

Reprocessed single-use devices and third-party inspections; changes resulting from MDUFMA

Kenneth Sumner, Jeff Baetz and Diane Mandell continue their discussion of the impact of new US legislation.

This article is the second and final part in a series that examines major recent changes affecting the medical device industry in the US resulting from passage of the *Medical Device User Fee and Modernization Act* (MDUFMA) on 26 October 2002. In Part I, we discussed the collection of user fees for the review of medical device applications by the FDA's Center for Devices and Radiological Health (CDRH)¹. Part II examines two other significant changes brought about by the passage of MDUFMA: new regulatory requirements for reprocessed single-use devices (SUDs) and establishment inspections performed by accredited third parties².

Reprocessing single-use devices

Current medical practice includes the reprocessing of some medical devices even if they are labeled for single use, as one measure to reduce ever-escalating medical costs. The single-use labeling on many devices results partly from the more expeditious route to market and partly from the lower regulatory burden for SUDs compared to devices labeled for reuse, despite the fact that some of these SUDs can safely be used multiple times. Physicians and other end users of devices perceive that the original equipment manufacturer (OEM) has an economic incentive to label their product for single use. This perception is fostered by the occasional letter from an OEM stating that the device is for single use only, then goes on to explain how to sterilize the device if the facility intends to reuse it. Other manufacturers of SUDs provide services to 'recycle' the devices, leading to the perception that these devices are not truly for single use.

Faced with the knowledge that reprocessing occurs, the FDA strives to ensure that the reuse of still-functional devices is achieved with agency oversight, with the requirement that the reprocessed device is as safe and effective as when it was manufactured by the OEM. Analyses by organizations such as the General Accounting Office (GAO) relating to the reprocessing of SUDs highlight the lack of comprehensive information regarding the prevalence of reprocessing, the potential risk to patients, and the knowledge that certain devices should not be reprocessed while others are likely to be safely reprocessed. The analyses conclude that 'oversight is warranted'³. Reprocessors that are currently required to comply with the new requirements include hospitals that reprocess SUDs and third-party reprocessing firms.

Between 14 August 2001 and 26 October 2002, when MDUFMA was signed into law, reprocess manufacturers (both hospitals and third-party reprocessors) were required to:

- submit a 510(k) Premarket Notification or a Premarket Approval Application (PMA), depending on the class of the device;
- register the facility using Form 2891⁴;
- list each class of reprocessed device using Form 2982;
- comply with requirements of the Quality System Regulation (QSR), including sterilization activities and tracking of reprocessed devices, correcting and removing unsafe devices from the market; *and*
- submit adverse event reports (AERs).

Once MDUFMA is fully implemented, reprocess manufacturers will be required to:

- submit either a 510(k) containing 'validation data' (regarding cleaning and sterilization and functional performance) or a 'premarket report,' which is a new type of premarket application (the FDA has not yet released guidance on 'validation data' and 'premarket reports');
- register their facility, as before;
- list each class of reprocessed device, as before;
- comply with QSR requirements, as before, including sterilization activities and tracking of reprocessed devices, correcting and removing unsafe devices from the market;
- submit AERs on specially modified MedWatch forms (described below); *and*
- clearly label the device as a reprocessed SUD along with the name and address of the reprocess manufacturer.

The Agency's listing of which devices belong in the exempt and in the 510(k) category is undergoing revision, as discussed below. The FDA has dedicated a portion of its web site to SUD-related questions and issues⁵.

Physicians perceive that OEMs have an economic incentive to label their product for single use

There will be new rules for reprocess manufacturers

Previously exempt devices will be re-evaluated to determine if a 510(k) and validation data are necessary

26 April 2003 was the deadline for the FDA's listing of 'critical reprocessed SUDs' (defined as those devices that contact normally sterile tissue or body spaces during use) to appear in the *Federal Register*. The notice, which was actually published on 30 April, provides a listing of 15 critical reprocessed device classifications that are currently exempt from the 510(k) process, but will now require submission of a 510(k) with validation data, such as manual surgical instruments and certain dental instrumentation. The submissions will be due within 15 months of the *Federal Register* notice⁶. 26 April 2004 is the deadline for review of 'semi-critical reprocessed SUDs' (defined as those that contact intact mucous membranes but do not penetrate sterile areas of the body). On or by this date, the FDA will list those that require submission of a 510(k) with validation data. Any device that does not appear on either list can continue to be marketed as before.

