Guidance for Industry and FDA Staff

Medical Device User Fee and Modernization Act of 2002, Validation Data in Premarket Notification Submissions (510(k)s) for Reprocessed Single-Use Medical Devices

Document issued on: September 25, 2006

This guidance supersedes the document issued under this title on June 1, 2004

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

Office of Device Evaluation

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Preface

Public Comment

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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.

I. Introduction

Background

On October 26, 2002, the Medical Device User Fee and Modernization Act of 2002 (MDUFMA), P.L. 107-250, amended the Federal Food, Drug, and Cosmetic Act (the Act) by adding new section 510(o), which provided new regulatory requirements for reprocessed single-use devices (SUDs). According to this new provision, in order to ensure that reprocessed SUDs are substantially equivalent (SE) to predicate devices, premarket notification submissions (510(k)s) for certain reprocessed SUDs identified by FDA must include validation data. These validation data include cleaning, sterilization data, and functional performance data demonstrating that each SUD will remain SE to a predicate device after the maximum number of times the device is reprocessed as intended by the person submitting the 510(k). The predicate device may be the Original Equipment Manufacturer's (OEM's) device, (i.e. the same device as originally manufactured), or any device of that type.

Before enactment of the new law, a manufacturer of a reprocessed SUD was required to obtain premarket approval or premarket clearance for the device, unless the device was exempt from the 510(k) requirements of the Act. Under MDUFMA, some previously 510(k)-exempt reprocessed SUDs are no longer exempt. Manufacturers of these FDA-identified (see below) reprocessed SUDs need to submit 510(k)s that include validation data. In addition, reprocessors of certain

FDA-identified SUDs that had cleared 510(k)s were required to submit validation data as specified by the Agency and to include validation data in any new 510(k)s for devices of this type.

On April 30, 2003, FDA identified those critical reprocessed SUDs that would no longer be exempt from 510(k) submission requirements.[1] Also on that date, FDA issued a list of the non-exempt reprocessed SUDs subject to the validation data submission requirement under MDUFMA. On April 13, 2004, FDA issued a list of semi-critical reprocessed SUDs that would no longer be exempt from 510(k) requirements.[2] On September 29, 2005, FDA updated these lists to include additional device types.[3] In this most recent FR notice, FDA also provided updated, current listings of all devices types subject to these MDUFMA requirements so reprocessors would not need to refer back to previous FR notices for a complete listing.

This guidance document describes the types of validation data that FDA recommends be submitted under section 510(o) of the Act. In addition, it provides guidance to industry and FDA staff on submission and review procedures for validation data in 510(k)s for reprocessed SUDs. This guidance supersedes the guidance of the same title, issued June 1, 2004. In this revised version, we clarify the use of FDA-recognized standards and the applicability of the Special 510(k) Program to 510(k)s submitted with validation data. We also clarify the obligations of an OEM who reprocesses SUDs. Lastly, the 2004 document addressed initial MDUFMA implementation issues; many of which are no longer relevant and have been removed. If, in the future, additional device types are added to the list of reprocessed SUDs requiring validation data, a Supplemental Validation Submission (SVS) will be required for those devices and this guidance will provide information on the type of validation data that should be submitted.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidance documents 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 certain reprocessed devices 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 comply with 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: www.fda.gov/cdrh/modact/leastburdensome.html.

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[1] See 68 FR 23139. A revised version of this list was published on June 26, 2003 (68 FR 38071).
[2] See 69 FR 19433.
[3] See 70 FR 56911.

Effect of this Guidance Document on Previous Guidance Documents

This guidance provides FDA recommendations on the content and format of cleaning, sterilization, and functional performance validation data in 510(k)s for reprocessed SUDs that are required by MDUFMA to include such data. MDUFMA and this guidance on validation data submissions supersede any other guidance document that recommends less complete data and information than we have described in this document.

