On June 14, 2023, FDA issued a guidance titled "Content of Premarket Submissions for Device Software Functions."[1] This final guidance supersedes the Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices, issued on May 11, 2005. The final guidance issued on June 14, 2023, provides information regarding the recommended documentation sponsors should include in premarket submissions for FDA's evaluation of the safety and effectiveness of device software functions. In particular, the final guidance includes information to help determine a device's Documentation Level (formerly known as Level of Concern). The purpose of the Documentation Level is to help identify the minimum amount of information that would support a premarket submission that includes device software functions.

Within the framework of the superseded guidance, nocturnal home hemodialysis systems were considered a device with a Major Level of Concern. Based on the device's risk in the context of the device's intended use, as discussed in the final guidance "Content of Premarket Submissions for Device Software Functions," nocturnal home hemodialysis systems should generally address the recommendations for an Enhanced Documentation Level. The actual Documentation Level for your device may vary based on the specifics of your device. For more information about the Documentation Level and recommended documentation for a premarket submission, sponsors are encouraged to review the guidance "Content of Premarket Submissions for Device Software Functions."

[1] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/content-premarket-submissions-device-software-functions.

Guidance for Industry and FDA Staff

Investigational Device Exemptions (IDEs) for Devices Indicated for Nocturnal Home Hemodialysis

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Gastroenterology and Renal Devices Branch
Division of Reproductive, Abdominal, and Radiological Devices
Office of Device Evaluation

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Preface

Public Comment

Written comments and suggestions may be submitted at any time for Agency consideration to the Division of Dockets Management, Food and Drug Administration, 5630 Fisher Lane, Room 1061, (HFA-305), Rockville, MD, 29852. When submitting comments, please refer to the exact title of this guidance document. Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

Additional copies are available from the Internet at http://www.fda.gov/cdrh/ode/guidance/1650.html. You may also send an e-mail request to dsmica@fda.hhs.gov to receive an electronic copy of the guidance or send a fax request to 240-276-3151 to receive a hard copy. Please use the document number (**1650**) to identify the guidance you are requesting.

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Guidance for Industry and FDA Staff

Investigational Device Exemptions (IDEs) for Devices Indicated for Nocturnal Home Hemodialysis

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

1. Introduction

FDA has developed this guidance document to assist industry in preparing Investigational Device Exemption (IDE) applications for nocturnal home hemodialysis (NHHD) systems. These dialysis devices are intended to administer dialysis therapy in the home setting, while the patient is expected to be asleep.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

The Least Burdensome Approach

The issues identified in this guidance document represent those that we believe need to be addressed before your device can be marketed. In developing the guidance, we carefully considered the relevant statutory criteria for Agency decision-making. We also considered the burden that may be incurred in your attempt to follow the guidance and address the issues we have identified. We believe that we have considered the least burdensome approach to resolving the issues presented in the guidance document. If, however, you believe that there is a less burdensome way to address the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html.

2. Scope

This guidance document addresses IDE applications only for the clinical investigation of a hemodialysis delivery system for NHHD. Manufacturers of delivery systems for conventional hemodialysis should refer to the **Guidance for the Content of Premarket Notifications for Hemodialysis Delivery Systems**.[1] For the purposes of this guidance, FDA defines conventional hemodialysis and NHHD systems as shown below.

> **Conventional Hemodialysis**
> Conventional hemodialysis is a type of chronic hemodialysis that takes place in a clinical environment and typically includes treatments performed three times per week for approximately four hours per treatment. The therapy is administered by a trained medical professional.
>
> **Nocturnal Home Hemodialysis (NHHD)**
> NHHD is a type of chronic hemodialysis that takes place in the home while the patient is sleeping, typically at night, up to seven times per week, for approximately six to ten hours per treatment, depending on the individualized dialysis prescription. It is administered by the patient or a trained partner, rather than by a trained medical professional.

