responsibility of the patient's physician. This recommended practice, therefore, is addressed to the physician responsible for the hemodialyzer reprocessing program.

The committee recognizes that such dialyzer characteristics as biocompatibility and clearance of larger molecules may be affected by reuse. Those factors are beyond the scope of this document.

This recommended practice does not address every risk that may be associated with reprocessing.

### 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: record keeping, 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, and quality assurance and quality control.

### 1.2 Exclusions

This recommended practice does not cover the reprocessing of blood tubing sets nor address labeling and performance requirements for first-use hemodialyzers. Transducer protectors are not covered in this guideline.

## 2 Normative references

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

ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *First use hemodialyzers*, 1st ed. ANSI/AAMI RD16-1984. Arlington (Va.): AAMI, 1984. American National Standard. ISBN 0-910275-41-6.

ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Hemodialysis systems,* 2nd ed. ANSI/AAMI RD5-1992. Arlington (Va.): AAMI, 1992. American National Standard. ISBN 0-910275-70-X.

## 3 Definitions

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

**3.1 AOAC:** Association of Official Analytical Chemists.

**3.2 artificial kidney:** See **hemodialyzer.**

**3.3 ASHRAE:** American Society of Heating, Refrigerating and Air Conditioning Engineers.

**3.4 cleaning:** The passage of a solution or solutions through the blood and dialysate compartments to purge the dialyzer of blood and other substances.

**3.5 clearance:** A measure of net flux 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 due to ultrafiltration. See also **clearance**, **open-loop system**.

**3.6 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:

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

*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;

$Q_{UF}$= ultrafiltration rate.

**3.7 dialysis:** The act of performing hemodialysis therapy with a hemodialyzer on a patient at a dialysis facility.

**3.8 dialyzer:** See **hemodialyzer**.

**3.9 disinfection:** A process for killing vegetative microorganisms.

**3.10 disinfection, high level:** A procedure with a germicide approved by EPA as a sterilant/disinfectant that results in inactivation of all vegetative microorganisms.

**3.11 disinfection, low level:** A procedure that inactivates most vegetative bacteria except *M. tuberculosis*, some fungi, and some viruses.

**3.12 documentation:** Any record, notice, or other written material used by the dialysis facility to comply with the recommendations of this recommended practice.

**3.13 endotoxin:** Toxic substance (lipopolysaccharide [LPS]) from gram-negative bacteria that has a broad spectrum of biological activities, including pyrogenicity.

**3.14 EPA:** The U.S. Environmental Protection Agency, the federal agency responsible for identifying and controlling environmental pollutants of air and water, solid waste, pesticides, toxic substances, radiation, and energy.

**3.15 fiber bundle volume (FBV):** The aggregate volume of patent hollow fibers contained within the blood compartment of a hollow-fiber dialyzer. Sometimes used interchangeably with total cell volume (TCV), but not equivalent.

**3.16 first use:** The use of a hemodialyzer before it has been reprocessed.

**3.17 first-use syndrome:** 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. The mechanisms are, as yet, unclear.

**3.18 formaldehyde:** Formaldehyde (HCHO) solution, USP (nominal concentration 37 percent by weight [W/W] or 40 percent by volume [W/V]). Generally contains 8-16 percent Methanol for stabilization. A dilution of 1 part of formaldehyde with 9 parts of water yield 4.0 percent (W/V). Also called formalin. Concentrated formaldehyde stored under adverse conditions can polymerize to form paraformaldehyde, a

white precipitate.

**3.19 germicide:** An agent that kills microorganisms.

**3.20 hazard:** An actual event detrimental to patients and/or staff.

**3.21 hemodialyzer:** An 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. Types of dialyzers include: *parallel plate*, which incorporates a membrane in tubular or sheet form supported by plates in a sandwiched configuration; and *hollow fiber*, which incorporates the membrane in the form of very small fibers having a microscopic channel running through them.

**3.22 labeling:** The display of written, printed, or graphic matter upon a dialyzer including all packaging.

**3.23 lipopolysaccharide (LPS):** Group of structural molecules unique to the outer membrane of gram-negative bacteria. Purified LPS is O-antigen and bacterial endotoxin. LPS is not destroyed by disinfection procedures commonly used with dialyzer reuse.

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

**3.25 membrane:** A semipermeable material between the blood and dialysate compartments in a hemodialyzer.

**3.26 multiple use:** The use of a device for more than one procedure after suitable reprocessing of the device.

**3.27 NFPA:** National Fire Protection Association.

**3.28 OSHA:** Occupational Safety and Health Administration.

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

**3.30 port, blood:** An opening in the blood compartment of a hemodialyzer.

**3.31 port, dialysate:** An opening in the dialysate compartment of a hemodialyzer.

**3.32 ppm:** Abbreviation for parts per million.

**3.33 pre-processed dialyzer:** Dialyzer subjected to reprocessing procedure prior to first use.

**3.34 pyrogen:** A fever-causing substance. Bacterial LPS is one of the most potent pyrogens. If introduced into the blood stream, as little as 5 endotoxin units (1 nanogram) per kilogram of body weight causes fever in rabbits and humans.

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

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

**3.37 rebound:** Chemical disinfectants tend to bind in the solid components of the disinfected, reprocessed dialyzer. When the dialyzer is rinsed of disinfectant to a particular level, if the rinsing process is stopped, the concentration of residual disinfectant may rise or "rebound" to a significantly higher level as the chemical diffuses from the solid components into the (static) fluid solution in the dialyzer.

**3.38 removal of germicide:** The passage of a solution through the blood and dialysate compartments of a hemodialyzer to purge it of the germicide.

**3.39 reprocessing:** The act of restoring a previously used device so that it is suitable for using again.

**3.40 risk:** An event considered likely or possible which is potentially hazardous but has not yet occurred or resulted in detrimental clinical consequences.

**3.41 sterile:** Free of all microbial life, including highly resistant bacterial endospores.

**3.42 total cell volume (TCV):** The 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. Sometimes used interchangeably with fiber bundle volume (FBV), but not equivalent.

**3.43 toxic agent:** A substance that in sufficient amounts causes harm to an exposed organism.

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

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

*where*:

$P_{Bi}$ = 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; and

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

**3.45 validation or process validation:** The establishment of documented evidence providing a high degree of assurance that a given process will consistently yield a product meeting predetermined specifications and quality characteristics.

**3.46 ultrafiltration:** The transfer of fluid between the blood and dialysate through the dialysis membrane due to a pressure gradient (transmembrane pressure) existing between the blood and dialysate compartments.

**3.47 use number:** The number of times a hemodialyzer has been used in patient dialysis treatments.

## 4 Records

All records described in this recommended practice should meet the requirements for medical records, including completeness, legibility, and security. 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.

### 4.1 Dialyzer reprocessing manual

The dialyzer reprocessing manual should be a compilation of all specifications, policies, training materials, manuals, methodologies, and procedures which 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.

### 4.2 Reprocessing record

Records must be kept that identify the new dialyzer, the date of each reprocessing step, the person performing the procedure, their 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 should be permitted to read records pertaining to the reprocessing

and reuse of their own dialyzers.

### 4.3 Equipment maintenance record

A log must be maintained of the date of preventive maintenance procedures and the date of 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 to monitor exposure to substances of known or suspected toxicity that may be required by OSHA or other regulatory agencies.

### 4.5 Complaint investigation record

A file must be kept of all complaints by patients and staff about failures of reprocessed dialyzers or possible adverse reactions to reprocessed dialyzers; the results of a comprehensive investigation of these alleged problems; and if appropriate, the corrective actions taken. The file should be reviewed periodically for trends that may contribute to patient morbidity and mortality.

### 4.6 Quality assurance and quality control record

A record must be kept of the date and results of QA and QC evaluations and the person(s) conducting the evaluations.

## 5 Personnel qualifications and training

### 5.1 Qualifications

Personnel should possess adequate education or experience to understand and perform procedures outlined by the individual dialysis facility relevant to the facility's multiple use program. These people currently range from those with no medical background who are fully trained by the facility, to licensed practitioners with extensive medical background.