Fifteen currently exempt 'critical' reprocessed device classifications will require submission of a 510(k) with validation data

Reprocessed SUDs currently requiring a 510(k) will also require 'validation data'

The FDA identified which of the currently reprocessed 510(k) devices will now require validation data in addition to submission of a 510(k) in the 30 April 2003 *Federal Register* notice. This six-page listing provides a new series of product codes to identify reprocessed 510(k) devices that are required to submit validation data. Validation data are due for these devices by 26 January 2004. The purpose of submitting validation data is to demonstrate that the reprocessed device remains substantially equivalent after reprocessing, up to the maximum number of times the device can be reprocessed. If a reprocessed device already has a cleared 510(k), the manufacturer must submit validation data or cease marketing the device. The validation data is required within nine months of the *Federal Register* notice.

Reprocessed devices previously requiring a PMA will now require submission of a 'premarket report'

In a premarket report, the manufacturer will be required to describe the methods, facilities and controls used for reprocessing and packaging the device instead of the methods used by the original manufacturer⁷. The new requirement is expected to be more realistic for reproprocessors because the reprocess manufacturer does not have access to OEM data files and pertinent information. An example is cited where four out of four ablation catheter reproprocessors were unable to achieve PMA approval prior to MDUFMA because of the lack of ability of the reprocess manufacturer to obtain confidential company information that was considered necessary for the PMA application⁸. The MDUFMA-revised requirement for a premarket report may lower the hurdle for approval by the agency because the required data (i.e. the methods, facilities, and controls used for reprocessing and packaging the device) will now be under the control of and accessible to reprocess manufacturers. Agency guidance on the content of the premarket report is pending.

Other Requirements

Other SUD reprocessing requirements that result from MDUFMA include:

- MedWatch forms must be modified to facilitate adverse event reporting associated with reprocessed devices, by the deadline of 26 April 2003. Section 303 requires the FDA to revise MedWatch forms 'to facilitate the reporting of information by user facilities or distributors as appropriate relating to reprocessed SUDs, including the name of the reproprocessor and whether the device has been reused'⁹; and
- reprocess manufacturers must clearly provide labeling that specifies that the device is a reprocessed SUD, along with the reproprocessor name, by the deadline of 26 April 2004. The label should state: Reprocessed device for single use. Reprocessed by [name of manufacturer that reprocessed the device].

A summary of the proposed action dates for reprocess-related activities has been reproduced from a larger table published by the FDA (*see* Table 1 on opposite page).

Impact of the MDUFMA Changes on Reprocessed SUDs

There are several outcomes of the changes described for reprocessing SUDs. The new provisions for 510(k) submissions requiring validation data may make bundling of devices into one 510(k) submission more difficult. Although there is still an opportunity for a manufacturer to bundle some SUDs, if validation data for different products is significantly different, bundling of these submissions may not be acceptable. This has cost implications for the reproprocessor.

On the positive side, the requirement for a premarket report may be more achievable for reprocess manufacturers to provide than the original data requirement in a PMA, thus resulting in more premarket approvals than before MDUFMA.

