DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	8/20/2018-8/28/2018*
	FEI NUMBER 3013712903

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Nitish N. Chakravarty, Chief Manufacturing

FIRM NAME	STREET ADDRESS
Liva Pharmaceuticals Limited	Survey No 434-6/B and 434-1/K, Village Jarod,Taluka, Waghodia
CITY, STATE, ZIP CODE, COUNTRY Vadodara-Halol Highway, Gujarat, 391510 India	TYPE ESTABLISHMENT INSPECTED Manfacturer

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 OBSERVED:

OBSERVATION 1

Procedures designed to prevent microbiological contamination of sterile small volume parental drug products purporting to be sterile are not followed.

Specifically,

SOP entitled: "Aseptic Process Simulation (Media Fill)", QA-00024, Version:4.0, Effective date:07/09/2018, page 31,6.4.15 (D) reads in parts: "***Containers having obvious breach of container/ closure integrity such as cracked container, broken container, containers with missing (b) (4) stopper/closures shall be sorted out and rejected** The rejection shall be discarded with rationale. Justification after identifying reasons for obvious breach of container closure integrity**The same shall be followed by documentation***". For one of the (b) (4) media fill batch performed between (b) (4) (b) (4) to demonstrate commercial readiness, there is no documentation identifying the reasons for the breach of the container closure integrity of the non-integral vials that were rejected prior to incubation. A summary is given below:

Media Fill Number	Number of defects observed as non-integral vials during (b) (4) visual inspection	Type of defect	Reference in the Batch Master Record

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	Satheesh Thomas, Investigator - Dedicated Drug Cadre	X Satheesh Thomas Investigator - Dedicated Drug Cadre Signed By: Satheesh Thomas -S Date Signed: 08-28-2018 11:23:27	8/28/2018

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(b) (4)	08	04 vials type of defects not recorded	129-136

OBSERVATION 2

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically,

Investigations for the below listed Out of Limits (OOL) for environmental monitoring in Suite (b) (4), used in the manufacture of (b) (4) is incomplete.

OOL NO.	Grade	Type of monitoring	Result	Limit	Product manufacturing (Yes/ No)	Activity
M-EM/18/072	C	Active air sampling	(b) (4) cfu/m3	≥ (b) (4) cfu/m3	No	Cleaning
M-EM/18/086	C	Active air sampling	(b) (4) cfu/m3		No	Cleaning
M-EM/18/079	C	(b) (4)	(b) (4) cfu/plate	≥ (b) (4) cfu/plate	No	Cleaning
M-EM/18/041	B	Personnel monitoring	(b) (4) cfu/plate	≥ (b) (4) cfu/plate	No	Cleaning and Sanitization

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M-EM/18/042	B	Personnel monitoring	(b)(4) cfu/plate		No	Cleaning and Sanitization
M-EM/18/043	B	Personnel monitoring	(b)(4) cfu/plate		No	Cleaning and Sanitization
M-EM/18/050	B	Personnel monitoring	(b) cfu/plate		No	Cleaning and Sanitization
M-EM/18/058	B	Personnel monitoring	(b)(4) cfu/plate, (b)(4) cfu/plate		No	Cleaning and Sanitization
M-EM/18/065	B	Personnel monitoring	(b)(4) cfu/plate		No	Cleaning and Sanitization
M-EM/18/069	B	Personnel monitoring	(b)(4) cfu/plate		No	Cleaning and Sanitization
M-EM/18/073	B	Personnel monitoring	(b)(4) cfu/plate		No	Cleaning and Sanitization
M-EM/18/080	B	Personnel monitoring	(b) cfu/plate		No	Cleaning and Sanitization
M-EM/18/081	A	Settle plate	(b)(4) cfu/plate	≥ (b)(4) cfu/plate	No	Assembling
M-EM/18/068	B	Surface monitoring	(b)(4) cfu/plate	≥ (b)(4) cfu/plate	No	Cleaning and Sanitization

OBSERVATION 3

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Employees engaged in the manufacture, processing and packing of a sterile small volume parental drug product, lack the training and experience required to perform their assigned functions.

Specifically,

a) Per SOP entitled: "*Qualification and requalification of Visual inspectors", PK-002-00, Effective:01/12/2017*, the acceptance criteria for qualifying a visual inspector is listed below. During the inspection on 08/20/2018, I had randomly picked a qualified visual inspector with initials (b) (6) to perform visual inspection of the visual inspection test kit containing a sample set of (b) (4) vials, used to qualify visual inspectors. However, the aforementioned visual inspector failed to meet the below listed acceptance criteria that is required to qualify visual inspector.

Acceptance Criteria	Result
Total Quantity of Defective Containers (Not Less than (NLT) (b) (4))	(b) (4)
Total Quantity OF Good Containers (NLT (b) (4))	(b) (4)
Acceptance Criteria NLT (b) (4) % (Critical Defect)	(b) (4) %
Acceptance Criteria ≥ (b) (4) % of total defects (other than critical)	(b) (4) %
False reject rate ≤ (b) (4) % (Good Vial)	(b) (4) %

b) Per SOP entitled: "Manual Visual Inspection of filled and sealed containers", SOP Number: PK-004-00, Effective Date:01/10/2017, defects such as "(b) (4) and black Particles" for small volume parental, liquid vial ((b) (4)), are classified as critical defects. Per the current SOP entitled: "Manual Visual Inspection of filled and sealed containers", Document

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Number: 2261-SOP-PK-00005, Version 2.0, Effective Date:03/19/2018, for small volume parental, liquid vial ((b) (4)), black particles is classified as critical defects and (b) (4) Particles has been re-classified as a major defect. The re-classification of (b) (4) particles in the current SOP, is not scientifically justified. Furthermore, during my inspection, a qualified visual inspector failed to meet acceptance criteria for being qualified visual inspector (see aforementioned Observation 3-a)

OBSERVATION 4

Failure to follow established and approved Standard Operating Procedures.

Specifically,

SOP entitled: "*Procurement, receipt, storage, and handling of* (b) (4) *microbial cultures and re-hydrating fluid*", Document Number :2261-SOP-QC-00090, Effective Date:05/10/2018,Version 2.0, Section 6.0 (G) reads in parts: "*** (b) (4) received lot of (b) (4) culture shall be checked for its purity, which is to be done by colony morphology and characteristics, gram staining and microbial identification through (b) (4) as per SOP No.:2261-SOP-QC-00121***".However, all microbial cultures used for the growth promotion test has not been verified for its purity.

OBSERVATION 5

Investigation invalidating an Out of Specification (OOS) during the real-time stability studies is not scientifically justified.

Specifically,

For (b) (4) , Lot number (b) (4) , (b) (4) , there was an Out of Specification (OOS) for particulate matter at 183 days (real- time study). The OOS was invalidated and the investigation reads in parts: "*** due to lack of cleanliness of the test tubes, aluminum foil and the test environment

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***". However, there is no history of cleaning in any of the aforementioned areas, except for the environment, for real-time stability studies performed on other (b) (4) batches. The investigation lacks any scientific rationale as to why the aforementioned OOS related to real-time stability was invalidated.

***DATES OF INSPECTION**

8/20/2018(Mon), 8/21/2018(Tue), 8/22/2018(Wed), 8/23/2018(Thu), 8/24/2018(Fri), 8/25/2018(Sat), 8/27/2018(Mon), 8/28/2018(Tue)

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