### 5.2 Training

#### 5.2.1 Curriculum

The dialysis facility's physician/director shall establish a training course for the persons performing hemodialyzer reprocessing. A written document should give details about the curriculum and should in particular address the potential risks to patients and staff 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;

j) the principles of dialysis, emphasizing the characteristics of the hemodialyzer.

### 5.2.2 Documentation

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

## 6 Patient considerations

### 6.1 Medical issues

A decision to reprocess hemodialyzers should be made by a physician knowledgeable about reprocessing and its medical and economic implications. Dialyzers shall 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 shall stipulate whether and how reprocessing will be done for patients who have shown sensitivity to materials used in the reprocessing of hemodialyzers. Since the current human immunodeficiency virus (HIV) or hepatitis B status of the patient cannot be known with certainty, all staff potentially exposed to patients' blood should observe universal precautions.

### 6.2 Informed consent

Opinions differ about the need for specific informed consent for reprocessing hemodialyzers. If informed consent specifically for hemodialyzer reprocessing is obtained, the informed consent form should be in the medical record. The physician director and staff are responsible for fully informing patients of the dialysis facility's practices with regard to reuse of hemodialyzers and other dialysis supplies (as required by HCFA).

## 7 Equipment

Each piece of equipment used for reprocessing must 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 should be ensured by appropriate functional tests. Strict quality control (QC) must be maintained for either type of dialyzer reprocessing equipment. Additionally, complete documentation of system function, operating procedures, potential system failures and dialyzer-reuse criteria must be in the dialyzer reprocessing manual, known to the operator and available for review.

### 7.1 Water systems

The system providing water for reprocessing must meet all the requirements for pressure, flow rate, bacteriological and pyrogenic contamination, and other requirements for operating the reprocessing equipment under minimal and peak load conditions.

### 7.1.1 Disinfection

The design of the water system should facilitate easy cleaning and disinfection of the entire system. Disinfection of the water system, including any booster pumps and water storage tanks, should be done whenever necessary to achieve the quality of water specified in 11.2.2 and 11.4.1.2. The disinfection procedure must include purging all portions of the system so that the residual germicide is reduced to safe

levels as demonstrated by an appropriate test. The dates of disinfection and the dates and results of tests for residual disinfectant should be recorded in the equipment maintenance record (see 4.3), accompanied by the signature or other unique means of identification of the person performing the procedure.

### 7.1.2 Testing water quality

Product water used for rinsing, cleaning, and to dilute the germicide must be tested for the degree of bacterial and/or endotoxin contamination as specified in 11.2.2 and 11.4.1.4. Water bacteriology monitoring should 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's 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

Dialyzer test methods (11.3) and the test for the concentration of germicide shall be established prior to clinical use of the reprocessed dialyzers (see 11.4.1.5 and 12.3.2 or 12.3.3). For automated systems, this can be done by following the manufacturer's instructions. For manual systems, this can be done by confirming the accuracy of total cell volume (TCV) measurement and germicide concentration. Verification of tests should be repeated after each significant change in the reprocessing system.

### 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 alternative approaches are supported by documented experience. If these guidelines are not available, inspection should be semiannual. A record should 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, the problem should be investigated and repaired by qualified personnel. The reprocessing system function testing should be repeated after repairs of automated equipment and, if appropriate, after repairs of manual equipment before the reprocessed hemodialyzer 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 to maintain acceptable ambient concentrations of harmful substances. The area should be kept clean and sanitary. It may be part of the dialysis treatment area, as long as properly designed and vented equipment is used that meets the requirements for environmental safety (see 8.5).

## 8.2 Storage area

Reprocessing materials, devices awaiting reprocessing, and reprocessed devices should be stored so as to minimize deterioration, contamination, or breakage. Segregation of new, used, and reprocessed dialyzers should be maintained to make clear the status of each group of dialyzers. When appropriate, environmental contamination of the storage area should be controlled and monitored. 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, 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

Durable gloves and protective clothing should be worn when handling the dialyzer during initiation and termination of dialysis and during the reprocessing procedure. Universal precautions shall be observed. Eye protection should be worn when performing steps that may result in spills or splashes of substances of known or suspected toxicity. These agents should only be handled in areas with adequate ventilation, washing facilities, eye wash stations, appropriate respirators, and spill control materials. When handling concentrated toxic substances, aprons impervious to these substances should be worn.

### 8.5 Environmental safety

The dialysis facility should have written procedures for safe storage and handling of chemicals used in reprocessing (see National Institute of Safety and Health (NIOSH)/OSHA, 1980 and Sax, 1979 cited in annex D, and material data safety sheets cited in section 3 for useful information). Vapors from reprocessing materials should be maintained below potentially toxic levels (see table 1).

**Table 1—OSHA Environmental exposure limits (*29 Code of Federal Regulations* [CFR] 1920-1990)**

| Substance/material | Limits |
|---|---|
| Formaldehyde | 0.75 ppm TWA<br>3 ppm STEL<br>0.5 ppm action level |
| Glutaraldehyde | 0.2 ppm |
| Phenol | 5 ppm TWA |
| Acetic acid | 10 ppm |
| Peracetic acid | None developed |
| Chlorine dioxide syn: Chlorine oxide | 0.1 ppm TWA |
| Hydrogen peroxide | 1 ppm TWA |

TWA = time weighted average
STEL = short term exposure limit
ppm = parts per million

## 9 Reprocessing supplies

### 9.1 Specifications and testing

Each reprocessing material should meet a certain level of quality that ensures its suitability for the intended purpose. This requirement may be determined by certification by the supplier of the product that the product meets necessary specifications, or by relevant identification or testing procedures by trained personnel, as appropriate. When testing is performed, a log of the date, the identifying number for the delivery or batch, and test results should be maintained.

### 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 must be used for only one patient. The labeling therefore must 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 should be labeled prior to or at the first use of the device, and the label should 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 and/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 must be labeled with the patient's name, the number of previous uses, and 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 identification of the person performing the various steps in the reprocessing procedure, and the reference values for performance parameters. When this information appears on the label, a permanent record should also be kept (see 4.2).

## 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 C (normative). The results of the tests and the signature or other unique means of identification of 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.

### 11.1 Transportation and handling

Dialyzers should be handled and transported in a clean and sanitary manner. Persons handling used dialyzers during transportation should do so in a clean and sanitary manner maintaining universal precautions until disinfection is complete.

### 11.2 Rinsing/cleaning

**11.2.1** Dialyzer reprocessing should be initiated in sufficient time to produce a reprocessed device that meets the requirements of 11.3. Each dialysis facility should establish its time limits. Staff involved in the handling, transport, or storage of dialyzers, locally or at remote locations, should take necessary precautions to prevent exposure to possibly infected blood.

**11.2.2** The dialyzer should be rinsed and cleaned with a fluid or fluids that enable it to meet the specification of 11.3. Both the blood and dialysate compartments should be flushed with a rinsing/cleaning solution. The water should have a bacterial colony count of less than 200 per ml or a bacterial lipopolysaccharide (LPS)

concentration of less than 1 ng/ml as measured by the *Limulus* amebocyte lysate assay.

**11.2.3** Diluted solutions of hydrogen peroxide, sodium hypochlorite, peracetic acid, or other chemicals may be used as cleaning agents for the blood compartment, providing that the cleaning agent has been shown to be reduced to safe levels by subsequent flushing and that the structural integrity and performance of the dialyzer are not significantly affected adversely.

Each chemical must be removed before the next is added, unless mixing is known to be safe and effective for reprocessing. A cleaning agent, such as sodium hypochlorite, must be cleared before adding formaldehyde in order to avoid noxious fumes and degradation of disinfectant. Combining sodium hypochlorite and peracetic acid may produce hydrochloric acid vapors.

