Gmail

Gautham H <gauthamh@aurigaresearch.com>

[WARNING: MESSAGE ENCRYPTED]FDA FMD145 EIR

2 messages

Angela.Glenn@fda.hhs.gov <Angela.Glenn@fda.hhs.gov> Tue, Aug 30, 2022 at 6:27 PM
To: gauthamh@aurigaresearch.com

Dear Gautham H. :

Attached to this email is a copy of the establishment inspection report (EIR) for the inspection completed at your establishment located at Plot No 136, 6th Cross, Bengaluru, Karnataka conducted on 07/22/2022 by or on behalf of the U.S. Food and Drug Administration (FDA). The Agency concluded that the inspection is "closed" under 21 C.F.R.20.64(d)(3), and therefore is releasing a copy of the EIR to you.
The copy provided to you is the narrative portion of the report. It may contain redactions in accordance with the Freedom of Information Act (FOIA) and 21 CFR part 20. You may request additional information under FOIA. For more information on how to make a FOIA request click here
The attached EIR is password protected to secure your firm's proprietary information and/or trade secrets. The password needed to open and/or print the document will be forwarded to you in a separate e-mail. You may need to check your Spam folder if you do not see the password in your e-mail inbox. If you did not receive the password in a separate e-mail, please contact the POC below.
If there are any questions about the released information, feel free to contact the Acting DCB at 1-214-253-4995 or ORAPHARM2ACTINGDCB@FDA.HHS.GOV.

FDA U.S. FOOD & DRUG ADMINISTRATION

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Gautham H <gauthamh@aurigaresearch.com> Fri, Oct 14, 2022 at 4:23 PM
To: Chethan <chethan@aurigaresearch.com>

fyi
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SUMMARY

Initial and preapproval inspection of this contract testing facility, initiated by inspection request Operation ID 223364, FACTS ID 12174222, Trip 2022-072D, was conducted in accordance with Compliance Program 7346.832, Pre-Approval Inspections. There is no previous inspectional history for this firm.

This inspection included coverage of the following application product that names Thinq Pharma-CRO [redacted] as the application holder [redacted] Auriga Research Private Limited as the contract testing facility that performs [redacted]

The current inspection included a review of portions of the Quality, Facilities & Equipment, and Laboratory Control systems. Coverage included review of training records, equipment calibration/qualification, equipment cleaning and use logbooks, and analytical worksheets.

On 07/22/2022, a close out meeting was held with management and selected employees. A Form FDA 483, Inspectional Observations, was issued to Mr. Guatham H., General Manager for the following [redacted]

[redacted]

Results of this inspection were emailed to Foreign Pre-Approval Manager, CDER Surveillance, and CDER PAI Program on 07/25/2022. Profile code LMN was added and updated as acceptable. Firm management was cooperative and there were no refusals. No samples were collected.

ADMINISTRATIVE DATA

Inspected firm:	Auriga Research Private Limited
Location:	Plot No 136, 6th Cross Bengaluru, Karnataka, 560022 India
Phone:	(++91)80-35229344
FAX:	
Mailing address:	Plot No 136, 6th Cross Bengaluru, Karnataka, 560022 India
Email address:	gauthamh@aurigaresearch.com
Dates of inspection:	7/20/2022-7/22/2022
Days in the facility:	3
Participants:	**Nicole E Knowlton, Investigator - GDUFA**

On 07/20/2022 credentials were presented to Mr. Guatham H., General Manager, who identified himself as the most responsible person for the site. Dr. Saurabh Arora, Managing Director, confirmed Mr. Guatham H. was the most responsible person for the firm.

On 07/22/2022, a Form FDA 483, Inspectional Observations, was issued to Mr. Guatham H., General Manager.

Mr. Guatham H., General Manager, stated there is no fax line at the firm.

No representatives from a foreign regulatory body were present during this inspection.

HISTORY

Dr. Saurabh Arora, Managing Director, explained his father, Mr. Vijay Kumar Arora, Chairman, started Arbro Group in 1985. He stated the business originated with raw material and finished product trading and product testing started in 1990. There are 1500 employees across six laboratories and two manufacturing facilities and thirty regional offices. The manufacturing facilities produce

tablets, capsules, and syrups (nonsterile oral) for the domestic market as well as Ghana, Afghanistan, and Nigeria. This site was established in 2013 and performs microbiological and chemical testing for pharmaceuticals, food, cosmetics, and nutraceuticals. Business hours are 9am-6pm Monday through Friday and alternate Saturdays. The laboratory is staffed seven days a week: the first shift is 7am-4pm, the general shift is 9am-6pm and the second shift is 1pm-10pm. There are 153 employees at the site: 20 in quality assurance, 77 in quality control, 12 in microbiology, 2 in information technology, and 25 in marketing. The firm has future plans to open an office in the US or partner with a US laboratory.

Exhibit 1 is the firm's Welcome PowerPoint presentation.

Post inspectional correspondence including FMD-145 should be addressed to:
Mr. Guatham H., General Manager
Auriga Research Private Limited
Plot No. 136, 6th Cross
Bengaluru, Karnataka, 560022, India
gauthamh@aurigaresearch.com

JURISDICTION (PRODUCTS MANUFACTURED AND/OR DISTRIBUTED)
Auriga Research Private Limited conducts testing on [redacted] to be used in production of [redacted] intended to be distributed in the United States and is subject to the Food Drug & Cosmetic Act. **Exhibit 2** is [redacted] received for analysis.

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED
Exhibit 1, page 11 shows the Management Team.

