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UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

UNITED STATES OF AMERICA,

Plaintiff,

v.

Undetermined quantities of boxes of articles of device, labeled in part:

(box)

"* Shelhigh No-React® VascuPatchÔ *** Shelhigh, Inc. ***,"**

undetermined quantities of boxes of articles of device, each box containing one jar, which contains the device labeled in part:

(box)

"* Shelhigh Pulmonic Valve Conduit No-React® Treated *** Model NR-4000 *** Shelhigh, Inc. ***,"**

(jar)

"* Shelhigh No-React® Pulmonic Valve Conduit *** Shelhigh, Inc. ***," and**

all other quantities of all articles of device, with any lot number and in any size or type container that are labeled or

Hon.

Civil Action No.
07 CV 1769 WJM

VERIFIED COMPLAINT FOR FORFEITURE *IN REM*

unlabeled, including finished products, in-process materials, and raw materials used in the manufacture of such finished products, that are located anywhere on the premises of Shelhigh, Inc., 650 Liberty Avenue, Union, New Jersey,

and

all other quantities of all articles of device that are labeled as manufactured by Shelhigh, Inc. that are located anywhere on the premises of:

Future Medical Diagnostics Manufacturers Inc., 141 South Avenue, Suite 200-205, Fanwood, New Jersey,

Defendants in-rem.

Plaintiff, United States of America, by and through its attorney, Christopher J. Christie, United States Attorney for the District of New Jersey (By: Peter W. Gaeta, Assistant United States Attorney), respectfully brings this complaint and alleges as follows in accordance with Supplemental Rule G(2) of the Federal Rules of Civil Procedure:

NATURE OF THE ACTION

1. That this complaint is filed by the United States of America, and requests seizure and condemnation of articles of device, as described in the caption, for violations of the Federal Food, Drug, and Cosmetic Act (Act), 21 U.S.C. 301, et seq.

2. That there are at Union, New Jersey, in the possession of Shelhigh, Inc. ("Shelhigh" or "the firm"), 650 Liberty Avenue, and at Fanwood, New Jersey, in the possession of Future

Medical Diagnostics Manufacturers Inc., 141 South Avenue, Suite 200-205, or elsewhere within the jurisdiction of this Court, articles of device, as described in the caption.

JURISDICTION AND VENUE

3. That plaintiff brings this action *in rem* in its own right to condemn and forfeit the defendant property. This Court has jurisdiction over an action commenced by the United States under 28 U.S.C. 1345 and 21 U.S.C. 334, which provides the Court with jurisdiction over seizures brought under the Act.

4. That this Court has *in rem* jurisdiction over the defendant property because the defendant property is located in the District of New Jersey. Upon filing of this complaint, the plaintiff requests that the Court issue an arrest warrant *in rem* pursuant to Supplemental Rule G(3)(b), which the plaintiff will execute upon the property pursuant to Supplemental Rule G(3).

5. That venue is proper in this district pursuant to 28 U.S.C. 1395(b) and 21 U.S.C. 334(a)(1) because the defendant property is located at Shelhigh, Inc., 650 Liberty Avenue, Union, New Jersey, and at Future Medical Diagnostics Manufacturers Inc., 141 South Avenue, Suite 200-205, Fanwood, New Jersey.

BASIS FOR FORFEITURE

6. That the defendant articles of device are adulterated under 21 U.S.C. 351(h) because the methods used in, and the facilities and controls used for, their manufacture, packing, storage, and installation are not in conformity with current good manufacturing practice (CGMP) requirements for devices as set forth in the QS regulation, 21 CFR Part 820.

7. That by reason of the foregoing, the defendant property is held illegally within the jurisdiction of this Court and is liable to seizure and condemnation pursuant to 21 U.S.C. 334.

FACTS

8. That the articles of device manufactured by Shelhigh are cardiovascular, neurological, and general surgery sterile implantable medical devices, including pulmonic and aortic heart valves and pericardial patches that are surgically implanted, often in compromised patients and infants. All of the devices that the firm manufactures undergo a No-React® rinse that occurs after sterilization. The purpose of this final rinse process is to stabilize the sterilant to prevent it from leaching off the device and causing an allergic reaction in patients. This No-React® process is performed in the firm's purported class 100 aseptic manufacturing room (class 100 room), the purpose of which is to prevent contamination of the sterile devices.