**11.3 Performance measurements**

**11.3.1 Performance test after each use**

*In vitro* clearance of a small molecule such as sodium or urea or a comparable clearance, should be used as the actual reject criterion unless there is a strong correlation between clearance and another measurement. If clearance is used, a 10 percent loss is acceptable. Total cell volume (TCV) may be used for hollow-fiber dialyzers. The acceptable TCV is at least 80 percent of the original TCV.

**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 must be treated by a process that prevents adverse effects due to microbial contamination. The blood and dialysate compartments of the dialyzer must be sterilized or subjected to high-level disinfection because an inadequate germicide will result in infection in the patient. Low-level disinfection is sufficient for the exterior of the device.

**11.4.1 Interior (blood/dialysate compartment)**

**11.4.1.1 Germicide**

Chemical germicides or other disinfection procedures used for disinfection of hemodialyzers must have been shown to accomplish at least high-level disinfection when tested in a variety of dialyzers artificially contaminated with appropriate microorganisms, including the highly resistant water-adapted forms. If formaldehyde is used as the sole germicidal agent, the Centers for Disease Control (CDC) recommends that a concentration of 4 percent (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 Pharmacopeia (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, be sure that the chemical is not outdated. Some germicides have recommendations for maximum storage time after dilution and/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 this date should be checked at the beginning of each day, before reprocessing begins. If the temperature of the disinfection process is elevated,

appropriate recording means must be employed to assure that this criterion has been met. If maximum storage temperature limitations exist, records should be maintained to document this criterion. The disinfection process must not adversely affect the integrity of the dialyzer. Germicides must 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, care should be taken not to mix reactive materials such as sodium hypochlorite and formaldehyde.

#### 11.4.1.2 Chemical germicide diluent

The water used to prepare the germicide solution should have a bacterial colony count of less than 200 per ml or a bacterial LPS concentration of less than 1 ng/ml as measured by the *Limulus* amebocyte lysate assay.

#### 11.4.1.3 Chemical germicide procedure

The hemodialyzer should be filled with the germicide solution until the concentration in the hemodialyzer is at least 90 percent of the prescribed concentration. The ports of the dialyzer should 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, with any other germicide approved by the EPA as a disinfectant, by steam, or by ethylene oxide gas.

#### 11.4.1.4 Monitoring

The water used to rinse and clean dialyzers and to dilute the germicide should be tested for bacterial contamination (culture and/or pyrogen testing—see 11.2.2 and 11.4.1.2) before a reprocessing program is undertaken. After 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 the results are considered satisfactory.

#### 11.4.1.5 Chemical germicide concentration

With reprocessing systems where each batch of germicide is manually prepared, each batch of germicide should be tested prior to use to verify the proper concentration of the germicide. 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, using at least a low-level germicide which is compatible with the dialyzer materials of construction. Sodium hypochlorite at a concentration of 0.05 percent is usually suitable for this purpose. 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, that the dialyzer is not damaged, and that rinsing of blood has been satisfactorily completed. The dialyzer should also be aesthetically acceptable in appearance.

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

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

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

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

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

**11.5.6** The label should be properly filled out and legible.

### 11.6 Disposition of rejected dialyzers

Reprocessed dialyzers which have been rejected for failure to meet performance, inspection, or other release criteria should either be immediately discarded or be further reprocessed and subjected to the performance requirements of 11.3, 11.4, and 11.5. In the latter instance, the dialyzer must 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 one month) must be documented to be safe and effective.

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

A written procedure should be followed which renders the reprocessed dialyzer safe for subsequent use.

### 12.1 Visual inspection

The dialyzer should be inspected before preparing it for use. Completion of this inspection should be recorded in the reprocessing record (see 4.2), accompanied by the signature or other unique means of identification of the person completing the inspection. The inspection should include the following features:

a) The label on the reprocessed dialyzer should be intact, affixed to the device, legible, and should contain 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; the presence of germicide in the dialysate and blood compartment, including headers, should be confirmed; and there should be no evidence of leakage from the ports or other portions of the dialyzer;

d) the duration of storage should be appropriate for the agent or method used to sterilize or disinfect the dialyzer;

e) the cosmetic appearance of the dialyzer should be aesthetically acceptable.

### 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 should be recorded in the reprocessing record (see 4.2), accompanied by the signature or other unique means of identification of the person verifying patient identification.

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

### 12.3 Verification of germicidal contact

The contact time of the germicide or disinfection procedure must comply with the facility's protocol. The presence of chemical germicide in each hemodialyzer must be assured through direct testing or on-line process and procedural control. If other disinfection procedures are employed, there must be methods to assure that each hemodialyzer has been properly subjected to the disinfection process. An individual mark should clearly identify the operator responsible for this verification.

### 12.3.1 Time period

The period of time that each hemodialyzer was filled with germicide or exposed to the disinfection process must meet or exceed the minimum time specified by a written procedure or manufacturer's recommendations.

### 12.3.2 Presence test of each hemodialyzer

Certain germicide manufacturers require the testing for presence of germicide in each hemodialyzer prior to rinsing. These instructions must be followed.

### 12.3.3 Process control and sampling

In the absence of the requirement in 12.3.2, the presence of germicide may be assured by a direct presence test of each hemodialyzer or the use of process control and sampling of the dialyzer for germicide.

#### 12.3.3.1 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, such as FD&C Blue #1 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 the use of dye may be inappropriate with certain germicides.

#### 12.3.3.2 Sampling

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).

b) For germicide prepared in batches, sample at least one hemodialyzer from each batch with a direct presence test.

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

## 12.4 Priming the dialyzer and rinsing of the germicide

The dialyzer shall be rinsed and primed according to a procedure that has been documented to produce a reduction in the concentration of germicide to an acceptable level and to result in a physiological solution in the blood and dialysate compartments.

### 12.4.1 Testing for residual germicide

Residual germicide shall be measured by a test of appropriate sensitivity according to a written procedure in order to ensure that the germicide level is below the maximum recommended residual concentration. In the case of formaldehyde, the recommended maximum level is 5 ppm. Completion of this step should be documented in the reprocessing record (see 4.2), accompanied by the signature or other unique means of identification of the person performing the test. A written policy should establish the maximum allowable time between rinsing the germicide from the dialyzer and beginning dialysis.

### 12.4.2 Repeat of germicide removal and testing steps if required

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 prior to the initiation of dialysis. Define and document your rinse procedure step by step, and assure that all personnel are familiar with it and follow it.

### 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. Any alterations in the procedures shall be approved by the physician in charge of the reuse program.

## 13 Monitoring

### 13.1 Dialysis

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

### 13.2 Symptoms

#### 13.2.1 Fever and chills

Temperature should be measured and recorded at least before and after dialysis with new and reprocessed dialyzers. A temperature of over 37.8°C (100°F), taken orally, or chills should be reported to the physician. Unexplained fever and/or chills occurring more often than just during dialysis with new dialyzers should be promptly evaluated for endotoxin contamination of the water used for reprocessing (see 11.2.2 and 11.4.1.2) and of the sterilization or disinfection process (see 11.4 and table 2).

#### 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 the new or reprocessed dialyzer. Suspected reactions to the residual germicide should prompt reevaluation of the rinsing procedure and test for residual germicide (see 12.4.1 and 12.4.2 and table 2).

#### 13.2.3 Recording

Any significant events such as the symptoms listed above should be recorded on an incident report form which includes the results of any evaluations conducted by the physician and others and reported to the manufacturers in accordance with the Safe Medical Devices Act of 1990. 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 or excessive deviations from the expected ultrafiltration (weight loss) should be recorded in a log kept in the complaint investigation file (see 4.5). If there is excessive deviation from the expected ultrafiltration, testing should be repeated (see 11.3.2) and appropriate adjustments made in the reprocessing procedure or the algorithm for estimating the expected ultrafiltration. Deterioration of a patient's clinical condition or variability of routine dialysis procedures (heparinization, ultrafiltration, transfusion requirement) require investigation of all practices, including reuse. Reports of investigations should be filed in the complaint log. A progressive, otherwise unexplained rise in serum creatinine should also be recorded in the complaint investigation file and properly investigated.

