GMP Trends

DISTRICT ADDRESS	DATE OF ISSUE
GMP Trends LLC P.O. Box 1111 Firestone, Colorado 80520	Introductory
	C.I. ISSUE MMCX

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

To: Responsible Person, Director of Quality Assurance

FIRM NAME	STREET ADDRESS
Pharmaceutical and Related Industries	5600 Regulation Lane
CITY, STATE AND COUNTRY United States of America and Worldwide	TYPE OF ESTABLISHMENT INSPECTED Pharmaceutical and Medical Device

DURING A REVIEW OF INSPECTION REPORTS OF U.S. FIRMS (I) (WE) OBSERVED:

MANUFACTURING-ACTIVE PHARMACEUTICAL INGREDIENTS (API)

1. …..The type and extent of control to be exercised over suppliers was not clearly defined.

   Material Supplier Audits – Although your firm performs periodic audits of starting material suppliers, they do not always conduct timely follow-up to known reported deficiencies. For example, the audit report for ….. includes concerns of lack of equipment maintenance, supervision and a corroded roof. There was no evidence of follow-up available. This firm is currently a supplier of ….. intermediate.

2. …..Manufacturing equipment is not fully and adequately qualified for its intended use prior to being placed into production.

   Specifically,

   a. The firm's SOP ….. Inspection and Testing of Manufacturing Equipment does not adequately describe the information necessary for completing an Installation Qualification (IQ). For example, environmental and operational requirements, ancillary equipment and maintenance. Further, IQ processes are not required to be reviewed and approved by the quality control unit (QCU).

   b. The firm's SOP ….. Inspection and Testing of Manufacturing Equipment does not adequately describe the steps necessary to perform an Operational Qualification (OQ) or the necessity for OQ protocols. For example, the SOP states that OQ will be performed using ….. which mimics the manufacturing process (usually water will be used). There is no requirement to demonstrate that the simulation process adequately mimics normal production activities. The OQ processes are not required to be reviewed and approved by the QCU.

   c. The firm's SOP ….. Inspection and Testing of Manufacturing Equipment does not adequately describe the requirements for Performance Qualification (PQ). There is no requirement for a PQ protocol or for the PQ final report to be reviewed and approved by the QCU. Further, PQ is accepted once ….. lots have been manufactured. There is no requirement for the lots to have been manufactured in succession.

3. …..Failure to maintain API Processing Equipment in a sanitary manner.

   Specifically, an accumulation of debris was observed on the exterior of the sight glass located on the top of fermentation vessel ….. In addition, standing water was observed on the sight glass atop fermentation vessel ….. These sight glasses are used to perform a visual inspection of the interior of the reaction prior to charging.

4. …..The Quality Unit has failed to fully investigate or implement adequate corrective measures in response to contamination of API batches.

   Regarding the investigations and corrective actions associated with both …..:

   a. Both investigations are silent with respect to identification of and consideration for all other potentially affected API batches. For example, reactor ….. is not dedicated to ….. API and is also used in the manufacture of ….. API's.

   b. Both investigations are silent with respect to evaluating the various equipment (i.e.; piping, fixtures, I-beam) above the charge in port (manway) on reactor ….. as potential sources for contamination of process materials. No corrective measures had been implemented to minimize potential for contamination when charging materials during processing of ….. API. No effective controls had been implemented to ensure that the various equipment (i.e., piping, fixtures, I-beam) located above the charge in port (manway) on reactor ….. are properly maintained and are free of filth, rust, blistering paint, or chipping paint.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE **GMP Trends LLC**	EMPLOYEE(S) NAME AND TITLE **Editor**	DATE ISSUED **Introductory**

— Contents of GMP TRENDS® are protected by U.S. Copyright Law. Reproduction of any type is strictly prohibited by law. Authorization to photocopy for internal or personal use can be granted by contacting Copyright Clearance Center, 222 Rosewood Drive, Danvers, MA 01923, (978) 750-8400 or (855) 239-3415. E-mail: info@copyright.com, www.copyright.com