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March 14, 2003

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U.S. Food and Drug Administration
Dockets Management Branch (HFA-305)
5630 Fisher's Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. 02N-0534

To Whom It May Concern:

Alliance Medical Corporation, a leading reprocessor of used single use devices, appreciates the opportunity to offer comment in the matter of implementing Section 302 of the Medical Device User Fee and Modernization Act of 2002, specifically as it pertains to Validation Data for Reprocessed Single Use Devices

Alliance Medical Corporation recognizes the extreme importance of ensuring the single use devices we reprocess are as safe and effective as the original, unused device. Safety is ensured when the processes and equipment used to clean and sterilize the devices have been validated with scientifically valid and defensible studies which demonstrate, with a high level of assurance, that the devices are both clean and sterile. Effectiveness of the reprocessed device requires reasonable and appropriate performance evaluation activities to demonstrate the reprocessed devices functions as designed by the original manufacturer after the maximum number of reprocessing cycles designated for the device.

Cleaning

Scientifically valid and defensible demonstration of the cleaning processes are based on "worst-case" contamination and inoculation, followed by demonstrated and measurable bioburden reduction studies. Bioburden reduction studies of sterile devices should be expected to demonstrate at least three replications of 99%, or three log, reduction in bioburden. Non-sterile devices should be expected to demonstrate at least 75%, or two log, reduction in bioburden.

Test articles should be clean, sterile devices. Test article contamination should be based on a suitable test soil, such as the US Pharmacopoeia standard for artificial soils. Considering this, devices used primarily in or around the vascular system would be contaminated with artificial blood soil. Devices used primarily in or around the gastrointestinal tract would be contaminated with artificial fecal matter. Devices used primarily in or around mucosal tissue would be contaminated with artificial mucosal soil. In each case, the test article should contaminated to a "worst-case level" indicating the contamination includes the most difficult to clean areas of the test article.

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Test article inoculation should expect to represent a "worst-case" level of bacterial contamination with a non-pathogenic, Gram-Positive, endospore-forming organism recognized to be resistant to drying and heat. The bioburden reduction determination would reasonably expect to include a suitable extraction efficiency, such as sequential extractions.

In addition to the 90% and three log reduction requirements for cleaning validations, sterile products should also demonstrate lack of pyrogenicity based on the international standards for endotoxins.

Sterilization

Sterility of reprocessed devices should only be predicated on a sterility assurance level of 1.0×10^{-6}, or a 12 log reduction in bioburden. Sterilization processes require performance qualification/validation in accordance with FDA-recognized, internationally developed standards, such as AAMI/ANSI/ISO 1135:1994.

Each batch or lot of reprocessed single use devices should be monitored to ensure each critical sterilization parameter is met (that no planned or unplanned deviations were observed) and appropriate sterilization process documentation has been established. Chemical and biological indicators of sterility may supplement the measurement of critical sterilization parameters; no batch or lot may be released parametrically. All devices must be held in quarantine pending final release.

Reprocessed single use devices sterilized by exposure to a sterilant gas, such as ethylene oxide (EO) are to be evaluated for sterilant residuals. All EO-sterilized devices should be expected to comply with the FDA-recognized ISO 10993-7 standard for ethylene oxide residuals, as augmented by the AAMI Technical Information Report on EO residuals (TIR 19).

The packaging of sterilized reprocessed single use devices must be validated to assure the efficacy of the packaging. Ship tests are conducted to validate the secondary packaging of devices.

Pyrogen-free devices, such as those intended for use in or around the vascular system, need to be evaluated using a test for endotoxins with a high degree of acceptance and reliability, such as the Limulus Amebocyte Lysate (LAL) test. All reprocessed single use devices designated as pyrogen-free also need to comply

with the FDA-recognized, internationally developed standards for endotoxins, ISO 10993.

Performance/Function

Performance evaluation of reprocessed single use devices needs to be specific to the device type. All devices should be evaluated in accordance with applicable FDA Reviewer Guidances, and other appropriate performance testing developed based on a device risk analysis. Each device should have an identified maximum number of reprocessing cycles, based on functional performance data which may include actual or simulated clinical use evaluation, and materials characterization tests, such as FTIR.

For example, reprocessed electrophysiology catheters should be evaluated for the full range of electrical function, such as continuity, resistance, and conductivity. Deflectable catheters need also be evaluated for the extent of deflection, plane of deflection, and other appropriate tests. In addition, steerable catheters should be evaluated against a written standard.

Other single use devices, such as compressible limb sleeves, can be evaluated against manufacturer performance specifications, e.g., the ability to inflate to the specified pressure and deflate with unfailing repetition.

Surgical instruments with electrical function, such as for diathermy or tissue ablation, may also be evaluated for fitness based on tests such as the dielectric withstand test (a measure of mechanical integrity). Devices designed for cutting, such as surgical scissors, should be evaluated for compliance with the recognized standard for sharpness, ASTM F1079.

Devices subject to component fatigue should reasonably be evaluated to assess the affect, if any of reprocessing on the device. For example, external fixation devices should be evaluated to identify the fatigue failure point.

Pre-production Process Validation

All automated equipment utilized in the reprocessing operation and test equipment used to measure product performance should be validated in accordance with the requirements of 21 CFR 820.

Procedures used for device reprocessing must include a mechanism to exclude devices that have exceeded the maximum number of reprocessing cycles, and include a mechanism for determining when a cycle count is increased, such as when a non-conforming device is re-worked.

Continued biocompatibility of reprocessed single use devices must be evaluated following the completion of all reprocessing activities, including cleaning, sterilization and performance testing after the maximum number of reprocessing cycles. This testing should be completed in accordance with FDA-recognized internationally developed standards for biocompatibility, including ISO 10993-5 (Cytotoxicity), 10993-10 (Intracutaneous Reactivity), and ISO 10993-10 (Sensitization).

Alliance Medical Corporation is deeply committed to pre-production process validation. While this may commonly be associated with Class III devices, we remain convinced this is a necessary and appropriate requirement for commercial reprocessors.

We appreciate the opportunity to provide comment on this issue.

Sincerely,

Don Selvey, Vice President
Regulatory Affairs and Quality Assurance
Alliance Medical Corporation