For example, Blue Book document K90-1 describes information on sterilization processes that FDA recommends manufacturers submit in 510(k)s. Section 302(b) of MDUFMA and this guidance supersede K90-1 as it relates to the scope of the validation data to be submitted in 510(k)s on the cleaning, sterilization, and functional performance aspects of reprocessed SUDs that require the submission of such validation data.

Definitions

Section 201 of the Act (302(d) of MDUFMA) includes the following relevant definitions:

Single-use device: "The term 'single-use device' means a device that is intended for one use, or on a single patient during a single procedure."

Reprocessed: "The term 'reprocessed', with respect to a single-use device, means an original device that has previously been used on a patient and has been subjected to additional processing and manufacturing for the purpose of an additional single use on a patient. The subsequent processing and manufacture of a reprocessed single-use device shall result in a device that is reprocessed within the meaning of this definition."

Original device: "The term 'original device' means a new, unused single-use device."

Critical reprocessed single-use device: "The term 'critical reprocessed single-use device' means a reprocessed single-use device that is intended to contact normally sterile tissue or body spaces during use."

Semi-critical reprocessed single-use device: "The term `semi-critical reprocessed single-use device' means a reprocessed single-use device that is intended to contact intact mucous membranes and not penetrate normally sterile areas of the body."

II. Questions and Answers on the MDUFMA 510(k) Requirements for Certain Reprocessed SUDs

Unless otherwise stated, a reference to "requirements" in the following questions and answers refers to the requirements of MDUFMA section 302(b) (the Act § 510(o)).

MDUFMA 510(k) Requirements for Certain Reprocessed Single-Use Devices

1. What are the requirements under MDUFMA for critical and semi-critical reprocessed SUDs that were previously exempt from 510(k) submission requirements?

The new law required FDA to review the *critical and semi-critical* reprocessed SUDs that were exempt from the 510(k) requirements and determine which of these devices require 510(k)s to ensure their substantial equivalence to predicate devices. On April 30, 2003, FDA identified in the Federal Register those critical reprocessed SUDs whose exemption from 510(k) would be terminated.[4] On April 13, 2004, FDA identified those semi-critical reprocessed SUDs whose exemption would be terminated.[5] On September 29, 2005, FDA updated and consolidated the lists of the critical and semi-critical reprocessed SUDs that would no longer be 510(k) exempt.[6]

In accordance with the statute, manufacturers of reprocessed SUDs whose exemption from 510(k) submission requirements was terminated must submit 510(k)s that include validation data regarding cleaning, sterilization, and functional performance, in addition to all the other required elements of 510(k)s identified in 21 CFR § 807.87, within fifteen months of publication of the relevant Federal Register notice or no longer market their devices.

2. What are the requirements under MDUFMA for reprocessed SUDs that were already subject to 510(k) submission requirements?

MDUFMA required FDA to review the types of reprocessed SUDs already subject to the 510(k) requirements and identify which of these device types required the submission of validation data to ensure their substantial equivalence to predicate devices. FDA published a list of these devices in the Federal Register on April 30, 2003[7], and updated the list on September 29, 2005.[8]

For a device type on this list that already had been cleared through the 510(k) process, the statute required manufacturers to submit validation data regarding cleaning, sterilization, and functional performance within nine months of publication of the Federal Register list or cease marketing. Beginning nine months after publication of the list, FDA may take action against a marketed device on the list if the validation data required by MDUFMA were not submitted.

For a device type on this list that has not yet been cleared through the 510(k) process, MDUFMA requires manufacturers to submit 510(k)s that includes validation data regarding cleaning, sterilization, and functional performance, in addition to all other required elements of 510(k)s identified in 21 CFR Part 807.87, in order to market these devices.

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[4] See 68 FR 23139. A revised version of this list was published on June 26, 2003 (68 FR 38071).
[5] See 69 FR 19433.
[6] See 70 FR 56911.
[7] See 68 FR 23139. A revised version of this list was published on June 26, 2003 (68 FR 38071).
[8] See 70 FR 56911.

