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January 20, 2003

Food & Drug Administration
Dockets Management Branch
CDRH/OHIP/DSMICA (HFZ-220)
1350 Piccard Drive
Rockville, MD 20850-4307
Attn: Bill Sutton

Re: Docket No. 02N-0534

Dear Sir or Madam:

Boston Scientific Corporation ("BSC") submits these comments in support of the listing of reprocessed, single-use ureteral stone dislodgers as critical, single-use devices for which the exemption from premarket review pursuant to Section 510(k) of the Federal Food, Drug and Cosmetic Act (FFDCA) should be terminated in accordance with Title III, Section 301(b)(2) of the Medical Device User Fee and Modernization Act of 2002 (MDUFMA).

The safety and effectiveness of reprocessed ureteral stone dislodgers cannot adequately be assured without premarket review to ensure their substantial equivalence to the single-use predicate device. These devices are designed for first-use performance, not for amenability to cleaning and sterilization. Indeed, the structural features of ureteral stone dislodgers – small movable parts and narrow crevices – prevent adequate cleaning and sterilization. Moreover, reprocessing of stone dislodgers may compromise their physical integrity and increase the risk of malfunction. Therefore, FDA must terminate the exemption for reprocessed, single-use ureteral stone dislodgers pursuant to Title III of MDUFMA.

02N-0534 C11

I. FDA MUST EVALUATE THE EXEMPTIONS FOR CRITICAL REPROCESSED, SINGLE-USE DEVICES AND IDENTIFY THOSE WHICH MUST BE TERMINATED TO ASSURE SAFETY AND EFFECTIVENESS

Pursuant to FDA regulations at 21 C.F.R. § 876.4680(b), ureteral stone dislodgers are classified as exempt Class II medical devices. Under FDA's Enforcement Guidance for Reprocessed Single-Use Devices, the reprocessing and reuse of these devices are exempt from premarket review under section 510(k) of the FFDCA.[1]

Congress enacted Title III of MDUFMA in response to significant safety concerns regarding the reprocessing and reuse of devices that were approved by FDA for single-use only. Title III requires FDA to "identify [critical or semi-critical reprocessed, single-use devices that are exempt from premarket notification requirements] for which such exemptions should be terminated in order to provide a reasonable assurance of the safety and effectiveness of the devices." Under MDUFMA, FDA is required to "publish in the Federal Register a list of the devices so identified."[2] The exemption for each device included on the list is terminated upon publication of the list.[3] In order to provide reasonable assurance of their safety and effectiveness when reused, these reprocessed devices will be subject to review pursuant to section 510(k) to ensure that they remain substantially equivalent to the single-use, predicate device.

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1 *See* FDA, "Enforcement Priorities for Single-Use Devices Reprocessed by Third Parties and Hospitals" (August 14, 2000).

2 MDUFMA § 302(b)(2).

3 Manufacturers and distributors of reprocessed single-use devices will have fifteen (15) months from the date on which a device is included on the list to submit to FDA a 510(k) premarket notification including validation data supporting the maximum number of times the device may be used safely and effectively. *Id.*

II. REPROCESSED, SINGLE-USE URETERAL STONE DISLODGERS ARE CRITICAL REPROCESSED SINGLE-USE DEVICES THAT PRESENT A HIGH DEGREE OF RISK TO PATIENT SAFETY

A. Characteristics of Single-Use Ureteral Stone Dislodgers[4]

Single-use ureteral stone dislodgers are used during urological procedures to endoscopically grasp, manipulate and remove foreign objects from the upper urinary tract. Generally, a ureteral stone dislodger includes a grasping or capture component attached to a drive wire. The capture component and drive wire are typically covered by a polymer sheath, which itself is attached to a handle used to manipulate the drive and capture wires by extending and retracting them into and out of the sheath. Stone dislodgers vary in length from approximately 90 to 120 cm. The polymer sheath has an extremely narrow cross sectional diameter of approximately 3 Fr or 1 mm. The thickness of the sheath wall is approximately 0.002 inches, or about half the thickness of a sheet of paper. The drive wire itself varies from 0.01 to 0.015 inches in diameter, and the very delicate capture wires of the capture component vary from 0.004 to 0.008 inches. The clearance between the sheath and the drive wire is approximately 0.002 to 0.004 inches.

