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	10/20/2022-10/29/2022* FEI NUMBER 3014362214

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Bhaskar Krishna Arumugam, Managing Director and CEO

FIRM NAME	STREET ADDRESS
Maiva Pharma Private Limited	No 32 Sipcot Industrial Complex, Phase I
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Hosur, Tamil Nadu, 635126 India	Sterile 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 WE OBSERVED:

OBSERVATION 1

Appropriate controls are not exercised over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.

Specifically,

A- during the manufacturing process documents are printed out from computerized systems and attached to the batch manufacturing records. However, the soft copy of the record is not stored. For example,

a. (b) (4) (equipment # (b) (4) (b) (4) used in Line (b) (4) captures data for temperature, humidity and differential pressure for the manufacturing of sterile products.

b. Environmental Monitoring System (EMS) used in Line (b) (4) captures data for temperature, humidity and differential pressure for the manufacturing of sterile products

B- Your firm does not back up files for the following equipment

a. (b) (4) (equipment # (b) (4) used in Line (b) for (b) (4) g of sterile products

b. (b) (4) (equipment # (b) (4) and the (b) (4) (equipment # (b) (4)) used in Line (b) (4) for (b) (4) production parts and equipment for the production of sterile products. (b) (4) ((b) (4) equipment # (b) (4) used in Line (b) (4) used for (b) (4) vials

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(b) (4) sterile products

c. (b) (4) used in Line (b) used for (b) (4) filling operations.

d. (b) (4) used in Line (b) (4) used for (b) (4) vials during (b) (4) filling operations.

C- Your firm has equipment that are used by employees during production and / or processing sterile products where employees are using common user names and shared passwords. Examples of equipment are as follows:

a. Line (b) (b) (4), equipment # (b) (4) (b) (4) equipment # (b) (4) equipment # (b) (4) (b) (4) equipment # (b) (4) (b) (4) equipment # (b) (4), (b) (4) equipment #'s (b) (4)

b. Line (b) (b) (4) equipment # (b) (4) and (b) (4) (b) (4) equipment # (b) (4)

D- (b) (4) to is used to monitor (b) (4) (b) (4) (b) (4) . (b) (4) (b) (4) The (b) (4) has been in place since September 2015, which has been subject to an initial design qualification (DQ) and subsequent installation and operational qualification (I/OQ). The DQ states "The purpose of this document is to qualify the appropriate design and performance requirements for procurement of the (b) (4) (b) (4) to meet the URS and Purchase order requirement includes, for example, the Engineering, Production and Quality Assurance departments are to "Verify the DQ document with URS and PO" and/or "Review of DQ with respect to URS and PO" and "Review & Approval, Authorization of DQ and clearance for proceeding to next stage", respectively. The Assistant General Manager of Engineering, the Assistance General Manager

of Production and the Assistance General Manager of Quality Assurance confirmed that there is no URS for the (b) (4)

E- The "Validation Master Plan for Computerized Systems" document number Maiva/VMP/CSV/001-V01 define User Requirement Specification (URS) as "A requirement specification that describes what the equipment or system is supposed to do, thus containing at least a set of criteria or conditions that have to be met." Despite not having a URS for the (b) (4) the September 2015 OQ Report, document number Val/Rep/Prod/OQ (VP/Prod (b) (4) (b) (4) evaluation and conclusions report that the (b) (4) has been qualified and (b) (4) performance meeting the acceptance criteria. Based on the above results review it concluded that the (b) (4) can be implemented for routine (b) (4) " The report is approved by the Validation Team Members i.e., Production, Engineering, Quality Control and Quality Assurance.

