



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration  
New England District

2015d

One Montvale Avenue  
Stoneham, Massachusetts 02180  
TEL (781) 596-7700  
FAX (781) 596-7899

November 29, 2001

**WARNING LETTER**

**NWE-04-02W**

**CERTIFIED MAIL**  
**RETURN RECEIPT REQUESTED**

Mr. Thomas Glover  
President and Chief Executive Officer  
Vasca, Inc.  
3 Highwood Drive  
Tewksbury, MA 01876

Dear Mr. Glover:

An inspection of your facility located at 3 Highwood Drive, Tewksbury, MA was initiated by Food and Drug Administration (FDA) Investigator Edward Janik on July 5, 2001 and completed on July 17, 2001. This inspection confirmed that your firm manufactures the LifeSite® Hemodialysis Access System. This product is a medical device, as defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The inspection revealed that the LifeSite® device is *adulterated* within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformity with the Quality System Regulation, Title 21, Code of Federal Regulations (CFR), Part 820, promulgated under Section 520(f)(1) of the Act. The following deviations were noted:

- 1) Records of complaint investigations do not demonstrate that complaints are adequately evaluated to determine their MDR reportability, as required by 21 CFR § 820.198(a)(3); and
- 2) Records of complaint investigations do not always include the results of the investigations, as required by 21 CFR § 820.198(e)(6).

Examples of these deviations include:

Three complaints listed as closed (Nos. 01022601, 01030901, and 01050201) and one open complaint (No. 01031201) were not reported as MDRs and did not include complete investigations. Files for the three closed complaints did not include medical records. All four complaints involved patient deaths.

The inspection also revealed the LifeSite® device is *misbranded* within the meaning of section 502(f)(1) of the Act, in that it fails to bear adequate directions for use for the purposes for which it is intended as described in 21 CFR § 801.4. As the manufacturer, you have knowledge of facts that would give you notice that this device, which you have introduced into interstate commerce, is being used for conditions, purposes, or uses other than the ones for which it is offered for sale. You are required to provide adequate labeling for such device that accords with such other uses to which the device is being put, such as implanting procedures for femoral and direct thoracotomy placement.

The inspection also revealed that the LifeSite® device is *misbranded* within the meaning of Section 502(t)(2) of the Act, for the following two reasons:

- 1) Information required to be submitted to the Food and Drug Administration (FDA) by the Medical Device Reporting (MDR) regulation specified in 21 CFR Part 803 was not submitted within 30 days as required. Since the commercialization of this device—in the European Union in July 1998, in Canada in January 1999, and in the United States in August 2000—there have been at least 129 complaints reported to your establishment involving death or serious injury.

For example, our review of the records for twenty (20) of these complaints found information to reasonably suggest that your device may have caused or contributed to a death or serious injury or malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Your firm filed MDRs past the 30 day due date for fourteen (14) of the reviewed complaints:

Four (4) events where bleeding from the valve or pocket was reported and the valve was explanted:

<b>Vasca Complaint Number</b>	<b>MDR Report Number</b>
00101701	1225459-2001-00031 filed 8/1/01
00101702	1225459-2001-00034 filed 8/1/01
00110801	1225459-2001-00035 filed 8/1/01
01041002	1225459-2001-00025 filed 8/1/01

Six (6) events that reported infection or necrosis, with valve explanted:

<b>Vasca Complaint Number</b>	<b>MDR Report Number</b>
01050203	1225459-2001-00023 filed 8/1/01
01050801	1225459-2001-00022 filed 8/9/01
01051401	1225459-2001-00021 filed 8/1/01
01052304	1225459-2001-00020 filed 8/1/01
01050202	1225459-2001-00019 filed 8/1/01
00010401 (Europe)	1225459-2001-00026 filed 8/10/01

One (1) event that reported difficulty accessing valve, with valve repositioned to correct:

<b>Vasca Complaint Number</b>	<b>MDR Report Number</b>
01042002	1225459-2001-00024 filed 8/1/01

Two (2) events that reported catheter detachment from the valve:

<b>Vasca Complaint Number</b>	<b>MDR Report Number</b>
99041501 (Europe)	1225459-2001-00041 filed 8/10/01

Two (2) events that reported problems with flow:

<b>Vasca Complaint Number</b>	<b>MDR Report Number</b>
99082001 (Europe)	1225459-2001-00029 filed 8/10/01 (also infection)
99122301 (Europe)	1225459-2001-00030 filed 8/10/01

An additional six (6) complaints concerning nine (9) patients are considered MDR reportable, but your firm has not filed MDRs for these adverse events:

<b>Vasca Complaint Number</b>	<b>Nature of Adverse Event</b>
01022601	abdominal pain reported after dialysis, and patient died the next day
01031201	four patients experienced problems with hematoma and/or bleeding (each adverse event should be reported separately)
01050201	infection
01052305	necrosis
99092001	catheter came loose from valve
00082101	flow problems

- 2) The inspection also revealed you failed to furnish material or information as required by Section 519 of the Act. Specifically, you failed to submit written reports to FDA of corrections or removals, as required by 21 CFR § 806.10. For example:

Sometime in March 2001, Vasca, Inc. revised the instructions for the use of the LifeSite® device. Users of your device were notified of this revision—recommending the use of an initial heparin lock concentration of 1000 units per milliliter instead of 5000 units per milliliter—through a “Dear Doctor” letter and a “Dear Healthcare Professional” letter. The correction did not include provisions for the removal from all channels of commerce of the obsolete instructions for use (pamphlet TM 0025).

