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Prequalification Unit Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Quality Control Laboratory

Part 1	**General information**		
Inspected laboratory details			
Name of Laboratory	Vimta Labs Ltd, Life Sciences Facility		
Address of inspected laboratory site	MN Park (Formerly Alexandria Knowledge Park) Plot No 5, Genome Valley, Shamirpet Mandal Hyderabad, Medchal-Malkajgiri District, Telangana 500 101, India		
Inspection details			
Dates of inspection	18 to 20 January 2023		
Type of inspection	Routine		
Introduction			
Brief description of testing activities	**Type of Analysis**	**Finished Products**	**Active pharmaceutical ingredients**
	Physical/ Chemical analysis	pH, Color test, Polarimeter, Density, Loss on Drying, Water Content, Disintegration, Dissolution, Uniformity of dosage units (mass content), Friability, Tablet Hardness, Particulate matter test, melting point, XRD, DSC, FT Raman, TGA, PSA, AAS, Particulate count, Water activity, Osmolality, Viscosity, Zetasizer, GC MS.	pH, Density, specific optical rotation, viscosity, Loss on drying, Melting Point, Water Content, Heavy metals, Sulphated ash, Acid insoluble ash, Acid value, Iodine value, Ester value, Acetyl value, Peroxide value, XRD, DSC, FT Raman, Particle Size Analyzer, AAS, TGA, Zetasizer, GC MS.
	Identification	HPLC (UV Vis), GC, (FID, ECD), TLC, UV-VIS Spectrophotometry, IR, AAS, XRD, DSC, FT Raman, PSA, Zetasizer, LCMS, IC, SDS-PAGE, Western blot, Isoelectric focusing, Intact mass, Charge variant analysis,	HPLC (UV Vis), GC (FID, ECD), TLC, UV-VIS Spectrophotometry, IR, FTIR, AAS, Chemical reaction, XRD, DSC, FT Raman, Zetasizer, LCMS, IC, SDSPAGE, Western blot, Iso-electric focusing, Intact mass,

		Glycan profiling, Disulphide mapping, Bioassays, GC MS.	Charge variant analysis, Glycan profiling, Disulphide mapping, Bioassays, GC MS.
	Assay, impurities and related substances	HPLC (PDA, Fluorescence, RI, light scattering detector), GC (FID, ECD), TLC, HPTLC, UV-Vis Spectrophotometry, AAS, Volumetric titrations, Potentiometry, Nitrogen Assay, UPLC, GC MS.	HPLC (Fluorescence, PDA, RI, light scattering detector), GC (FID, ECD), TLC, UV-VIS Spectrophotometry, AAS, Volumetric titrations, Potentiometry, Nitrogen Assay, UPLC, GC MS.
	Content	FT Raman, XRD, TGA, DSC, LCMS, IC, ICPMS, ICPOES, GCMS, DSC, RP-HPLC (PDA, RI and FLD), SEC-HPLC (GPC), ELISA.	FT Raman, XRD, TGA, DSC, LCMS, IC, ICPMS, ICP-OES, GCMS, RP-HPLC (PDA, RI and FLD), SEC-HPLC (GPC), ELISA.
	Microbiology Analysis	Sterility test, Microbial Limit Test, Bacterial Endotoxin Test (gel clot) and Sterility, Microbial Assay, antimicrobial Effectiveness Testing.	Sterility test, Microbial Limit Test, Bacterial Endotoxin Test (gel clot) and Sterility, Microbial Assay, antimicrobial Effectiveness Testing.
	Stability studies	Storage and testing as per client's Protocol based on ICH Guidelines	Storage and testing as per client's Protocol based on ICH Guidelines
	Other	Growth Promotion Testing of Media, Disinfectant Efficacy Evaluation, Invitro Microbial Kill Rate Study	
General information about the laboratory	Vimta Labs Limited, Life Sciences Facility (hereafter Vimta) was established in 1984 as a Partnership Firm and then converted to a Limited Company in 1991. Vimta Ltd consists of 18 sites, including the Headquarters and the site in the scope of this inspection. As of 2 January 2023, there were 1370 employees.		
History	The laboratory was inspected by WHO as part of the Pre-qualification of Medicines Program – Inspection of Quality Control Laboratory in March 2019, July 2018 (Desk Assessment), August 2013, December 2010 and April 2008.		