Ureteral stone dislodgers are inserted through an endoscope (typically a ureteroscope), either through the urethral opening or through a surgical incision in the back, into the bladder, ureter, and/or kidney. When the stone is located in the upper urinary tract, the capture wires are extended from the sheath to collect it. To retrieve the stone, a portion of the capture wires grasping the object are retracted into the sheath (the entire capture wire is not retracted into the sheath). The stone dislodger is then withdrawn through the endoscope, removing the stone from the body. In order to accomplish this intended use, the single-use stone

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[4] The design of a typical ureteral stone dislodger is included as Attachment A.

dislodger comes into contact with the normally sterile body spaces and tissue of the kidneys, bladder and ureters, and contacts (but does not penetrate) the mucosal barrier. Ureteral stone dislodgers are intended for single-use only, although they may be reprocessed and reused on multiple patients. Thus, ureteral stone dislodgers are critical, reprocessed, single-use devices subject to review under section 310(B)(2) of MDUFMA.[5]

B. Reprocessing Methods Do Not Assure the Cleanliness of Reprocessed, Single-use Ureteral Stone Dislodgers

Several structural features of single-use ureteral stone dislodgers prevent the thorough removal of tissue, blood, and other organic matter from used devices. Once the retrieval device is extended from the sheath, it contacts tissue, blood and urine in the upper urinary tract. The retrieval device may trap and hold particles of organic matter as it collects ureteral stones. These materials may be contaminated with bacteria if, as is frequently the case in patients undergoing these procedures, the patient suffers from a urinary tract infection. These particles of tissue, bacterial contamination, and biological material will then be drawn into the sheath with the ureteral stone when the retrieval device is retracted into the sheath.

The long (90 to 120 cm), extremely narrow (3 Fr or 1 mm diameter) lumen created by the polymer sheath covering the drive wire and capture component cannot be cleaned by flushing with cleaning fluid because it is open at only one end. Attempts to flush and aspirate cleaning fluid through a single opening have been shown to further distribute contaminated

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[5] MDUFMA defines a "critical reprocessed single-use device" as "a reprocessed single-use device that is intended to contact normally sterile tissue or body spaces during use." MDUFMA § 302(d). "Single-use devices" are defined in MDUFMA as "device[s] that [are] intended for one use, or on a single patient during a single procedure." *Id.*

tissue throughout a device.[6] In addition, there is a clearance of only 0.002 inches – approximately one-half the thickness of a sheet of paper – between the drive wire and the inner wall of the sheath. Thus, there is no way to remove residual tissue once it is retracted into the sheath. This attribute of ureteral stone dislodgers presents a significant barrier to adequate and verifiable cleaning of these devices for reuse.[7] The presence of residual biological material in stone dislodgers may create the risk of cross contamination, infection or pyrogenic reactions to the residues or plaque buildup on reused stone dislodgers.

C. Reprocessing Methods Do Not Assure the Sterility of Reprocessed, Single-use Ureteral Stone Dislodgers

Commonly-used sterilization methods do not ensure sterility of reprocessed, single-use devices. Most reprocessors use ethylene oxide gas to sterilize single-use devices. Ethylene oxide sterilization is a bioburden-based method and its effectiveness is limited by the inability of ethylene oxide gas to penetrate tissue. To ensure effective ethylene oxide sterilization, it is essential to ensure that the bioburden is consistently below that needed to achieve a sterility assurance level (SAL) of 10^{-6}.[8] Due to the nature of their use, device configuration, and cleaning difficulties, used single-use stone retrieval devices carry a high and variable bioburden. The bioburden may vary significantly, depending on the particular patient,

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6 Roth, K. *et al.*, "Quality Assurance on Reprocessing Accessories for Flexible Endoscopes – Just How Clean are Cleaned Instruments Really?," Central Service 7(2), at 7 (1999).

7 *See* ECRI, "Evaluating the Feasibility of Reusing a Single-Use Device," Special Report: Reuse of Single-Use Medical Devices: Making Informed Decisions, at 55 (1996) (noting that "[d]evices with long and/or small-diameter lumens, with rough or textured surfaces and deep groves or crevices, that are composed of porous materials and constructed with hinges or other features that may interfere with cleaning should probably not be considered [for reprocessing].").

8 This SAL represents the level at which there is a one in one million chance that a device is non-sterile. It is considered to be an industry standard. *See, e.g.*, BSEN Standard No. 556, "Sterilization of Medical Devices: Requirements for Medical Devices to be Considered Sterile," Section 4.1.

length and nature of the procedure, the presence of infection, and the like. Thus, it is virtually impossible to assure that used stone dislodgers do not exceed the SAL. As a result of this bioburden, ureteral stone dislodgers cannot adequately be sterilized with ethylene oxide gas.

Other sterilization methods are also unlikely to be effective in sterilizing used ureteral stone dislodgers. Steam sterilization is unlikely to be effective because the plastic and polyimide components of stone dislodgers melt if subjected to the extremely high temperatures of this technique (see Section II.D. below). Ionizing radiation, like ethylene oxide sterilization, is a bioburden-based method and also cannot adequately and consistently sterilize devices containing residual tissue. Additionally, due to the variable levels of bacteria that may be found on used stone dislodgers, the radiation level necessary for reprocessing may be very high. The effect of radiation treatment to sterilize used, single-use stone dislodgers likely would destroy the physical integrity of the devices. Thus, due to their design and the inevitable and variable bioburden on used devices, single-use ureteral stone dislodgers cannot adequately, reproducibly, and verifiably be sterilized by commonly-used sterilization methods.