The inspection also revealed that the LifeSite® device is *misbranded* under Section 502(f)(2) of the Act in that its labeling does not bear such adequate warnings against use in those pathological conditions, or against unsafe dosage or methods or duration of administration or application, in such manner and form as necessary for the protection of the user.

With regard to this charge it is noted that your access device is currently intended for use in hemodialysis patients that are awaiting creation and/or maturation of a permanent access. Review of post-market adverse event data, however, indicated that the majority of reported deaths and many reported injuries occurred in patients that were not candidates for permanent access placement. Information provided on adverse events indicated that many affected patients had a history of multiple access failures and access infections and would not be candidates for further permanent access placement. Moreover, several centers reported patient deaths for individuals that had been considered “last resort” patients by their healthcare providers, in that they were not candidates for permanent access, were very ill, and had limited options for dialysis access. Several reported deaths and many reported injuries occurred in patients that underwent access placement procedures (femoral or direct thoracotomy implantation) for which the device is not currently labeled.

In view of the number of reported deaths and injuries that have occurred in patients for whom the device is not specifically labeled, you should communicate this important safety information to health care professionals that use the device. More specifically, you should revise the labeling to incorporate important new post-market safety data. The labeling should be revised to warn the user about the risks of such use and expected outcome in patients with a history of multiple access failures or access infections, that are catheter dependent for dialysis access, and are not candidates for permanent access placement. The label should also warn the user that the safety and effectiveness of device implantation in sites other than jugular or subclavian vessels has not been evaluated. The labeling should also be revised to relate the new post-market safety information regarding reported deaths and injuries in such compromised patients that were not candidates for permanent access placement, including those that did not undergo jugular or subclavian vessel device implantation (femoral or direct thoracotomy implantation).

In view of the number of serious adverse events reported in the extended IDE, you should provide an IDE supplement providing all the details of all reported serious adverse events and deaths up to the date of mailing of the IDE supplement. You should also clarify the apparent concurrent use of other dialysis access devices in LifeSite® patients during the IDE (i.e., patient [REDACTED]).

Reviews of complaints indicate that there may be clustering of patient deaths and injuries [REDACTED].

You should evaluate this apparent clustering of adverse events to determine possible causes and potential corrections. For example, it may relate to more frequent use of the device in patients with serious medical problems or a need for further training of medical staff at specific centers.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and the regulations. The specific violations noted in this letter and the Form FDA 483 issued at the close of the inspection may be indicative of serious underlying problems in your establishment's Quality System. You are responsible for investigating and determining the causes of the violations identified by the FDA. You must also promptly initiate permanent corrective and preventive action on your Quality System.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for Class III devices to which the Quality System Regulation deficiencies are reasonably related will be cleared until the violations have been corrected. Also, no requests for Certificates for Products for Export will be approved until the violations related to the subject devices have been corrected.

We acknowledge the receipt of the following communications from your firm:

- 1) letter dated July 6, 2001 to Dr. Catherine Meyers, Gastroenterology and Renal Devices Branch, summarizing adverse events during the period of August 25, 2000 to June 26, 2001;
- 2) letter dated July 18, 2001 to Gail T. Costello, Director, New England District Office, responding to Form FDA 483 issued on July 17, 2001;
- 3) letter dated July 31, 2001 to Gail T. Costello, Director, New England District Office, providing a report pursuant to 21 CFR Part 806 (Corrections and Removals), along with additional information pertaining to MDR reportable events; and
- 4) series of weekly updates on complaints involving deaths, dating back to August 21, 2000 (No. 00082101)

You should take prompt action to correct these deviations. If they have already been corrected, you should take steps to prevent the recurrence of similar violations. Failure to promptly correct these deviations may result in regulatory action being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please notify this office within fifteen (15) working days of the receipt of this letter of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying system problems necessary to assure that similar violations will not recur. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

FDA also recommends that you consider sending a notification letter to dialysis centers and physicians regarding changes made to your device labeling.

In addition, we note that you have received complaints from dialysis unit staff that the training they received was not adequate to address relevant aspects of this device. Such complaints regarding training should be addressed. Further, all training should be documented by the firm and at each site of training.

Also, please clarify how you specifically address problems involving LifeSite® placement in sites other than jugular or subclavian vessels, when they are reported to you by dialysis centers.

Your response should be sent to: Mark Lookabaugh, Compliance Officer, U.S. Food and Drug Administration, One Montvale Avenue, 4th Floor, Stoneham, MA 02180. If you have any questions concerning this matter, please contact Mr. Lookabaugh at 781-596-7751.

Sincerely,



Gail T. Costello  
Director  
New England District