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Management & Quality Management System Documentation and Records, including data processing and archiving Personnel & training Premises and Equipment including Validation, Qualification and Calibration Contracts Method validation and verification Laboratory Practices, including evaluation of test results Safety Reference standards – Reagents - Water
Restrictions	Nil
Out of scope	The facility was also responsible for clinical diagnostics, the testing of food and agricultural products, electronic and electrical testing and environmental testing and consultancy. Only divisions involved in the quality control of pharmaceutical products were in the scope of the inspection.
Abbreviations	**Meaning**
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
CoA	Certificate of analysis
FPP	Finished pharmaceutical product
FTIR	Fourier transform infrared spectrophotometry or spectrophotometer
GMP	Good manufacturing practices
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
KF	Karl Fisher titration
LIMS	Laboratory information management system
MB	Microbiology
MR	Management review
NC	Non conformity
NCA	National control authority
NCL	National control laboratory
NRA	National regulatory agency
OOS	Out-of-specifications test result
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
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometry or spectrophotometer

Part 2	**Summary of the findings and comments**

1. Organization and Management

The organization and management structure of the laboratory was clearly documented and defined within the organisational chart. Roles and responsibilities were available with the overall reporting structure.

The laboratory implemented policies and procedures in accordance with the Quality Manual to ensure the confidentiality of documentation/information received as well as generated. These procedures ensured that its management and personnel were not subjected to commercial, political, financial, and other pressures or conflicts of interest that might adversely affect the quality of their work. The signed forms for Priyanka V. (dated 2022/09/22) were reviewed. The laboratory had a policy in place to ensure the confidentiality of information contained in marketing authorizations and test reports.

The laboratory had an established Quality Policy. The inspectors verified that the laboratory had established processes that mostly met the requirements of WHO good practices for pharmaceutical quality control laboratories (Annex 1), the standard (ISO 17025:2017), and other applicable regulations (notwithstanding the nonconformities identified during this inspection).

A quality manager was designated to ensure compliance with the quality management system and reported directly to top management to ensure that decisions were taken on laboratory policies and resources.

The laboratory was comprised of the following sections:

- Samples accession
- Archives
- Ultra-Trace Laboratory
- Physical Characterization
- Trace Analysis Laboratory
- Industrial Chemistry
- Food and Water Laboratory
- Drug Laboratory
- Contract Laboratory
- Biopharma
- Microbiology Laboratory

2. Quality management system

The Laboratory's Quality Manual adequately addressed and reflected the intended practices of the laboratory, with a clear commitment from top management for the continual improvement and support of the QMS. The manual was set out according to the requirements of various standards including but not limited to ISO 17025:2017. Safety requirements and requirements of applicable regulatory/accreditation bodies were also included. Principles of GXPs were implemented in applicable areas of testing and research services.

The QMS consisted of organization structure, policies, procedures, processes, and resources needed.

Internal Audits:

The laboratory implemented an internal audit program including documented requirements. This high-level corporate document described the requirements for independent auditors, and for all departments of the laboratory to have an internal quality audit performed at least once per calendar year.

Management review (SOP and list of performed management reviews):

The SOP for Management review was checked. The SOP described in general terms what topics would be monitored through the review. Meetings were held twice a year (around February and September).

CAPA handling:

Handling and disposition of non-conformity events, as well as a related CAPA plan, took place in accordance with the procedure titled Corrective Action. The laboratory had a maximum timeline for implementation of 90 calendar days.

CAPAs were to be initiated from findings from a laboratory deviation, laboratory error or a stand-alone CAPA.

Out of Specification:

The SOP for the OOS investigation was available, with a flow chart on the process to be followed. It included the different phases in investigation, hypothesis testing, re-testing, re-sampling and averaging of results. The SOP made provision for the inclusion of an OOS result in the averaging of results. An annual report was prepared based on OOX results, with trending, conclusion and CAPAs.

Complaints:

The laboratory had a customer complaint process available titled Handling Complaints. All communication between the facility and the complainant was available, including all email exchanges.

Change control:

The laboratory had a documented procedure for change control.

Disaster recovery and backup:
The laboratory had a procedure in place for IT backup of data. Daily and weekly backup was performed for IT systems connected to the server and standalone systems were backed up every 15 days. A check of the transfer of data was performed.

The server room was protected with three locks, with controlled access into the room. The room was clean and orderly, with a self-cooling unit within the server unit, along with external room air conditioning. The system was connected to the BMS and monitored.

3. Control of documentation

There were documented procedures for document and record control which met the requirements of the standard. A master list identifying the current issue number status and distribution of documents was available. Each controlled document had a unique identifier, issue number and effective date. The documents were authorized by the QA-Head. Once authorized, two copies were provided, i.e., a controlled copy and a master copy which were kept by the QA unit.

The training was conducted when changes had occurred to a document. Hardcopies were available at the relevant location based on a distribution list. All staff had access to a computer and SOPs were mostly available at the point of use.

The review period of documents was 2 years.

The document archive facility was secured by a heavy fireproof door and an additional security door, it was clean and orderly, with separate rooms for the different departments. A sign-in procedure was required to enter the facility. Internal staff sprayed the facility every 15 days for flying and crawling insects, rodent traps were present. Fire detectors and extinguishers were available.

4. Records

Records were available of analytical tests, including calculation and derived data, instrument use, calibrations and maintenance, and sample receipts in logbooks containing consecutively numbered pages.