F- The (b) (4) requires the use of a password with regards to configuration setting, time & date settings, (b) (4) time settings, (b) (4) settings, alarm indication status, copy memory and print & download memory. The Senior Executive of Production explained that there can be up to (b) (4) individuals that can use the (b) (4) . The Senior Executive of Production and the Senior Manager of IT confirmed that there is no password for the (b) (4) (b) (4)

G- There is a permanent change management (PCM) document number PCM/001/22/045, dated 09 Mar 2022, that describes a proposed change i.e., "It is proposed to replace the new hard disk for (Maiva/QC-INS/2T-001) HPLC System with a reason for the change is due "Hard disk failure has been identified" and "Based on the QA Assessment the following actions shall be proposed - Based on the evaluation the hard disk has to be replaced." From 15 Mar 2022 to 20 Oct 2022 there were 119 HPLC analyses that consisted, for example, of Assay, Related Substances and Preservative Content of various finished drug products manufactured in Line #(b) and Line #(b)

Regarding the installation of a new hard drive, the Senior Executive IT, Senior Manager of IT and the Assistance General Manager Quality Assurance confirmed that there has been no validation performed for the HPLC System.

H- There are (b) (4) legacy systems that include for example the (b) (4) (b) (4) and (b) (4) system for example (b) (4) (b) (4) (b) (4) systems The Assistance General Manager of Quality Assurance confirmed that these systems rently comply with the established requirements described in the Validation Master Plan for Computerized Systems" document number Maiva/VMP/CSV/001-V01.

I- The VMP for Computerized Systems defines and establishes the requirements regarding the computer access via the use of an individual password there is a "common password" that is used by multiple individuals, for example there are (b) (4) ndividuals that can access the (b) (4) (b) (4) individuals that can access the (b) (4) (b) (4) ls that can access the (b) (4) The Senior Executive of IT and the Assistance General Manager o med there are no provisions and/or language within their policies and procedures that allows or approves the use of a "common password".

J- (b) (4) system is used to (b) (4) (b) (4) for example, from (b) (4) (b) (4) (b) (4) ılity Test. The (b) (4) system can be remotely accessed by the manufacturer of the (b) (4) System. The Assistance General Manager of QC Microbiology, the Senior Executive IT and the Assistance General Manager Quality Assurance confirmed they do not know the extent of the vendor's remote monitoring capabilities and/or knowledgeable if the (b) (4) process parameters and the electronic raw data has been compromised.

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K- The "Validation Master Plan for Computerized Systems" document number Maiva/VMP/CSV/001-V01 establishes the requirements for all computerized bases systems. The Assistance General Manager of QC Microbiology, the Senior Executive IT and the Assistance General Manager Quality Assurance confirmed there is no language in the VMP that allows or approves remote access to the computer-based systems.

OBSERVATION 2

Equipment used in the manufacture, processing, packing or holding of drug products is not of adequate size to facilitate operations for its intended use and cleaning and maintenance.

Specifically,

A- Cleaning validation is conducted in accordance to SOP/QA/GEN/047, 'Cleaning Validation', with effective date August 10, 2022. The cleaning validation for Line (b) is conducted report QPR/QC/CV/EA003-027/21/122, dated September 11, 2021. In reviewing the report (page (b) (4) states (b) (4) (b) (4) There are no microbiological and / or chemical cleaning evaluations performed for the aseptic manufacturing lines from where the products are aseptically filled (b) (4)) and up to the end of the process. Once the vials are filled, they remain open for approximately (b) (4) mm (approximately (b) (4) feet) before the vials get stoppered.

B- The initial validation for disinfectant (b) (4) efficacy study was performed on March 23, 2018 for the aseptic Line (b that consisted of taking (b) (4) samples from the vial filling room. A second study was conducted on October 20, 2020 that consisted of taking (b) (4) samples from the vial filling room. Your firm did not provide any rationale for the redu ing. On page 4

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of the validation study, it states, "The purpose of the protocol is to determine the disinfectant (b) (4) efficacy, while applying with (b) (4) disinfectant solution, when a (b) (4) in conjunction with (b) (4) ge 21, section 14.6 states "Placeme emical indicators at the w se location will be helping to access the reach ability of the (b) (4) to all the locations of the room and the same will be representative for the respective ro o assure microbial contamination." However, the chemical indicator locations that are selected include the (b) (4) LAF and the (b) (4) LAF, which do not appear to be the worst-case location.

