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

Re: Docket No. 02N-0534

Dear Sir or Madam:

Aircast Incorporated ("Aircast") submits these comments in support of the listing of reprocessed, single-use compressible limb sleeves ("CLSs") as reprocessed, single-use devices for which validation data must be included in submissions made pursuant to Section 510(k) of the Federal Food, Drug and Cosmetic Act (FFDCA) in accordance with Title III, Section 302(b) of the Medical Device User Fee and Modernization Act of 2002 (MDUFMA).

The safety and effectiveness of reprocessed CLSs cannot adequately be assured without premarket review to ensure their substantial equivalence to the single-use predicate device after the maximum number of times the device is reprocessed. These devices are designed for first-use performance, not for amenability to repeated cleaning and sterilization. In fact, reprocessing of CLSs may compromise their physical integrity, increasing the risk of malfunction and, consequently, danger to patients who require them. Therefore, FDA should require the submission of validation data regarding cleaning, sterilization, stability and functional performance from reprocessors of reprocessed, single-use CLSs pursuant to Title III of MDUFMA.

I. FDA MUST EVALUATE REPROCESSED, SINGLE-USE DEVICES SUBJECT TO PREMARKET NOTIFICATION REQUIREMENTS AND IDENTIFY THOSE FOR WHICH REPORTS MUST INCLUDE VALIDATION DATA

Pursuant to FDA regulations at 21 C.F.R. § 870.5800(b), CLSs are classified as non-exempt Class II medical devices. Under FDA's Enforcement Guidance for Reprocessed Single-Use Devices, reprocessors of CLSs are subject to the premarket reporting requirements set forth under section 510(k) of the FFDCA.[1]

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

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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 that, with respect to reprocessed, single-use devices, FDA "identify such devices or types of devices for which reports under [section 510(k)] must, in order to ensure that the device is substantially equivalent to a predicate device, include validation data, the types of which shall be specified by the Secretary, regarding cleaning and sterilization, and functional performance demonstrating that the single-use device will remain substantially equivalent to its predicate device after the maximum number of times the device is reprocessed . . . ." Under MDUFMA, FDA is required to "publish in the Federal Register a list of the types so identified."[2] Manufacturers and distributors of reprocessed, single-use devices will have nine (9) 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.* 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 after the maximum number of times the device is reprocessed. *Id.*

II. REPROCESSED, SINGLE-USE COMPRESSIBLE LIMB SLEEVES ARE REPROCESSED, SINGLE-USE DEVICES THAT PRESENT A MODERATE DEGREE OF RISK TO PATIENT SAFETY

A. Characteristics of Single-Use Compressible Limb Sleeves

Compressible limb sleeves are inflatable cuffs for the arm, leg, or foot that, together with tubing and a pump, comprise a pneumatic compression device.[3] CLSs are often constructed out of lightweight, hypoallergenic material, such as brushed nylon, and may be placed directly against the skin. CLSs are often secured using hook and loop fasteners. Attached to the cuff are tubes which connect to an electric pump by way of tubing connectors sealed with gaskets. The pump controls compression, inflating the aircell or bladder according to specific inflation and deflation cycles. As the aircell inflates and the CLS compresses the affected area, the veins collapse longitudinally, forcing increased venous blood flow. After compression, the aircell deflates allowing the veins to refill and bring oxygenated blood to the limbs.

Aircast pioneered and sells a particular pneumatic compression device called the VenaFlow® system. Each VenaFlow® system includes a pump with tube assembly that is designed to operate with inflatable cuffs, of which there are three designs – the calf, foot and thigh. The cuffs are secured with hook and loop fasteners and are designed for single-use only. The VenaFlow® pump's pressure and its inflate/deflate cycle are preset to operate automatically with any of the three cuff designs. Pressures are shown on the pump's digital display. If the

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2 MDUFMA § 302(b).

3 A photograph of Aircast's Venaflow® system with a calf cuff is attached as Appendix A.

pressure is out of the appropriate range, due to a kinked tube for example, a pressure alarm is activated and corrective instructions are illuminated on the display.

The pressure alarm on the VenaFlow® pump goes a long way toward minimizing danger to patients as a result of inadequate pressure in the cuff. However, not every pump used with a CLS has such an alarm. Patients who are unaware that their particular device is malfunctioning and who therefore do not receive timely, effective treatment may be in danger of serious harm, such as stroke or infection requiring amputation, or even death. Moreover, in some circumstances, even patients using a system equipped with a pressure alarm may be unable to return a defective device for one that functions properly in time without compromising treatment and increasing the risk of harm or death.

Pneumatic compression devices are used to prevent deep vein thrombosis ("DVT") and associated pulmonary embolism, which can result in significant morbidity and mortality following major surgery or multiple trauma. The VenaFlow® system prevents DVT using a combination of graduated sequential compression and rapid impulse inflation. This combination helps to prevent the formation or presence of a blood clot in a blood vessel by accelerating blood flow and enhancing the breakdown of fibrin, a protein that facilitates blood clotting. Prevention of DVT is particularly important for preventing pulmonary embolism because the majority of patients with fatal embolisms are diagnosed within 30 minutes of the onset of symptoms – too late for the administration of DVT therapy or surgical intervention.