9. That the Food and Drug Administration (FDA) issued Warning Letters to the firm on April 26, 2000, and December 14, 2005. The December 14, 2005 Warning Letter advised Shelhigh that it was, among other things, violating the Quality System (QS) regulation. In addition, in a regulatory meeting held on June 16, 2006, the firm was again warned by FDA that continuation of the violative conduct could result in seizure, injunction, and/or civil money penalties. The deficiencies identified during the recent inspection of Shelhigh demonstrate that the firm continues to violate the QS regulation in many significant respects and that the firm has not established and maintained a quality system that is appropriate for the medical devices it designs and manufacturers. 21 C.F.R. 820.5.

10. That FDA inspected Shelhigh on October 11-December 20, 2006. The inspection revealed that the methods used in, and the facilities and controls used for, the manufacture, design, packing, storage, and installation of the above-captioned articles of device do not comply with the QS regulation, 21 CFR Part 820, which was promulgated pursuant to 21 U.S.C. 360j(f)

to assure that the devices will be safe and effective and otherwise in compliance with the Act. These QS deviations include, but are not limited to, the following:

A. Procedures for the acceptance or rejection of finished device production runs, lots, or batches were not complete and adequate [21 CFR 820.80(d)]. For example:

(i) The firm does not have a procedure describing how samples used to test for sterility are processed and controlled prior to sterilization to ensure that they are representative of finished devices. Specifically, the firm's sterility samples are selected from products that fail initial leak testing early in the manufacturing process and are commingled, and thus are not representative of the finished product lot and do not permit lot traceablility. Accordingly, those samples are not subject to the additional manual manipulation of the manufacturing process that occurs prior to the No-React® rinse process and are not representative of the lot that is released;

(ii) The firm allowed at least four lots of devices that failed sterility testing to be released for distribution in the last two years. FDA reviewed all 89 initial sterility tests performed for Shelhigh by its independent testing contractor (contract laboratory) during 2005 and the first 10 months of 2006. This review showed that 7.4% of samples tested in 2005 failed sterility and that 5.7% failed sterility testing in 2006. Although retesting failed to find non-sterile product, such retesting was not justified (and should not have been conducted) under accepted industry standards because the firm had not first shown that the initial positive test results were due to errors committed by its contract laboratory. (In fact, in the one instance in which Shelhigh asked its contract laboratory to evaluate its positive result for laboratory error, no such error was found.) In addition, because of the inherent limitations of sterility testing (e.g., contamination is random and sampling amounts are very low) and in the absence of a showing of meaningful laboratory error, a retest result of apparent sterility does not establish sterility; and

(iii) The firm failed to identify device lots that did not meet specifications during endotoxin testing. Specifically, the firm released two lots of devices that failed initial endotoxin testing, even though initial tests and retests were performed on an inadequate sample size (one sample unit from each lot), which could lead to a false negative result. See also 21 C.F.R. 820.250(b) (manufactures must establish and maintain procedures to ensure that sampling methods are adequate for their intended use; sampling plans must be based on a valid statistical rationale). Endotoxins can cause fever, shock, coagulation of blood, and a rapid fall in blood pressure when introduced into blood or tissues of the body.

A. manufacturer's final acceptance activities are the last chance to assure that finished devices meet specified requirements. Failure to verify that appropriate acceptance criteria have been met can result in the distribution of defective finished devices.

B. Adequate procedures to control product that does not conform to specified requirements were not established and maintained [21 CFR 820.90(a)]. For example:

(i) The firm does not investigate initial sterility failures for devices that it manufactures. As set forth above, the firm does not investigate to determine whether laboratory error or the manufacturing process caused a non-sterile result before permitting a retest for sterility; nor does the firm investigate its manufacturing process to identify the source of contamination; and

(ii) The firm failed to identify non-conforming results during the pulmonic valve pressure leak testing (a test conducted to ensure that the device will not leak after it is implanted in patients) and subsequently released non-conforming products for distribution, despite the firm's procedure which required that such devices be rejected.