### 13.4 Clinical results

In order to assure that all parameters relating to hemodialyzer clearance are being met, monitoring of relevant patient results is recommended. Specifically, regularly sequential pre- and post-dialysis blood urea

nitrogen (BUN) ratios (or formal urea kinetic modeling studies) should be done. The failure of these results to meet the expectations of the dialysis prescription should be investigated.

**Table 2—Patient safety**

| Patient health effect | Probable underlying cause |
|---|---|
| Infection | Improperly used or selected germicide or method |
| | Contamination or break in sterile procedure during dialyzer rinsing, priming, or set-up |
| Pyrogen reaction, endotoxemia | Improper processing technique, contaminated water used to rinse dialysers or to prepare germicide solutions |
| Acute chemical reactions | Inadequate dialyzer preparation and priming procedures |

## 14 Quality assurance

It is the responsibility of all staff to carry out critical scrutiny of 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, from consensus documents such as AAMI guidelines or standards, from aggregated regional or national data, or from other accepted norms. The criteria chosen as the internal standards of a facility must 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 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 reuse processes.

### 14.1 Records

A record of review, comments, trend analysis, and conclusions arising from quality assurance (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 followed up until a solution is in place and demonstrated to be effective. High volume tasks of recognized hazard should have frequent (weekly or daily) oversight. Practices with little potential for harm may only need critical scrutiny on a quarterly or annual basis. The medical director is responsible for the schedule of review, endorsement of findings, and, where appropriate, implementation of changes.

### 14.3 Patient considerations

Personnel should audit compliance with policy for informed consent at least annually.

### 14.4 Equipment

Designated staff 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. At least twice a year, designated staff should verify the testing procedures recommended in 7.1.1, 7.1.2, and 7.2.2.

### 14.5 Physical plant and environmental safety considerations

Designated staff should audit the provisions of 8.1 through 8.3 at least annually. The provisions of 8.2 should be audited at least quarterly. Designated staff should verify the tests(s) specified in 8.3 at least quarterly.

### 14.6 Reprocessing supplies

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

### 14.7 Hemodialyzer labeling

The provisions of section 10 should be audited by designated staff at least quarterly.

### 14.8 Reprocessing

Designated staff should audit the written procedures for the various steps in this process and verify implementation, at least monthly to begin with. Semiannual audits may be sufficient, based on a documented history of favorable results. Designated staff should perform the necessary testing specified in section 11. Trend analysis should be done.

### 14.9 Preparation for dialysis

Designated personnel should audit the written procedures and verify their implementation at least quarterly. Designated staff should verify the tests for the presence of germicide and the test for residual germicide by using positive and negative control solutions at least quarterly.

# Annex A
(Informative)

**Rationale for the development and provisions of this recommended practice**

## A.1 Scope

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 exists 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.

Labeling and performance requirements for new hemodialyzers are covered by the American National Standard, *First Use 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.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 quality control (QC) and quality assurance (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, those reprocessing records 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, since both of these are traceable, permanent records and it may be inconvenient to record all the information in one location. The committee decided not to include a specific recommendation for a checklist for initiating dialysis, because although this 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.5 Personnel qualifications and training

The committee did not accept a proposal to include curriculum covering the entire range of technical activities related to dialysis. It was 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 accepted since certification of training (see 5.2.2) renders the recommendation superfluous.

## A.6 Patient considerations

### A.6.1 Medical issues

The primary objective of the committee was not to recommend medical indications for reprocessing or to evaluate the medical or economic implications of reprocessing, but to provide recommendations for safe reuse practice. Many professionals consider the "first-use syndrome," (see Definitions) to be a specific indication for reprocessing.

At the time of this writing, the Centers for Disease Control (CDC) does not object to reprocessing and reusing dialyzers from patients with C hepatitis due to lower viral burden. CDC is also not opposed to the reprocessing of dialyzers from patients with known HIV infection. The committee recommends, however, that universal precautions be used in the reprocessing of all dialyzers. These precautions include the use of gowns, masks, and gloves. Each facility must 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 is 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. It is also asserted that for most patients honest, trusting interaction with their personal physicians is a sufficient guarantee of quality, but the imposition of a dictatorial relationship may lead patients to seek recourse through legal means. 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 due to the confusion that could be created by personal preferences for, as examples, length of dialysis, choice of blood flow, fluid removal rate, etc. They argue that multiple use of hemodialyzers can properly be implied in the consent for hemodialysis therapy just as are other treatments.

The topic of physician/patient relationships is important to mention 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 improve the quality of care. The committee also considered the question of the right to freedom of choice 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 (see Rettig, 1982).

Fear of increased risk, anger over presumed profits, and frustration surrounding consent issues have been expressed by some patients. Establishing QA practices such as those recommended here and sharing information with patients to educate them, responding to questions, and eliminating any impression of secrecy are encouraged as effective solutions to these problems.

The fact that the majority of dialysis facilities reprocess hemodialyzers and the long history of this technique

support the conclusion that the 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.

## A.7 Equipment

Validation of dialyzer performance and 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 the replacement of hoses, valves, and the like in these simple systems will not affect performance. The recommendation was subsequently changed to testing the function of the reprocessing system because the committee judged that demonstration of proper system function 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 it) 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 not accepted, because these measures to control bacterial contamination were deemed inappropriate for reprocessing since the exposure of the dialyzer to bacterial contamination is limited to making connections comparable to setting the device up for dialysis. Another proposal that the reprocessing area be negatively pressurized to control odors was not accepted because the committee agreed that odor control can be achieved by other methods. The committee also determined that it was not necessary to recommend facility design, since a number of configurations have been shown to be satisfactory, including the 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. The importance of trained personnel evaluating the supplies is illustrated by an instance where formaldehyde contained a hydrocarbon contaminant from a storage tank. This is also the rationale for recommending USP grade formaldehyde.

### A.9.2 Inventory control

The committee suggests 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 dialyzer to be reprocessed should be labeled prior to or at the first use to ensure that the patient will be correctly identified and to have the label available for the information recommended in 10.3.

### 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 not accepted because space limitations may make this impractical, and there is no need to have all of the information on the label. Display of the number of previous uses on the label is recommended so that this information is readily available. 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 where confusion with another patient's dialyzer will not occur.

## A.11 Reprocessing

### A.11.1 Termination of dialysis

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

### A.11.2 Rinsing/cleaning

**A.11.2.1** The committee considered stipulating a period of time after dialysis within which reprocessing must 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 fluids for rinsing and cleaning (Bass et al., 1973). Some clinics have refrigerated dialyzers until they are reprocessed to retard bacterial growth and clotting.

**A.11.2.2** A proposal that only treated water or physiological saline be used was not accepted at first, because some safe and effective techniques employ 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 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 lipopolysaccharide (LPS) of 1 ng/ml.

The chemical quality of the water is 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 reverse osmosis quality water yields more reuses (F. Gotch, personal communication).

The committee had included a recommendation that any device which interfaces between the blood compartment and the permanent equipment must 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 are lacking.

### A.11.3 Performance measurements

As dialysis facilities have attempted to rigidly comply with the 1986 edition of this recommended practice due to adoption of this document by the Health Care Financing Administration [HCFA], some have misunderstood or expressed concern about the "validation" for indirect measures such as total cell volume (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, 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 Clearance

A measure of solute transport of the hemodialyzer, clearance must 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, 1981), the committee decided that the urea clearance should be the recommended criterion for rejecting a dialyzer. The alternative of sodium clearance was included since sodium and urea clearance are similar and the former may be more easily accomplished. The committee agreed that an acceptable tolerance for urea or sodium clearance is ± 10 percent because this amount of variation does not result in a clinically significant change in the BUN of the patient. The committee considered a proposal to include vitamin $B_{12}$ clearance as a criterion for rejection.

The committee recognizes that the clearance of larger molecules may be affected by the type of reuse cycle used, especially the cleaning agent. It was felt beyond the scope of this document to define this effect for all combinations of reuse cycles and dialyzer types.