Dr. Saurabh Arora, Managing Director: he explained his responsibility to this site is resource planning, approving resources and plans, approving documentation, instituting quality policy, reviewing top level documents, participating in management review meetings and internal audits. He stated he is located at their Delhi facility but is on site once a quarter and more often if required. Dr. Arora was present each day of the inspection and participated in the inspectional walkthroughs, discussions, and daily wrap up meetings. He was present at the closeout meeting and committed to corrections to the observations listed on the Form FDA 483, Inspectional Observations. He has been with the firm since 2007 and reports to Mr. Vijay Kumar Arora, Chairman.

Mr. Gautham H., General Manager: he was the main point of contact for the inspection. Mr. Gautham H. identified himself as the most responsible person for the site and Dr. Saurabh Arora, Managing Director, confirmed this. He stated he is responsible for site operations including the management part of business development, profit and losses, equipment, administrative activities, allocation, and operations. Mr. Gautham H. was present each day of the inspection and participated in the inspectional walkthroughs, discussions, and daily wrap up meetings. He accepted the Form FDA 483, Inspectional Observations, and promised corrections and a written response to FDA. Mr.

Gautham H. stated he has been with the company for twelve years and has been in his current position the entire time. He stated reports to Dr. Saurabh Arora, Managing Director.

Ms. Anitha, Technical Manager Microbiology: stated she is responsible for workload planning and reviewing and approving standard operating procedures and standard test procedures, deviations, change controls and out of specification investigations. Ms. Anitha explained she assigns the work to the analysts as well as a lot of media to use to conduct the testing. She was present each day of the inspection, participated in the inspectional walkthroughs, discussions, and daily wrap up meetings and was present at the closeout meeting. Ms. Anitha provided most of the information obtained during the inspection. She stated she has been with the firm six years and in her current position the entire time. Ms. Anitha reports to Mr. Kishor Kumar K. R., General Manager Technical.

Mr. Kishor Kumar K. R., General Manager Technical: he stated he is responsible for planning routine activities for microbiology and chemistry, identifying resources for activities and coordinating with management to obtain the resources, and handling issues such deviations and complaints. He was present each day of the inspection, participated in the inspectional walkthroughs, discussions, and daily wrap up meetings and was present at the closeout meeting. Mr. Kishor Kumar K. R. stated he has been with the firm for two years and eight months and in his current position the entire time. He stated the heads of quality control and quality assurance report to him. Mr. Kishor Kumar K. R. reports to Mr. Gautham H., General Manager.

Mr. Gurunatha Kini, Senior Manager Quality Assurance: he stated he is responsible for the quality management system, approving standard operating procedures and standard test procedures, approval of the certificates of analysis, compliance for client audits, and handling change control, deviations, out of specifications and audits. Mr. Gurunatha Kini explained he has been with the firm and in his current position for seven months. He reports to Mr. Kishor Kumar K. R., General Manager Technical.

Ms. Sruthi Medkal, Team Leader for Microbiology: she stated she is responsible for performing bacterial endotoxin and sterility testing, preparing standard operating procedures and standard test procedures, training personnel, work planning, and validations. In addition to the above listed responsibilities, Ms. Sruthi Medkal stated in the absence of the Technical Manager Microbiology, she is responsible for the microbiology department. She stated she has been with the firm for over five years and in her current position for two months. Ms. Sruthi Medkal reports to Ms. Anitha, Technical Manager Microbiology.

FIRM'S TRAINING PROGRAM

Mr. Gurunatha Kini, Senior Manager Quality Assurance, explained training is based on the employee's job description and a microbiology degree is required to work in the microbiology area. Personnel are required to pass an assessment after training on the procedures. Analysts must perform a qualification which is based on the task they will be performing.

Procedure Qualification of Microbiologist ARLBL/QA/SOP-085 effective 21/4/2022 governs the

qualification program. Personnel must pass the qualification test prior to performing routine analysis. The technical manager reviews the results and gives their recommendation to the quality manager. If the employee fails the qualification, they will undergo retraining and a qualification exercise before they again attempt qualification. The qualification is a monograph test that is quantitative. The requalification period is every two years.

I reviewed Microbiologist Validation for MLT/Water Test for Navyashri P. performed 2/3/2021.

I reviewed the training for Ms. Sruthi Medkal, Team Leader for Microbiology, including her training on bacterial endotoxin testing. The qualification date was 23/9/2020 and was approved by the quality assurance manager 6/10/2020.

I verified Mr. Sidharth P.K.'s training on procedure Good Documentation Practices dated 12/5/2022 and noted he passed the assessment with 12/12 correct. I also verified Ms. Anitha participated 3/12/2021 in a group training on procedure Good Documentation Practices. Mr. Gurunatha Kini explained the group training was part of the annual training, so no assessment was given; the assessment is only given for new employees.

MANUFACTURING/DESIGN OPERATIONS

Auriga Research Private Limited performs microbiological and chemical testing for pharmaceuticals, food, cosmetics, and nutraceuticals. The coverage of this inspection was limited to [redacted]

The three primary inspectional objectives of the PAI program were covered during this inspection and a summary of the findings are detailed below.

Objective 1: Readiness for Commercial Manufacturing

Coverage included a review of the firm's Quality, Facilities and Equipment, and Laboratory Control Systems. I observed the facilities and equipment, and reviewed documents pertaining to [redacted] including training records, equipment calibration/qualification, equipment use logbooks, and analytical worksheets. I observed no issues with the firm's readiness for commercial manufacturing.

Objective 2: Conformance to Application

I reviewed the application along with a review of the firm's current activities. I reviewed and verified the analytical methods were consistent with the descriptions contained in the drug application.