Proper control of non-conforming product is critical to ensure that finished devices and products that do not conform to specifications are not used or distributed. The investigation of non-

conformances is an essential part of ensuring ongoing control of a manufacturing process, to determine the cause and effect of a non-conformance and to prevent its recurrence.

C. Adequate quality requirements that must be met by suppliers were not established, and procedures to ensure that all purchased or otherwise received services conform to specified requirements were not complete [21 CFR 820.50(a)]. For example:

(i) Appropriate quality requirements have not been established for the firm's contract laboratory, which supplies bioburden testing, environmental monitoring, *Limulus Amebocyte Lysate* (LAL) testing, and sterility testing; the firm did not require the sterility test used for its products to be validated by its contract laboratory. The firm's sterility test method only includes the use of one culture medium, Soybean Casein Digest Broth (SCDB), which does not support the growth of anaerobic microorganisms. Accordingly, the test will not detect such organisms, which may be present and contaminate the devices and infect patients. In addition, the SCDB was incubated at an improper temperature, which may reduce the recovery of certain microbiological contaminants.

Failure to establish and maintain procedures to assure appropriate services to test a finished device can result in failure of the device to meet its specifications and distribution of non-conforming product.

D. Production processes were not adequately developed, conducted, controlled, and monitored to ensure that devices conform to their specifications [21 CFR 820.70(a)]. For example:

(i) The firm's procedure for testing quality of water used to process products does not include analysis for the presence of endotoxins, even though its device specifications require that the level of bacterial endotoxins in finished devices not exceed a specific limit. This water is used to prepare various solutions that come in direct contact with raw materials, components, and

finished devices. Minimizing the presence of endotoxins in process components is important because the firm has no process to remove them in subsequent processing steps.

Production and process controls are necessary to ensure that each manufacturer produces devices that conform to their specifications. Where any deviations from specifications could occur during manufacturing, process control procedures must be established to ensure conformance to specifications.

E. A critical process whose results cannot be fully verified by subsequent inspection and test has not been adequately validated, and procedures were not established to monitor and control process parameters for validated processes [21 CFR 820.75(a),(b)]. For example:

(i) The firm has not adequately validated the No-React® detoxification process, a final rinse process used on all devices after sterilization and performed in the class 100 room, to demonstrate with a high degree of assurance that the process will not adversely affect the sterility of all devices manufactured at its facility. Although the firm stated that it had submitted validation data to FDA, the firm submitted only a procedure and general data that were not generated by the procedure. Also, the procedure submitted for the No-React® process is different than that actually performed by the firm.

Because the firm's devices are implanted into patients, ensuring continued sterility is critical. The microbiological control of the Shelhigh No-React® process cannot be fully verified by subsequent inspection and testing because the firm cannot perform sterility testing on every finished device without destroying the devices. Thus, the firm is required to validate the process with a high degree of assurance and thereafter follow the precise process that was validated. Process validation means confirmation by objective evidence that a process consistently produces a result or product meeting its predetermined specifications. 21 CFR 820.3(z). Examples of factors

that must be considered when validating an aseptic manufacturing process include the absence of microbiological, and the level of particulate, contamination contributed by the air, surfaces, and employee practices, among others.