The scope of this document is limited to IDE applications for the device types identified below when used for NHHD:

- § 876.5600 Sorbent regenerated dialysate delivery system for hemodialysis
- § 876.5820 Hemodialysis system and accessories
- § 876.5860 High permeability hemodialysis system

The procodes for these devices are ODM, ODN, and ODO, respectively. This guidance does not address the investigation of hemodialyzers, hemofilters, or hemoconcentrators.

FDA believes that the NHHD systems described in this guidance document are significant risk devices, as defined in 21 CFR 812.3(m); therefore, any clinical investigation must be conducted in conformance with the Investigational Device Exemptions (IDE) regulations, 21 CFR Part 812. In addition to the requirement of having an FDA-approved IDE, sponsors of such trials must comply with the regulations governing institutional review boards (21 CFR Part 56) and informed consent (21 CFR Part 50). FDA recommends that you contact us before submitting a 510(k) or IDE to discuss clinical data requirements unique to each system. For general information regarding IDEs, please refer to **Investigational Device Exemptions Policies and Procedures in CDRH Device Advice.**[2]

In addition to the information described above, we recommend that IDEs for NHHD systems contain the information described in the following sections.

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[1] http://www.fda.gov/cdrh/ode/hemod.pdf
[2] http://www.fda.gov/cdrh/devadvice/ide/index.shtml

3. Device Description

We recommend that you include detailed information describing the safety features and basic components of the NHHD system in your device description. This information should include a description of the physical and electronic components, system features and functions, and software as discussed below.

Physical and/or Electronic Description

You must provide a description of the NHHD system.[3] We also recommend you provide the information in the form of a block diagram that identifies the interconnections between the various sub-systems, system components, user interfaces, and networks.

You must provide a description of the important individual components of the NHHD system.[4] You should provide specifications, if applicable. Important components of a NHHD system generally include the following:

- pumps;
- valves;
- ultrafiltration controller mechanism;
- air detector systems;
- blood leak detectors;
- patient disconnection or exsanguination preventers and detectors;
- heat exchangers;
- access ports for external remote monitoring devices;
- anticoagulant pumps or supply; and
- other safety features.

Some NHHD systems may also include the following important components:

- water treatment system;
- integrated remote patient monitors; and
- dedicated tubing sets.

We recommend you provide a diagram (in color, if possible) that identifies the fluid paths (e.g., blood, dialysate, effluent) and indicate how each path interacts with the components of the NHHD system.

We recommend you identify each of the system components and the corresponding materials that are either patient-contacting or indirect patient-fluid contacting, including dialysate distribution lines, monitors, and sensors applied to the patient. For the purpose of this

[3] See 21 CFR 812.25(d).
[4] See 21 CFR 812.25(d).

guidance, you should consider a system component in the dialysate fluid path to be patient-fluid contacting.

We recommend you provide a description of the system's patient/user interface (also called the "device-user interface," "use interface," "man-machine interface" or "usability").

We recommend you describe how the patient or user interacts with the system, with emphasis on designed-in prevention of potentially dangerous errors, detection of errors, and recovery from hazardous situations. The user interface includes all components and accessories necessary to perform the tasks related to safe and effective use of the device (e.g., installation, calibration, operation, maintenance, and ultimately disposal of parts and supplies). The user interface components generally include controls, displays, connections, alarms, device logic (software), labeling, and training materials.

We recommend you provide a description of the dialysate used with the NHHD system (e.g., type of concentrate used, whether it is prepared on-line or pre-mixed). If the dialysis solution is prepared on-line during the dialysis treatment, we recommend you provide the following information:

- the ratio of the mixture of concentrates and water used;
- the minimum quality of water that is to be mixed with the dialysate (e.g., following the American Association for Medical Instrumentation (AAMI) standard RD62:2001, *Water treatment equipment for hemodialysis applications*, or an equivalent current, FDA-recognized standard);
- the type of concentrates that may be used (e.g., acid and bicarbonate, acetate); and
- the way incoming water is fed into the NHHD system (i.e., we recommend you describe how connections are made, the flow path, and identify the use of flow-limiting valves).

