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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Active Pharmaceutical Ingredient Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**M/s Arene Life Sciences Private Limited, Unit-1**
Corporate address of manufacturer	M/s Arene Life Sciences Private Limited S. R. CHAMBERS 3-58 Ramachandrapuram Hyderabad 502 032, Telangana India
Inspected site	
Name & address of inspected manufacturing site if different from that given above	M/s Arene Life Sciences Private Limited, Unit-1 Plot No. 48, 49 & 50, 209, 210 & 211, Phase-II, IDA Pashamylaram, Patancheru (M) Sangareddy Dist.- 502 307 Telangana, India
Synthetic unit /Block/ Workshop	Block B (Module II), Block E (Module I), Pilot Plant (extension of Block D)
Inspection details	
Dates of inspection	22-25 January 2024
Type of inspection	Routine GMP inspection
Introduction	
Brief description of the manufacturing activities	Arene Life Sciences Private Limited, Unit 1, is engaged in manufacturing APIs and drug intermediates for human use of various categories like analgesic, anti-retroviral, anti-hypertension, anti-viral, anti-bacterial, anti-mycobacterial, anti-coagulant, antihistamine, and anti-depressant. β-lactams are not manufactured on-site. The site has seven manufacturing blocks (MB), including one pilot plant, a solvent recovery plant, and warehouses. Additionally, there are buildings and areas dedicated to Quality Assurance, Quality Control, maintenance, EHS, and administrative offices. There is also a process development laboratory.
General information about the company and site	Arene Life Sciences Private Limited, Unit 1, was established in 2004 and has been registered under the Companies Act., 1956. The site is located at an industrial area, approximately 45km from Hyderabad and 55 Km from Hyderabad International Airport. There are two more manufacturing Units. More specifically, Unit 2 located at Choutuppal and Unit 3 located at Sadasivpet.

History	This was the second WHO Prequalification inspection. The site had also been inspected by OGYEI National Institute of Pharmacy and Nutrition, Hungary in October 2019, US FDA in February 2023 and ANVISA in June 2023. The site was periodically inspected by the national and local authorities. The last inspection by the Drugs Control Administration, Government of Telangana was carried out in June 2023.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Documents reviewed included but were not limited to: - Job descriptions for key personnel - Training - Product Quality Review - Quality Risk Management - Management Review - Complaints and Recalls - Deviation control - Change Control - OOS/OOT and investigations - Batch Release - Validation/ Qualification/ Calibration - Sampling and testing of materials - Batch processing records - Materials Management System - Purified Water System - HVAC System <u>Areas inspected</u> - Production operations with focus on concerned APIs - Warehouses - Chemical laboratory
Restrictions	N/A
Out of scope	APIs not submitted to WHO Prequalification were excluded from the scope of this inspection
WHO APIs covered by the inspection	Efavirenz Linezolid Darunavir Ethanolate Nirmatrelvir
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
BMR	Batch manufacturing record
BPR	Batch production record

CC	Change control
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EHS	Environment, Health and Safety
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification
KF	Karl Fisher
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MR	Management review
NC	Non conformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
RO	Reverse osmosis
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer

Part 2	Summary of the findings and comments (where applicable)

1. Quality management

The company had established a QMS based on Indian drug Schedule M, ICHQ7, WHO TRS No. 957 Annex 2, 21 CFR Parts 210 and 211, and EU GMP Part-II. The principles of the system were described in the Quality Manual (QM). Quality risk management was integrated into all aspects of the QMS, and the basic concepts were aligned with ICH Q9 and described in the QM. The QM provided details on the company's organization including but not limited to the responsibilities, and authorities of various levels of employees, and a description and monitoring of all QMS processes for continuous improvement. The Quality Policy and the establishment of measurable quality objectives were adequately described. Quality and Production functions were independent of each other.

Management Review

Management Review was described in a written procedure. Management review meetings were held monthly. The Head of the QA department or designee prepared the monthly and quarterly management reports including the quality events, investigations resulting from OOS/OOT, deviations, complaints and change control. The minutes of the meeting covering October 2023 were reviewed. Moreover, the CAPA annual summary report for 2023 was presented.