F. Adequate procedures to prevent contamination of equipment or product by substances that could reasonably be expected to have an adverse effect on product quality were not established and maintained [21 CFR 820.70(e)]. For example:

(i) The firm's class 100 room has no separate gowning room for employees to dress in sterile garments before entering the room;

(ii) Employees do not wear sterile shoe covers before entering or when inside the class 100 room. In the class 100 room, the entire body should be covered by sterile garments. Sterile shoe covers are necessary to cover shoes, which are recognized vectors for transporting high levels of microorganisms throughout a facility;

(iii) Employees use a broom to sweep the floor of the class 100 room. Such sweeping causes dust, bacteria, and mold spores to spread throughout the ambient air of the room onto table tops, walls, shelves, and other surfaces that later may be touched by personnel who process product. Although this sweeping is done prior to disinfection, the firm's standard operating procedures provide for inadequate disinfection of surfaces, and the firm's disinfectant does not kill microbiological spores;

(iv) A non-sterile stainless steel cart is transported into the class 100 room during product processing;

(v) Pieces of raw and painted wood were observed in the firm's class 100 and class 1,000 rooms. Wood is porous, difficult to disinfect, can allow for the growth of bacteria and mold

and contamination of the environment, and is inappropriate in a class 100 and class 1,000 environment; and

(vi) The following conditions were also observed in the firm's controlled manufacturing areas immediately adjacent to the class 100 room, where fresh porcine and bovine tissue products are processed: ceiling panels stained with unknown substances; dislodged ceiling panels; portions of ceiling panels missing; and air diffusers with corrosion and dirt accumulation.

Each manufacturer is required to establish and maintain procedures to prevent contamination of components, manufacturing materials, in-process devices, finished devices, equipment, and returned devices by substances that could adversely affect device safety or effectiveness.

G. Adequate procedures to control environmental conditions that could reasonably be expected to have an adverse effect on product quality were not established and maintained [21 CFR 820.70(c)]. For example:

(i) The firm's procedure for determining whether surfaces in the class 100 room are contaminated requires the use of Isopropyl Alcohol to wipe down only one small area prior to sampling for contamination. In addition, because Isopropyl Alcohol may prevent growth of microorganisms and Shelhigh does not add a neutralizing agent to its surface monitoring media, this process kills many surface microorganisms prior to monitoring, masking the true count and types of potential microbes on work surfaces that are used during device manufacturing in the class 100 room. Accordingly, even the limited surface sampling performed by Shelhigh (see (ii) below) is not reliable. Lack of accurate sampling results fundamentally undermines the ability of a firm to detect when hazards are present during processing that can result in device non-sterility;

(ii) Monitoring for air and surface contamination in the class 100 room is rarely performed and, when performed, not done adequately. Shelhigh conducts surface monitoring only once every three months; the firm's surface monitoring is performed only on one spot in the class 100 room. Air monitoring is done with only one exposure plate after each manufacturing shift under static conditions and therefore does not reflect actual processing conditions.

(iii) The class 100 room is not properly constructed to perform sterile operations and control contamination. For example, there are gaps at the bottom of the walls and at the top of each corner of the room, which are twenty feet from a door to an environmentally uncontrolled warehouse area that may be opened during product processing; the entryway to the room consists of a series of plastic strips, which are located approximately two feet from the work bench on which devices are finally processed; and the high efficiency particulate air (HEPA) filters, which are used to bathe the room in filtered air, are periodically turned off thereby allowing unfiltered and ambient air to enter the class 100 room. (See also 21 CFR 820.70(f)).

Manufacturers are required to establish and maintain adequate procedures to carefully monitor and control environmental conditions that could reasonably be expected to have an adverse effect on product quality. As a part of the requirement, manufacturers are required to frequently monitor and periodically inspect environmental control systems to verify that the systems, including necessary equipment, are adequate and functioning properly. In addition, these monitoring activities must be documented and reviewed. To determine whether appropriate environment and process controls are being maintained, manufacturers who aseptically process products sample air and surfaces every day and typically during each shift, using an appropriate number and location of environmental monitoring plates.

H. Adequate requirements for the health, cleanliness, personal practices, and clothing of personnel were not established and maintained [21 CFR 820.70(d)]. For example:

(i) Employees who handle porcine and bovine materials, finished devices, sutures, surgical instruments, and solutions used during the manufacture of the devices were observed leaving the controlled manufacturing environment in their gowned attire entering the restroom, and re-entering the controlled manufacturing areas without changing their gowned attire, in violation of the firm's procedure. These employees were working in a critical device processing area that is in close proximity to the class 100 room.

