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AdvaMed
Advanced Medical Technology Association

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket Number 02N-0534 - Medical Device User Fee and Modernization Act (MDUFAMA)

Dear Sir/Madam:

As FDA begins implementation of key provisions of the Medical Device User Fee and Modernization Act (MDUFAMA), in particular, Section 302, establishing new requirements for the reprocessing of single-use devices, AdvaMed appreciates your consideration of our views and comments in this area.

AdvaMed, the Advanced Medical Technology Association, represents more than 800 innovators and manufacturers of medical devices, diagnostic products and medical information systems. Our members produce nearly 90 percent of the $68 billion in health care technology products consumed yearly in the United States and nearly 50 percent of the $159 billion purchased around the world annually.

AdvaMed has a number of comments, both general and specific, discussed below:

General Comments

AdvaMed strongly supports the inclusion of new requirements for the reprocessing of single-use devices in MDUFAMA because we believe that single use devices (SUDs) that are reprocessed pose risks to patients of cross-infection, cross-contamination, and impaired performance if they are not properly cleaned and resterilized, and demonstrated to be capable of withstanding the stress of repeated uses.

Congress concurred in this assessment. The House report accompanying the Committee on Energy and Commerce's consideration of the MDUFAMA legislation states that "The

Committee also recognizes that the reprocessing of a single-use device may raise issues that are not addressed and need not be addressed when the device is originally manufactured. The Committee wants to ensure that devices that undergo reprocessing continue to be safe for use on patients and continue to work as intended."[1]

Congress established a strong statutory safety standard for both 510(k) and PMA reprocessed devices. For 510(k)s, Congress requires that cleaning, sterilization and functional performance validation data "demonstrate that the [reprocessed] device will remain substantially equivalent to its predicate device after the maximum number of times the device is reprocessed as intended by the person submitting the premarket notification."[2] For PMA devices, Congress established a new type of application – a "premarket report" – specifically tailored to reprocessed devices, that must meet all the requirements of a premarket approval application in addition to cleaning, sterilization and functional performance validation data "that demonstrates that the reasonable assurance of the safety or effectiveness of the device will remain after the maximum number of times the device is reprocessed as intended by the person submitting such report." [3] To ensure the safety of patients, Congress provided FDA with explicit and additional authority to require any other additional data and information that the "Secretary determines is necessary to determine whether there is reasonable assurance of safety and effectiveness for the reprocessed device."[4]

Congress also intended that end users of reprocessed devices be made aware of the fact that they are using a reprocessed device as well as who reprocessed the device through the identification and labeling provisions of Sec. 301 and 302, respectively. MDUFAMA also requires FDA to modify its MedWatch forms to begin to capture adverse event reporting data in recognition that "FDA has not been able to compile information regarding adverse events associated with reprocessed devices . . . in part, because reports may not be identifying certain devices as reprocessed."[5]

Importantly, Congress intended that the new reprocessing requirements be rigorous and thorough: "Additionally, the Committee recognizes there is a difference between validation and verification. The former involves a level of rigor and statistical probability that a device or process will consistently perform as intended; the latter demonstrates through testing or observation that a specific requirement has been fulfilled."[6]

AdvaMed has specific and comprehensive recommendations regarding the type of cleaning, sterilization and performance validation data that should be required to meet the strong safety

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1 House of Representatives Report 107-728, p. 44.
2 Section 302(b) of H.R. 5651, the Medical Device User Fee and Modernization Act of 2002
3 Section 302(c) of H.R. 5651, the Medical Device User Fee and Modernization Act of 2002.
4 Section 302(c) of H.R. 5651, the Medical Device User Fee and Modernization Act of 2002.
5 House of Representatives Report 107-728, p. 45.
6 House of Representatives Report 107-728, p. 46.

standard set by Congress for reprocessed 510(k) and PMA devices which follow in our specific comments and in Attachment A – "Validation and Routine Control Recommendations for Reprocessing Medical Devices Labeled as Single Use."

We would also like to bring to your attention key findings in a recent article, "Development of a Program Model to Evaluate the Potential for Reuse of Single-Use Medical Devices: Results of a Pilot Test Study" authored by Dr. Eduardo Abreu, M.D. of the Cleveland Clinic Foundation.[7] The article outlines the key steps and factors to consider when reprocessing single use devices including: a device audit; a three-part comparative evaluation of sterilization and its impact on the device materials and device function through pilot feasibility, base-line, and simulated-use studies; biocompatibility evaluation; and clinical evaluation which includes reliable device and patient tracking systems and continuous quality assessment. Among other findings, the authors note that some single use devices (SUDs) cannot withstand reprocessing.

