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

**Food and Drug Administration**  
**555 Winderley Pl., Ste. 200**  
**Maitland, Fl 32751**

**WARNING LETTER**

**FLA-03-19**

January 6, 2003

Mr. Terence D. Wall  
Chief Executive Officer  
Vital Pharma, Inc.  
20 Campus Road  
Totowa, New Jersey 07512

Dear Mr. Wall:

From September 27 to October 4, 2002, an investigator from the Food and Drug Administration (FDA) inspected your contract manufacturing establishment located at 971 and 1006 W. 15th Street, in Riviera Beach, Florida. The investigator determined that your manufacturing operations for Intergel Adhesion Prevention Solution (Intergel), an intraperitoneal instillate intended to reduce adhesions following peritoneal cavity surgery, do not comply with FDA's Quality System (QS) Regulation for medical devices, located at Title 21, Code of Federal Regulations (CFR), Part 820. These violations cause Intergel to be adulterated within the meaning of section 501(h) of the Act, 21 U.S.C. § 351(h).

The inspector noted the following violations:

1. Your firm has failed to establish and maintain process control procedures describing the process controls necessary to ensure conformity with specifications, as required by 21 CFR § 820.70(a). Specifically, your firm's process control procedures do not address power outages, or the maximum time the device can remain in the aseptic fill line during machine down-time.
2. Your firm did not conduct process controls in accordance with documented instructions and SOPs, as required by 21 CFR § 820.70(a)(1). Specifically, your firm continued producing VPI-011 lot 2L010 on May 20, 2002, even though the quality control unit did not document clearance of the fill line, as required by your firm's own procedure.
3. Your firm did not verify or validate a change to a process, as required by 21 CFR § 820.70(b). Specifically, you did not complete validation activities or close the change control form before changing molds.

4. Your firm did not validate and approve according to established procedures a process whose results cannot be fully verified by subsequent inspection and test, as required by 21 CFR § 820.75(a). Specifically:
  - a. In conducting retrospective process validation VP 702 of the BFS process for Intergel, your firm did not: (1) determine process parameters for the validation lots; (2) establish quantitative acceptance criteria for defects; or (3) specifically qualify control mechanisms of critical process parameters.
  - b. In conducting process validation VP 642 of the aseptic process for Intergel, your firm: (1) exceeded worst case filling times; (2) did not address worst case times between the steam-in-place sterilization of equipment and the BFS processing; (3) did not address worst case down time for equipment with product in the aseptic filling line; (4) did not include a simulated power outage in its worst case disruptions; and (5) failed to determine, in conducting the review of the validation and supporting documents, that the entry-exit log did not document that an operator was present at all times during processing, as required by the protocol.
  - c. Your firm has not determined whether the cleaning process for the BFS machine adequately removes media used as part of media fills.
5. Your firm failed to (1) establish and maintain procedures for monitoring and control of process parameters for validated processes and (2) document the monitoring and control methods and data for such processes to ensure that the specified requirements continue to be met, as required by 21 CFR § 820.75(b). Specifically, your firm did not identify critical process parameters or establish acceptable ranges for the BFS system.
6. Your firm failed to establish and maintain procedures for finished device acceptance as required by FDA regulations. Specifically, your firm's acceptance procedures do not require your firm to review the data and documentation associated with the activities required in the device master record, as required by 21 CFR §820.80(d). In addition, your firm's procedures for acceptance of finished device production runs, lots, or batches did not include requirements to review BFS production process parameters as part of the device history review for final release.
7. Your firm did not establish and maintain procedures addressing evaluating nonconforming product, including determining the need for an investigation, as required by 21 CFR § 820.90(a). Specifically, your firm has not established

criteria for determining when to conduct an investigation of nonconformance or procedures governing the documentation of evaluations of nonconformance.

8. Your firm did not establish and maintain procedures for implementing corrective and preventive action (CAPA) in accordance with FDA regulations, as required by 21 CFR § 820.100(a). Your firm's procedures for implementing corrective and preventive actions do not include requirements for analyzing quality data to identify recurring quality problems. In addition, your firm's procedures for implementing corrective and preventive actions do not include requirements for submitting relevant data for management review.
9. Your firm has failed to establish and maintain CAPA procedures that include requirements for identifying the actions needed to correct and prevent recurrence of nonconforming product and other quality problems, as required by 21 CFR § 820.100(a)(3). Specifically, your firm did not implement a procedure to identify cosmetic defects on the inside of containers for lots IN049, IN055, and IN137 that resulted in complaints 01-07 and 02-04 as a quality problem and did not take action to prevent this problem from recurring.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure that your manufacturing operations comply with all applicable requirements of the Act and of FDA regulations.

Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties. Moreover, uncorrected QS Regulation violations can provide a basis for FDA to deny export certification for medical devices. FDA also advises other federal agencies of the issuance of Warning Letters about medical devices so that they may take this information into account when considering the award of contracts.

We have received and reviewed your October 30, 2002, response identifying proposed and on-going corrective actions. Please provide documentation for our

review and file after all of these measures have been implemented. Your response should be sent to Timothy J. Couzins, Compliance Officer, Food and Drug Administration, 555 Winderley Place, Suite 200, Maitland, Florida 32751, (407) 475-4728.

Sincerely,

*Ken Hester*

*for*

Emma Singleton  
Director, Florida District

cc:



William F. Stringer, President  
Vital Pharma, Inc.  
1006 West 15<sup>th</sup> Street  
Riviera Beach, Florida 33404