Manufacturers are required to establish and maintain adequate procedures for the health, cleanliness, personal practices, and clothing of their personnel who are working in areas where contact between personnel and product or the environment could adversely affect the product. Requirements for sterile devices and environmentally-controlled room operations necessitate a high level of control in order to minimize the bioburden and particulate contamination of the devices and the contamination of the environment.

I. Procedures were not followed to confirm that the design changes made to the Pulmonic Valve Conduit, a device used to replace a diseased, damaged, or absent pulmonic artery in infants and children, were controlled to include the identification, documentation, validation or, where appropriate, verification, review, and approval of the changes prior to their implementation [21 CFR 820.30(i)]. For example:

(i) The Pulmonic Valve Conduit design was changed from a straight inflow conduit to a curved inflow conduit. This design change was not adequately evaluated for the potential impact on the functional, physical, or mechanical property features of the device as a whole.

Manufacturers are required to have procedures to ensure that after design requirements are established and approved, changes to the design requirements are also documented, reviewed, validated, and approved. The records of the design changes create a history of the evolution of the design. Such records are integral to failure investigations and preventing the repetition of errors and the development of unsafe or ineffective designs.

J. Adequate design validation requirements to ensure that devices conform to defined user needs and intended uses were not established and maintained [21 CFR 820.30(g)]. For example:

(i) Although documentation submitted by the firm to FDA supported only a three year product shelf-life, the firm's labeling claims a four year shelf-life for all devices. The shelf-life testing used to support the firm's claimed four-year expiration date was inadequate because it did not evaluate device performance for the extended period and did not include all devices.

(ii) The firm has no test data to support multiple resterilizations of its devices, which the firm believes may extend the shelf-life of these devices to 12 years.

Because the firm produces tissue-based devices, it is critical to conduct design validation studies to ensure that any processing and reprocessing of these devices does not compromise performance and adversely affect the safety and effectiveness of devices, e.g., by degrading the products.

K. Adequate procedures for ensuring that all personnel are trained to adequately perform their assigned responsibilities and for identifying training needs were not established, maintained, and documented [21 CFR 820.25(b)].

(i) In addition to the many clear deviations set forth above, the lack of adequate training is also evident from the fact that an employee of the firm fabricated shrink temperature test

results on retained samples and presented the data to an FDA investigator because she could find no record of the original test results;

(ii) The firm has not adequately documented the training of its employees. There are no current records documenting CGMP, Quality System, or microbiological training for Shelhigh's Chief Scientific Officer (CSO), who is responsible for training quality assurance auditors, or the firm's General Manager, who acts in the CSO's absence.

In order for a manufacturer's quality system to reliably function, all personnel must be properly trained. At a minimum, such training must include the consequences of improper performance so that personnel will be aware of the effects that their actions can have on the safety and effectiveness of the device and know what process and product defects can occur as a result of deficient practices, procedures, or conditions.

WHEREFORE, the plaintiff requests that the Court issue a warrant and summons for the arrest and seizure of the defendant property; that notice of this action be given to all persons who reasonably appear to be potential claimants of the defendant property; that the defendant property be condemned and forfeited to the United States; that the defendant property be disposed of as this Court may direct pursuant to the provisions of the Act; and that plaintiff be awarded its costs and disbursements in this action, and for such other and further relief as this Court deems proper and just.

CHRISTOPHER J. CHRISTIE
United States Attorney

By:

PETER W. GAETA
Assistant U.S. Attorney

STATE OF NEW JERSEY : SS VERIFICATION
:
COUNTY OF :

ROBERT MAFFEI, of full age, being duly sworn according to law, upon his oath deposes and says:

1. I am a Compliance officer, New Jersey District Office, United States Food and Drug Administration, and as such am presently assigned to the above-captioned matter.

2. I have reviewed the attached Complaint and the allegations it contains are true to the best of my knowledge, information, and belief.

Robert Maffei
ROBERT MAFFEI

Sworn and subscribed to
before me this 16th day
of April, 2007, at
Newark, New Jersey

PETER W. GAETA
Attorney-at-Law
State of New Jersey