3. How does a manufacturer know if its device is on one of the MDUFMA lists?

As mentioned above, FDA published Federal Register notices listing the affected devices. On April 30, 2003, FDA published a Federal Register notice containing two lists. List I identified those critical reprocessed SUDs that were previously exempt from the 510(k) requirements but now require the submission of 510(k)s with validation data. (On June 26, 2003, FDA published a correction to this notice to include an additional device type whose exemption from 510(k) requirements would be terminated.) List II identified those reprocessed SUDs already subject to 510(k) requirements that now require the submission of validation data. On April 13, 2004, the Agency published the list of semi-critical reprocessed SUDs that were previously exempt from 510(k) requirements but that now require the submission of 510(k)s with validation data.

Finally, on September 29, 2005, FDA updated the lists to include two additional device types that would be subject to these MDUFMA requirements. In addition, the September 2005 FR notice included consolidated lists from all previous FR notices so reprocessors would not need to refer to previous notices in order to obtain a complete listing of all device types subject to these requirements. [9]

4. How does a manufacturer know what type of validation data to submit in order to comply with the law?

As discussed above, MDUFMA requires that manufacturers of listed reprocessed SUDs submit cleaning, sterilization, and functional performance validation data in order to demonstrate that reprocessed devices remain substantially equivalent to the relevant predicate devices. Section III of this guidance provides a detailed discussion of the Agency's recommendations on the types of data to be submitted to comply with this requirement.

5. Is FDA able to take enforcement action against a manufacturer who does not submit the validation data required by MDUFMA?

Yes, but for any reprocessed SUDs that are newly listed under section 510(j) of the Act, there will be a grace period during which FDA may not take action. As stated above, MDUFMA requires that validation data be submitted to FDA for listed reprocessed SUDs within nine months (for devices already subject to 510(k) submission requirements that had 510(k)s submitted before the device was listed) or fifteen months (for critical and semi-critical reprocessed SUDs whose 510(k) exemption was terminated) after publication of the list in the Federal Register. Therefore, until the grace period expires, FDA may not take action against reprocessed SUDs identified in the published lists solely on the basis that validation data have not yet been submitted to the Agency. After the submission of validation data, a manufacturer may continue to market the reprocessed SUD until FDA determines whether the data are acceptable.

[9] See 70 FR 56911 for a complete listing of all device types subject to these MDUFMA requirements.

6. What information should be included in a 510(k) for a reprocessed SUD if the device type is not included on one of the published lists requiring a 510(k)?

A 510(k) for a reprocessed SUD must include all the information required by 21 CFR § 807.87. In addition, FDA recommends that the 510(k) include any additional information recommended in an applicable FDA device-specific 510(k) guidance. If the device type is not one of those included in the published lists (hereafter referred to as "listed"), validation data are not required in a 510(k).

7. May a manufacturer submit a Special 510(k) for a reprocessed SUD?

The Special 510(k) program is designed to be based on the review of the basic elements of a 510(k) set forth in 21 CFR 807.87 and a declaration of conformity with design controls in place of actual data. If the reprocessed SUD does not require validation data, and is otherwise eligible for a Special 510(k) submission, the reprocessor may submit a Special 510(k).
If the reprocessed SUD is of a type that requires validation data, it should not be submitted as a Special 510(k) because special 510(k)s do not include validation data.

8. Do any of the requirements under section 510(o) of the Act discussed above apply to original equipment manufacturers (OEMs)?

The statutory requirements apply to all manufacturers who reprocess SUDs. This includes OEMs who reprocess SUDs. The requirement does not apply to OEMs' manufacture of the original, non-reprocessed device, however.

Overview of Validation Data

9. In general, what validation data must be included in a 510(k) for a listed reprocessed SUD under MDUFMA?

MDUFMA requires that 510(k)s for listed reprocessed SUDs include "validation data, [as] specified by the Secretary, regarding cleaning and sterilization, and functional performance demonstrating that the [SUD] will remain substantially equivalent to a predicate device after the maximum number of times the device is reprocessed as intended by the person submitting the premarket notification." MDUFMA section 302(b) (the Act § 510(o)(1)(A)).

