Premarket Guidance: Reprocessing and Reuse of Single-Use Devices; Draft Guidance for Industry and FDA Staff

Draft Guidance – Not for Implementation

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Center for Devices and Radiological Health

Infection Control Branch
Division of Dental, Infection Control, and General Hospital Devices
Office of Device Evaluation

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Preface

Public Comment

For 90 days following the date of publication in the Federal Register of the notice announcing the availability of this guidance, comments and suggestions regarding this document should be submitted to the Docket No. assigned to that notice, Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852.

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Premarket Guidance: Reprocessing and Reuse of Single-Use Devices; Draft Guidance for Industry and FDA Staff

This document is intended to provide guidance. It represents the Agency's current thinking on this topic. It does not create nor confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute and regulations.

Introduction

This document provides premarket guidance to the medical device industry, including third party and hospital reprocessors, and to Center for Devices and Radiological Health (CDRH) staff who are responsible for the premarket evaluation of submissions for reprocessed single-use devices or related enforcement activities.

On August 14, 2000, FDA published a policy entitled **Enforcement Priorities for Single-Use Devices Reprocessed by Third Parties and Hospitals**, August 14, 2000 http://www.fda.gov/cdrh/reuse/1168.html (Enforcement Priorities document). The Enforcement Priorities document provides guidance to third parties and hospital reprocessors about their responsibilities as manufacturers engaged in reprocessing devices labeled for single use (SUDs) under the Federal Food, Drug, and Cosmetic Act (the Act).

The Enforcement Priorities document finalizes the FDA priorities for enforcing premarket submission requirements for reprocessed SUDs based upon the regulatory class of the device (i.e., Class I, II, or III). Prior to the effective date of the Enforcement Priorities document, FDA had not actively enforced premarket submission requirements for reprocessed SUDs for third party reprocessors and hospitals. The agency now intends to actively enforce premarket requirements if reprocessors of SUDs have not filed premarket submissions or applications, and received marketing clearances or approvals by the dates described below:

Priorities timetable

Enforcement Dates for Premarket Submissions and Approvals		
	Filing Date:	Clearance or Approval Dates:
Class III	2/14/2001	8/14/2001
Class II non-exempt	8/14/2001	2/14/2002
Class I non-exempt	2/14/2002	8/14/2002

This guidance, **Premarket Guidance: Reprocessing and Reuse of Single-Use Devices; Guidance for Industry and FDA Staff**, expands upon the summary premarket information in the Enforcement Priorities document. For a more detailed explanation of FDA's enforcement priority timetable, refer to the Enforcement Priorities document.

Intent of this Guidance Document

This guidance is intended to inform the device industry and CDRH staff on the current policies and recommendations regarding premarket regulatory and technical issues for reprocessed SUDs. This guidance may be modified or updated. This guidance may also be supplemented by questions and answers posted by CDRH on its reuse internet web site.

Who to Contact in CDRH with Premarket Regulatory or Technical Questions Related to Reprocessed SUDs

For questions on Office of Device Evaluation (ODE) policies and procedures - the following CDRH personnel are coordinating reuse activities within ODE:

Timothy A. Ulatowski	301-443-8879
Barbara Zimmerman	301-443-8517
Philip J. Phillips	301-594-2022
Heather Rosecrans	301-594-1190

For product specific technical questions - the following ODE personnel are coordinating reuse activities within each of their divisions:

DCRD:	Bill Letzing	301-443-8320
DDIGD:	Elaine Mayhall	301-443-8913
	Feli Marshall	301-443-8913
DOED:	Jake Romanell	301-594-1744
DRARD:	Mary Cornelius	301-594-2194
	Miriam Provost	301-594-1220
DGRND:	Neil Ogden	301-443-8262
DCLD:	Kaiser Aziz	301-594-3084

The Infection Control Branch, DDIGD, provides consulting reviews within ODE on data and information related to sterilization, cleaning and packaging. FDA staff or industry may contact the Branch Chief, Chiu Lin, Ph.D. (301-443-8913), regarding these specific issues.

Requests for meetings – The industry may request meetings as outlined in CDRH guidance on communication with industry, **Meetings with the Regulated Industry**, (I89-3), November 20, 1989 http://www.fda.gov/cdrh/i89-3.html. Meetings require multidisciplinary participation and time for preparation. Therefore, industry and FDA

should agree on a meeting date that affords both parties ample time for preparation. Meetings should be preceded by submission to FDA of a complete agenda, names of meeting attendees, and background information.