During the device audit stage, the study authors evaluated single use devices "in relation to their characteristics (i.e., materials of construction, geometry [especially any complexities of design or construction that would hinder the cleaning and sterilization], and function)" and identified and analyzed issues that would affect cleaning, sterilization and reprocessing including "areas on the SUD that are difficult to clean and sterilize, such as inner cavities, dead-end lumens, etc."[8] Of interest, through their case studies, the authors found that one of the most difficult aspects of reprocessing was the cleaning and decontamination phase because it relied on busy cardiac catheterization laboratory personnel to follow a specific subprotocol to "maximize the removal of clinical soil from the devices."[9] The subprotocol included aspiration and flushing of portions of the SUD as well as soaking to prevent damage to the device from drying.

During the evaluation stage, the authors evaluate the effect of the sterilization process on the SUD materials and on its function using visual and microscopic (where applicable) inspection, dimensional measurements (using calibrated instruments), and functional testing which in some cases included input from clinical users. Importantly, the authors found during their case study that some SUDs were "rendered . . . unusable" at this stage because the "SUD's materials had been affected by the reprocessing."[10] The material effects included brittleness, tackiness, "crimp and kink deformations," and "material stresses that led to cracks."[11]

7Eduardo L. Abreu, M.D., Donna M. Haire, M.S., Paul S. Malchesky, D. Eng., David F. Wolf-Bloom, M.S., and J. Fredrick Cornhill, D.Phil., "Development of a Program Model to Evaluate the Potential for Reuse of Single-Use Medical Devices: Results of a Pilot Test Study," *Biomedical Instrumentation &Technology* Volume 36/Number 6, (November/December 2002), p. 389.
8 Ibid., p. 392.
9 Ibid., p. 397.
10 Ibid., p. 398.
11 Ibid., p. 398.

During the clinical evaluation stage, the authors point out that "reliable device and patient tracking systems must be developed to assure that a device is not reused more than the number of times for which it was validated and that traceability of the device can be maintained."[12] They also note the importance of maintaining an historical log in the "case of any problem arising from clinical use."[13]

Specific Comments

FDA requires extensive and rigorous validation of SUDs to prove safety, efficacy and sterility. These validations are generally performed according to industry recognized standards. Reprocessed SUDs should also be required to undergo extensive validation testing. The validation requirements for reprocessed SUDs must take into consideration the collection processes, cleaning, sterilization, drying, and packaging of the products.

AdvaMed's validation recommendations represent all of the steps a manufacturer of a reusable device would take to validate how the device can be cleaned and sterilized after every use and still remain functional. We believe that the same standards should apply to the reprocessing of devices designed for single use. Importantly, because the design criteria for single use devices do not take reuse into consideration, FDA must be extremely rigorous in establishing comprehensive cleaning, sterilization and performance validation requirements for each original device type from each original equipment manufacturer to ensure that these devices can be safely and effectively reprocessed. Where specific features of a device model within an original equipment manufacturer's device type affects the reprocessor's ability to safely and effectively clean, sterilize, and ensure the functional performance of the device, FDA should also require a separate 510(k) submission or premarket report application.

Further, FDA should review all data relating to cleaning and sterilization, and their affect on device function in the 510(k) submission. For premarket reports, consistent with the statutory requirements of Sec. 302, FDA should review all the data that they would normally review for a premarket application, except that for the manufacturing section, FDA should review "a full description of the methods used in, and the facilities and controls used for, the reprocessing and packing of the device."[14] In addition, equipment qualification data is clearly within the purview of the quality system regulation and should be reviewed as part of the quality system inspection process for both 510(k)s and premarket reports.

Of note, several European countries have banned the practice of reusing SUD's because of concern associated with infectious diseases, including transmissible spongiform encephalopathies. Re-sterilization processes validated and controlled in accordance with recognized manufacturing and sterilization standards should not be assumed to be effective in inactivating the causative agents of spongiform encephalopathies.

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12 Ibid., p. 395.
13 Ibid., p. 395.
14 Section 302(c)(2)(A)(vii) of H.R. 5651, the Medical Device User Fee and Modernization Act of 2002.

The attached document – " Validation and Routine Control Recommendations for Reprocessing Medical Devices Labeled as Single Use" – represents AdvaMed's recommendations regarding the type of cleaning, sterilization and performance validation data that should be required to meet the strong safety standard set by Congress for reprocessed devices.

Sincerely,

Tara Federici

Tara Federici
Associate Vice President
Technology and Regulatory Affairs

Enclosure (1) - **Attachment A**