If the dialysis solution is not prepared on-line, we recommend you provide a complete description of the type of solution that may be used, how it is prepared and stored before use, and how it is delivered into the fluid path system.

We recommend you describe the water treatment system, if one is used within the NHHD system to purify tap water for the preparation of dialysate. You should explain the various components of this water treatment system and how they may be arranged and optimized for each home setting.

We recommend you describe all intended clinical configurations that are mentioned in the device labeling (e.g., single-needle, double needle) and explain which features of the system are used for each configuration.

We recommend you identify the accessories that may be incorporated within the NHHD system (e.g., patient data card, network interface, non-invasive blood pressure (NIBP) monitor, water treatment system, dedicated tubing sets, electrocardiogram (ECG)). If the system incorporates a device component for which there is a device-specific guidance

document issued by FDA (e.g., NIBP monitor,[5] water treatment system[6]) you should refer to those documents for additional recommendations.

We recommend you indicate whether any external accessories (e.g., wetness detectors, external blood flow and/or hematocrit monitors) that may be used with the NHHD system in the clinical study are legally marketed. For accessories that are not legally marketed, we recommend you provide detailed information on the accessories.

If the system does not include a dedicated tubing set, we recommend you identify the legally marketed tubing set compatible with your device and include this information in the device labeling and the investigational plan for the clinical study. Where applicable, we recommend you conduct the functional testing described in **Section 4. Reports of Prior Investigations** with the tubing set identified in your IDE.

System Features and Functions

We recommend you provide a list of the performance specifications for the controllable parameters of the NHHD system, including both the range of allowable values and the default. We recommend you provide information for each of the following parameters:

- flow rate that each pump can deliver;
- transmembrane pressure;
- ultrafiltration rate;
- dialysate temperature;
- dialysate conductivity;
- arterial and venous pressure;
- length of treatment;
- volume of water that can be purified, if applicable;
- rate of production of purified water, if applicable;
- water conductivity and purity, if applicable; and
- volume of dialysate that can be processed.

You should provide a list of the alarms in the NHHD system. Since the study subject and the care partner may be sleeping during treatments, the alarms should be able to awaken them in the event of an alarm condition. For each alarm, we recommend you identify the design (e.g., audible, visible, tactile, vibration). In addition, we recommend you identify:

- the hazard condition that triggers the alarm;
- how the subject or the trained care partner should respond to and resolve the condition that triggered the alarm; and
- how the machine responds to the alarm condition (e.g., system shut down).

[5] http://www.fda.gov/cdrh/ode/noninvas.html
[6] http://www.fda.gov/cdrh/ode/hemodial.pdf

Since alarms are part of the patient/user interface, we recommend you describe the alarms from the perspective of human factors or usability. In addition, we recommend you describe whether you followed any standard pertaining to alarms in designing or validating the alarm system (e.g., IEC 60601-1-8, *Medical electrical equipment Part 1-8: General requirements for safety - Collateral standard: general requirements, tests and guidance for alarm systems in medical electrical equipment and medical electrical systems, Edition 1*).

We also recommend you describe the role of the system's integrated remote monitoring system, if a component of your device, or interface with an external remote monitoring system.

Due to its inherent design and operational properties, we recommend the NHHD system include several key design features, associated alarms, and fail-safe responses. We recommend you incorporate the following features:

- disinfection, cleaning, and reprocessing capabilities and cycles;
- dialysate conductivity monitor, if your device contains a dialysate mixing system;
- water conductivity monitor; if your device contains a water treatment system;
- pH sensor;
- ultrafiltration controller;
- air detector system;
- blood leak detector;
- patient disconnect preventers and detectors;
- temperature monitor;
- anticoagulant administration system;
- access port for external remote patient monitoring device;
- integrated remote patient monitor, if a component of your system; and
- fail-safe design features in the event of power failure.