Note: All interactions with the industry on premarket submissions for reprocessed SUDs should include one of the ODE policy staff listed above or the division technical contact, if possible. It is also important to maintain cross-division communication to help ensure consistency.

Premarket Information Related to Reprocessing of SUDs on the CDRH Internet

FDA has posted a variety of information relevant to reprocessing of SUDs on its reuse web site. Refer to http://www.fda.gov/cdrh/reuse/index.shtml. The web site includes information such as:

- frequently asked questions and answers
- full text of the August 14, 2000, Enforcement Priorities document
- guidance documents and other documents that are helpful to those considering premarket submissions for reprocessed SUDs
- reprocessing-related standards information

Devices Excluded from the SUD Reprocessing Enforcement Strategy

The August 14, 2000, Enforcement Priorities document does **NOT** apply to:

- Permanently implanted pacemakers;

  Reuse of these devices is addressed in Compliance Policy Guide 7124.12.

- "Opened-but-unused" SUDs;
- Healthcare facilities that are not hospitals;

  FDA may consider expanding its enforcement strategy to additional types of facilities in the future.

- Hemodialyzers.

Persons interested in premarket submissions for hemodialyzers should refer to the available specific guidance on these devices.

Enforcement Priorities Related to Premarket Submissions

The August 14, 2000, Enforcement Priorities document http://www.fda.gov/cdrh/comp/guidance/1168.pdf contains important policy and information related to premarket submissions for reprocessed SUDs. Premarket review staff and other interested parties should refer to this document. The relevant premarket sections of the August 14, 2000, Enforcement Priorities document include:

- Section E.7, Regulatory requirements for SUD reprocessors under the Act, Premarket Requirements

  This section includes some basic questions and answers related to premarket submissions.

- Section F.1, Enforcement, Premarket Requirements

  This section states the dates that FDA intends to begin actively enforcing the requirements for filing premarket submissions and its requirements for marketing clearances and approvals.

- Appendix B, Definition of terms

  This appendix includes important definitions related to reprocessing of SUDs.

- Appendix E, FDA's Intended Timeline for enforcing specific premarket submission requirements.

  This appendix summarizes the enforcement timeline.

Premarket Issues Related to Submissions for Reprocessed SUDs

The following information may be helpful to SUD reprocessors who submit premarket notification submissions and applications. Information marked by an asterisk (*) is directed primarily to CDRH staff, although the device industry may find this information informative.

1. In premarket notification submissions and approval applications, will FDA evaluate only manufacturing information related to reprocessing?

No, FDA will evaluate all the criteria required by its statutes and regulations in making marketing determinations.

a. For premarket notification (510(k)) submissions

A 510(k) submission must contain enough information for FDA to determine whether the device is as safe and effective as a legally marketed predicate device (i.e., "substantially equivalent" within the meaning of section 513(i) of the Act). The 510(k) applicant is responsible for identifying a legally marketed predicate device for the SUD they wish to reprocess. The predicate device selected must have the same intended use as the device in the 510(k) submission. For a reprocessed SUD, the legally marketed predicate device for comparison may be the SUD of the Original Equipment Manufacturer (OEM). The reprocessor must submit information in the 510(k) submission comparing the characteristics of their device to the predicate device to establish that they are equivalent with respect to safety and effectiveness factors in all respects. These factors include, but are not limited to, design, sterility, biocompatibility, strength of materials, and functionality. Accordingly, information that addresses only the steps used in reprocessing the device would not be sufficient to receive marketing clearance.

The criteria that FDA uses in deciding to grant marketing clearance for 510(k) submissions are more fully described in section 513(i) of the Act and 21 CFR 807.100. A 510(k) submission must include all the information described in the 510(k) regulation, 21 CFR 807.87.

b. For premarket approval (PMA) applications

FDA's basis for approval of a PMA application is a finding that the device has a reasonable assurance of safety and effectiveness for its intended uses based on valid scientific evidence. Section 515 (d) (2) of the Act. A PMA application must include valid scientific evidence that demonstrates the safety and effectiveness of the reprocessed SUD. 21 CFR 814.45(c) and 860.7. Submission of clinical data may be necessary in order to establish reasonable assurance of safety and effectiveness. A PMA application from a reprocessor also should evaluate the unique characteristics of the reprocessed device, including but not limited to design, sterility, construction or assembly, biocompatibility, strength of materials, and clinical functionality. Accordingly, premarket information that addresses only the steps used in reprocessing the device would not be sufficient to receive marketing approval. The factors that FDA uses to grant marketing approval of PMA applications are more fully described in section 515(d) of the Act and 21 CFR 814.44.