Objective 3: Data Integrity Audit

I audited the analytical worksheets against the media preparation, autoclave, and incubator logbooks to authenticate the data. Data was complete and accurate.

Quality

The firm has established a Quality Unit comprised of Quality Assurance and Quality Control that is responsible for reviewing, approving, and implementing procedures and analytical methods; reviewing and approving change controls; releasing analytical results; and conducting investigations. The quality department is responsible for reviewing investigations, including deviations and out of specification reports.

The dates on the documents are written as day, month, year. The firm's master procedures are paper copies and subject to review every three years.

Dr. Arora stated management review meetings are held annually and quality issues including but not limited to findings of audits, improvements and customer complaints are discussed.

Procedure Deviation Control ARLBL/QA/SOP-019 issue 08 1/7/2022 details the procedure for deviation handling. A deviation is defined as a departure from standard operating procedures or specifications resulting in non-conforming material processes or where there have been unusual or unexplained events which have the potential to impact on quality, system integrity or personal safety.

I reviewed the deviation logbooks for 2021 and 2022 [redacted] observed no deviations related to this drug substance.

[redacted]

OOS procedure
Procedure Handling of Out of Specification (OOS) Results in Microbiology Laboratory ARLBL/MB/SOP-070 06/07/2022 defines an OOS as a test value that falls outside the specification or acceptance criteria established in Regulatory submission, Official Compendia or In-House Company specification. The procedure explains the Phase IA as a review of the testing procedure by the microbiologist to eliminate the possibility of laboratory introduced error or contamination and Phase 1B requires an in-depth investigation. The Phase 1B investigation includes but is not limited to a review of the documentation and logbooks, exam of equipment used, and environmental conditions.

If there is no assignable root cause in Phase 1B the sample is retested in triplicate by a different analyst. If there is assignable root cause in Phase 1B the sample is retested two times with two different analysts, if the original sample is in the laboratory. If the sample is exhausted, they will contact the client and request an additional sample. Once the testing is complete, they will determine if the results are out of specification.

Section 4.2.7.19 of the procedure requires the analyst to immediately notify the technical manager microbiology in the case of a bacterial endotoxin failure and notify the client within twenty-four hours of the OOS.

Dr. Arora stated there were no OOS for [redacted] reviewed the OOS logbook and observed no OOS for [redacted]

Change Control
Procedure Change Control ARLBL/QA/SOP-016 issue 07 effective 01/07/2022 details the procedure to control and manage all changes that can impact quality and safety of products. This procedure applies to changes in all systems and documents. Changes are classified as critical, major and minor. Assessments are made by the department heads which determines the impact. Change controls are approved by quality assurance and time frames for closure is based on the classification.

I reviewed the change control logbook and noted the changes are documented in the logbook with description of the change, affected department, date, number and completion date. I did not observe any changes that related to [redacted]

Sample Management
Sample management is handled on the basement level- and the samples are received by customer support. The samples arrive with a Test Request Form which includes the name of the product, batch number, method of analysis and the specifications. The samples are taken to the booking area. The samples and are logged into the Y Laboratory Information Management System (YLIMS). The samples are assigned an Analytical Report (AR) number and a barcode and are placed in trays based on the sample type and held in access-controlled cabinets until they are taken to the required testing area by the booking personnel. The Booking area maintains room temperature conditions and there are chambers for 5°C±3°C and -20°C±5°C.

To enter the microbiology area, a lab coat, hairnet, and shoe covers are required, and hands must be sanitized with 70% isopropyl alcohol. The samples are stored in plastic baskets in the Balance Room and Sample Storage Area. The baskets are identified for samples to be analyzed, analyzed, and by type of sample such as sterility, pharmaceutical, food, ayurvedic and cosmetic.

Facilities and Equipment
I conducted a walkthrough inspection of the facilities on July 20, 2022, including the sample receipt area, sample storage area and the microbiology laboratory. I did not observe issues with the number of laboratory staff and equipment relative to the volume and type of testing performed. I did not observe laboratory instrumentation without identification or out of calibration. I did not observe cross-contamination issues with the layout of the laboratories and flow of samples and personnel. I did not observe concerns with lighting, cleanliness, and organization.

Exhibit 3 is Photo DSCN0619 showing the ground floor facility layout and **Exhibit 4** is Photo DSCN0620 showing the basement floor layout.

The controlled area in the microbiology laboratory contains a sample preparation room, sterility room and a biosafety room and requires appropriate gowning to enter. Firm personnel explained the sample preparation room contains three laminar air flow hoods (LAFH) that are used for sample

preparation; the LAFHs are Class A, and the surrounding area is Class B. The other rooms are Class C and each contains a LAFH which are also Class A.

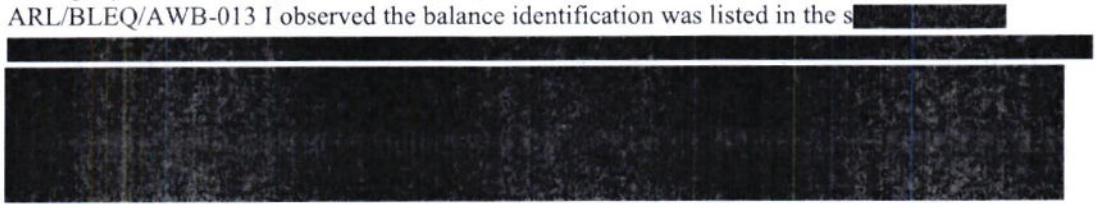
Sample Preparation Area
Sterile garments are required to enter the controlled microbiology areas. Samples are received from a pass box and are prepared under a laminar air flow hood (LAFH). The three LAFHs were identified, and stickers showed the equipment was current with their qualifications. Samples move through a separate pass box to the incubation room. There are Biosafety and Sterility Rooms within the controlled area.

