DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Detroit District Office 300 River Place, Suite 5900 Detroit, MI 48207 313-393-8100 Industry Information: www.fda.gov/oc/industry	8/20-28/2013*
	FEI NUMBER 3008716173

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Thomas J. Ross, President

FIRM NAME	STREET ADDRESS
Grand River Aseptic Manufacturing, Inc.	140 Front Ave. SW, Suite 3
CITY, STATE AND ZIP CODE Grand Rapids, MI 49504	TYPE OF ESTABLISHMENT INSPECTED Manufacturer

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS; AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

1-The responsibilities and procedures applicable to the quality control unit are not in writing and fully followed. Specifically,

A-Acceptance criteria for the contracted HEPA Filter Integrity Testing and Aseptic Core (b) (4) CERTIFICATION OF THE CLEANROOM FACILITY provider are not specified to assure all reported findings from the provider meet your facility's intended use. Products filled in the cleanroom (APA) of your facility include: Products coded as 001-100A and 008-109A.

For example,

i- The differential pressure measures noted on the "ROOM PRESSURE SURVEY" provided by the contracted tester/provider (report dated 2/13/2013) indicated differential pressures below in house differential pressure specifications. For example, between room (b) (4) the provider reported a value of 0.006" water gauge. Your in house specification at this same ISO 6 to ISO 7 (room (b) (4) threshold is not less than 0.05" water gauge.

ii- The airflow velocity uniformity within a room/suite, including the acceptability of variances in velocity from each HEPA filter within a room/suite is not specified. For example and as noted by this same contract tester (report dated 2/13/2013), a HEPA filter was noted with an average velocity of (b) (4) feet per minute at one side of room (b) (4) while another HEPA filter in this same room was noted with an average of (b) (4) feet per minute.

B- The scientific rationale for the change to the functional requirements of the Building Monitoring System specifications for differential pressure monitoring was not provided for the alarm delay change from (b) (4) seconds to (b) (4) seconds. In addition, this change is not reflected in the current "Building Monitoring System Functional Requirements Specification" (remains noted with action alarm after a (b) (4) minute time delay"). This change

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	R E Dombrowski	Rebecca E. Dombrowski, Investigator	8/28/2013

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occurring on or about 11/28/2011 was also not reported through the formal Validation Change Control system, as required according to written procedure QA-SOP-003, Validation Change Control.
This observation is applicable to manufactured products including product 001-100A and 008-109A.

2-Certificates of testing of closures are accepted in lieu of testing without establishing the reliability of the supplier's test results through appropriate validation of the test results at appropriate intervals.
Specifically,

Ready to Sterilize Stoppers, material code (b) (4) [redacted] used as part of the container closure system for product 001-100A, are received with a Quality Certificate providing the report of analysis for various tests, including bacterial endotoxin and particulates on the stoppers. The reliability of the reported particulate levels has not been established through appropriate validation of the test results. Reported values for this measure included both visible and sub-visible particulates.

For example, stoppers of incoming lot (b) (4) [redacted] accepted and released for use on 12/10/2012, and used in the filling/closure of product 001-100A, Lot # L-12-023.

3-Laboratory controls do not always include the establishment of scientifically sound and appropriate test procedures designed to assure that in-process materials conform to appropriate standards of identity, strength, quality and purity.
Specifically,

The in-process product 001-100A bulk formulation bioburden test method has not been fully validated to address the recover-ability of representative microbial organisms. Specifically, the validation of this bioburden test method included only confirmation of recovery of Geobacillus stearothermophilus in the presence of the bulk formulation. This method has been used in bioburden evaluation of product 001-100A bulk formulation lots L-12-023, L-12-024, and L-12-025.

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4-Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not written.
Specifically,

As observed during a water fill simulation on 8/20/2013, three operators within the Aseptic Fill Suite were observed passing through the ISO 5 defining curtains into the ISO 6 Aseptic Processing Support room and back into the ISO 5 Aseptic Fill Suite on numerous (three observed) occasions within a short (approximately (b)(4) min.) time, making contact with the curtains with their sterile garb. Restrictions against such movements between the air spaces were not defined in written procedures at the time of this observation.
This same fill suite was used in the filling of product 001-100A lot L-12-023.

*Dates of Inspection: 8/20/2013 (Tues.), 8/21/2013 (Wed.), 8/22/2013 (Thrs.), 8/23/2013 (Fri.), 8/27/2013 (Tues.), 8/28/2013 (Wed.).

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