



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration  
Rockville MD 20857

JAN 23 2006

The Honorable Tom Davis  
Chairman  
Committee on Government Reform  
House of Representatives  
Washington, D.C. 20515-6143

Dear Mr. Chairman:

Thank you for your letter of December 16, 2005, co-signed by Representative Henry A. Waxman, regarding the Food and Drug Administration's (FDA or the Agency) oversight of reprocessed single-use devices (SUDs).

As you know, the reprocessing of SUDs is legally permissible in the United States in compliance with the Federal Food, Drug, and Cosmetic (FD&C) Act. The Medical Device User Fee and Modernization Act (MDUFMA) of 2002 mandated changes to the regulation of SUDs. MDUFMA created a number of new requirements for reprocessors and for FDA's review of these products. These new requirements were motivated by concerns about the growth of the reprocessing industry and the difficulty of reprocessing increasingly complex and hard to clean medical devices. Additional information regarding FDA's efforts in this area as well as answers to your questions is provided below.

**1. What specific steps is FDA taking to ensure that reprocessed single-use medical devices are safe and efficacious?**

Reprocessors of SUDs are considered "manufacturers" under the FD&C Act. They are subject to the same requirements under the Act as other manufacturers of medical devices. For example, like all device manufacturers, reprocessors are required to: register their establishments and list their devices; report adverse events; follow good manufacturing practices as required by the quality system regulations and label devices appropriately.

In addition, under the FD&C Act, reprocessors of some SUDs must obtain pre-market clearance before distributing their devices even though the original device is exempt from pre-market review. Further, some SUDs are subject to the pre-market report requirement, which is similar to a pre-market approval application, but with data related to reprocessing required (section 515(c)(2) of the FD&C Act). Reprocessors may be required to include validation data in pre-market submissions relating to cleaning, sterilization, and functional performance following reprocessing. The FD&C Act also requires reprocessors to state in their labeling that the device has been reprocessed, and beginning in August 2006, requires reprocessors to physically mark the actual device with a name or symbol that identifies the reprocessor.

To help ensure that these requirements are met, FDA, among other actions, reviews the validation data, issues not substantially equivalent orders when appropriate, conducts inspections of reprocessors, and undertakes enforcement actions.

**2. Has FDA received complaints through the MedWatch adverse event reporting system of illnesses or injuries resulting from reprocessed medical devices that were designated for single-use?**

The Center for Devices and Radiological Health searched the Medical Device Reporting database for adverse event reports where the reporter responded "Yes" in Block D8 ("is this a single use device that was reprocessed and reused on a patient?"). This question was added to the MedWatch reporting form in the fall of 2003 in accordance with Section 303 of MDUFMA. The search produced 176 cases of apparent malfunction or injury associated with reprocessed devices. These reports were received by FDA between October 22, 2003, and December 13, 2005. Upon analysis of these reports, FDA determined that these adverse events are not related to the reprocessing of the SUD.

**a. If so, please provide a list of the types of illnesses and injuries reported correlating with the type of device and the name of the reprocessing company.**

As noted above, we did not identify any adverse events that were actually related to the reprocessing of the SUD. However, if you would like, we can provide on your request a list of the reported illnesses and injuries from the 176 reports identified above.

**b. Please provide the specific action taken by FDA in response to each reported illness or injury to ensure the malfunction of the reprocessed medical device in question was not reflective of a systemic problem.**

We have not identified in our database any reports of illness or injury that are due to reprocessing of SUDs. In general, however, we would respond to any report of death or serious illness or injury by investigating the report, and taking any appropriate follow-up actions, which may include recalls and notifications.

**c. Who is required to submit reports of such adverse events to FDA? Are both the hospital and the reprocessors responsible for reporting adverse events to FDA?**

Any firm or hospital that reprocesses an SUD is considered a medical device manufacturer and, as such, is subject to all the regulatory requirements applicable to original equipment manufacturers. When the device is reprocessed by a third-party reprocessor, the hospital, as a user facility, and the reprocessor, as a manufacturer, are responsible for reporting adverse events in accordance with the Medical Device Reporting Regulation (21 Code of Federal Regulations [CFR] part 803). However, if an adverse event involved a SUD that was reprocessed by a hospital, the hospital would be required to report as both the user facility and the manufacturer.