Discard Area
The firm maintains a separate room with an autoclave for decontamination of media. The media is autoclaved and sent away as medical waste.

Equipment Calibration
Firm personnel explained every instrument/equipment is calibrated externally annually and in-house verifications are performed monthly for balances, incubators, and micropipettes and quarterly for the digital colony counters.

Balances
The firm utilizes numerous balances throughout the microbiology laboratory. Daily, weekly and monthly verifications are performed in-house and the balances are calibrated annually by a third-party vendor. Firm personnel explained they have three sets of standard weights used to verify the balances. I reviewed Logbook Format for Weighing Balance Monthly Calibration and noted the weight verification was performed from 500mg to 2000g. I asked if the firm had 500g, 1000g, and 2000g weights and was told yes. I requested the weights and noted the weights were not documented in the Balance Monthly Calibration for July 2022 **(FDA 483 Observation 1C)**.

During my review of Logbook for Weighing Balance Daily Calibration for balance ID: ARL/BLEQ/AWB-013 I observed the balance identification was listed in the s[redacted]



Laminar Air Flow Hoods
I reviewed Re-Performance Qualification Protocol of Aseptic Area ARLBL/AVP/001 effective 28/6/2022 which was performed by a third-party servicer except for the airborne viable count which was performed in-house with settle plates. I reviewed the environmental monitoring logbook titled Area Qualification by Settle Plate Method, Air Sampler Method and Swab Method and noted the date of exposure for the plates was 29/6/2022 and the report was dated 4/7/2022. I noted all the samples tested met specification.

pH Meter
Calibration of the pH meter is conducted daily prior to use. A three-point calibration is performed using 4.0, 7.0, and 10.0 buffer solutions. Calibration and use are documented. I verified the buffer solutions were within expiration.

Incubators
The firm maintains numerous incubators with various conditions. Firm personnel explained the incubators that would be utilized for the micro limit test.

- Incubator ARL/BLEQ/BOD-006 with a set temperature of 22.5°C is used for media storage
- Incubator ARL/BLEQ/BIC-001 with a set temperature of 32.5°C is used for pre-incubation
- Incubator ARL/BLEQ/BOD-001 with a set temperature of 22.5°C is used for sample inoculation for bacteria and fungi
- Incubator ARL/BLEQ/BIC-006 with a set temperature of 37°C is used for E. coli
- Incubator ARL/BLEQ/BIC-008 with a set temperature of 32.5°C used for micro limit testing

The incubators are qualified annually by a third-party service, and I reviewed the most recent qualification of an incubator used for micro limit testing; incubator ARL/BLEQ/BIC/008 which has a set temperature of 32.5°C. I reviewed the following documents:

- Installation Qualification of Bacteriological Incubator RSECA-428A8 IQ/RSECA-428A2 R. 0 approved 6/7/2022 covering Incubator 428A81999 performed by Rising Sun Enterprises. Firm personnel showed documentation correlating Incubator 428A81999 and incubator identification ARL/BLEQ/BIC/008.
- Operation Qualification of Bacteriological Incubator RSECA-428A8 OQ/RSECA-428A8 R. 00 approved 6/7/2022
- Performance Qualification of Bacteriological Incubator RSECA-428A8 PQ/RSECA-428A8 R. 00 approved 6/7/2022
- Temperature mapping Performed by TempSense Bangalore Calibration Certificates for ARL/BLEQ/BIC-008 Cert TI/22/S140-02 dated 14/07/2022

When I reviewed Temperature mapping Performed by TempSense Bangalore Calibration

[redacted]

Additionally, I reviewed Qualification of Bacteriological incubator SN 76720813 ID ARL/BLEQ/BIC-001 which was installed 24/8/2013 and calibration certificate dated 11/11/2021 cert TI/21/107-04 from TempSense. The chamber was qualified across four temperatures from 30.0°C-42.5°C.

Autoclave
The firm utilizes a Manchin Fabrik steam sterilizing autoclave (ARL/BLEQ/AC-002) to sterilize media, utensils, and garments. There are two generators on site that will automatically initiate within thirty seconds of a power outage. Autoclave cycle times have been validated. Firm personnel

explained the autoclave is operated manually; they manually set the vacuum and temperature, turn on the steam, open the exhaust, and turn on the filter air in. Dr. Saurabh Arora, Managing Director, explained the vendor provided the values for the vacuum and chamber pressure. He stated these values were utilized in the operational qualification and are the set values listed in the procedure for everyday use. Operation and Instruction Manual for H.P.H.V. Steam Sterilizer SR. NO. 4303/2437/13 provides the instructional set up the firm follows in their procedure for operation of the autoclave.

Procedure Operation of Horizontal Autoclave ARLBL/MB/SOP-097 Issue 10 effective 5/7/2022 details the procedure for operating the horizontal autoclave. Section 5.3 of the procedure provides specific instructions for HPHV Operation (High Pressure High Vacuum) cycle which Ms. Anitha, Technical Manager Microbiology, stated was used for the garments and accessories load. She stated the standard process listed in Section 5.3.2 is used for media.