10. How does FDA define "validation"?

FDA has defined validation in the context of the Quality System Regulation, 21 CFR Part 820, as follows:

> **§ 820.3(z)** "*Validation* means confirmation by examination and provision of objective evidence that the particular requirements for a specific intended use can be consistently fulfilled.
>
> 1. *Process validation* means establishing by objective evidence that a process consistently produces a result or product meeting its predetermined specifications.*
> 2. *Design validation* means establishing by objective evidence that device specifications* conform with user needs and intended use(s)."

§ 820.3(y) "Specification* means any requirement with which a product, process, service, or other activity must conform."

11. Where can I obtain more information on design and process validation?

Design and process validation requirements are further detailed in 21 CFR Part 820, Quality System Regulation. An educational guidance document is available for design controls, which include design validation, on FDA's web site at www.fda.gov/cdrh/comp/designgd.html. Also, the Global Harmonization Task Force has an educational guidance document on process validation found at www.ghtf.org/sg3/sg3-final.html. (Note: FDA's Quality System regulation does not permit the use of option E in Figure 1 of the Global Harmonization Task Force's Process Validation Guidance.)

12. How does FDA interpret the scope of validation data required under MDUFMA?

FDA interprets validation data as broad in scope, including information about processing at the point of use to the completion of packaging and sterilization, and other post-process considerations. This guidance provides more discussion on validation data in Section III. Cleaning, sterilization, and functional performance validation of reprocessed SUDs include aspects of both design validation and process validation. Design validation, in this case, should incorporate both the design of the product and the design of the processes to be used in reprocessing the device.

FDA interprets the cleaning process to include all steps to remove, inactivate, or contain contamination, beginning immediately after clinical use of the device, and all subsequent steps to decontaminate and clean a device up to packaging and prior to the first step of the sterilization process. This includes all quality control tests.

A clean device, as specified by the reprocessor, should be the input for the sterilization process. FDA interprets the sterilization process as beginning after packaging and any preconditioning other than cleaning (e.g., prehumidification for ethylene oxide (EO)) to the end of any post-process conditioning.
Manufacturers should assess functional performance after the cleaning and sterilization process validations. Successful process validations then support the overall design validation. The results of the cleaning and sterilization validations provide objective evidence that the particular requirements for a specific intended use can be consistently fulfilled and are equivalent to those of the predicate device.

13. What are some general considerations regarding validation of reprocessed SUDs?

Proper design validation helps ensure equivalent functional performance of the device for established user needs and intended uses. The design of the product, in part, is dictated by the design of the original device because the manufacturer is starting with an existing device, albeit used at least once. Therefore, it is vital that the manufacturer understand and document the incoming device specifications important to safe and effective use (i.e., those of the original device), in order to understand the effects of any reprocessing, to develop the acceptance criteria for both the processes and the finished product that will be distributed, and to help establish

equivalent performance. The design validation must be performed according to established procedures. The established procedures that define device specifications should include processing specifications, operating conditions, and acceptance criteria for both product and processes. See 21 CFR § 820.30.

The design validation must also include a risk analysis when appropriate. See 21 CFR § 820.30(g). The risk analysis should document: the identification of hazards originating from the product, the processes utilized by the manufacturer and the users of the device both before reprocessing and after; the tools utilized to analyze the source(s) of the hazard(s); and the risk estimation. Additionally, the design validation should then address how these risks are managed and shown to be acceptable and equivalent to those of the original device. (For further information and guidance on Risk Management and Risk Analysis, see ISO 14971.)

Design validation should also encompass a procedure for keeping track of and assessing any OEM changes in specifications, components, or materials in the original devices. The analysis of changes ensures that the design validation performed originally continues to be valid for the devices being reprocessed. Further, there should be a method that analyzes and demonstrates that any repairs or part replacements are equivalent to the original specifications used as the basis for the reprocessor's design validation.