User facilities must report deaths that are suspected to be device related to both FDA and the device manufacturer within 10 days of becoming aware of the information. The user facility is afforded the same amount of time to report device related serious injuries. However, serious injury reports are reported only to the device manufacturer. If the device manufacturer is unknown, the user facility sends the report to FDA (21 CFR 803.30). Manufacturers must report device related deaths, serious injuries, and malfunctions to FDA within 30 days after they become aware of a reportable event (21 CFR 803.50).

**3. Please provide information on the number of adverse events reported for the original (first) use of single-use devices:**

The combination of manufacturer reported data from Blocks H5 (labeled for single use) and H8 (usage of Device) from MedWatch form 3500A, between November 1, 2003, and the present shows a total of 65,325 adverse event reports for the initial use of devices labeled for single use.

**a. Including any information about the comparative rates of injury from original use vs. reuse.**

FDA does not have information about the comparative rates of injury from original use versus reuse. MedWatch, although a source of useful adverse event information, is not a reliable source for comparative data. As discussed next, conducting this type of comparative analysis requires comprehensive information that is not readily available through MedWatch.

**b. If comparative information is unavailable, what actions would be necessary to develop such information?**

At a minimum, the necessary data would include: 1) identification of the specific type of device and adverse event to be detected; 2) the number of original and reprocessed SUDs of that type in use; 3) a mechanism to track the number of times that each reprocessed SUD has been used; 4) the rate of adverse event for the original device, and 5) a study sample large enough to be able to detect any differences in the rates of adverse events between original and reprocessed SUDs. In order to extract meaningful information this analysis may need to be conducted for each type of device type. These data would have to be available for over 200 device types.

**4. What is the current Good Manufacturing Process (cGMP) for the reprocessing of single-use medical devices?**

Reprocessors, like other manufacturers, are subject to the Quality System Regulation, which sets forth cGMP requirements (21 CFR part 820).

**a. What are the consequences for reprocessors if they violate the cGMP?**

Failure to meet the cGMP requirements could lead to FDA enforcement actions, including product seizure, injunction, civil penalty fines, and prosecution. These actions are typically

preceded by a warning letter, which provides an opportunity for response and time for correction.

**b. In total, how many violations has FDA documented since the enactment of the Medical Device User Fee and Modernization Act (MDUFMA) in 2002?**

FDA has documented four inspections since the enactment of MDUFMA in which the overall inspection was classified violative. Each inspection typically included violations of multiple requirements such as cGMP, registration and listing, adverse event reporting, labeling, and pre-market requirements. Three of the four violative inspections resulted in the issuance of regulatory correspondence to the facility outlining the specific violations identified. The fourth resulted in an injunction.

**5. Please provide a list of any enforcement action taken against reprocessors since the enactment of MDUFMA in 2002. This list should include the name of the company, type of device, date of the enforcement action, and reason for violation.**

There have been four violative inspections since the enactment of MDUFMA. One of the violative inspections (Medical Device Services) resulted in an enforcement action, an injunction, and the other three received regulatory correspondence. Information on the four inspections follows:

- Medical Device Services, Inc., St. George, UT; Injunction May 2003; cGMP violations
- Medi-stat, Inc., Denver, CO; Warning Letter October 2003; cGMP violations
- Bowie Memorial Hospital, Dallas, TX; Warning Letter May 2003; cGMP violations
- Haskell County Healthcare System, Dallas, TX; Untitled Letter November 2002; cGMP violations

Additionally, the following firm had a violative inspection before MDUFMA, which led to an enforcement action after MDUFMA was enacted: Adven Medical, Lubbock, TX; Injunction April 2003; cGMP violations.