Quality Risk Management

The principles of QRM were described in high level, in the QM and SMF and indicated that they were applied to all GMP related operations and activities for APIs.
The risk evaluation report on nitrosamine formation during the manufacture of Efavirenz API was reviewed.

Product Quality Review

PQRs were conducted based on a written procedure for batches manufactured between January and December every year and had to be completed within three months after the set review period. The QA department was responsible for the preparation of the PQRs. At the beginning of the current calendar year a master list was prepared by using the format Annual product review/product quality review master list covering all the APIs and intermediates. The Annual PQR master list for products manufactured in 2023 was presented.
The PQR of Linezolid API for the period January to December 2023 was reviewed. Five batches were manufactured. The PQR included a review of the manufacturing process, OOS results, rejected batches, incidents/deviations, changes, validation, stability, regulatory agency deficiency letters/queries, CAPAs, CAPA of previous PQR, packaging materials, API starting materials manufacturers, yield at different stages, critical process parameters, supporting systems (PW, Nitrogen, AHU, compressed air), qualification/calibration status, and stability.
The PQR of Efavirenz API for the period January to December 2023 was also reviewed. No batch was produced in 2023. The PQR included a review of changes, recalls, returns, complaints, deviations, and ongoing stability.

Deviations

A procedure for handling deviations was in place and was discussed in detail. The procedure was applicable to all deviations from approved procedures related to manufacturing, packing, storage, and

issuance of material related to raw materials, intermediates, APIs, equipment, system test procedures, and computerized systems. Any incidents related to QC laboratory such as for example instrument breakdown or calibration failures were managed according to a different SOP, while data error corrections in completed documentation were handled separately using a dedicated procedure. Additionally, there was a procedure in place for handling incidents. Deviations had to be reported and documented within 24 hours from the time they were identified. The QA department was responsible for assigning a unique identification number. The QA department in collaboration with the affected department were responsible for conducting the root cause investigation which had to be completed within 30 days, including a check for recurrence. CAPAs were identified and proposed by the affected department and were approved and monitored for implementation by the QA department. Deviations were reviewed every six months and a report was compiled. The second half of 2023 deviation report was reviewed along with some deviation handling examples.

The observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

2. Personnel

Organization charts were in place depicting the hierarchical and administrative structures. There were separate organograms for the technical and quality operations. Quality Assurance and Quality Control departments were independent of production and were reporting to the Site Quality Head. Job descriptions for key personnel were in place. The job descriptions of the Production Shift Supervisor, the QA department Senior Manager and the QA department Deputy Manager were reviewed. Qualifications and delegation of duties were described in the procedures.

The procedure for personnel training was presented. There were several types of training including induction training, on the job training, annual GMP training and external training. The Human Resources department in collaboration with the QA department were responsible for the organization of trainings. Induction training was provided to both short-term contract workers and long-term employees. A training programme per department was prepared annually, and the training sessions were conducted by qualified trainers. The relevant qualifications, training and evaluation of the trainers were defined in the training SOP and training records were spot-checked. The 2024 list of qualified trainers was made available. The 2023 and 2024 production training programmes were presented.
The training record for the batch-to-batch cleaning procedure was reviewed.
The procedure for personnel medical examinations was discussed. A pre-employment medical check-up was conducted and after recruitment personnel were medically examined annually. A list of the medical tests was included in the SOP. There was a procedure in place defining hygiene practices on site. Food and drinks were not allowed in the manufacturing and laboratory areas. Protective clothing and gear had to be worn in the manufacturing areas and the laboratories. Personnel with open lesions/ wounds and/or feeling unwell were not allowed in the manufacturing areas.

3. Buildings and facilities

The campus consisted of several buildings and workshops. Layouts of the facilities were made available. In general, premises were constructed, designed, and maintained to suit the operations to be conducted and prevent the risk of contamination of materials and products. At large, the design of the premises was such as to minimize the risk of errors and permit effective cleaning and maintenance. There was no restrictive access to the manufacturing buildings. Personnel from different workshops could enter any