The committee recognizes that larger molecule clearances, such as that for vitamin $B_{12}$, are largely membrane limited (Collins and Ramirez, 1979; Dorson, et al., 1983) as opposed to small molecule clearances, such as that for urea, which are largely flow-rate limited. Larger molecule clearances will therefore be disproportionately decreased by loss of membrane area or increased membrane resistance due to protein coating of the membrane (Pizziconi, 1985). It was 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).

Although direct clearance measurements fulfill these needs, determining the clearance for each hemodialyzer reprocessed may be impractical; moreover, there are indirect tests that reflect the mass transfer characteristics of the device which may be used in lieu of clearance measurements.

The residual TCV of hollow-fiber hemodialyzers, the most widely used indirect test for clearance, has been found to yield mortality and morbidity results as good or better than those for dialyzers that have not been reprocessed in studies that do not include randomized, controlled trials (Deane & Bemis, 1981). 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. Using certain methods of reprocessing that do not cause a significant change in the permeability or geometry of the membrane, a loss of TCV of 20 percent corresponds to a loss

of urea clearance of less than 10 percent (Gotch, January 1984). The committee decided not to use this as the only criterion, however, since certain methods of reprocessing could conceivably change this relationship (Pizziconi, 1985). At present, volume change is recommended as a QC test only for hollow-fiber hemodialyzers because other hemodialyzers 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 instance, 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. While it might appear that this would cause lower urea clearance, it does not. The shorter diffusion distances of the smaller fiber diameter causes an increase in urea transport rate, offsetting the loss in surface area. Following similar scientific principals, 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 the fiber. This is the reason that a 20 percent loss in surface area only yields about a 10 percent 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 recommends that, whenever possible, the user measure the original volume of each hemodialyzer prior to the first patient use and record this value as the reference TCV (reprocessing volume) for all subsequent reprocessings. It is also recognized that this is not always practical. In the absence of 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 percent of the monthly usage of dialyzers, whichever is less) for each hemodialyzer model. This should be rechecked monthly. Substantial changes in average preprocessing volume should be investigated.

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

a) fistula recirculation;

b) accurate blood and dialysate flow rate;

c) accurate time of dialysis;

d) compliance with dietary limitations;

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

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

g) variations in the original clearance and $K_{uf}$ of the hemodialyzer;

h) variations in the clearance and $K_{uf}$ of the hemodialyzer due to reuse.

A proposed indirect measure of solute clearance, other than changes in TCV, is the *in vitro* ultrafiltration coefficient of the hemodialyzer ($K_{uf}$), or its inverse, the membrane hydraulic resistance ($R_m$) (Pizziconi, 1985). Unlike TCV, measurement of $K_{uf}$ is purported to detect changes in membrane resistance as well as

changes in surface area. It has been shown, however, that the standard deviation for the regression of urea clearance vs. $R_m$ is nearly twice that of the available data for the regression of urea clearance vs. TCV in reprocessed hollow-fiber hemodialyzers (Gotch, 1985). The clinical validity of this conclusion is a matter of controversy (Gotch and Pizziconi, personal communication).

The committee recognizes that measurement of $K_{uf}$ is potentially more sensitive for large molecule clearance than for small molecule clearance (i.e., there is a greater decline in vitamin $B_{12}$ clearance than urea clearance for a given decrease in membrane surface area). It is also acknowledged that measurement of TCV and $K_{uf}$ may yield overlapping information.

The 1986 edition of this recommended practice included language that allowed a change of ±20 percent in the *in vitro* $K_{uf}$ to be used as an indirect indicator of dialyzer clearance. Due to the controversy in originally adopting this recommendation, and the fact that this technique has lost favor in actual practice, the specific recommendation was removed from this edition. However, if suitable correlation of dialyzer $K_{uf}$ (or other appropriate test) to dialyzer clearance can be demonstrated, such techniques may be used.

Of particular concern to this committee are any variations in hemodialyzer functions related to reuse procedures. While there have been documented cases (Delmez, 1989), they are very rare, especially as compared to the other factors listed above. For this reason, the committee strongly feels that the monitoring requirements of section 13 are of great importance to use in conjunction with the individual hemodialyzer measurements recommended in 11.3.2.

### 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 ultrafiltration coefficient of the hemodialyzer ($K_{uf}$), 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.

*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 occurs in part due to 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 since clotting also occurs in these devices, it was decided that *in vitro* $K_{uf}$ should not be recommended to predict in vivo ultrafiltration performance in these devices as well.

The committee recognized the possibility 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. It was 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 percent per degree centigrade. Thus, care must 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. Based on recommendations of 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 percent of the test pressure. A maximum allowable pressure drop is not given because of variations among test systems and dialyzers.

## A.11.4 Germicide

The terms "high-level disinfectant" and "low-level disinfectant" are taken from Dr. Earl Spalding, whose system classifies a germicide as a high-level disinfectant if it inactivates all vegetative organisms in a specified, relatively short period of time (i.e., 10-30 minutes) (Spalding, 1972). This implies a destruction of pathogenic bacteria and viruses but not large numbers of bacterial spores. When exposure time is extended (i.e., 6-10 hours), the same formulation often inactivates large numbers of bacterial spores which changes the classification to a sterilant (an agent that inactivates all forms of microbial life, including spores) or a sporicide (an agent that inactivates bacterial spores—this usually means inactivation of all microbial life and therefore is synonymous with "sterilant"). An example is 2 percent activated glutaraldehyde which is used as a high-level disinfectant for exposure times of 10 to 30 minutes for certain types of medical devices; this same formulation can accomplish sterilization of other types of medical devices when the exposure time is 10 hours.

A low-level disinfectant in the Spalding classification has limited activity and is not effective for bacterial spores, mycobacteria, or certain types of viruses, but is effective for other types of organisms. Low-level disinfectants are used primarily to reduce microbial contamination to a comparatively safe level.

The committee is aware that the EPA regulates and registers germicides formulated as "sterilants," "sporicides," "disinfectants," and "sanitizers" and that these terms may or may not be synonymous with the Spalding classification used in this recommended practice. The EPA classification is based primarily on specific label claims as well as the intended use of the chemical germicide. The definitions for "sterilant" and "sporicide" are the same as the Spalding definitions, but the definition for "disinfectant" is not. For example, according to Spalding a disinfectant which is labeled a "hospital disinfectant" has been tested against certain species of *Salmonella*, *Staphylococcus* and *Pseudomonas*. If the label claims that the formulation is also mycobactericidal, then *Mycobacterium bovis* is also tested. No such differentiation is made in activity in the term "disinfectant" by the EPA. Consequently, a "high-level" disinfectant in the Spalding classification may or may not be the same formulation as an EPA "disinfectant." The EPA "sanitizer" is synonymous with "low-level disinfectant" in the Spalding classification. ("Antiseptics," which are chemical germicides formulated for use on skin and tissue, should not be confused with "disinfectants," which are formulated for hard surfaces or medical devices; antiseptics are regulated by the FDA Center for Drugs and Biologics.)

The EPA requires manufacturers of chemical germicides formulated as general disinfectants, hospital disinfectants and disinfectants applied in other industries (e.g., food) to test these formulations by using certain protocols for microbiological efficiency, stability, and toxicity to humans. The decision to register a

disinfectant and to approve label claims is based on data provided to the EPA by the manufacturer.

EPA approval differs from approval by CDRH. The FDA considers a germicide used in reprocessing of hemodialyzers a medical device and regulates the labeling of such products. The agency also relies on the testing submitted by the manufacturer. Rather than using the definitions given above, the FDA at present requires that the label indicate the organisms tested and the conditions of the tests.

### A.11.4.1 Interior (blood/dialysate compartment)

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

Over the years, a variety of 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 percent, glutaraldehyde solutions, solutions containing peracetic acid as the active ingredient and, more recently, heat sterilization.