We recommend you describe all prescription profiling features used within the NHHD treatment (e.g., dialysate, ultrafiltration, sodium). We recommend you identify the profiles available to the user, describe the process for selecting a particular profile, and describe how the NHHD system reacts to a particular profile during machine use. In addition, in the event that profiles require different operating conditions or parameters, we recommend you clarify whether one profile has precedence over another.

Software

We recommend you submit the information for software-controlled devices described in the **Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices**.[7] The type of information we recommend you submit is determined by the "level of concern," which is related to the risks associated with software failure. The level of concern

[7] http://www.fda.gov/cdrh/ode/guidance/337.html

for a device may be minor, moderate, or major. We believe the level of concern for NHHD systems is major. If your device incorporates off-the-shelf software, refer to the **Off-the-Shelf Software Used in Medical Devices**[8] guidance. You can find additional information on software validation in the **General Principles of Software Validation**[9] guidance.

4. Reports of Prior Investigations

IDEs for NHHD systems must include the results from pre-clinical testing performed prior to a clinical study.[10] Your testing information should include the information described below.

Bench Testing

We recommend you conduct functional testing that demonstrates the system and its components perform as designed and expected. This functional testing should include validation of all of the system features under both standard operating conditions and worst-case conditions (e.g., treatment features, user interface, disinfection procedures, disconnect preventers and alarms, system sensors, controllers, monitors, alarms, and if applicable, water treatment and integrated remote monitoring capabilities).

We recommend you conduct a system-level hazard analysis including use error-related hazards. You should correlate this analysis to the functional testing of the system to confirm that the device does not perform in an unexpected or unsafe manner, or provide a declaration of conformity with risk management standard ISO 14972.

We recommend you conduct electrical safety testing and submit the results, or provide a declaration of conformity with IEC 60601-1, *Medical Electrical Equipment – Part 1: General Requirements for Safety*.

We recommend you conduct electromagnetic compatibility (EMC) testing, or describe whether you followed any EMC standard (e.g., IEC 60601-1-2, *Medical Electrical Equipment – Part 1-2: General Requirements for Safety; Electromagnetic Compatibility – Requirements and Tests*) and to what extent you followed the standard. Since the NHHD system is intended for use in a home environment, we recommend you conduct testing that addresses the potential hazards in the home environment, including radiated immunity testing at the 10 V/m level at all tested frequencies.

We recommend you conduct performance testing demonstrating your device has the capability of transmitting real time alarms to a remote monitoring station (i.e., over the internet or direct phone line), either using an integrated remote monitoring system, if a component of your system, or by interfacing with an external monitor.

If your device contains dedicated tubing sets, we recommend you conduct testing of those sets and disposable components. For information on dialysis system tubing sets, refer to the guidance Hemodialysis Blood Tubing Sets – Premarket Notification (510(k)) Submissions.

[8] http://www.fda.gov/cdrh/ode/guidance/585.pdf
[9] http://www.fda.gov/cdrh/comp/guidance/938.pdf
[10] See 21 CFR 812.20(b)(2).

Biocompatibility Testing

We recommend you conduct biocompatibility testing, as described in the FDA-modified **Use of International Standard ISO-10993, Biological Evaluation of Medical Devices Part-1: Evaluation and Testing**,[11] for all direct and indirect patient-fluid contacting components of the NHHD system. In addition, we recommend you select biocompatibility tests appropriate for the duration and level of patient contact with your device. If identical materials and identical material processing are used in a comparable, marketed predicate device with the same type and duration of patient contact, you may identify the predicate device in lieu of providing biocompatibility testing.

Alternatively, we recommend you conduct leach testing that identifies and characterizes the potential leachables using appropriate chemical analyses for indirect patient-fluid contacting materials, such as dialysate. In addition, we recommend you conduct a risk assessment of the toxic potential of these leachables. The risk assessment should be supported by the referenced literature.