2. What is the difference between premarket requirements for OEMs and SUD reprocessors?

Any person engaged in activities that trigger premarket requirements, as described in 21 CFR 807, must comply with the same requirements. A 510(k) submission or PMA application from a reprocessor should address any applicable FDA guidance, laws or regulations. There are no additional regulatory requirements for reprocessed SUD submissions or applications, nor are there special allowances for these submissions or applications.

3. What is the difference in premarket requirements if a reprocessor labels an SUD for single use versus multiple use by the end user?

Provided there is sufficient valid scientific information, a reprocessor has the option of labeling a reprocessed SUD for either single use or multiple use (reusable) by the end user. For a single use device, the reprocessor reprocesses a used SUD, labels it for single use only, and distributes it to an end user for one use. For a multiple use device, the reprocessor reprocesses a used SUD, labels the device with adequate directions for use that instruct the end user how to reprocess the device, and distributes it to an end user for multiple use. The end user is responsible for reprocessing the multiple use device according to the directions for use.

a. For 510(k) submissions

For a single use device, the submission should include information requested in Blue Book K90-1, Sterilization Data, http://www.fda.gov/cdrh/k90-1.html, as well as other information needed for 510(k) submissions as described in question 1 above. Labeling for a multiple use device should include validated directions for cleaning and sterilizing or disinfecting the device by the end user.

b. For PMA applications

For a single use device, the application should include validation data and information on the entire reprocessing procedure, as well as other information needed in a PMA application as described in question 1. Labeling for a multiple use device should also include validated directions for cleaning and sterilizing or disinfecting the device by the end user. The application should include a summary of the data validating the directions for reprocessing the device by the end user.

For a multiple use device, ODE staff and reprocessors should refer to the recommendations outlined in the guidance document entitled **Labeling Reusable Medical Devices for Reprocessing in Health Care Facilities**, April 1996 http://www.fda.gov/cdrh/ode/198.pdf, and the Questions and Answers document for this guidance, September 3, 1996 http://www.fda.gov/cdrh/ode/1198.html.

4. What type of manufacturing information and data analysis should be submitted in a PMA application or a 510(k) submission?

FDA will evaluate the manufacturing process validations as part of the review of PMA applications and associated premarket quality systems regulation (QSR) inspections. FDA expects PMA applications for reprocessed SUDs to have complete manufacturing sections addressing all relevant aspects of the statute, regulations and applicable guidance. FDA will not ordinarily evaluate the manufacturing process as part of its review of a 510(k) submission, unless FDA would request such manufacturing information for the same type of product from an OEM.

A "right of reference" may be a least burdensome approach to help ensure complete PMA manufacturing sections and design control documentation. A right of reference may also be useful for 510(k) submissions. Refer to question 12 for more information on rights of reference.

5. ***How does the Center for Devices and Radiological Health's Office of Device Evaluation and Office of Compliance plan to address the reprocessing procedures that are beyond the scope of a 510(k) submission review?**

FDA will address reprocessing procedures that are beyond the scope of a 510(k) submission review by cooperative efforts within the Center for Devices and Radiological Health on (a) reprocessor-related, directed or periodic QSR inspection reports, (b) process-related information in a 510(k) submission, and (c) reprocessing procedures in reprocessor-related PMA applications and premarket QSR inspections.

a. Directed or periodic inspection reports

The Office of Compliance (OC) and the Office of Device Evaluation (ODE) will engage in a cooperative effort on evaluation of directed or periodic inspection reports. The cooperative effort includes the following:

- Resources permitting, OC intends to inspect all commercial reprocessors.
- Staff from the Infection Control Devices Branch (INCB) will evaluate all inspection reports of reprocessor facilities. INCB's will identify and resolve any safety or effectiveness issues associated with the manufacturing process. Any INCB staff questions or observations will be forwarded by INCB to OC, which then will take action as needed. INCB staff should seek consultation with other ODE components and the Office of Science and Technology (OST) on the evaluations, as needed. The evaluations and correspondence will be shared among CDRH offices.
- OC may request participation of ODE and OST staff in inspections of reprocessors.

b. Process-related information in a 510(k) submission

The cooperative effort between OC and ODE will include action on process-related information contained in a 510(k) as follows:

- Unless applicable product-specific guidance recommends otherwise, manufacturing data and information are ordinarily not submitted in a 510(k), except for certain sterilization information. However, if any manufacturing process data and information are included or referenced in a 510(k), CDRH may review the data to evaluate any potential risk to public health that may be associated with that information.