The logbook for Autoclave Sterilization Record documents the load details, lot number, sterilization hold time, pressure, temperature, the person that operated the load, and the person that reviewed the entry [redacted]

I reviewed Instruments/Equipment Preventative Maintenance Schedule for 2022 and Preventive Maintenance Record Logbook and noted the preventive maintenance was conducted as scheduled. The most recent preventive maintenance conducted by the service vendor Sree Ganesh Enterprises was 13/7/2022 and was a routine check that included but was not limited to checking the chamber condenser valve adjustment, joint leakage, and electrical terminals.

Third-party TempSense conducts the annual qualification and calibration, Sree Ganesh Enterprises conducts preventative maintenance every six months and in-house preventative maintenance is conducted every six months. All calibrations and qualifications were current.

I reviewed Validation Protocol for Autoclave (Horizontal) Equipment ID ARL/BLEQ/AC-002 Protocol No.: ARL/VP/AC-01/05 effective 28/12/2020 which included heat distribution studies for and empty chamber, media and garment loads, heat penetration with garment and media loads, a Bowie Dick test and leak test. Biological indicator strips with Bacillus Stearothermophilus were used in the validation; [redacted] Chemical indicator strips are used in routine autoclave runs, as per their current procedure, and documented for traceability. Firm personnel explained biological indicators are not used in routine autoclave runs but are used every three months as a check.

[redacted]

[redacted]

I reviewed Validation Protocol for Autoclave (Horizontal) ARL/VP/AC-01/06 effective 17/12/2021 for autoclave ARL/BLEQ/AC-002. The qualification included heat distribution and heat penetration studies, a Bowie Dick test and leak test. During my review of this qualification, I noted the load patterns were more clearly defined than the previous qualification and that chemical indicators and steam tape were used in each load.

I reviewed the most recent calibrations for the gauges and the temperature display on the autoclave and the stopwatch used to verify the exhaust time.

Media Preparation
The firm has established written procedure Preparation, Pre-Incubation, Growth Promotion Test, Reconciliation and Storage for Microbiological Media ARLBL/MB/SOP-076 Issue No. 09 effective 05/07/2022 which governs the handling of the firm's media.

The firm prepares dehydrated media in-house for use in microbial limit tests, they do not purchase any prepared media. I reviewed the Media Preparation Logbook and noted firm personnel document the name of the media, in-house batch number, quantity prepared, quantity weighed, pH prior to sterilization, and pH post sterilization. The printout from the pH meter is attached to the media preparation logbook.

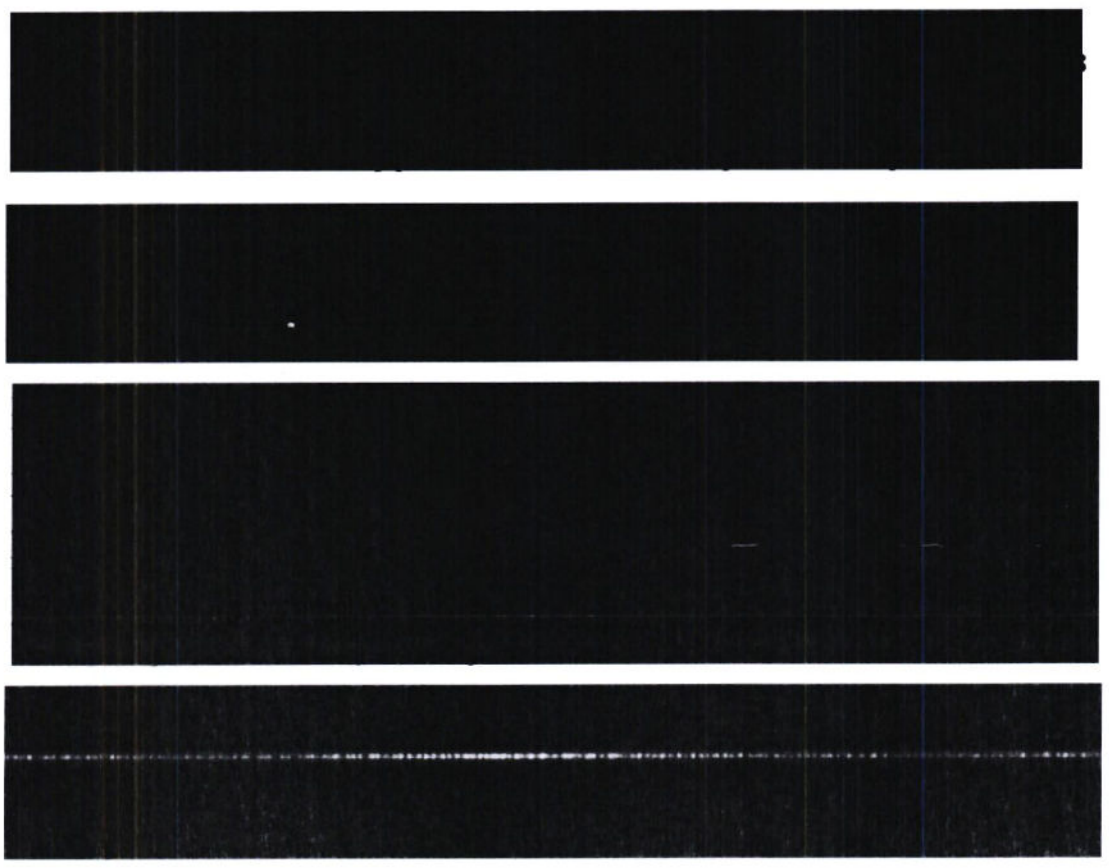
I verified the media preparation for a recent batch of prepared media, R2A (Reasoner's 2A agar) including the logbook entries, the autoclave load, sterilization cycle and pH values.