The reason, in part, for using formaldehyde at concentrations that are less than the sterilization cycle concentration (i.e., 8 percent 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 dialyzers; 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 endotoxin which cause pyrogen reactions in dialyzing patients if the endotoxins are introduced into the blood stream. Outbreaks of pyrogenic reactions during dialysis have ceased when steps were taken to reduce the colony count in the dialysate at the end of dialysis to less than 2000 per ml. The maximum allowable colony count in the water used for dialysis was estimated to be 200 per ml (AAMI, 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 was decided to add the alternative of a maximum bacterial LPS concentration of 1 ng per ml for the water used to dilute the germicide since the association of reprocessed hemodialyzers with pyrogenic reactions has been defined by the LAL test rather than culture (Petersen, et al., 1981), and since 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, 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 USP for detecting bacterial endotoxin in water. Further, the committee believes that reliable, reproducible LAL tests are readily available.

Another group of water bacteria can constitute a hazard in a dialysis center. These are the nontuberculous mycobacteria, which 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 lipopolysaccahrides, 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 2 percent alkaline glutaraldehyde. By comparison, *Pseudomonas aeruginosa* at a concentration of $10^6$/ml would be

inactivated within a matter of minutes. Using 8 percent 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 that CDC has conducted have demonstrated that the nontuberculous mycobacteria associated with the water systems in this center can readily survive 2 percent formaldehyde after 24 hours of exposure; in other instances, some strains survived for up to 96 hours. Obviously, this is not high-level disinfection. Further laboratory studies have shown that if the concentration of formaldehyde is increased to 4 percent, 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 CDC has stockpiled and which include 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), CDC also showed incomplete kill of mycobacteria in manually reprocessed high flux dialyzers using 2.5 percent 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 upon 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 to either use 4 percent instead of 2 percent formaldehyde or 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 is a much simpler approach. Moreover, there appears to be a scientific basis for considering 4 percent formaldehyde at a 24-hour exposure as at least a high-level germicide process. All laboratory data acquired so far show that 24 hours of exposure with 4 percent 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 percent formaldehyde is used, both the dialysate and the blood compartment must 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 percent formaldehyde through each compartment before the dialyzer is sealed for storage. The committee decided to specify an effluent within 10 percent of the original concentration to avoid a design standard that might not be appropriate in the future.

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

The committee is aware of published information regarding the use of 1 percent 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 this seems to be an acceptable alternative to 4 percent formaldehyde at 20°C.

There is, unfortunately, no realistic procedure whereby a dialysis center can monitor the effectiveness of the disinfection procedure. Such sophisticated microbiologic tests cannot be performed in dialysis centers. Moreover, this means of verification should not be attempted because it requires the use of specialized

equipment and highly trained microbiologists. Instead, a center should adhere rigidly to established protocols for QC and QA. Monthly tests for total bacteria and/or endotoxin levels in the water used to make up the germicide should be conducted. Testing of the germicide's final-use concentration should be 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 percent 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 for making the dialysate. This was deleted because of the lack of consensus on this issue, as noted above (see 7.1).

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.

HCFA requires (42 CFR 405.2150) that dialyzers shall not be subjected to multiple germicide solutions due to possible combined actions of the germicides on the hemodialyzer membrane. This 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 feel that this requirement is unnecessary if each hemodialyzer is subjected to an air pressure leak test as part of the reuse process.

### A.11.4.2 Exterior

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

### 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 since the allowable clots must 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 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 provided.

### A.11.7 Storage

The committee acknowledged that the selection of one 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 one month, and therefore felt that this was a reasonable period of time.

## A.12 Preparation for dialysis and testing for potentially toxic residues

The committee considered methods other than direct testing of the germicide as a process control in each hemodialyzer. It was 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 are 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. Certain germicide manufacturers recommend this procedure, and their recommendation should be followed. If each hemodialyzer is not tested for presence, then a combination of process control and sampling was considered to be adequate. By conducting the test prior to use of any of a batch of dialyzers, all dialyzers from these batches may be quarantined or released.

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 due to formaldehyde in reused dialyzers, does not occur below a residual formaldehyde level of 10 ppm (see Howell, 1972; White, 1977; Crosson, 1976); (b) the maximum daily dose of formaldehyde from dialysis is less than the California OSHA daily limit, which is based on a 5-day week, whereas dialysis patients usually dialyze three or fewer times a week (Gotch, 1984); (c) there is no evidence of toxicity due to 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; and (d) residual formaldehyde levels lower than 5 ppm are difficult to monitor and considerably increase the time required to prepare the dialyzer for dialysis.

The committee considered establishing maximum residual levels for germicides other than formaldehyde. Consensus could not be reached on this issue because of the relative lack of experience with these agents in reprocessing hemodialyzers. It was noted that toxicology studies are favorable for some of these agents and that the labeling information for them, which includes the maximum residual level, is reviewed by the FDA.

### A.12.1 Visual inspection

See section A.12.

### A.12.2 Verification of patient identification

See section A.12

### A.12.3 Verification of germicidal contact

See section A.12.

### A.12.4 Priming the dialyzer and rinsing the germicide

See section A.12.

### A.12.4.1 Testing for residual germicide

See section A.12.

### A.12.4.2 Repeat of germicide removal and testing steps if required

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, while not all- inclusive, should be carefully considered when developing the 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 connection to the hemodialyzer. If peracetic acid-type germicide is used, be sure the blood side is flushed 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 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) Care must be taken to avoid a false negative residual disinfection test by sampling too quickly after a quantity of saline has been infused. Equilibration must take place before sampling.

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 bloodline.

## A.13 Monitoring during dialysis

### A.13.1 Dialysis

No additional rationale 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 due to other factors such as infections not attributable to dialysis and to hypovolemia.

### 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 Monitoring of clinical results

Critical assessment of chemistries, as are 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. Instead of measuring only the clearance of the dialyzers, the overall effectiveness of the entire treatment is measured. No other measure of the effectiveness of new or reused dialyzers is as clear or relevant. Trend lines developed from these data characterize the quality of therapy. Information concerning protein intake and catabolic rate may be necessary because of their effect on BUN concentration. Other processional 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). In order to document adequate mass transfer, parallel measurements of pre- and post-creatinines may be helpful. When problems develop with any patient or group of patients, monitoring intensity must be increased and other methods 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, 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: (a) adequate device cleaning and sterilization; (b) the lack of adverse effects on device quality or physical characteristics; and (c) that the device remains safe, reliable, and effective for its intended use. The committee believes that compliance with these recommendations necessitates use of regularly examined reprocessing procedures based on methods of demonstrated effectiveness carried out under conditions safe to the patient and to the personnel.

# Annex B
(Informative)

### Formaldehyde assay method

The following assay method for formaldehyde in the range 0.5 – 5 percent W/V is simple, accurate, and rapid. Formaldehyde reacts with sodium sulfite to effect a quantitative release of sodium hydroxide. The concentration of formaldehyde is computed from the volume of a *standard* sulfuric acid solution required to neutralize the sodium hydroxide. This method is a minor modification (for the concentration range of interest) of the Sodium Sulfite Method developed by Lemme and improved by Seyewetz and Gibelo and Sadtler.

In addition, other analytical and commercially available methods may be used.

## B.1 Materials

a) 125 ml glass, polystyrene or polymethylpentene Erlenmeyer flask;

b) 1 ml pipette or disposable syringe;

c) 3 ml disposable syringe (use 1 ml syringe for F concentration <1.5 percent);

d) 5 percent (W/V) sodium sulfite solution;

e) 0.1 – 1 percent (W/V) thymolphthalein solution (in reagent alcohol);

f) sulfuric acid solution, 0.5 N (N/2), certified, 1 liter.

## B.2 Purchase

a) Sodium sulfite anhydrous, crystal, certified or reagent grade, 500 grams;

b) reagent alcohol, or ethyl alcohol denatured, 500 ml;

c) thymolphthalein reagent, 25 grams or thymolphthalein solution 0.1 – 1 percent (for 2 and 3);

d) sulfuric acid solution, 0.5 N (N/2), certified, 1 liter.