- ODE staff may request consults on the process information (e.g., from INCB or OST). Staff should document deficiencies regarding the process information and obtain concurrence through the management chain. These process-specific deficiencies should not be considered as part of the substantial equivalance decision (unless recommended in a product-specific gudiance) and should not delay a final decision on a 510(k).

- ODE's identification of specific deficiencies in the manufacturing process should be sent to OC. OC will evaluate the deficiencies under the QSR and will take action as needed. OC will share its review with other CDRH offices.

c. Reprocessor-related PMAs and premarket QSR inspections

As noted, FDA does not ordinarily evaluate manufacturing procedures in 510(k) submissions. However, some reprocessors who submit 510(k) submissions, may also submit PMA applications for their other devices that share the same manufacturing processes and procedures as their 510(k) cleared devices. PMA applications are subject to FDA evaluation of manufacturing procedures and premarket QSR inspections. Information in these PMA applications and premarket inspections may be relevant to the procedures used to reprocess SUDs subject to 510(k) submissions, such as quality control procedures and process validations. Therefore, the coordinated FDA evaluation of PMA applications and premarket inspections from reprocessors should address some aspects of reprocessing procedures for their devices that are subject to 510(k) submissions.

6. What labeling requirements apply to reprocessed SUDs?

Reprocessed SUDs must be labeled according to the requirements of the Act and 21 CFR Part 801. PMA applications and 510(k) submissions must include proposed labeling for the reprocessed SUD (21CFR 807.87(e) and 21 CFR 814.20(b)(10)). CDRH will post additional information on labeling on its reuse internet web site http://www.fda.gov/cdrh/reuse/index.shtml.

7. ***Is reprocessing an SUD considered a new intended use within the meaning of section 513(i) of the Act?**

For generic types of devices that do not require PMA applications, ODE staff should not ordinarily consider the reprocessing of an SUD as a new intended use that would preclude an SUD from going through the 510(k) route to marketing. The reviewer should still be vigilant for any differences in labeling of the reprocessed device compared to the predicate that may create a new intended use.

8. ***How will FDA's reviewers use ODE's 510(k) Decision Flowchart to evaluate 510(k) submissions?**

ODE reviewers use the 510(k) substantial equivalance decision-making process flow chart that is based on the criteria in section 513(i), for documenting the rationale for their decisions. In terms of this flow chart, it is unlikely that a reprocessed SUD will present a new intended use or new types of safety and effectiveness questions than legally marketed predicates. There may be differences in specifications and tolerances between the predicate device and reprocessed SUD. ODE reviewers may request information about these differences. It is also possible that submissions for reprocessed SUDs, as with OEM submissions, may be based on descriptive information alone, unless applicable product-specific guidance recommends otherwise.

9. **Can I combine several different models and brands of the same type of device into one 510(k) submission or PMA application?**

510(k) submissions and PMA applications are device specific; FDA requires a 510(k) or a PMA for each device. Only closely related variations of the same type of device should be grouped in one submission or application. FDA advises reprocessors to examine device groupings that OEMs have developed in previous submissions as models that may be useful in considering the groupings of reprocessed SUDs. Data and information in the submission or application must support the substantial equivalence (510(k)) or safety and effectiveness (PMA) of each device within the entire group of devices in a marketing application or submission.

10. **What additional information should be included on the cover sheet in a 510(k) submission or PMA application?**

The applicant should clearly identify the device as a reprocessed SUD in the cover letter of the submission or application in order to facilitate FDA tracking. FDA staff enter a reuse notation on a tracking computer sheet attached to each submission. ODE staff should ensure that the reuse flag on the tracking sheet has been properly noted.

11. Can SUD reprocessors submit special 510(k) submissions, abbreviated 510(k) submissions, or modular PMA applications?

Reprocessors may avail themselves of every premarket process available to OEMs including, when appropriate, special and abbreviated 510(k) submissions and modular PMA applications. It is conceivable that if a reprocessor receives clearance of a traditional 510(k) submission, then the special 510(k) submission option would be available to the reprocessor for requesting clearance of significant modifications to the same device. For more information about these alternative processes, consult applicable guidance http://www.fda.gov/cdrh/ode/parad510.pdf and http://www.fda.gov/cdrh/pmat/modpmat.html.