C- The "Validation of Disinfectant (b) (4) Efficacy Study on Clean and Controlled Environments" document number QD/PQ/QC/20/20-21-RV01 dated 8/8/19 concludes that the concentration of (b) (4) % of (b) (4) with a contact time of (b) (4) is an effective surface infectant. However, the disinfectant process consists of (b) (4) rocess, which the (b) (4) manufacturer's recommendations as follows i.e., (b) (4) (b) (4) The Assistance General Manager of QC Microbiology confirmed that the aforementioned efficacy study did not include an evaluation of a (b) (4) process.

D- The disinfectant efficacy study included test coupons that consisted of a variety material of construction. However, the Assistance General Manager of QC Microbiology confirmed the study did not include an evaluation of, for example, (b) (4) (b) (4)

E- A mobile LAF cart is used to transfer (b) (4) material and parts to the Grade A aseptic filling (b) (4) RABS. The mobile LAF mately (b) (4) mm (b) (4) ft (W)] x (b) (4) mm (b) (4) ft (D)] x (b) (4) mm (b) (4) ft (H)] and the LAF cart is positioned e Grade B area and placed adjacent to the (b) (4) RABS fill equipment. There is inadequate space available to

perform the various manual transfer operations of sterile material into the Grade A interior of the (b) (4) RABS.

OBSERVATION 3

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

Specifically,

A-The "Procedure for Off Line NVPC Monitoring at Maiva Facility" document number SAOP/QA/Gen/048 establishes the Non-Viable Particle Count (NVPC) monitoring, the monitoring frequency and the NVPC acceptance limits for the classified manufacturing areas (i.e., Grade A, B, C & D). The procedure establishes for example, the frequency for Grade A areas is performed on an (b) (4) for "All LAF, (b) (4) (Other than filling zone established for the Grade B "All Sterile area". For Grade C & Grade D classified areas the monitoring frequency is on a (b) (4) (b) (4) base. The Assistance General Manager of Quality Assurance confirmed there is no rationale for the NVPV monitoring frequency.

B-The above frequency is applicable for the mobile laminar air flow (LAF – Grade A) cart that is used to transfer, for example, sterile fill equipment parts, (b) (4) stoppers, environmental monitoring materials and related materials that are used during the aseptic filling processing (Line #(b) & Line #(b)).

C-Regarding particle [Nonviable particle (NVP)] monitoring, there is no particle monitoring performed for the Grade A (ISO 5) (b) (4) RABS (Line #(b) (4) & Line #(b) or for the Grade A biological safety cabinet that is used for USP Sterility Tests.

D-Aseptic vial filling operations are performed in manufacturing room #(b) (4). The manual transfer operations consist of manually transferring material from the mobile LAF cart into the restricted access barrier (b) (4) RABS), which is performed in a Grade B classified area. There is no NVPC monitoring performed within the Grade B area to assure that the established acceptance criteria are achieved.

E-The (b) (4) process is performed in the (b) (4) RABS, with the (b) (4) vials at approximately (b) (4) nm ((b) (4) ft) away from the nearest (b) (4) (b) (4) The area between the (b) (4) and the (b) (4) RABS is partially blocked by the (b) (4) stopper equipment and (b) (4)

F-For Line #(b), the particle monitoring device is located in the Grade B area i.e., the (b) (4) of the aseptic filling line. The particle monitoring device is not located in the Grade B area where there is a greater number of personnel activities that are performed during the routine aseptic filling process.