Prepared media is held in the Incubation and Observation Room; during the inspection walkthrough on July 20, 2022, I observed a rack with prepared liquid media and prepared media plates in an incubator.

Procedure Growth Promotion Test for Microbiological Media ARLBL/MB/SOP-195 issue 03 effective 05/07/2022 states every new batch of dehydrated media is to be tested for growth promotion. I verified the firm conducts growth promotion on each batch of media prepared. They use positive and negative controls, and all controls are ATCC. Ms. Anitha, Technical Manager Microbiology, explained they are using the microorganisms listed in USP 61 for growth promotion. I noted the controls were listed on the test packets for [redacted]

Sterile Garments and Accessories
Sterile garments are worn in the controlled microbiology areas such as sample preparation. The sterile garments are stored in a cupboard in the gowning area prior to entering the controlled microbiology area. During the inspection walkthrough of the facility on July 20, 2022, the technical

manager microbiology removed the autoclaved garments from the cupboard and placed them on the crossover bench. [redacted]



Procedure Cleaning, Sterilization and Destruction of Clean Room Gown and Accessories and Washing of Lab Shoes ARLBL/MBS/OP-272 issue 01 effective 5/7/2022 provides instructions for handling gowns and accessories. Section 4.3.1 states to destroy the garments after one hundred sterilization cycles and if any damages are observed, whichever is earlier. Check the tick mark on the respective gown cover on the gowns.

I asked how they determined the garments could withstand one hundred sterilization cycles and Ms. Anitha stated they are following the recommendation of the gown manufacturer for the number of uses. I reviewed a letter from Sunbeam Creations dated 21/7/2022 stating the garments are manufactured with GMP Cleanroom Standards and can be autoclaved for 100+cycles.

I asked if there was a documented check of the garments for wear and tear and Ms. Anitha stated they are only making the mark on the gown cover. I asked who was responsible to make the mark and she stated it was the person operating the autoclave. I reviewed how the firm placed a tick mark on the garments as well as documentation showing the last shipment of garments received.

[redacted]

Bacterial Endotoxins and Micro Limit Test
Exhibit 2 is a list of [redacted] and Result showing the sample receipt date, booking date, report number, sample name, client name, parameters, result, pass/fail, and upper limit. Dr. Saurabh Arora, Managing Director, explained the list was printed from the YLIMS system and includes all the samples that have been received [redacted]

Exhibit 10 is Report BG202201100065 showing the micro limit testing.
Exhibit 11 is Report BG202205130168 showing the micro limit testing.
Exhibit 12 is Report BG202107150090 showing the bacterial endotoxin testing.

The firm performs bacterial endotoxin testing by gel clot. No bacterial endotoxin testing was being performed during the inspection. I verified the firm maintained current LAL Water and it was stored at appropriate conditions. The firm utilizes a Neolab heating block for incubation of LAL assays. Calibration of the heating block was current. The firm has established procedure Receipt, Storage and Handling of LAL Test Kits and Operation of Heating Block SRLBL/MB/SOP-092 effective 11/7/2022 which provides guidance for storage and handling of the LAL water and use of the heating block.

I reviewed the analytical worksheets with the corresponding logbooks [redacted] BG202107150090 including media preparation, sterilization, chemical indicator used, controls, incubators and incubation periods.

Laboratory Water
Veero Labwater (ARL/BLEQ/VWP-002) generates the water used in the microbiological laboratory. Procedure Operation of Veero Labwater ARLBL/MB/SOP-259 issue 02 effective 05/07/2022 provides instructions for operation and monitoring. The specification for pH is 5-7 and conductivity is <1µs/cm. I observed the parameters were within specification.

OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE

Observations listed on form FDA 483

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

Specifically,

A. Your firm has not established a written procedure describing the steps to check the garments for damage prior to sterilization. The garments are worn in the controlled microbiological areas including the Sample Preparation Room. These areas are used or have the potential to be used in the handling [redacted] drug substance samples.

B. [redacted]

C. [redacted]

D. [redacted]

E. Weighing balance ARL/BLEQ/AWB-013 is used in the preparation of media for microbial limit testing and this testing is performed on [redacted] samples as listed in the drug application for ANDA 216724 [redacted]

F. There was no documented review of the temperature mapping of incubator ARL/BLEQ/BIC-

008 (32.5°C) performed by third party vendor 7 July-8 July 2022.This incubator may be used in microbial limit testing for [redacted]

Reference: 21 CFR 211.22(d)

Supporting Evidence and Relevance:
Please note that 1E is not an observation; it is a statement of the use of the balance.

Evidence 1A:
Exhibit 13 is Procedure Cleaning, Sterilization and Destruction of Clean Room Gown and Accessories and Washing of Lab Shoes ARLBL/MBS/OP-272 issue 01 effective 5/7/2022. There is no requirement in the procedure to check the garments for cuts, holes, deterioration or fraying.

I spoke to a junior microbiologist who stated she checks for damages such as cuts and stains on the garments. I asked if there was a specific procedure she follows [redacted]

Evidence 1B:
Exhibit 14 is Photo DSCN0625 of Logbook for Weighing Balance Daily Calibration showing on 06/07/2022 the value under 5g was originally 4.90. This value was struck through, initialed, and dated but no reason was listed why the value was changed to 5.0. [redacted]

Exhibit 14 also shows this entry was checked by the Microbiology Manager.

Exhibit 15 is procedure Good Documentation Practices ARLBL/QA/SOP-003 issue 09 effective 01/01/2022. **Page 6** Section 5.3.4 requires a brief comment why the change is required.