NOTE—This solution is the *standard* for the formaldehyde concentration measurement. It must be carefully

stored, tightly capped, and protected from contamination or corruption.

## B.3 Prepare solutions

a) *Sodium sulfite solution, 5 percent*. Dissolve 50 g (a 30 ml—one ounce—dry measure is sufficiently accurate for this purpose) in sufficient reverse osmosis water to make one liter. Store in tightly capped glass bottle. Discard when 500 ml is consumed.

b) *Thymolphthalein solution*. Dissolve 1 gram (3 ml—1/2 tsp—dry measure) in 100 ml alcohol. Store in tightly capped glass bottle.

## B.4 Method

a) Pour approximately 10 ml of 5 percent sodium sulfite solution into clean Erlenmeyer flask;

b) add one drop (0.1 ml) of thymolphthalein to flask;

c) add 0.5 N acid drop by drop (from 3 ml syringe) until blue color disappears (one drop is usually sufficient);

d) add 1.0 ml (accuracy is important) of formaldehyde to be tested to flask. An intense blue color will immediately develop;

e) titrate 0.5 N acid until blue color disappears, swirling contents of flask after each addition. The initial addition may be 80 percent of the volume expected to be required. Thereafter, add drop by drop by drop. View the solution from the side at the bottom of the flask;

f) the percent formaldehyde = 1.5 times the volume (ml) of acid required in the titration.

| Acid | Percent formaldehyde (W/V) |
|---|---|
| 3.0 | 4.5 |
| 2.9 | 4.4 |
| 2.8 | 4.2 |
| 2.7 | 4.0 |
| 2.6 | 3.9 |
| 2.5 | 3.7 |
| 2.4 | 3.6 |
| 2.3 | 3.4 |
| 2.2 | 3.3 |
| 2.0 | 3.0 |
| 1.9 | 2.8 |
| 1.8 | 2.7 |
| 1.7 | 2.5 |
| 1.6 | 2.4 |
| 1.5 | 2.2 |

## B.5 Suggestions to technicians

a) Rinse the flask with purified water between uses. It is not necessary to dry it. Small amounts of residual water will not affect tests.

b) Prepare a standard 4.0 percent formaldehyde solution by diluting 10.0 ml of 37 percent (W/W) (40 percent [W/V]) with 90.0 ml of purified water. Carefully store solution (it is perfectly stable) and assay it over time.

c) Practice the procedure until the maximum variability in acid volume required (when testing the 4.0

percent standard) does not exceed ± 0.1 ml.

d) FD&C Blue #1 dye added to the formaldehyde will not interfere with the interpretation of this test unless it is present in excessive amounts.

## B.6 Short version

a) Pour 10 ±1 ml of 5 percent (W/V) sodium sulfite solution into a 125 ml glass Erlenmeyer flask;

b) add 1 drop (0.1 ml) of 1 percent thymolphthalein solution;

c) add 0.5 N standard sulfuric acid solution drop by drop to decolorize;

d) add 1.0 ml of formaldehyde sample;

e) titrate with 0.5 N sulfuric acid, mixing after each addition until blue color disappears;

f) percent formaldehyde = 1.5 × volume (ml) of 0.5 N acid used in titration.

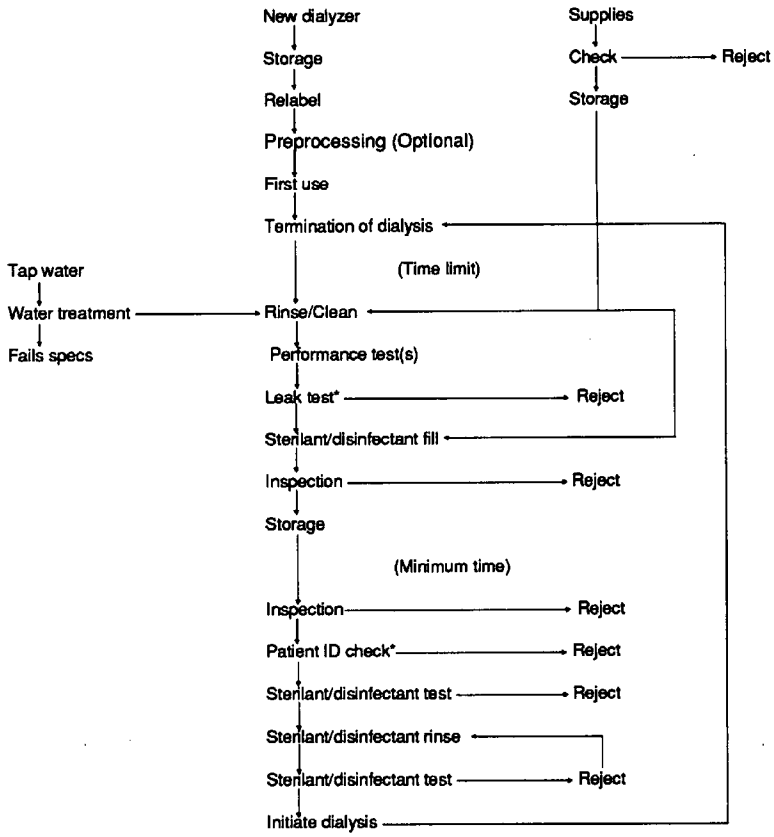
## B.7 Reference

WALKER, JF. Quantitative analysis of formaldehyde. In *Formaldehyde*, 3rd ed. New York: Reinhold; 1964, p. 486-488.

# Annex C

(Normative)

**Systems diagram for reprocessing dialyzers**




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

# Annex D
# (Informative)

## Bibliography

ALTER, MJ., FAVERO, MS., et al. Reuse of hemodialyzers: Results of nationwide surveillance for adverse effects. *Journal of the American Medical Association*, 1988, vol. 260, no. 14, p. 2073-2076.

ALTER, MJ., FAVERO, MS., MOYER, LA., BLAND, LA. National surveillance of dialysis-associated diseases in the United States, 1989. *Trans Am Soc Artif Internal Organs*, 1991, vol. 37, p. 97-109.

AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS. *Industrial ventilation: A manual of recommended practice*. 16th ed. Lansing (Mi.): ACGIH, 1980.

AMERICAN SOCIETY OF HEATING, REFRIGERATING, AND AIR-CONDITIONING ENGINEERS. *Ventilation for acceptable indoor air quality*. Atlanta (Ga.): ASHRAE Standard 62-1981. ASHRAE, 1981.

ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *First use hemodialyzers*. ANSI/AAMI RD16-1984. Arlington (Va.): AAMI, 1984. American National Standard. ISBN 0-910275-41-6.

ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Hemodialysis systems*. ANSI/AAMI RD5-1982. Arlington (Va.): AAMI, 1982. American National Standard. ISBN 0-910275-70-X.

ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Hemodialyzer reuse: Issues and solutions*. TAR #10. Arlington (Va.): AAMI, 1985. AAMI Technology Analysis & Review. ISBN 0-910275-51-3.

BASS, OE., et al. Detrimental effects of air rinsing on dialysis membranes. *Trans Am Soc Artif Internal Organs*, 1983, vol. 19, p. 466-470.

BECK-SAGUE, CM., JARVIS, WR, et al. Outbreak of gram-negative bacteremia and pyrogenic reactions in a hemodialysis center. *Am J Nephrol*, 1990, vol. 10, p. 397-403.

BERKSETH, R., et al. Peracetic acid for reuse of hemodialyzers, Clinical Studies. *Trans Am Soc Artif Internal Organs*, 1984, vol. 30, p. 270.

BLAND, LA., ALTER, M., et al. Hemodialyzer reuse: Practices in the United States and implication for infection control. *Trans Amer Soc Artif Internal Organs*, 1985, vol. 31, p. 556-559.

BLAND, LA., FAVERO, MS. Microbial contamination control strategies for hemodialysis systems. *Joint Commission on Accreditation of Healthcare Organizations: Plant, Technology & Safety Management Series: Infection control issues in PTSM*, 1990, p. 30-36.