G-The "Monitoring and Recording of (b) (4) for All Clean Rooms" document number SOP/PROD/FIL/003 establishes the procedure for monitoring of (b) (4) (b) (4) The air pressures are monitored on a routine base. In addition, "All the identified critical area (b) (4) monitoring is carried out by using the (b) (4) parallel with manual monitoring. These (b) (4) will monitor the (b) (4) continuously and print out the data (b) (4) " The Assistance General Manager of Production and the Assistance General Manager of Quality Assurance confirmed that the (b) (4) (b) (4) records are not reviewed and approved by either the production or QA departments.

H-The "Trending of Temperature, Relative Humidity, (b) (4) Offline NVPC Monitoring and Viable Particle Count Trend Review for Line (b) (4) & Line (b) (4) (Sep 2021 to Feb 2022)" document number QD/PQ/PROD/21/053-PV (b) (4) establishes the purpose "…is to analyze

the observed data through trending of results obtained for Temperature, Relative humidity, (b) (4) offline NVPC monitoring and Viable particle count taken from the production critical processing areas of (Line (b) (4) and Line (b) (4) for the month of SEP 2021 to FEB 2022." The Assistance General Manager of Production and the Assistance General Manager of Quality Assurance confirmed that the (b) (4) data obtained by the (b) (4) is not part of, or included with, the (b) (4) analysis and trends.

I-The firm's conducted a preventive maintenance for Line (b), Facility Maintenance Record dated July 19, 2022, as stated in item # (b) (4) "(b) (4) . According to section 3.2 of Standard Operating Procedure SOP/ENGG/GEN/002, document titled 'Facility Maintenance' with effective date March 25, 2022, which states "(b) (4) (b) (4) (b) (4) " However, a gap was observed on the electrical conduit piping in Line-(b) that leads directly into the ceiling. We observed an approximate ¼ inch opening between the wires in the pipe that is locate in the ceiling's (b) (4) . With the Assistant General Manager of QA we detected the air coming out of the opening from the aseptic area and into the (b) (4) area. The rest of the wiring in the pipe was covered with silicon.

J-Light fixture located in the (b) (4) area leaked air from the aseptic area and into the (b) (4) on the (b) (4) side of the fixture. This was confirmed by Assistant General Manag

K-Light fixture located in the (b) (4) area leaked air from the aseptic area and into the (b) (4) on the (b) (4) side of the fixture. This was confirmed by Assistant General Manager of QA

L-On October 21, 2022 we observed what appeared a mold like growth in the Line (b) (4) aseptic room.

For example, three sections in the lower bottom of the fill line near the floor; Two area in line (b) (4) i.e., one on top of the viewing panels and one on the bottom of the viewing panels.

M-On October 26, 2022 during manufacturing of batch (b) (4) (b) (4) we witnessed three (3) employees improperly gowned in the aseptic, Line (b) (4) manufacturing area i.e.,

1-Employee # (b) (6), Microbiologist was observed changing (b) (4) settle plates in the Grade A area.

2-Employee # (b) (6) Microbiologist was observed changing agar settle plates in the Grade A area.

3-Employee # (b) (6), Operator Production was observed in Grade B area working on the operating the line.

All of the employees had an approximate ¼ inch gap between the bottom of the goggles and headdress of the aseptic gown.

OBSERVATION 4

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile did not include adequate validation of the aseptic and sterilization process.

Specifically,

A- The "Aseptic Process Simulations" document number SOP/QA/GEN/044 establishes for example, that "The purpose of the aseptic process simulation is to demonstrate the capability of the aseptic processing operation and environment to produce sterile drug products consistently and it is a simulation of the entire aseptic process, which substitutes a microbiological growth

medium for a sterile drug product." The procedure establishes "Whenever contamination exists in a media fill run, it should be considered indicative of a potential sterility assurance problem, regardless of run size." The aseptic processing simulation (APS) batch manufacturing records document the removal of (b) (4) mls from the initial (b) (4) -micron filtrated sterile solution vessel located in the (b) (4) Grade A LAF (b) (4) . The (b) (4) ml of microbial growth media is not included with f, the media filled vials that are incubated, which prevents the ability to ascertain that the (b) (4) ml microbial growth media is not contaminated and to demonstrate that the aseptic process simulation is acceptable.