**6. Under the MDUFMA, reprocessing firms seeking 510(k) approval must demonstrate that the reprocessed single-use device will remain “substantially equivalent” to the predicate device after the maximum reprocesses as proposed by the company filing the application.**

**a. How often has FDA issued a “Not Substantially Equivalent” letter to firms seeking to legally market a reprocessed single-use medical device?**

FDA has received 199 510(k) submissions for reprocessed single use devices. Of these, FDA found 134 substantially equivalent and 20 not substantially equivalent. In addition, 20 510(k)s were withdrawn by the applicant, 3 were exempted from pre-market notification requirements, 6 were deleted for lack of response to an agency request for additional information, and 16 are currently under review.

**7. Does FDA have limits on how many times a medical device can be reprocessed?**

FDA does not set limits on the number of times a medical device can be reprocessed. The reprocessor determines how many times their product can be reprocessed; however, they are responsible for validating the number of reprocessing cycles allowed for each SUD. FDA, in turn, is responsible for evaluating these validation data that the reprocessor submits in support of the number of times the product can be reprocessed.

**a. If so, how does FDA enforce compliance to ensure that a device is not reprocessed beyond the set number of times?**

During inspections of reprocessors, FDA investigators review the firm's procedures and protocols to determine the nature of their reprocessing operations, which typically would include reviewing the firm's specification for the number of times their device is to be reprocessed. Investigators also review data for processes in use to determine, among other things, whether the number of times they reprocess a device is appropriately validated. They also review product specifications, testing specifications, controls, and records to determine how the firm screens incoming used product for reprocessing and whether they stay within their specification limits and parameters for reprocessing. Failure to comply with such specifications and controls is a violation that FDA would identify to the firm.

**8. Please provide a list (separated by class) of all reprocessed single-use devices along with a correlating list of companies who reprocess those devices.**

Enclosed.

**9. Not all reprocessed single-use devices are required to obtain 510(k) approval before being marketed; how does FDA determine which medical devices require approval and which do not?**

In accordance with MDUFMA, FDA categorized device types that are known to be reprocessed as: critical (device intended to contact normally sterile tissue or body spaces), semicritical (device intended to contact intact mucous membranes and not penetrate normally sterile areas of the body), or noncritical (device intended to make topical contact and not penetrate intact skin). Next, FDA evaluated the potential risk (high, moderate, or low) associated with a SUD based on: (1) risk of infection, and (2) risk of inadequate performance following reprocessing. This process for risk categorization is called the Review Prioritization Scheme (RPS). FDA identified an additional risk criterion as those reprocessed SUDs intended to come in contact with tissue at high risk of being infected with the causative agents of Creutzfeldt-Jakob Disease (CJD).

Using this methodology and these criteria, the FDA identified those critical and semicritical reprocessed SUDs that were previously exempt from pre-market notification requirements and that were either high risk according to the RPS or intended to come in contact with tissue at high risk of being infected with CJD. These devices are no longer exempt and now require submission of 510(k)s that include validation data on cleaning, sterilization, and functionality.



The Agency additionally identified those reprocessed SUDs already subject to pre-market notification requirements that were either high risk according to the RPS or intended to come in contact with tissue at high risk of being infected with CJD. These SUDs now require the submission of validation data if already cleared by FDA or the submission of a 510(k) that includes validation data if the device is newly proposed for marketing in the United States.

Validation data was submitted for several previously cleared SUDs categorized as critical under the RPS. Based on this data, some SUDs were found to be substantially equivalent to a predicate device and could continue to be legally marketed and other SUDs were found not substantially equivalent and could no longer be marketed. FDA has conducted inspections to confirm that these critical devices are no longer being marketed. FDA will also conduct inspections of reprocessors to verify that "semi-critical" devices are no longer being reprocessed unless a 510(k) has been submitted and cleared by the Agency.

We hope this information is helpful. Please do not hesitate to contact us if you have any questions or need additional information. A similar letter has been sent to Representative Waxman.

Sincerely,

A handwritten signature in black ink, appearing to read "Patrick Ronan". The signature is written in a cursive, flowing style.

Patrick Ronan  
Associate Commissioner  
for Legislation

Enclosures