Changes make bundling devices into one 510(k) submission more difficult

Table 1. Actions and reports with due dates as outlined by the US FDA¹⁰

Date Due (Time beyond Effective Date)	By	Requirement	Citation (to FD&C Act, where possible)
<i>26 October 2002 – MDUFMA signed by President, becomes law. This is the effective date of most provisions of the act.</i>			
26 April 2003 (Six months)	FDA	The FDA must identify the types of reprocessed SUDs for which 510(k)s will be required in the future, and must publish a list of those devices in the <i>Federal Register</i> . 510(k)s for these devices must include 'validation data... regarding cleaning and sterilization, and functional performance' to show that the reprocessed device 'will remain substantially equivalent...after the maximum number of time the device is reprocessed as intended' by the person who submits the 510(k). § 510(o)(1)(A). Publication of this list also triggers the timeframe for submission of validation data for devices on this list that <i>already have</i> a 510(k); see below at 26 January 2004.	§ 510(o)(1)(A)
26 April 2003 (Six months)	FDA	The FDA is to review the types of <i>critical</i> reprocessed SUDs that are currently exempt from 510(k), and determine which of these exemptions is to be terminated. The FDA must publish a <i>Federal Register</i> notice listing these devices. 510(k)s submitted for these devices must include validation data, and must be submitted within 15 months of publication of the list.	§ 510(o)(2)
26 April 2003 (Six months)	FDA	The FDA must modify MedWatch forms to facilitate reporting of information relating to reprocessed SUDs.	MDUFMA Sec. 303
<i>26 January 2004 (15 months, at most) – Holders of 510(k)s for reprocessed devices included on the list published by the FDA pursuant to § 510(o)(1)(A) (see entry at 26 April 2003) must submit validation data to the FDA within nine months of publication of the list. § 510(o)(1)(B).</i>			
<i>26 January 2004 (15 months) – Requirement for labeling of reprocessed SUDs becomes effective. § 502(v)(2).</i>			
26 April 2004 (18 months)	FDA	The FDA is to review the types of <i>semi-critical</i> reprocessed SUDs that are currently exempt from 510(k), and determine which of these exemptions is to be terminated. The FDA must publish a <i>Federal Register</i> notice listing these devices. 510(k)s submitted for these devices must include validation data, and must be submitted within 15 months of publication of the list.	§ 510(o)(2)

FDA and reproprocessors have various deadlines to meet over the next year

Third-party inspections

The intention of the provision for third-party inspections was to increase the number of facility inspections performed under MDUFMA Section 704; therefore, device manufactures may contract FDA-accredited third parties to conduct biennial inspections of Class II and Class III devices. This enables FDA to concentrate its limited inspection resources on higher-risk devices. The first provision that an eligible manufacture must satisfy relates to the most recent inspection at its own facility. The manufacturer's facility must have been classified as 'no action indicated' or 'voluntary action indicated,' and the manufacturing entity must notify the FDA of the accredited agency it intends to use and have the FDA's agreement of that selection.

However, the FDA and industry have recently agreed that, in order for third-party inspections to be a viable programme, the provisions governing its use under the newly enacted MDUFMA require simplification. Specifically, both the FDA and industry agree that particular attention is needed to clarify problematic wording outlining manufacturer and prospective third-party eligibility. Currently, the conditions are cumbersome, create potential legal impossibilities and could ultimately keep third-party inspections from being a viable option for manufacturers.

The majority of the language problems stem from last-minute additions made in Congress to appease members of the Senate HELP Committee¹¹. Members of the committee were concerned that if a manufacturer were able to choose and pay for its own inspection, the inspection would be less rigorous than one conducted by the FDA. Ultimately these concerns were satisfied with additional conditions, and MDUFMA was passed. However, what had initially started as an attempt to create a simple third-party accredited inspection programme has ended in a complex set of provisions with numerous challenges. As a result, the FDA and industry continue to examine ways in which to both accommodate the law and provide the beneficial programme they had originally intended.

Provisions governing third-party inspections are cumbersome and require simplification

Manufacturing eligibility criteria

For a manufacturer to market a device in both the US and in ‘one or more foreign countries,’ the agency must also be certified, accredited, or otherwise recognized by one of the countries in which the device is to be marketed.

The law restricts repeated use of the same accredited third party

The most problematic requirement relating to manufacturers in a foreign country arises from the mandate that the manufacturer must submit to the FDA a statement that the law of the [foreign] country in which a device will be marketed recognizes an inspection of that establishment by the FDA. Mark Heller, of the law firm Hale & Dorr (Washington, DC), was one of the first to publicly address this provision as a potential ‘legal impossibility written into the statute.’ Furthermore, Heller noted that ‘at this juncture, it is not clear that there is any country that has recognized as a matter of law [FDA’s] inspection authority’¹².

Several possible resolutions to this legal hurdle have been proposed in an effort to try to make third-party inspections a legitimate option for manufacturers. Possible solutions that have been suggested draw upon current regulatory practices in place with foreign establishments. For example, current mutual recognition agreements (MRAs) established between countries or jurisdictions could be used as a way around the problematic wording, as suggested by CDRH director David Feigal¹³. Others have suggested that export certificates could be recognized as a current procedure whereby recognition of the FDA’s inspectional authority abroad could be inferred.