In addition, the design validation should specify how many times the particular device being validated can undergo reprocessing. This helps decrease the risk of long-term adverse effects and helps ensure that the manufacturer can demonstrate after each reprocessing that the device is substantially equivalent to the originally marketed device and meets its intended use and user needs. The maximum number of times the reprocessor recommends that the device be reprocessed should also play an important role in the cleaning and sterilization process validations.

While cleaning and sterilization procedures, materials, and product performance/verification testing are developed and assessed during design, these processes must also undergo process validations, as required by 21 CFR § 820.75. Traditionally, process validation encompasses a series of installation qualifications, operational qualifications, and performance qualifications.

14. How does MDUFMA affect documentation of validation reports by a reprocessor?

There is no change to the requirements under the quality system regulation for documentation of validation for a device. Reprocessors must continue to maintain records of their validation activities. See 21 CFR 820.30(j). Prior to MDUFMA, validation data could be requested by FDA on a device-specific basis if FDA believed it was pertinent to a finding of substantial equivalence. MDUFMA adds the requirement that validation data pertaining to cleaning and sterilization, and functional performance must now be submitted with the 510(k) for certain devices identified by FDA.

FDA-Recognized Standards and Validation Data

15. Can a manufacturer use FDA-recognized standards to reduce the amount of specific validation documentation in a 510(k) submission for a reprocessed SUD?

FDA can not accept a declaration or statement of conformity in lieu of cleaning, sterilization, or functional performance validation data for those reprocessed SUDs listed in the FR because [10] MDUFMA requires the submission of validation data for those device types.

Submission of Validation Data to FDA

16. What is the recommended format and content for 510(k)s subject to the MDUFMA validation data requirements?

A 510(k) for a listed reprocessed SUD should be identified as such and:

- must include the information described in 21 CFR § 807.87, Information Required in a Premarket Notification Submission. (The general format and content for a 510(k) is described in the regulation. Additional general format and content guidance is available in our Guidance for Industry and FDA Staff – Format for Traditional and Abbreviated 510(k)s. See CDRH's website at www.fda.gov/cdrh/ode/guidance/1567.html.
- should address information discussed in any relevant FDA device-specific guidance and guidance generally applicable to premarket submissions for medical devices; and
- must contain validation data (MDUFMA § 302(b)). This should be included in the test report section of the 510(k).

FDA accepts and encourages the submission of electronic copies from any manufacturer that wishes to submit an electronic copy with a premarket submission. (See CDRH's website at entitled, Electronic Copies for Premarket Submissions, at www.fda.gov/cdrh/elecsub.html.)

17. If a 510(k) is submitted prior to publication of a MDUFMA list adding that device type and the substantial equivalence (SE) decision is still pending, must the reprocessor submit the validation data before FDA renders its decision?

No. If FDA publishes a list adding a device type, we may still clear a 510(k) for a reprocessed SUD of that device type that now requires validation data, even if the validation data are lacking, provided the 510(k) was under review when the MDUFMA list published and clearance will occur no later than nine months after publication. If nine months have passed, the manufacturer must submit the cleaning, sterilization, and functional performance validation data required by MDUFMA for the cleared device. While FDA reviews these data, the device may stay on the market. If the manufacturer does not submit the data by the nine-month deadline, the device may no longer be

[10] See 70 FR 56911 (www.fda.gov/ohrms/dockets/98fr/05-19509.pdf) for a complete listing of all device types subject to the validation data requirement.

marketed. Alternatively, the manufacturer may supplement the pending 510(k) with the validation data, thus obviating the need for a post-clearance submission to the Agency of the validation data.

18. How should a reprocessor submit validation data for previously cleared 510(k)s subject to these requirements?

The Agency has published notices identifying the types of devices that require submission of validation data. The Agency did believe a new 510(k) was needed in order to submit solely the validation data for devices with previously cleared 510(k)s. When submitting the validation data required under MDUFMA for an already cleared 510(k), a reprocessor was to clearly label the submission as a "Supplemental Validation Submission (SVS)" and reference the cleared 510(k) number. It is possible that the Agency may identify future device types that if reprocessed will require validation data. If that is the situation, to facilitate the review process, reprocessors should either: (1) incorporate by reference or (2) again provide the required elements of a 510(k), as identified in 21 CFR 807.87, in the SVS. Reprocessors should send these submissions to the CDRH Document Mail Center (DMC). FDA accepts and encourages the submission of electronic copies from any manufacturer that wishes to submit in this format. (See CDRH's website at www.fda.gov/cdrh/elecsub.html.)