Pneumatic compression devices are also used to treat venous leg ulcers, some of which can be limb and life threatening for particular patients such as diabetics, by increasing the flow of oxygenated blood to the lower limbs. In light of these potential consequences associated with the malfunction of CLSs, it is important that reprocessed, single-use CLSs be safe and effective each time they are used to treat the conditions for which they are indicated.

Current original equipment manufacturer ("OEM") specifications do not sufficiently assure the integrity and effectiveness of reprocessed, single-use compression limb sleeves because they are set without regard to reprocessing methods. For some single-use devices, OEM specifications require that CLSs be designed for up to 50 cycles[4] before degradation may affect CLS performance. In addition, OEM specifications typically require that CLS performance be within certain ranges for, among other things, aircell strength, burst test results, and shear and peel tests,[5] which measure the strength of the hook and loop closures. Tests show that, without regard to reprocessing methods, the integrity and performance of CLSs degrade over time. *See* VenaFlow Sterile Cuff Product Performance Evaluation ("Evaluation") attached hereto as Appendix B; QI Test Results attached hereto as Appendix C. For example,

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4 A 'cycle' is defined as one closure and release.

5 Shear tests measure the force required to pull apart on the same plane two pieces that comprise the hook and loop fastener. Peel tests measure the force required to lift one piece of the hook and loop fastener from its counterpart.

data show that, for sterile cuffs after three years, the shear strength of a hook and loop fastener significantly decreases, making the product unsound for medical use. *See* Evaluation. Accordingly, individual manufacturers set expiration dates for their sterile CLSs three years from the date they are manufactured. *See* VenaFlow Sterile Cuff 4 Year Aging Test ("Aging Test") attached hereto as Appendix D (concluding after that three year aging will be used on all sterile VenaFlow® cuffs).

In addition, CLSs degrade with use, something neither the manufacturer nor the reprocessor can track over the life of a CLS. For example, test data indicate that there may be a marked drop in peel strength after 50 cycles. In these tests, peel strength after 50 cycles was less than 25 percent of that for new devices. *See* QI Test Results. A single-use CLS is expected to undergo fewer than 50 cycles during use by one patient. The manufacturer, therefore, can be reasonably certain that its product will perform effectively during the first use, involving fewer than 50 cycles, so long as it is used before the expiration date if sterile. Reprocessors must similarly validate the cumulative number of cycles a CLS has been through in order to establish the total number of uses the device may undergo before the peel strength significantly declines.

Reprocessing methods hasten the degradation process. For example, tests were conducted on cuffs aged less than 6 months, after being subjected to a double exposure to the gamma radiation sterilization process. The cuffs had much lower average seal strength than unaged sterile cuffs and sterile cuffs aged six months, two and three years. For the twice-sterilized cuffs, shear strength after 50 cycles was comparable to that of a sterile cuff aged 4 years. *See* Evaluation. These results show that reprocessing methods can have a significant affect on product degradation. Consequently, OEM specifications are an irrelevant benchmark for product safety and effectiveness with regard to reprocessed, single-use compression limb sleeves. Reprocessors of CLSs should be required to submit validation data, including stability data and expiration dates for reprocessed CLSs, to ensure that reprocessed CLSs are substantially equivalent to the single-use predicate device.

B. Reprocessing Methods in General Do Not Assure the Integrity and Effectiveness of Reprocessed, Single-use Compression Limb Sleeves

Compressions cuffs frequently are secured with hook and loop fasteners. Repeated use, cleaning, disinfection, and sterilization of the device can degrade the integrity of the hook and loop closures. Testing demonstrates that shear and peel values, measurements reflecting the strength of the hook and loop bond, are reduced with repeated cleaning and sterilization, regardless of the method. *See* Evaluation; QI Test Results. Reduced shear and peel strength will cause the compression cuff to become loose. A loosely fitting cuff compromises treatment by reducing compression of the affected area which reduces the device's effect on blood flow.

In addition, repeated cleaning, disinfecting or sterilizing agents used to reprocess the sleeve may weaken the seal between the tube and sleeve. Resulting air leakages from the device will reduce inflation of the compression cuff, thereby reducing compression of the

affected area and the attendant effect on the patient's blood flow. If a pump attached to a compression sleeve is programmed with compression profiles, the effectiveness of which depend on accurate inflation sequences, air leakages resulting from poor connection between the tube and sleeve may significantly alter the sequences, compromising treatment and possibly endangering the patient.

Finally, some cuffs may be constructed from materials, that are not fully compatible with common cleaning or disinfection methods. *See* Sterilization Stability of Resin Materials ("Sterilization Stability chart") attached hereto as Appendix E. Improper cleaning, disinfection or sterilization poses a moderate risk of infection to the patient.