D. Reprocessing Methods May Damage Single-use Ureteral Stone Dislodgers and Cause Them to Malfunction

Single-use ureteral stone dislodgers are designed for first-use performance, rather than for ease of cleaning and resterilization. The component parts of ureteral stone dislodgers, and the mechanisms which hold them together, are extremely delicate and are not designed to withstand reprocessing. The stainless steel or nickel titanium drive wires of such devices are only 0.01 to 0.015 inches in diameter and the capture wires are even finer – only 0.004 to 0.008 inches. Therefore, the physical integrity of these devices may be seriously compromised by cleaning and sterilization procedures.

The delicate drive and capture wires were not selected and designed to withstand reprocessing. The components may be degraded due to the use of harsh cleaning agents and procedures, stress of repeated use, or rigorous sterilization methods. Such degradation creates an increased risk of device breakage or malfunction and can dull and erode the retrieval wires. This may result in serious patient injury, including perforation, scraping, or severing of the ureter, evulsion, hemorrhage, and edema.

Single-use stone dislodgers may also be functionally altered as a result of stress induced by the sterilization techniques discussed above. Treatments using heat and chemicals may cause the polymer sheath to melt onto the drive wire inside the sheath, causing the retrieval mechanism to malfunction during extension or retraction. Further, the presence of blood, residual tissue and other organic material remaining within the sheath may adversely impact the performance of these devices after first use. Specifically, due to the miniscule clearance space (0.002 inches) between the drive wire and the sheath, the presence of biological residue may interfere with the smooth extension and retraction of the capture wires and otherwise impair the performance of these extremely delicate moving parts. Premarket review of these reprocessed devices is therefore required to provide reasonable assurance of their continued safety and effectiveness.

E. Quality System Regulations Alone Do Not Ensure the Safety and Effectiveness of Reprocessed, Single-use Ureteral Stone Dislodgers

The Quality System Regulations (QSR) do not ensure that reprocessors will attain proper sterility and performance with respect to ureteral stone dislodgers. The QSR is designed and intended to be a post-market manufacturing control. It is not intended to supplant FDA's premarket review process, which is the cornerstone of FDA's mission to ensure that

products are both safe and effective before they are used on patients. In fact, in its Annual Report for Fiscal Year 1999, FDA reported that a study at Walter Reed Army Hospital of the reprocessing and reuse of single-use coronary catheters and endoscope accessories demonstrated model-specific cleaning and disinfection problems as well as varied effects of disinfection on performance characteristics. According to FDA, the "research [was] demonstrating that device-specific issues of reuse of single-use devices must be addressed on a model-by-model basis."[9] Single-use stone dislodgers are not intended to be reused. The design and features of these devices raise serious concerns with respect to their ability to be cleaned and their ability to withstand a pre-specified number of cleaning cycles without functional deterioration. These issues can only be effectively addressed by a premarket review of the validation data and procedures for the new intended use of the devices. Postmarket enforcement of the QSR requirements – which presume the device is both safe and effective to enter the market – is inadequate to ensure that sterility and performance testing are appropriate for a particular device.

III. CONCLUSION

MDUFMA requires FDA to evaluate the exemptions from premarket notification requirements for all exempt, critical reprocessed single-use devices to determine whether to terminate those exemptions. Reprocessed, single-use ureteral stone dislodgers are critical, reprocessed, single-use devices that present a high degree of risk to patients. The design and structural features of ureteral stone dislodgers prevent adequate cleaning and removal of residual tissue and other organic materials from these devices. Further, reprocessing methods are generally not adequate to ensure the sterility of these devices without damaging their structural

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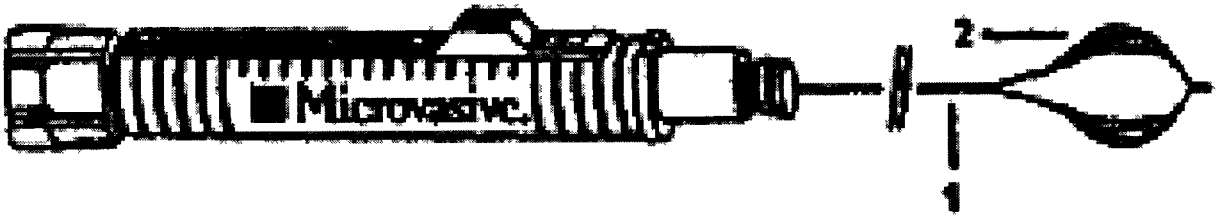
[9] FDA, "Annual Report Fiscal Year 1999" (November 30, 1999).

integrity and effectiveness. Finally, reliance on post-market controls alone does not provide adequate assurance of the safety and effectiveness of these devices.

Therefore, premarket review of reprocessed single-use ureteral stone dislodgers is essential to provide reasonable assurance of the devices' continued safety and effectiveness. Thus, MDUFMA requires that the exemption for reprocessed, single-use ureteral stone dislodgers be terminated. As a result, BSC urges FDA to list reprocessed single-use ureteral stone dislodgers pursuant to Section 301(b)(2) of MDUFMA.

ATTACHMENT A

Device Illustration



1. 3Fr Sheath
2. Multi-Wire Design