19. Will manufacturers have to pay user fees when they submit the validation data?

According to MDUFMA, any 510(k) submitted on or after October 1, 2002, is subject to a user fee unless it meets one of the requirements for exemption (e.g., when solely indicated for pediatric use).[11] Manufacturers submitting new 510(k)s with validation data for listed devices will need to include user fees for this type of submission. If, however, the listed device was already cleared for marketing and the manufacturer only submits a SVS, no user fee is required.

20. What will happen if FDA decides that validation data is needed for a device under review but not yet listed?

Section 510(o)(1)(C) of the Act enables FDA to require the submission of validation data for a reprocessed SUD before it is cleared for marketing, even if it is not yet listed by the Agency. This allows FDA to identify new types of reprocessed SUDs for which validation data should be reviewed prior to marketing clearance. When FDA determines that validation data should be submitted for a type of reprocessed SUD that has not yet been listed, it will promptly post a notice on the web to inform reprocessors of the need to submit such data for that device type. The Agency will then publish a notice in the *Federal Register* identifying that additional device type(s) as requiring validation data.

In order to ensure consistency in the requests for validation data, FDA intends to designate each ODE Division Director as the person responsible for determining whether validation data

[11] See MDUFMA section 102(b) (the Act § 738(a)(1)(B)).

are necessary for an unlisted device. The Division Director should notify the 510(k) Staff of these determinations so that the list of devices subject to validation data submission requirements can be updated. When a reprocessed SUD is listed, and the date of the requirement is in effect, all subsequent new submissions for the same type of reprocessed SUD must contain validation data.

21. Can master files be used to document validation data?

Yes. Master files are a means to reduce the potential documentation burden relating to the submission of validation data.

FDA enables manufacturers to submit master files with information that may apply to more than one submission. A master file is not cleared but rather is a depository of information that may be referenced by the manufacturer or by those with a right of reference given by the submitter of the master file. For more information on master files, see the guidance entitled, "Master Files Part III; Guidance on Scientific and Technical Information" at /www.fda.gov/cdrh/ode/338.pdf.

If there are common aspects of the design and process validation data for multiple devices, then the common validation data may be provided in a master file. FDA will review the file when referenced in a 510(k), PMA, or premarket report.

22. Can the validation data for multiple devices be bundled in a single application?

Bundling is the combination of more than one device or multiple indications for use for one device in a single premarket submission. Validation data should be applicable to all the specific finished device(s) covered by each submission. Although there may be common aspects of validation (see previous discussion of Master Files) for reprocessed SUDs, there may also be unique aspects of designs (e.g., different OEMs) and unique process validations for each device type. Therefore, the manufacturer should justify how the data submitted apply to all the devices in the submission and only bundle those devices or indications that can be reviewed together. For more information on bundling, see the guidance entitled, "Guidance for Industry and FDA Staff: Bundling Multiple Devices or Multiple Indications in a Single Submission" https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089732.pdf

III. Specific Validation Data Recommendations

The following section provides recommendations on the specific types of validation data and information a person submitting a 510(k) for a listed device should provide to the Agency.

Overview Information on Reprocessing Procedure

FDA recommends that the submission:

- Provide a complete summary overview of the reprocessing procedure for the device beginning from the point of use of the device to the release of product at the end of the process. A detailed graphical presentation (e.g., flow chart, diagram, or drawing) will be helpful to orient the FDA review staff. The

overview should be sufficiently clear to identify all the steps of the process related to cleaning, disinfection and/or sterilization, and functional performance of the device.