manufacturing facility.There were two warehouses and seven manufacturing blocks on the campus. The Nirmatrelvir API was manufactured in the pilot plant, on the second floor of MB-D.
Linezolid and Efavirenz were manufactured in MB-B (Module-II). The first floor included the reactors' area, a material staging area, and the HVAC system for the clean area (ground floor) and the drying area. The HVAC system consisted of three units (AHU-204, 5, 6). AHU-204 supplied 100% fresh filtered air to the crystallization and centrifuge area. The other two units provided a mixture of fresh and recirculated air to the clean area (AHU-205 drier, quarantine, milling, and sifting room, AHU-206 change room 1, change room 2, corridor, wash area, PM entry, exit room). The procedure for monitoring differential pressure (DP) across filters and cleaning the filters was reviewed. A list of AHU filters for MB-B (Module II), was in place. The AHU filters cleaning records for 2023, the schedule of cleaning for 2024 and the logbook on differential pressure of AHUs 204, 205 and 206 were spot-checked. Cleaning was performed every 3 months and in case of product change. The ground floor included the centrifuge area and the clean area. The entry to the clean area was separated from the synthetic area.
Darunavir Ethanolate API was manufactured in MB-E. The first floor included the reactors area, a dispensing room, and the crystallization area (clean area) which was accessed through a separate entry and change room. On the ground floor, there were two dyer rooms, one centrifuge and a reactor, as well as the clean area which was accessed through a separate entry.

There was one PW generation system supplying all manufacturing blocks except the laboratories.
The procedure for the operation and maintenance of the PW generation and distribution system was reviewed. Potable water was used in the generation of PW. The procured potable water was unloaded to the storage tank (30KL), chlorinated, filtered through a multi-grade filter, treated with Sodium Metabisulphite, and neutralized with NaOH. The water was then passed through a fine filter 5µm and fed to the RO membrane. The RO permeate water was then passed through the EDI, followed by a UV chamber, collected in the PW storage tank (4KL), and distributed to user points. The vent filter was replaced annually.

The observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

4. Process equipment

Reactor systems, equipment, and utilities were installed to allow reflux, distillation, cooling, crystallization, centrifugation, drying, and milling required to make the APIs of interest. The material of construction of all major equipment where the product was directly in contact was SS316/Glass Line. Tools and equipment were uniquely identified, and status labels were normally used. In general, they were maintained according to written procedures. The procedure for preventive maintenance of process equipment was presented and discussed. The procedure provided detailed instructions on performing maintenance on key equipment like the reactors, the tray dryers, the sifters, the blenders, the rotary cone vacuum driers, the centrifuges etc. The maintenance department was responsible for performing the preventive maintenance of process equipment in coordination with production personnel. The annual preventive maintenance schedule for 2023 was presented. The preventive maintenance record of the crystallizing reactor (clean area, MB-B) was spot-checked. Similarly, the preventive maintenance record of the sifter (clean area, MB-B), the GL reactor (pilot plant) and the Micron Filter (pilot plant,) were reviewed.

The procedure for batch to batch, idle and skip cleaning of manufacturing equipment was presented. Centrifuge bags were changed after every 5 API batches while for intermediates or APIs (before the final processing stage) centrifuge bags were changed every 5-10 batches. Similarly, the Micron filter cartridges were replaced after filtering 5 API batches (final processing stage) and after 5-10 batches when filtering intermediates or APIs (before the final processing stage). Additionally, filter cartridges used for filtering solvents for the final processing stage were to be changed every 15-20 batches.

The observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

5. Documentation and records

The company had established a documentation system. An overview of the documentation system hierarchy was included in the QM. The documentation system was divided into three levels: Level 1 (Quality Policy and objectives), Level 2 (SOPs, STPs, process flowchart, VMP, checklist, drawings) and Level 3 (formats that were needed to provide evidence for all activities carried out).
The procedure for the Batch Numbering System was presented. The QA department was responsible for assigning the batch number.

The observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

6. Materials management There were written procedures describing the receipt, quarantine, storage, and handling of materials, as well as procedures for sampling, testing, and approval or rejection of materials. The receipt of bulk solvents was performed in an undercover area of the tank farm. The tanker and solvent documentation were checked upon receipt. The bulk solvent was sampled and tested, and the test results were taken into account before introducing the solvent into the tank using dedicated, flexible hoses. Following mixing with the existing solvent in the tank, a new sample was withdrawn and analyzed, and a new batch number was assigned following positive test results.
There were two warehouses. On the ground floor of Warehouse-1 there were: an area dedicated to the storage of liquids in drums, a temperature-controlled room, a quarantine area, a sampling/dispensing room, a rejected material area, and a carbon room with a separate entry. The 1st floor was dedicated to solid raw materials (transferred by hoist from the ground floor) and included sampling and dispensing rooms, a hazardous material room, a rejected materials room, and a quarantine area. The 2nd floor was dedicated to intermediates including a quarantine area, an approved material area and a rejected material area. Warehouse-2 was used for solid raw materials. The ground floor included a quarantine area, an approved material area, a dispensing/sampling area, a rejected material room, and a hazardous material room. The procedure for entry and exit from the sampling/dispensing area and the usage sampling/dispensing logbook were spot-checked. The 1st floor was used for storage of packaging materials. There were separate rooms for primary and secondary packaging materials, respectively. The primary packaging material room included a sampling/dispensing area and a rejected material room. On the first floor, there was also a separate area for final processing (drying, blending, micronization) of APIs with a separate entry. The second floor included the finished product goods, including tail batches (handled as finished API batches) and an area dedicated to intermediates with a rejected intermediates room. Additionally, there was a room for rejected finished goods and for returned finished goods. Recalled batches were stored in the returned storage area.

Receipt of materials at warehouses 1 and 2 was performed based on a check list. The received materials were registered in the raw material inward register.

The procedure for sampling and release of raw materials and packaging materials was reviewed. Samples were drawn from all containers for Key Starting Materials (KSMs). However, for the KSMs received from a sister site the rule of √n+1 applied, where n was the total number of containers received. For the general raw materials, the rule of √n+1 was also applied.

The observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

7. Production and in-process controls The production operated in three shifts. In general, production operations followed defined procedures. Process flows and routes of synthesis were made available.
On the first day of the inspection, the inspection team visited the warehouses, the tank farm, and the pilot plant, where the Nirmatrelvir API was manufactured.
A procedure for product changeover was presented. The production department was responsible for initiating the changeover and ensuring the cleaning verification and line clearance. The head of the QA department was responsible for reviewing and approving the product changeover. Centrifuge bags, filter bags, filter cartridges and flexibles hoses from the previous product had to be disposed and new ones had to be used. There was a provision to clean production rooms and equipment after every ad hoc or periodic maintenance.
In the morning, of the second day, the inspectors visited the first floor of MB-B where production of Linezolid Stage-II was on-going. Additionally, the inspection team visited the clean area (Grade D) of MB-B where the crystallization process of Linezolid Stage III took place. Spot checks on BMRs of on-going processes were made.
In the afternoon of the second day, the inspectors visited the clean area of MB-E, where the crystallization of Darunavir Stage II was on-going. The inspectors observed the filtration and distillation steps and checked the relevant BMR and equipment logbooks.

The observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

8. Packaging and identification labelling of APIs and intermediates
The APIs were packed in translucent polythene bags under Nitrogen, tied with a strip, then placed in a secondary black polythene bag under Nitrogen, tied with a strip and finally placed in a high-density polyethylene container.
The procedure on Control of labels and seals was reviewed. The product labels for the "in-house release" were prepared by the QA department including details such as product name/chemical name, batch No, manufacturing date, retest/expiry date, drum No, gross/tare/net weight, storage conditions, and drug license number.
The product labels for commercial dispatch with QR codes were generated by validated software. Upon receipt of the request for product release labels, the QA authorized personnel printed the required labels. The QA personnel removed the approved/under test labels and pasted the in-house release labels. Upon receipt of the dispatch request, in-house labels were replaced by commercial ones. After completion of labelling, the containers were sealed by self-locking SS tamper proof seals.

The observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

9. Storage and distribution

A procedure for the transportation of finished products was available. The QA department was responsible for ensuring that the materials were transported as per customer requirements. The storage and transport temperature restrictions were based on documented stability /hold time studies. Transport companies were identified by the logistics department. The template of the technical/quality agreement for contract transportation was presented. A checklist for transport vehicle was filled out before dispatch.

The observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

10. Laboratory controls

The Quality Control (QC) operations were independent from production. The QC laboratory was divided in different sections and included several areas/rooms like the instrumentation laboratory, the wet chemistry laboratory, the retention sample room, the sample preparation room, the glassware cleaning room, the chemicals storage room, the stability room (including the stability chambers 25ºC/60%, 30ºC/75%, 30ºC/65%, 40ºC/75%), the balance room, and the microbiological laboratory. The analytical laboratory was equipped with instruments like Karl Fischer Titrator, pH meter, Gas Chromatography, Conductivity meter, High Performance Liquid Chromatography, LCMS, Polarimeter, Analytical balances, UV spectrophotometer, and FTIR. Spot checks on usage, calibration and qualification records were made. Similarly, examples of analytical records for Nirmatrelvir and Darunavir were reviewed in detail.

Reference and Working Standards

There was a procedure in place describing the storage dispensing and inventory management of Reference and Working Standards. Records for the use of Darunavir Ethanolate WS and Nirmatrelvir WS were reviewed in detail.

Analytical method validation

A procedure for analytical method transfer validation was in place. The procedure defined the steps for the transfer of analytical methods and the acceptance criteria between sending (SU) and receiving unit (RU). The analytical method transfer validation for related substances by HPLC and for assay for the API Nirmatrelvir was discussed.

OOS results

A procedure for handling OOS results was in place. The procedure was applicable to all types of analyses. The 2023 OOS results logbook was presented. Examples of OOS results handling were reviewed.

Retention samples.

Retention samples of key starting materials, intermediates, and finished APIs were stored in a designated storage area in the chemical laboratory. The inventory of the retained samples was in place. In case of

withdrawal of a retention sample, the quantity to be used was registered in the consumption record. The temperature and relative humidity were monitored on-line.

The observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

11. Validation

The procedure for the qualification of equipment was presented. The procedure defined responsibilities and provided definitions for URS, DS, FAT, SAT, DQ, IQ, OQ and PQ. Each stage of qualification had to be completed, checked, and approved before the following stage could be initiated. Equipment re-qualification was performed every 5 years ±45 days and after any major change. An annual plan for re-qualification was prepared and monitored monthly. After completion of the re-qualification, the equipment card was updated. Examples of equipment qualification/requalification were reviewed.

HVAC clean area - MB-B (Efavirenz, Linezolid)

The HVAC qualification of the clean area of MB-B was discussed. AHUs 204, 205 and 206 supplied air to the MB-B clean area. The air was circulated through a series of filter (10µm and 5µm) and finally passed through HEPA (0.3µm). The PQ protocol and report executed by a contractor were reviewed in detail. The PQ included the following tests: the air velocity and number of air changes per hour, HEPA filter integrity test, Differential pressure, temperature/humidity, particle count test, recovery test, and air flow direction.

Cleaning Validation

Cleaning verification and validation were carried out according to a written procedure. Cleaning methodologies were adequately described. The QA department was responsible for the preparation of the cleaning validation protocol in coordination with the concerned department.

The observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

12. Change control

A procedure for managing changes was in place. The scope covered all GMP areas affecting product quality, including but not limited to materials, facilities, equipment, processes, specifications, analytical methods, and quality documentation. Changes were categorized as major or minor and temporary or permanent. The initiating department raised a requisition for change control. The change request was forwarded to the Quality Assurance department for logging and approval. A change implementation review was done within 60 days of the initial approval date. Change control trend analysis was performed every six months.

The change control logs for 2023-2024 were presented, and examples of change management were reviewed.

The observations related to this section have been adequately addressed, and the implementation of CAPA will be verified at the next inspection.

13. Rejection and re-use of materials

The company had separate procedures for reprocessing and reworking. Reprocessing was handled through the change control system and there was a provision to place samples on stability depending on

the reprocessing activity and production stage. The procedure defined the stages when reprocessing could take place and the level of testing to be performed and the supporting documentation to be generated. Examples of reprocessed batches were reviewed.
Reworking involved subjecting an intermediate or an API that did not conform to standards or specifications to one or more processing steps that were different from the established manufacturing process. Before reworking a batch, an investigation had to be performed to identify the root cause of the non-conformance. A batch production record (BPR) had to be developed and approved, defining the steps to be followed. The batch had to be tested according to specifications, and additional testing could take place if appropriate. Provisions to place reworked batches in stability were described in the relevant procedure. A reworked batch was issued with a different batch number according to the SOP.