Sterility, Disinfection, and Expiration Date Testing

Sterility

FDA recommends that you provide sterilization information described in the guidance entitled, **Updated 510(k) Sterility Review Guidance K90-1**.[12] The device should be sterile with a sterility assurance level (SAL) of 1×10^{-6} using a sterilization cycle that has been validated in accordance with the quality system regulation (21 CFR Part 820).

Disinfection

We recommend you describe the complete system disinfection cycles, reprocessing cycles, and methods appropriate for disinfecting the NHHD system. This description should include the steps the operator should follow in order to complete machine disinfection, and methods for determining disinfectant residuals. If you identify a disinfection method, protocol, or agent not used in a legally marketed device or not used in a legally marketed dialysis system, you should provide validation of the method. If you have any questions about the data or information needed to support the safety of your proposed disinfection methods or protocols, we recommend that you contact the Gastroenterology and Renal Devices Branch prior to the submission of your IDE.

Expiration Date Testing

We recommend you identify all components of the NHHD system labeled with expiration dates. In addition, we recommend you substantiate these expiration dates with the appropriate testing data. Refer to **Guidance for the Content of Premarket Notifications**

[11] http://www.fda.gov/cdrh/g951.html
[12] http://www.fda.gov/cdrh/ode/guidance/361.pdf

for Conventional and High Permeability Hemodialyzers[13] for recommendations pertaining to expiration date testing for hemodialyzers.

Human Factors Recommendations

We recommend you provide validation of the patient/user interface, taking into account human factor considerations, such as potential user errors and ergonomic factors.

We also recommend you conduct a non-clinical, realistic "usability" (human factors) study to validate the device, as it may not be possible to evaluate the clinical device performance in potentially dangerous use scenarios. Usability testing should demonstrate that the device performs safely, under realistic conditions in the hands of prospective users, with minimal dependence on training and labeling as described in AAMI/ANSI HE74:2001, *Human Factors Design Process for Medical Devices* or equivalent methods.

Previous Clinical Data

You must submit a complete report of all prior clinical testing of the device, conducted at U.S. and outside U.S. (OUS) sites.[14] If the clinical testing is described in literature articles, we recommend you provide the articles. Foreign sites do not require IDE approval. However, if you intend to study your NHHD system in foreign centers, we recommend that you indicate this in the IDE application related to your U.S. study and include them in your statistical analysis plan. Clinical data obtained at foreign sites may be submitted in the marketing application as part of the primary data set. For future marketing applications using OUS data, we recommend you use the same clinical protocol as the IDE study for the foreign sites to minimize variability.

Bibliography

You must provide a bibliography of all publications, whether adverse or supportive, that are relevant to an evaluation of the safety or effectiveness of the device.[15] You should also include copies of all published or unpublished adverse event information.

5. Investigational Plan

You must provide a complete description of the investigational plan.[16] We recommend that you design your IDE study to obtain clinical data to demonstrate the safety of the NHHD system under actual use conditions. Your study should evaluate the incidence of adverse events, the device's ability to deliver prescribed treatments, and the subject's or care partner's ability, after appropriate training, to conduct the prescribed treatments in a nocturnal home hemodialysis setting. In general, we recommend you compare assessments for subjects over a period of time in-clinic, followed by a period of home-use. Please note that the study does not have to evaluate long-term effectiveness of nocturnal hemodialysis treatment as an endpoint.

[13] http://www.fda.gov/cdrh/ode/highpermhemo.pdf
[14] See 21 CFR 812.27.
[15] See 21 CFR 812.27(b)(1).
[16] See 21 CFR 812.25.

We recommend you consider the information below, specific to NHHD system clinical studies.

Study Design

We recommend that you design your study to incorporate an in-clinic period, followed by a home-use period. The appropriate length of the study and sample size will be dependent on the study endpoints, the indication for use, and any performance characteristics and claims you propose to include in labeling.