I reviewed the training record showing employee SPK was trained 12 May 2022 on the current version (issue 09) of procedure Good Documentation Practices ARLBL/QA/SOP-003 and the training for the Microbiology Manager who was trained on the previous version (issue 08) of the procedure 3 December 2021. No changes have been made to the procedure regarding the requirement to provide a brief comment why the change was made.

Evidence 1C:
Exhibit 16 is Photo DSCN0628 is Logbook Format for Weighing Balance Monthly Calibration showing the weight verification performed on Balance ARL/BLEQ/AWB-013 used in media preparation. The weight verification shows it was conducted using weights 500mg-2000g. The identification of the standard weight set used was ARL/BLEQ/WHB-004. This weight set contains weights from 1mg-200g.

Exhibit 17 is Photo DSCN0633 showing the exterior of standard weight set ARL/BLEQ/WHB-004.

Exhibit 18 is Photo DSCN0634 showing the weights in set ARL/BLEQ/WHB-004 from 1mg-200g.

Exhibit 19 is Photo DSCN0635 showing the exterior of the 500g weight ARL/BLEQ/WHT-003.

Exhibit 20 is Photo DSCN0636 showing the top of the 500g weight ARL/BLEQ/WHT-003.

Exhibit 21 is Photo DSCN0642 showing the 2000g (ARL/BLEQ/WHT-001) and 1000g (19935) weights.

Exhibit 22 is Photo DSCN0643 showing the top of the 2000g and 1000g weights.

Evidence 1D:
Exhibit 14 is Photo DSCN0625 of Logbook for Weighing Balance Daily Calibration showing the entries were not checked July 11-13, 2022.

Exhibit 23 is Photo DSCN0626 of Logbook for Weighing Balance Daily Calibration showing the entries were not checked July 14-19, 2022.

I asked if there was a required frequency the Logbook for Weighing Balance Daily Calibration was supposed to be checked and was told it was supposed to be checked at the time of performance.

Exhibit 24 is Procedure Operation & Calibration of Weighing Balance ARLBL/MB/SOP-243 Issue 02 effective 01/01/2022. This procedure does not specify a frequency for the Logbook for Weighing Balance Daily Calibration to be checked.

Evidence 1F:
Exhibit 25 is Temperature mapping Performed by TempSense Bangalore Calibration Certificates for ARL/BLEQ/BIC-008 Cert TI/22/S140-02 dated 14/07/2022. Firm personnel identified this document as the record of the temperature mapping performed on Incubator ARL/BLEQ/BIC-008.

I observed there was no signature on the records indicating they were reviewed. I asked if there was a report for the temperature mapping and was told no.

I explained to firm management they should indicate the documentation has been reviewed. I stated I normally see a protocol showing the work to be performed including the acceptance criteria or the expected outcome and a report that assess the results and reports the outcome and conclusions. Firm management stated they understood.

Discussion with Management:
Each point had been previously discussed at length during the inspection and Mr. Guatham H. and Dr. Arora stated they understood the observation.

OBSERVATION 2

[redacted]

Specifically, there second person verification of the manual control settings on the autoclave at the time of use. The manual settings include temperature and vacuum for the sterilization cycle and temperature and time for the drying cycle. Firm personnel explained the cycle information is documented at the end of the cycle.

The autoclave is utilized to sterilize media used in the microbial limit testing and garments worn in the controlled microbiological areas including the Sample Preparation Room. These areas are used or have the potential to be used in the handling of [redacted] drug substance samples.

Reference: 21 CFR 211.63

Supporting Evidence and Relevance:
Exhibit 26 is Operation and Instruction Manual for H.P.H.V. Steam Sterilizer SR. NO. 4303/2437/13 which provides the instructional set up the firm follows in their procedure for operation of the autoclave.

Firm personnel explained the autoclave is operated manually; they manually set the vacuum and temperature, turn on the steam, open the exhaust, and turn on the filter air in.

I asked how they verify the required vacuum hold period is complete. Firm personnel stated after the sterile hold start time, the pressure and temperature are documented, and the checker verifies after the cycle is completed. I asked if there is a second verification at the time of performance for the autoclave settings and cycles and firm personnel said Ms. Anitha, Technical Manager Microbiology, confirmed this.

Discussion with Management:
Each point had been previously discussed at length during the inspection and Mr. Guatham H. and Dr. Arora stated they understood the observation.

GENERAL DISCUSSION WITH MANAGEMENT

On 07/22/2022, a Form FDA 483, Inspectional Observations, was issued to Mr. Guatham H., General Manager. The following personnel were also present: Dr. Saurabh Arora, Managing Director; Mr. Kishor Kumar K. R., General Manager Technical; Mr. Gurunatha Kini, Senior Manager Quality Assurance; Mrs. Anitha Technical Manager Microbiology; Mr. Chethan B. N., IT Manager; and Mr. Veeresh Kumar M. S., Technical Manager. Each point had been previously discussed at length during the inspection and Mr. Guatham H. and Dr. Arora stated they understood.

I explained that the observations listed on the FDA 483 are my observations of objectionable conditions found during the inspection and are not intended to be an exhaustive listing. After further review by the Agency the conditions listed may be considered to be violations of the Food Drug & Cosmetic Act or other statutes. Legal sanctions available to FDA may include withhold on an application, re-inspection, Warning Letter, or detention/refusal of product upon entry to the United States. FDA may take action without further notice. Mr. Guatham H. and Dr. Arora stated they understood the warning, promised corrections and a written response within fifteen business days.