BLAND, LA., FAVERO, MS., et al. Effect of chemical germicides on the integrity of hemodialyzer membranes. *Trans Am Soc Artif Intern Organs*, 1988, vol. 34, no. 3, p. 172-175.

BOAG, J., VLCHEK, D. Clearance testing of dialyzers using conductivity. *Contemporary Dialysis & Nephrology*, 1987, p. 11-13.

California proposed hemodialyzer reuse regulations, May 1983.

CARSON, LA., BLAND, LA., et al. Factors affecting endotoxin levels in fluids associated with hemodialysis procedures. In *Detection of bacterial endotoxins with the* limulus amebocyte lysate test. WATSON, SW., LEVIN, J., and NOVITSKY, TJ. eds., 1987, p. 223-234.

CARSON, LA., et al. Growth characteristics of atypical mycobacteria in water and their comparative

resistance to germicides. *Appl Environ Microbiol*, 1978, vol. 36, no. 6, p. 839-846.

CARSON, LA., BLAND, LA., et al. Prevalence of nontuberculous mycobacteria in water supplies of hemodialysis centers. *Appl Environ Microbiol*, 1988, vol. 54, no. 12, p. 3112-3125.

COLLINS, MC., RAMIREZ, WF. Mass transport through polymeric membranes. *J Phys Chem*, 1979, vol. 83, no. 17, p. 2294-2301.

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

DEANE, N., 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.

DEPARTMENT OF HEALTH, EDUCATION AND WELFARE. *Evaluation of Hemodialyzers*. DHEW pub. no. NIH 73-103. Bethesda (Md.): NIH, 1973.

DEPARTMENT OF LABOR. 29, parts 1900 to 1910. In *Code of Federal Regulations*. Washington, DC: Government Printing Office, printed annually.

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, p. 11-39.

FASSBINDER, W., PILAR, J., SCHEUERMANN, E., KOCH, M. Formaldehyde and the occurrence of anti-N-like cold agglutinins in RDT patients. *Proc Eur Dial Transplant Assoc*, 1976, vol. 13, p. 333.

FAVERO, MS., BLAND, LA. Microbiologic principles applied to reprocessing hemodialyzers. In DEANE, WINEMAN, and BEMIS, eds.: *Guide to Reprocessing of Hemodialyzers*, 1986, p. 63-73.

FAVERO, MS., PETERSON, N. Microbiological guidelines for hemodialysis systems. *Dialysis and Transpl*, 1977, vol. 6, no. 11, p. 34-36.

FAVERO, MS. Chemical disinfection of medical and surgical materials. In BLOCK, SS., ed. *Disinfection, Sterilization and Preservation*, 3rd ed. Philadelphia: Lea and Febiger, 1983.

FDA. Reuse of medical disposable devices, chapter 24, devices. In *Food and Drug Administration Compliance Policy Guide*, 7124.16, July 1, 1981.

FDA. *Guideline on validation of the* Limulus *Amebocyte Lysate Test as an end-product endotoxin test for human and animal parental drugs, biological products, and medical devices.* U.S. Department of Health and Human Services, Public Health Service, December 1987.

FISCHBACH, LJ. *Dialyzer Reprocessing Guidelines*. Minneapolis (Mn.): Renal Systems, 1982.

FREEMAN, PB., et al. The affinity of synthetic membranes for calcium. *Trans Am Soc Artif Internal Organs*, 1965, vol. 11, p. 99.

GORDON, SM., TIPPLE, M., BLAND, LA., JARVIS, WR. Pyrogenic reactions associated with the reuse of disposable hollow-fiber hemodialyzers. *Journal of the American Medical Association*, 1988, vol. 260, no. 14, p. 2077-2081.

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

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

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, January 1984.

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

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.

GOULD, MJ. Performing the LAL gel-clot test in facilities. *Nephrology News and Issues*, 1988, vol. 2, no. 11, p. 26-27, 29.

HARRISON, PB., JANSSON, K., KRONENBERG, H., MAHONY, JF., and TILLER, D. Cold agglutinin formation in patients undergoing hemodialysis: A possible relationship to dialyzer reuse. *Aust NZ J Med*, 1975, vol. 5, p. 195.

HIMMELSTEIN, JS. and H., FRUMKIN. The right to know about toxic exposures: Implications for physicians. *New Eng J Med*, 1985, vol. 312, p. 687.

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

KAUFMAN, A., FRINAK, S., GODMERE, R., LEVIN, N. Clinical experience with heat sterilization for reprocessing dialyzers. *Trans Am Soc Artif Internal Organs*, 1992, vol. 38, p. 338-340.

KESHAVIAH, PD., LUEHMANN, D., SHAPIRO, F., COMTY, C. *Investigation of the Risks and Hazards Associated with Hemodialysis Systems*. Technical Report, contract #223-78-5046. Silver Spring (Md.): U.S. Dept. of Health and Human Services, Public Health Service/Food and Drug Administration/Bureau of Medical Devices, 1980.

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*, 1990, vol. 161, p. 85-90.

LOWRIE, EG., LAIRD, NM., PARKER, TF., SARGENT, JA. Effects of the hemodialyzer prescription on patient morbidity. Report from the National Cooperative Dialysis Study. *New Eng J Med*, 1985, vol. 305, p. 1176.

MAHER, JF., et al. Adherence of metals to cellophane membranes and removal by whole blood: A mechanism of solute transport during hemodialysis. *Trans Am Soc Artif Internal Organs*, 1965, vol. 11, p. 104.

MAHER, JF., et al. Medical Devices; medical device, user facility, distributor, manufacturing reporting, certification and registration. *Federal Register*, November 26, 1991, vol. 56, p. 60024-30.

MICHIGAN END STAGE RENAL DISEASE NETWORK COORDINATING COUNCIL. *Standards for Dialyzer Reuse*, second draft. Ann Arbor (Mi.): Michigan ESRD Network Coordinating Council, 1982.

NATIONAL FIRE PROTECTION ASSOCIATION. *Flammable and Combustible Liquids Code*. ANSI/NFPA 30-1984. Quincy (Mass.): NFPA, 1984.

NATIONAL KIDNEY FOUNDATION. National Kidney Foundation revised standards for reuse of hemodialyzers. *Contemp Dialysis*, 1984, vol. 5, no. 2, p. 29, 37.

NIOSH/OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION. Pocket Guide to Chemical Hazards. Pub. no. 78-210. Atlanta (Ga.): Centers for Disease Control, 1980.

OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION. Chapter 29, part 1910.20. In *Code of Federal Regulations*. *Federal Register*, May 27, 1992. Washington, DC: Government Printing Office.

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

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

PETERSEN, NJ. Microbiologic hazards associated with reuse of hemodialyzers. In SADLER, JH., ed. *Proceedings of the National Workshop on Reuse of Consumables in Hemodialysis*. Washington, DC: Kidney Disease Coalition, 1983.

PETERSEN, NJ., et al. Pyrogenic reactions from inadequate disinfection of a dialysis fluid distribution system. *Dialysis & Transpl*, 1978, vol. 7, p. 52.

PIZZICONI, VB. QA and QC aspects of reuse. In *Reuse of Disposables*. TAR #6. Arlington (Va.): Association for the Advancement of Medical Instrumentation, 1983.

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.

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.

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*, 1972, vol. 9, p. 5-31.

TRAPP, GA. Plasma aluminum bound to transferin. *Life Sciences*, 1983, vol. 33, p. 311.

UNITED STATES PHARMACOPEIA. Bacterial endotoxins test. Chapter 85, p. 1493-1495. In *United States Pharmacopeia*, Volume XXII. Easton (Pa.): Mack Publishing, 1990.

WHITE, WL., MILLER, GE., KAEHNY, WD. Formaldehyde in the pathogenesis hemodialysis-related anti-N antibodies. *Transfusion*, 1977, vol. 17, p. 443.

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