B- The 2020, 2021 & 2022 APS batch manufacturing records (BMR) document media filled vials that are rejected during the (b) (4) process. However, the BMRs do not document an assignable cause for rejecti d glass vials, which precludes the company from demonstrating that they met their acceptance criteria.

C- The Assistance General Manager of QC Microbiology confirmed that there are no incubation records for the media fill vials.

D- The "Entry and Exit Procedure for Production Block" document number SOP/Prod/Gen/006 established that personnel are required to "Remove the street foot wear along with socks and keep them in the locker/respective shoe rack provided." It is during this time that personnel are standing bare foot within the same area where they were standing with their street shoes. Prior to moving to the Grade D and Grade C areas personnel are required to don gowning attire that is commensurate with their respective work responsibilities that include donning factory shoes. As personnel don the subsequent gowning attire, they will stand bare foot within the Grade D and Grade C areas. The Assistance General Manager of QC Microbiology confirmed there is no environmental monitoring (EM) performed to determine that the bare feet in the Grade D and Grade C areas are not a source for microbial contamination.

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OBSERVATION 5

The batch production and control records are deficient in that they do not include identification of persons performing each significant step in the operation.

Specifically, the batch manufacturing record and the APS batch manufacturing records do not document the individuals that perform the work. Rather, the accomplishment of the various manufacturing steps is documented by an individual who observes the work that was being performed.

OBSERVATION 6

Air is recirculated to production areas, without adequate measures to control recirculation of dust.

Specifically,

A- The "Air Flow Visualization (Smoke Study) in Clean Rooms and Associated Clean Air Devices" document number SOP/QA/VAL/007 establishes "The test and visualization is to confirm that the airflow direction and its uniformity conform to the design and support the intended use of clean rooms, LAFs and clean air devices." The standard procedure defines unidirectional airflow as an "Air stream which has a defined direction." In addition, "Airflow patterns should be evaluated by smoke test to confirm the unidirectional air flow and also for presence of non-unidirectional air flow or eddy currents during operations if any. Routine operations under the HEPA Filter shall be mimicked for the same." The airflow visualization did not include an evaluation of the Grade A laminar air flow units that are used for the aseptic (b) (4) process performed in room #(b) (4) no "in operation" (dynamic) airflow visualization performed for the mobile transfer cart #(b) (4) (a Grade A interior environment) that is used to transfer sterile material from the Grade A (b) (4) (room # (b) (4) to the aseptic filling RABS in manufacturing room (b) (4) (Line #(b) , and no "in operation" airflow evaluation for performed for the Grade A (b) (4) RABS.

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B- The airflow visualization studies (videos) did not include all of the aseptic manual interventions that are commonly performed during the routine aseptic filling process and the manual aseptic connection process performed during the (b) (4) micron (b) (4) process.

C- The airflow visualization studies document numerous instances where the unidirectional airflow and impact upon the airflow could not be observed due to either the angle and position of the video camera, or due to an obstructive view caused by the filling equipment and/or due to a lack of smoke over the personnel's arms & hands.

D- The acceptance criteria include, for example, (b) (4) (b) (4) are not desirable in the Grade A area and should be identified and eliminated, when possible." However, there is no airflow visualization (smoke studies) performed for the Grade A (b) (4) to assure that the acceptance criteria are achieved.

E- There is an additional acceptance criterium e.g., (b) (4) (b) (4) The air flow visualization studies did not include an evaluation to assure that the (b) (4) RABS during the manual transfer operations that occur when using the mobile LAF cart.

F- The airflow visualization studies did not include an evaluation to verify that the (b) (4) (b) (4) and/or an evaluation of (b) (4) that commonly occur during routine manufacturing operation

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