Subject Selection

To avoid a possible bias from a recent hemodialysis initiation, we recommend you select subjects from a pool of established hemodialysis patients. We also recommend you include subjects with an established vascular access for hemodialysis and exclude subjects in transition from a cuffed catheter to an arteriovenous fistula.

We also recommend you consider the physical ability of the subject or care partner to perform the hemodialysis treatment.

Your investigational plan should include procedures for an inspection of the subjects' home environment to ensure that the environment has appropriate electrical connections, water supply, and any other features necessary for the use of the device. You should exclude subjects whose home environments are not suitable.

Endpoints

We recommend your study provide a comparison between in-clinic use and home-use, including:

- adverse events;
- ability to deliver the prescribed treatment, (e.g., delivery of prescribed parameters, achieving desired kt/V in prescribed treatment time); and
- the reliability of the device to provide each treatment as scheduled.

Statistical Plan

We recommend you provide a complete description of the statistical plan, addressing the sample size, proposed randomization scheme (if applicable), proposed interim analysis and early stopping procedures (if applicable), poolability of the data, and proposed analytical methods. For additional guidance on statistical methods for evaluation of clinical trial data, refer to **Statistical Guidance for Clinical Trials of Non-Diagnostic Medical Devices**.[17]

[17] http://www.fda.gov/cdrh/ode/odeot476.html

Subject Monitoring and Monitoring by the Care Partner

Your IDE application should include a description of the treatment monitoring plan and specify which features of the NHHD system will be used for subject monitoring. In order to address the safety concerns associated with dialyzing in a nocturnal hemodialysis setting, we recommend all studies incorporate the use of a care partner regardless of whether the device is used with real time remote monitoring. We recommend you design the study so that the care partner will be present throughout the dialysis treatment. We also recommend you not use remote monitoring as the sole method of subject monitoring.

Monitoring of Dialysate Chemistries and Water Quality

For NHHD systems that do not use pre-mixed dialysate solutions, the investigational plan should include procedures for monitoring the microbiological quality of the water coming into the system after purification. We recommend you perform periodic sampling and testing of the water quality (i.e., surveillance cultures, to ensure the water is within acceptable microbiological limits, as described in your protocol). We also recommend the investigational plan include instructions for monitoring the dialysate prepared by the NHHD system (i.e., instructions should be included to check dialysate conductivity, including the frequency of checks).

Training

We recommend subjects selected to participate in your clinical study undergo training on how to perform the entire hemodialysis treatment and vascular access procedures. You should evaluate the success of the training as part of your clinical study. We recommend you use a training team to observe the subject's or care partner's ability to perform the procedure in the clinic before starting the home period of study. The training team's observations should include observing the subject's or care partner's ability to troubleshoot the device and other procedure-related issues.

FDA believes that the actual time needed for successful training depends on factors specific to each subject (e.g., familiarity with hemodialysis, ability to follow directions, compliance, motivation). We recommend you use a practical test or written questions to assess the subject's comprehension and retention of the training received.

We recommend you outline the responsibilities of the care partner during the training sessions and provide instructions to subjects and care partners on emergency procedures, such as the procedures necessary if a serious adverse event occurs.

We recommend you provide training for the care of the vascular access (e.g., arteriovenous fistulas, grafts, cuffed catheters). In addition, we recommend you instruct subjects on procedures to avoid needle sticks, the use of aseptic techniques, and measures necessary to prevent hemodialysis related emergencies (e.g., disconnections, air emboli).

In addition, we recommend you include training on the regular maintenance of the device, management of supplies, necessary environmental features, such as the availability of electrical outlets and water supply, and sampling of dialysate chemistries and water quality.

Your IDE application should include copies of the training manual, questionnaires, checklists and any other training materials you plan to use in the study.

Labeling

The IDE application must comply with the labeling requirements described in 21 CFR 812.5. Your IDE application must include draft device labeling for the NHHD system (e.g., the operator's manual, patient labeling, any labels that will be affixed directly to the system or its accessories).[18]

We recommend your labeling include information about the safe use of the NHHD system, including device descriptions, instructions for the use of the system, and recommendations on what to do in the event of a problem.