- State the maximum number of times the device is intended to be reprocessed, the incoming raw material (processed OEM device) specifications, and the design specifications for the finished device.
- Provide a risk analysis, as discussed in Question 13.
- Provide the process specifications, operating conditions, and acceptance criteria for the product and process, as discussed in Question 13.
- Include in the validation report(s) the procedures and protocols utilized in the validation efforts, results, and other supporting information. The reports should summarize this information, and the appendices should include expanded information and/or the complete information referenced in the reports. Manufacturers may contact FDA to discuss the content of their reports before submitting this information to FDA.

Cleaning

The manufacturer should provide a thorough summary of data and information on the cleaning portion of the design and process validation. A number of formats for this information may be suitable. One format, using the following headings, is based on a process design and validation scheme adapted from ISO 14937, "Sterilization of medical devices – General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices:"

- Cleaning Agent Characterization
- Process and Equipment Characterization
- Product Definition
- Process Definition
- Process Validation, which includes:
  - Installation Qualification
  - Operational Qualification
  - Performance Qualification
- Routine Monitoring and Control
- Product Release
- Assessment of Change

Cleaning Agent Characterization

The submission should:

- Specify all the cleaning agents used, including products such as enzymes, water, rinses and detergents.
- Describe why each of the products was selected, and how the agents are prepared, used, and stored. Documentation of the labeling for the agents for conditions of use is acceptable.
- Document any deviation from the labeled conditions.
- Provide summary data on the safety of the cleaning agents under their conditions of use, specifically in regard to their toxic levels. This can be derived from Material Safety Data Sheets and/or from toxicological tests.
- Document the cleaning test methods, acceptance criteria, analysis and test results. The results should demonstrate the effectiveness of the cleaning agents when used as labeled or as intended by the reprocessor.
- Document all potential worst case degrees and type of contamination, as applicable, such as blood and other body fluids, fecal material, tissues, lubricants, and residual cleaning agents. The methods and results should document effectiveness of the agents on the specific device under the worst case contamination conditions.
- Describe the cleaning endpoint used in the tests and the rationale for the endpoint.
- Describe the sensitivity, specificity, reproducibility, accuracy, and precision (as applicable) of the analytical test methods for determining that the endpoint is achieved, (i.e., the device is clean).
- Describe the statistical considerations for the tests and explain how the samples used in testing represent the range of types of devices in the 510(k) submission.

Note: Tests demonstrating a reduction in contamination levels alone are insufficient as an endpoint. Although the common definition of a clean device is one that is visually free of contamination, this condition should be translated by the reprocessor into an objective and measurable endpoint specification. The endpoint should have a visual component but should be supplemented with chemical, microbiological, and/or other physical parameters with tolerances. Devices should not have an endpoint based on visual examination alone.

Tests should demonstrate that the cleaning endpoint is achieved independently of subsequent process steps. Test methods may utilize simulations of contamination under controlled lab conditions; however, actual contamination should be used to complete validation testing.

Process and Equipment Characterization

The submission should:

- Describe the cleaning process parameters and their tolerances. These parameters include all the variables of the process such as soak and rinsing amounts, process times, temperatures, brushing duration, and ultrasound bath parameters. The submission should describe how these process variables are controlled and monitored.
- Include quality control tests.
- Describe the specifications for the cleaning equipment, including, for example, physical description, instrumentation for monitoring and controlling the process, and fault recognition.

Product Definition

The submission should:

- Define the product to be cleaned and how it is presented for cleaning. This includes the acceptable degree of microbiological, organic and inorganic contamination of the device.
- Describe any steps in the cleaning process that have limits on the degree of incoming contamination. For example, initial defined steps of wiping, rinsing, and an enzyme soak may be needed to remove gross contamination prior to additional steps at the site of reprocessing.