There was a procedure in place for the recovery of solvents. Specifications for the recovered solvents had to be established. These solvents could only be used for the same stage or the previous production stage as per the validated process. Solvents used during equipment cleaning were excluded from recovery. A retest date of one year was assigned to all recovered solvents. The specifications for recovered solvents were checked.

The observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

14. Complaints and recalls
Handling of complaints was performed according to a written procedure. Market complaints were received by the Business Development department or the QA department and had to be registered within 24 hours. The QA department was responsible for reviewing the complaint information and categorizing the complaint according to its criticality (critical, major, or minor). The QA department in collaboration with other departments would validate the complaint and carry out the investigations within given timelines depending on the criticality of the complaint. The QA department was also responsible for checking the implementation and effectiveness of CAPA. The Business Development department was responsible for communicating to the customer the outcome of the investigations and CAPA.

A procedure for the timely withdrawal of defective APIs/intermediates from the market was in place. The Head of Quality and the Head of Technical in consultation with the Head of Regulatory Affairs were responsible for deciding and initiating the recall. A thorough investigation had to be conducted. The recall notification had to be sent out to customers and regulatory authorities within one day of the recall decision. Recalls were categorized into three classes (I, II, or III) based on potential impact to patient health. The procedure also included a protocol for performing mock recalls. The last mock recall was performed in December 2021 and was reviewed in detail.

The observations related to this section have been adequately addressed and the implementation of CAPA will be verified at the next inspection.

15. Contract manufacturers (including laboratories)
None of the production steps for any of the intermediates or APIs under WHO Prequalification were contracted out. Some analyses were contracted out (e.g., XRD, particle size distribution, elemental analysis, NMR).
The technical agreement with one of the contract laboratories was reviewed.

There was a procedure in place for qualifying suppliers. For the initial evaluation of potential suppliers of API starting materials, a questionnaire was used along with testing of 3 samples originating from different batches of the raw material to be procured, and an evaluation on nitrosamine formation, where applicable. After successful evaluation by the QA department, the vendor was assigned a provisional vendor status and was included in the relevant list. The QA department would then make arrangements to audit the vendor. After a successful outcome of the audit, the vendor was included in the approved vendor list and was periodically evaluated.

Part 3	**Conclusion – Inspection outcome**

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, ***M/s Arene Life Sciences Private Limited, Unit-1***,located at ***Plot No. 48, 49 & 50, 209, 210 & 211, Phase-II, IDA Pashamylaram, Patancheru (M), Sangareddy Dist.- 502 30, Telangana, India*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines for APIs.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR, were addressed by the manufacturer, to a satisfactory level, prior to the publication of the WHOPIR.

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 4	**List of WHO Guidelines referenced in the inspection report**

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eight Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2.
   Short name: WHO TRS No. 986, Annex 2
   https://www.who.int/publications/m/item/trs986-annex2

2. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2.
   Short name: WHO TRS No. 957, Annex 2
   https://www.who.int/publications/m/item/annex-2-trs-957

3. WHO guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report. Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 9.

Short name: WHO TRS 1010, Annex 9
https://www.who.int/publications/m/item/trs1010-annex9

4. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3.
Short name: WHO TRS No. 1033, Annex 3
https://www.who.int/publications/m/item/annex-3-trs-1033

5. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4.
Short name: WHO TRS No. 929, Annex 4
https://www.who.int/publications/m/item/annex-4-trs-929

6. WHO good practices for pharmaceutical quality control laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-seventh Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052), Annex 4.
Short name: WHO TRS No. 1052, Annex 4
https://www.who.int/publications/i/item/9789240091030

7. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3.
Short name: WHO TRS No. 957, Annex 3
https://www.who.int/publications/m/item/trs957-annex3

8. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty Second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8.
Short name: WHO TRS No. 1010, Annex 8
https://www.who.int/publications/m/item/Annex-8-trs-1010

9. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Third Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1019), Annex 2.
Short name: WHO TRS No. 1019, Annex 2
https://www.who.int/publications/m/item/trs1019-annex2

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
Short name: WHO TRS No. 1044, Annex 4

https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/production/trs1044-annex4-technology-transfer-in-pharmaceutical-manufacturing.pdf

11. WHO good manufacturing practices for sterile pharmaceutical products. Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
Short name: WHO TRS No. 1044, Annex 2
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