C. Gamma Irradiation in Particular Does Not Assure the Integrity and Effectiveness of Reprocessed, Single-use Compression Limb Sleeves

Gamma irradiation is the sterilization method commonly used to reprocess compression sleeves. Repeated or extreme exposures to gamma radiation will compromise the integrity and effectiveness of CLSs. In particular, repeated or extreme exposure of CLSs to gamma radiation can cause a male luer lock, which is used to connect the sleeve of the CLS to gamma radiation can cause the male luer lock, which is used to connect the sleeve of the CLS to the pump tubes, to become brittle and crack if it is constructed out of non-gamma-stable material. A brittle or cracked luer lock will create air leakage, which may result in CLS malfunction.

In addition, repeated or extreme exposure to gamma radiation will degrade CLSs designed with hook and loop closures. Exposure to gamma radiation will cause hook material to become increasingly brittle over time. Brittle hook material may not close tightly or securely, resulting in a loose fitting CLS. As mentioned, a loose fitting CLS may compromise treatment and endanger the patient because it necessarily reduces compression of the affected area which results in a decreased effect on blood flow.

Finally, multiple gamma exposure degrades both the performance and stability of the CLS in at least three ways – by compromising the strength of the aircell's seal, by reducing the hook and loop fastener's shear and peel strength, and by reducing the amount of inflation the aircell can withstand before bursting. Each of these effects will compromise the function of a pneumatic compression device, making it less dependable and less effective, if not completely ineffective.

D. Reprocessors Should Be Required to Submit Validation Data Demonstrating That CLSs Constructed Out of Particular Materials and Reprocessed Using Particular Methods Are Substantially Equivalent to the Predicate Device.

Reprocessors should be required to submit validation data demonstrating that particular CLSs reprocessed using a particular method are substantially equivalent to the predicate device. OEMs choose raw materials for their products based on first-use performance

and cost-effectiveness, not long-term durability or sterilization tolerance. For example, manufacturers can make CLSs using either gamma-stable or non-gamma-stable nylon. Companies manufacturing single-use devices may frequently choose to make their CLSs using non-gamma-stable nylon because it is considerably less expensive. Reprocessors, on the other hand, choose a reprocessing method based on its effectiveness, materials compatibility, and cost. Thus, gamma radiation is frequently favored over ethylene oxide sterilization because the latter is so costly.

These two variables, interacting, make it virtually impossible for reprocessors to establish global parameters within which all their reprocessing of all CLS devices can be considered to be safe and effective. Resin manufacturers establish stability guidelines for their products. These guidelines typically establish the cumulative exposure to gamma radiation exposure levels with which their material is compatible. A number of commonly used resins are compatible with gamma radiation at 5 – 10 MRad doses.[6] *See* Sterilization Stability chart. Because the effects of radiation on each material are different, reprocessors must evaluate and validate the effects of a particular reprocessing method on devices based on the material from which they are made. The reprocessor must demonstrate, not only that the material comprising a particular device is compatible with its sterilization and cleaning processes, but also, as in the case of gamma sterilization, that material stability and performance are not diminished up to the total acceptable dose of radiation to which the device will be exposed up to the maximum number of times the device is reprocessed. The reprocessor must demonstrate either that the reprocessing method has not exposed the product to levels of gamma radiation that exceed the raw-materials manufacturer's recommendation or must show that, if they exceed the manufacturer's recommended gamma exposure, the total gamma exposure does not compromise CLS integrity or effectiveness.

III. CONCLUSION

MDUFMA requires FDA to evaluate non-exempt reprocessed, single-use devices to determine whether they should be subject to the requirement that reprocessors submit in 510(k) premarket notification submissions validation data regarding cleaning, sterilization, stability and functional performance to demonstrate that the single-use device will remain substantially equivalent to its predicate device after the maximum number of times the device is reprocessed. Reprocessed, single-use CLSs pose a moderate risk to patients. Reprocessing methods in general and gamma irradiation in particular do not assure that reprocessed, single-use compression sleeves will be safe and effective after multiple uses. Cleaning and sterilization weaken fasteners, seals, air cells and other components of the device, causing them to degrade, break or malfunction thereby compromising patient treatment. Because CLSs are used to prevent the potentially serious effects of DVT, their continued efficacy is essential to patient treatment and safety. Therefore, premarket review of validation data for reprocessed, single-use

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[6] A typical sterilization dose of gamma radiation equals 2.5 to 4 MRads, depending on the bioburden.

CLSs is necessary to provide assurance of the devices' continued safety and effectiveness after reprocessing. Thus, pursuant to MDUFMA, FDA should require reprocessors of single-use CLSs to submit validation data, including stability data and expiration dates, in addition to the current premarket notification requirements under section 510(k). Aircast urges FDA to list reprocessed, single-use CLSs pursuant to Section 302(b) of MDUFMA.

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Aircast appreciates this opportunity to submit these comments on the listing of reprocessed, single-use compressible limb sleeves as reprocessed, single-use devices for which validation data must be included in submissions pursuant to Section 510(k) of the FFDCA. Please do not hesitate to call the undersigned if you require additional information regarding this matter.

Sincerely,

Daniel A. Berish
Vice President of Government Affairs

Attachments