In general, we recommend the operator's manual include the elements described below.

Therapy Background

We recommend you provide an overview of the therapies and modalities performed by the system, the target population, and general principle of operation. In addition, we recommend you include indications for use, contraindications, warnings, and precautions.

Device Description

We recommend you provide an overall description of the device and individual components. You should describe:

- the safety-related components included in the system (e.g., ultrafiltration controller, arterial and venous pressure sensors, disconnection preventers and sensors); and
- the accessories that need to be used with the system (e.g., extracorporeal tubing, replacement fluids).

We also recommend you identify:

- the dialysate solution to be prescribed by a physician and indicate whether it conforms to the AAMI RD62:2001 standard, or the equivalent current, FDA-recognized standard, in terms of chemical purity and microbiological quality;
- the operational parameters (e.g., flow rates, monitoring pressure) and, where appropriate, the accuracy of these parameters; and
- the model number and current software version of the machine.

Device Operation

We recommend you describe the pre-treatment, peri-treatment, and post-treatment steps needed to safely perform each available therapy mode. If the system may be used in

[18] See 21 CFR 812.20(b)(10).

different configurations (e.g., single-needle vs. double needle) we recommend labeling include clear instructions to distinguish between the configurations.

Alarms and Troubleshooting

We recommend you clearly identify the system alarms, their design and format, the suspected cause of the alarm condition, and how the subject or care partner should respond to the alarm.

Cleaning, Disinfection, and Preventative Maintenance

We recommend you provide detailed instructions for the subject or care partner to clean, disinfect, and maintain the dialysis machine. The disinfection instructions should be consistent with the information discussed in **Section 4. Reports of Prior Investigations**.

In addition, the operator's manual should include the following user-related instructions:

- instructions for the subject or their care partner to properly use, monitor, and verify the conductivity and temperature of the dialysate used in the NHHD system; and
- instructions for the subject or their care partner to properly monitor and adjust the dialysis treatment to ensure proper fluid balance.

The operator's manual should also include the following user-related precautions:

- a precaution regarding the possible susceptibility to electromagnetic interference and possible electrical hazards associated with the use of the NHHD system;
- a precaution to use high-permeability dialyzers only if the NHHD system is equipped with an ultrafiltration controller; and
- a precaution that the subject or care partner should not over-ride or bypass the air embolism/foam detector during treatment.

Because NHHD systems are designed for use at home and treatments are administered by subjects or their care partners, we recommend you provide patient labeling for subjects participating in the clinical study. For recommendations about preparing patient labeling, please refer to **Guidance on Medical Device Patient Labeling**.[19] Your patient labeling should include the same elements recommended above for the operator's manual, but written in layman's terms, that is, in a clear, concise fashion, directed to subjects or their care partners, who may not have any medical training. In addition, we recommend you provide detailed instructions for use, including:

- turning the device on and performing its setup;
- installing tubing sets;
- priming;
- setting up patient connections and disconnections;
- performing and monitoring treatments;
- cleaning and disinfecting the device; and

[19] http://www.fda.gov/cdrh/ohip/guidance/1128.pdf

- turning off the device.

In addition, we recommend you provide a pre-treatment device setup reference sheet, or task checklist, for subjects and their care partners.

We recommend you provide a list of settings and ranges of operation for all parameters that the subject or care partner may program or change at home, and explanations of these parameters' functions. In addition, we recommend you provide an easy-reference list of alarms, error conditions, and general troubleshooting directions.

We also recommend your patient labeling include a list of environmental features and supplies necessary to perform NHHD treatments, such as information on the home environment and preparations necessary to accommodate the NHHD system (e.g., electrical outlets, voltage, ground fault interrupters, water supply, drainage, phone line connection (if applicable), volume and type of dialysate concentrates or pre-mixed dialysate, information on disposables and consumables).