I provided the Foreign FDA 483 Response Handout.

ADDITIONAL INFORMATION

Original USB

Various documents (identified in the Exhibits Collected section) were provided on a USB drive on July 19, 2022. A working copy was burned onto a DVD-R. The original copy (USB drive) was maintained in my custody until it was placed into a Form FDA 525 (envelope) and officially sealed with an FDA 415a. The officially sealed original copy is **Exhibit 27**. The unsealed working copy disc is filed with the unlabeled exhibits and attachments.

Exhibit 28 is the Original DVD containing photos taken during the establishment inspection. The DVD was placed in a Form FDA 525 (envelope) and officially sealed with an FDA 415a. The unsealed working copy disc is filed with the unlabeled exhibits and attachments.

Accommodations

Accommodations were at Taj Yeshwanthpur 2275, Tumkur Rd, Yeshwanthpur Industrial Area, Phase 1, Yeswanthpur, Bengaluru, Karnataka 560022, India, which is approximately forty-five minutes from Rajiv Gandhi International Airport. The hotel was comfortable with restaurants on site and room service available. Wi-Fi was included in the accommodation charges. Transportation from the airport to the hotel was provided by the firm. The firm provided daily transportation between the hotel and the site.

EXHIBITS COLLECTED

1 Exhibit 1 Firm's Welcome PowerPoint presentation, 18 pages, 18 pages
2 Exhibit 2 Sample Details showing the [redacted]
3 Exhibit 3 Photo DSCN0619 showing the ground floor facility layout, 1 page, 1 page
4 Exhibit 4 Photo DSCN0620 showing the basement floor layout, 1 page, 1 page
5 Exhibit 5 Photo DSCN0650 showing sterilized bags of garments with condensation, 1 page, 1 page
6 Exhibit 6 Photo DSCN0651 showing sterilized bags of garments with condensation, 1 page, 1 page
7 Exhibit 7 Photo DSCN0652 showing the autoclave and a portion of the rack with the accessories, 1 page, 1 page

8 Exhibit 8 Photo DSCN0653 showing autoclaved accessories with condensation in the bags, 1 page, 1 page
9 Exhibit 9 Photo DSCN0654 showing autoclaved accessories with condensation in the bags, 1 page, 1 page
10 Exhibit 10 Report BG202201100065 showing the micro limit testing,13 pages, 13 pages
11 Exhibit 11 Report BG202205130168 showing the micro limit testing, 12 pages, 12 pages
12 Exhibit 12 Report BG202107150090 showing the bacterial endotoxin testing, 4 pages , 4 pages
13 Exhibit 13 Procedure Cleaning, Sterilization and Destruction of Clean Room Gown and Accessories and Washing of Lab Shoes ARLBL/MBS/OP-272 issue 01 effective 5/7/2022, 5 pages, 5 pages
14 Exhibit 14 Photo DSCN0625 of Logbook for Weighing Balance Daily Calibration showing on 06/07/2022 the value under 5g was originally 4.90 and the entries were not checked July 11-13, 2022, 1 page, 1 page
15 Exhibit 15 Procedure Good Documentation Practices ARLBL/QA/SOP-003 issue 09 effective 01/01/2022, 7 pages, 7 pages
16 Exhibit 16 Photo DSCN0628 of Logbook Format for Weighing Balance Monthly Calibration showing the weight verification performed on Balance ARL/BLEQ/AWB-013 used in media preparation, 1 page, 1 page
17 Exhibit 17 Photo DSCN0633 showing the exterior of standard weight set ARL/BLEQ/WHB-004, 1 page, 1 page
18 Exhibit 18 Photo DSCN0634 showing the weights in set ARL/BLEQ/WHB-004 from 1mg-200g, 1 page, 1 page
19 Exhibit 19 Photo DSCN0635 showing the exterior of the 500g weight ARL/BLEQ/WHT-003, 1 page, 1 page
20 Exhibit 20 Photo DSCN0636 showing the top of the 500g weight ARL/BLEQ/WHT-003, 1 page, 1 page
21 Exhibit 21 Photo DSCN0642 showing the 2000g (ARL/BLEQ/WHT-001) and 1000g (19935) weights, 1 page, 1 page
22 Exhibit 22 Photo DSCN0643 showing the top of the 2000g and 1000g weights, 1 page, 1 page
23 Exhibit 23 Photo DSCN0626 of Logbook for Weighing Balance Daily Calibration showing the entries were not checked July 14-19, 2022, 1 page, 1 page
24 Exhibit 24 Procedure Operation & Calibration of Weighing Balance ARLBL/MB/SOP-243 Issue 02 effective 01/01/2022, 18 pages, 18 pages
25 Exhibit 25 Temperature mapping Performed by TempSense Bangalore Calibration Certificates for ARL/BLEQ/BIC-008 Cert TI/22/S140-02 dated 14/07/2022, 8 pages, 8 pages
26 Exhibit 26 Operation and Instruction Manual for H.P.H.V. Steam Sterilizer SR. NO. 4303/2437/13 which provides the instructional set up the firm follows in their procedure for operation of the autoclave, 35 pages, 35 pages
27 Exhibit 27 Officially sealed original USB containing electronic documents collected during the establishment inspection, 1 page, 1 page
28 Exhibit 28 Original DVD containing photos taken during the establishment inspection, 1 page, 1 page

ATTACHMENTS

1 Issued 483, 4 pages

X Nicole E Knowlton
Investigator - GDUFA
Signed By: Nicole E. Knowlton -S
Date Signed: 08-19-2022 10:56:20