Finally, the law restricts a manufacturer’s repeated use of an accredited third party for facility inspections: three consecutive inspections of the same establishment are prohibited, unless the establishment petitions for a waiver. A waiver submitted to the FDA to continue the use of third-party inspections can follow one of two paths. The first is subject to FDA approval while the other is automatic, as shown in the chart below:

Table 2. Paths for approval of a waiver petition allowing the continued use of accredited persons to conduct inspections, US FDA¹⁴

FDA approval of a waiver must be sought if the	Automatic waiver approval is ‘deemed granted’ if the
<ul style="list-style-type: none"> • petition states a commercial reason for waiver; • FDA determines the public health would be served by the waiver; <i>and</i> • FDA had inspected the establishment within the past four years. 	<ul style="list-style-type: none"> • petition states a commercial reason for the waiver; • establishment had requested an FDA inspection within 18 months of its last inspection; <i>and</i> • FDA had not inspected the establishment within 30 months of the last inspection.

The restriction of consecutive inspections by a third party is intended to encourage the FDA to perform periodic inspections. However, the waiver exemption is included to avoid penalizing companies that are prepared for an inspection before the FDA can conduct one.

Preventing conflict of interest

For prospective third parties, Congress has outlined strict criteria that must be satisfied to prevent possible conflict of interest between the agency and a manufacturer (these are outlined in Section 704).

The third party may not be an employee of the federal government and they may not be owned by, or have an ‘affiliation (including a consultative affiliation)’ with a device manufacturer, supplier, or vendor. They cannot be engaged in the design, manufacture, promotion, or sale of FDA-regulated products. They must operate ‘in accordance with generally accepted professional and ethical business practices’ and must agree in writing to certain fundamental operating principles and they may not have a financial conflict of interest regarding any FDA-regulated product.

Prospective third parties worry that the specific exclusion of ‘financial’ and ‘consultative affiliations’ listed in these provisions could be problematic. This is because some organizations that could otherwise qualify as inspectors perform both auditing and consultative services. The FDA recognizes this as a potential problem and has stated its willingness to look at such situations on a case-by-case basis, as long as companies can demonstrate a clear separation between the two functioning groups.

Penalties for conflict of interest violations include criminal prosecution

Penalties for violations by a third party range in severity according to the type and extent of the violation. Examples include, but are not limited to, permanent disbarment, civil money penalties, and criminal prosecution.

Consideration of cost

Some have questioned the benefits of third-party inspections since the FDA sets no standardized cost for such inspections and places the onus of the cost (and the negotiation of that cost) on the

manufacturer. However, a distinct advantage especially for foreign manufacturers arises from an opportunity to bundle multiple audits during a single visit. Heinz-Jorg Steneberg, of TUV Rheinland of North America, has commented 'if you have to do [inspections] for two or three agencies, it costs a lot of money internally [and] costs manpower to support the audit.' He believes such hidden costs incurred in the preparation for each additional inspection would far exceed any fee that a third party would charge.

Procedure for requesting a third-party inspection

Upon receiving a written request from a manufacturer, the FDA has 30 days in which to respond by either approving the request outright, or asking for more information. If 30 days pass without notice from the FDA, 'the establishment is deemed to have clearance' to use the accredited entity it selected.

Additional information requests could relate to the relationship between a third party and the establishment, specifically requiring either entity (manufacturer or third party) to produce information on previous inspections of the establishment or any related establishment. An establishment can also be requested for additional information regarding compliance with quality systems and prompt correction of any quality system problems; this data must include complete reports of inspections or other quality audits within the prior two years.

The FDA has 60 days during which it must respond to the submission of the additional information. At that juncture, only a letter of denial from the FDA could prohibit the manufacturer from using the third party initially requested. If the FDA does deny an establishment's request, the establishment can either file a new request using an alternative third party or request a review of the denial. That review would be conducted by an FDA-appointed person and would begin within 30 days of the receipt of the request for review.

30-day deadline for FDA to respond to third-party inspection requests

Key dates

The FDA published a *Federal Register* notice providing criteria for the accreditation of third-parties to conduct inspections on 30 April 2003 (expected on 26 April 2003). By 26 October 2003, the FDA has been ordered to list, on the internet, no more than 15 accredited persons from which an eligible establishment could select. Finally, beginning FY 2005, no third-party inspections may be conducted if appropriations to the FDA for the given fiscal year fall below a certain level. The sunset date whereby authority for accredited third-party inspections expires is 1 October 2012.

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