Process Definition

The submission should:

- Provide a thorough summary of the specifications of the process and summarize the process definition activities. This includes information to demonstrate that the cleaning process attains the process parameters by objective endpoints. The biological safety of the product following exposure to the cleaning agents and after removal of residuals can be deferred to the sterilization validation step, if needed, since the end product of the entire process should be assessed.
- Identify and document, in the risk assessment, the limits for process residuals. The means to reduce the residuals should be documented.
- Demonstrate that the cleaned device meets the acceptance criteria.
- Specify the process used to determine the number of times each device has been reprocessed.
- Describe any procedures associated with repairing, refurbishing and/or replacing any device component as part of the reprocessing procedure. Characterize the replacement components and assess their suitability by appropriate engineering tests, and by preclinical or clinical tests when engineering tests alone are insufficient to assess clinical safety and effectiveness. Data regarding these activities should be provided.

Note: The functional performance assessment should be deferred until after the sterilization validation step, if sterilization is required. However, the effectiveness and safety of cleaning as a separate process should be individually documented. In other words, the manufacturer should show that the cleaning step results in a device that meets the cleaning endpoint and then show that the sterilization process achieves sterilization given worst case preprocess bioburden specifications (e.g., process achieves a sterility assurance level (SAL) of 10^{-6} with overkill).

Process Validation

The purpose of process validation is explained above. There are three steps used in process validation that can be adapted to a cleaning process, including both equipment and manual procedures. These steps are installation qualification, operational qualification, and performance qualification. The submission should provide a summary of each of the process validation steps as they apply to the reprocessing of the specific device:

- The installation qualification can be briefly summarized. For purposes of a 510(k), FDA is primarily interested in a summary of the operational and performance qualification where test and actual loads or sample runs are evaluated.
- The operational qualification summary data should demonstrate that the cleaning equipment is capable of delivering the specified process within defined tolerances.
- The performance qualification summary should demonstrate that multiple consecutive runs of the cleaning process with the specific type of device achieve the specified outcome. Explain any failures of the process and means to correct the process. The qualification should demonstrate effective and safe reprocessing after the defined number of iterations specified by the reprocessor.

Routine Monitoring and Control

The submission should describe how the cleaning process is monitored and controlled on a routine basis.

Product Release

The submission should provide the procedures for product release for return to the user or for further reprocessing, (e.g., packaging and terminal sterilization). This includes the criteria for designating the cleaning process as conforming to its endpoint specifications.

Assessment of Change

The submission should describe how changes to the incoming device will be assessed to identify significant changes that may impact the effectiveness of cleaning. (See also Question 13.)

Packaging

A manufacturer of a reprocessed SUD is not required to submit packaging validation data. However, any 510(k) premarket notification should contain a full description of the final packaging materials, packaging configuration, and shelf life. We recommend you retain the packaging validation protocol and data, and shelf life data on file at the manufacturing facility for review during a Quality Systems audit.

Sterilization

The submission should include a summary of the sterilization process design and validation activities. As explained above, the ISO 14937 scheme may serve as a template for this documentation. FDA does not believe that reiteration of the provisions of these standards is necessary for purposes of this guidance. They can be accessed at various websites for the standards development organizations.

Pyrogen Tests

Devices that come into direct or indirect contact with blood should be assessed for residual pyrogens after the sterilization process. FDA-recognized standards should be referenced when possible. A summary of the tests conducted during process definition should be described as well as routine monitoring.

Functional Performance

A reprocessor must evaluate functional performance of its reprocessed device(s) according to MDUFMA section 302 (the Act § 510(o)(1)(A), (2)(A)). Functional performance is a component of sterilization process characterization and validation, and also of cleaning process validation.

The reprocessor should assess functional performance on a worst case basis, i.e., after the maximum number of times the device is intended to be reprocessed as specified by the reprocessor. The reprocessor should simulate use of each sample of device between each reprocessing cycle and this step should be specified in the summary of the process design and validation. The specific types of engineering and other tests to be conducted will vary depending on the specific device.

The device should continue to meet its performance specifications after the reprocessor has tested the maximum number of intended cycles. Current FDA device-specific guidance may include performance tests that the reprocessor may use in validating functional performance. The performance tests should be summarized in the process design and validation documentation submitted for review.