12. How can I obtain information that is only in the possession of the OEM that is necessary to gain marketing clearance or approval?

As question 1 notes, SUD reprocessors are responsible for submitting information relating to characteristics of their device, including, but not limited to, design and materials. They may also need to submit information on their reprocessing procedures. If an SUD reprocessor does not have all the necessary information in its possession, it may need to obtain a written authorization from the person who has submitted the necessary information to FDA, providing FDA the right to reference the information on behalf of the reprocessor.

For example, an OEM may have on file at FDA a marketing submission, application, or master file related to the reprocessed SUD the reprocessor wishes to market. A right of reference from the OEM to FDA authorizing FDA to use the information on file, in whole or in part, may suffice as a portion of the reprocessors premarket submission or application.

13. In general, what aspects of premarket submissions and applications for reprocessed devices may be problematic?

As FDA evaluates premarket submissions and applications, we will identify common problems that may be unique to reprocessed SUDs. FDA has the following initial recommendations:

- Device descriptions should be relevant to the subject device and sufficiently detailed in terms of specifications and tolerances for FDA to evaluate substantial equivalence or safety and effectiveness.

- Validation data should use the specific device as the test article or justify why another device was used for tests. Tests used to support the design specifications and quality control procedures should include SUD samples exhibiting the range of tolerances for the specifications and procedures. For example, cleaning, sterilization, and performance tests should include SUDs

with the range of potential contamination and wear which the reprocessor intends to accept and process from incoming product.

- Validations should meet general norms, addressing the issues of both product performance and risk of infection.

- Referenced standards should be applicable to the device in question. Deviations from standards should be identified.

- Clinical data should be provided if recommended by guidance. Lack of appropriate clinical data in a submission when such information is ordinarily required of an OEM will delay the FDA review.

- Cleaning protocols and simulations should be rigorous and relevant. The soil should relate to the environment of use. Soil reduction, per se, should be insufficient as an endpoint. Elimination of visible soil is a qualitative endpoint that should be coupled with a quantitative assessment.

- For a critical device, a sterility assurance of one in one million non-sterile units should be demonstrated as an endpoint.

Quality System Related Aspects of Reprocessed SUDs

The following information describes issues that FDA considers under quality system evaluations, rather than as part of premarket evaluations for reprocessed SUDs:

- Incoming product control and acceptance. The reprocessor must have procedures for quality control of incoming used SUDs (21 CFR 820.80 and 820.86). The reprocessor should use acceptance criteria to determine if the incoming product can proceed to the next step in reprocessing or be discarded.

  The incoming control should identify devices that do not meet specifications. Incoming devices may not meet specifications because they have been degraded due to reuse or because the OEM has modified the device. Identifying when an OEM has modified the device is a significant challenge for a reprocessor.

- Production and process controls and nonconforming product. The reprocessor should have procedures to control processes and to identify, evaluate, and control product that does not meet specifications (21 CFR 820.70 and 820.90). These procedures may include in-process and final product quality control tests.

- Tracking the number of times a device has been reprocessed. The reprocessor should have a means to identify and track individual devices, when necessary, and to maintain a record of how many times the device has been reprocessed (21 CFR 820.60, 820.65, and 820.70). Rigorous tracking of the number of times the device has been reused may not be needed for some devices. For example, Class III EP catheters

may require a count of the number of uses while a stainless steel drill bit may not. The decision may depend, for example, on whether quality control measures alone can detect nonconforming product and whether design validation established that a limit was needed on the maximum number of times that a device could be reprocessed.

- Sterilization and cleaning validations. FDA ordinarily does not review process validation information in 510(k) submissions, but relies on post approval quality systems inspections to ensure validations are conducted appropriately. Refer to the Blue Book K90-1, Sterilization Data, http://www.fda.gov/cdrh/k90-1.html, and the 6 questions described in that document that may be posed to 510(k) applicants. Also, refer to the reviewer guidance on reusable device labeling previously referenced. PMAs should include details on reprocessing and these data are subject to premarket review. The Office of Compliance may involve the Office of Device Evaluation in reviewing manufacturing information.