5. Data processing equipment

An inventory of all computerised systems was available. Information such as the unique identification number of a software system or instrument, validation status, software version and system name were available. The laboratory had implemented procedures to protect the integrity- and confidentiality of data and records generated with the following exception. Excel was used for certain calculations and records.

6. Personnel

The laboratory was staffed with personnel who had the necessary education, training, technical knowledge, and experience for their assigned functions.

The skills matrix form was crosschecked with the above-listed analytical staff and found to match.

The staff interviewed were open and generally forthcoming with information.

Induction training was performed for all new staff, and in instances where a staff member had been away for greater than one year. The departmental head assigned the training schedule for the new staff member according to the tasks required with a training plan available in the individual's training record.

7. Premises

The laboratory facilities were of suitable size and design to suit the functions and to perform the operations to be conducted in them. The facility was well maintained, clean and orderly and clearly signposted. Access to the facility was controlled with the use of either fingerprint recognition or electronic card access with access restrictions assigned to high-risk areas. A list of staff who were trained and had access to the area was available at the entrance of most areas. All temperature-sensitive equipment was monitored 24/7 through a BMS.

All rooms containing instruments or required controlled conditions were temperature monitored, with very few humidity recordings. Calibrated temperature probes were placed in the hot spot of refrigerators and real-time temperature monitoring occurred.

There was a separate specimen reception area, with a separate area for the storage of samples.
A generator was used as backup in case of power failure. According to the company, this was challenged annually.

Microbiological facility:

Microbiological testing was performed in a contained laboratory unit. The laboratory was divided into areas such as sample receiving, sample storage, media storage, media preparation, reading room and testing room area. Cold stores were available for storage between 2 and 8 degrees Celsius.

The procedure for cleaning and disinfection in the microbiology laboratory was reviewed.

Incubators were available and kept at different conditions.

HVAC system:

There was a separate air supply to microbiology unit areas. Separate air-handling units and other provisions, including temperature and humidity controls, were in place for the microbiological laboratory unit.

Area qualification:

Entry to the facility took place via a system of airlocks and a change room where operators were required to wear suitable clean-room garments. Pictorial procedure for the gowning requirements was available at the entrance of the facility and personnel were aware of the proper entry and exit procedures.

Media:
Dry media was obtained from a supplier and stored on-site. Media was prepared in a separate area and the pH was checked before and after sterilization.

Incubators were available and kept at different conditions.

8. Equipment, instruments and other devices

The laboratory had a system for the calibration, maintenance and use of equipment with individual procedures available for all equipment. Preventive maintenance was to be performed at least annually unless otherwise stated. Calibration dates were determined either from the recommendation of the supplier of the equipment or from annual equipment re-evaluation.

The facility had a designated storage area for columns. All columns were purchased by Vimta Labs and assigned a unique identifier for ease of identification. Injection numbers were tracked.

All equipment selected had the maintenance and calibration logbooks readily available. All maintenance reviewed was within the period assigned by the laboratory.

Glassware and segregation:

The laboratory made use of automated and manual glassware cleaning procedures. The company procedure stated that glassware could be cleaned manually in the laboratory, or in a separate wash area. A glass washing machine could also be used.

Cleaning validation of glassware:

An exercise was undertaken to show that the cleaning procedure was effective.

9. Contracts

The laboratory had a process in place for the review and evaluation of suppliers in the Purchasing services and supplies procedure. Suppliers were classified as either critical or non-critical with the definition of critical being a vendor who provided consumables/reagents which require special storage conditions and directly impact the test results. All critical suppliers were audited every 2 years and all non-critical were reviewed every 5 years.

10. Reagents

The laboratory had a procedure for the evaluation and approval of suppliers (Purchasing services and supplies procedure.

The laboratory had a process in place for the labelling of chemicals and reagents upon receipt and again once opened that included using a sticker that contained the required information as per the standard.

Media components were supplied by approved and qualified vendors. Growth promotion and, if appropriate, other suitable performance tests were performed on all media on every batch received.

11. Reference substances and reference materials

The laboratory had a documented procedure for the use and control of reference substances and reference materials. Reference materials stored included those of sex hormones (ethinyl estradiol). The terminology used and defined in the mentioned SOP was found was aligned with that recommended by the WHO. The facility maintained a register for all reference substances.

Reference cultures:
Reference cultures were required to establish the acceptable performance of media (including test kits), validate methods, verify the suitability of test methods, and assess or evaluate ongoing performance.

Traceability was ensured using reference strains of microorganisms obtained directly from a recognized national or international collection.

12. Calibration, verification of performance and qualification of equipment, instruments and other devices

The list of all equipment, instruments and computerized systems was maintained by the laboratory. Unique identification numbers were assigned to all equipment and instruments used. The frequency of calibration, preventive maintenance and performance verification was determined by documented experience and was based on the need, type and previous performance of the equipment. Individual equipment's performance was reviewed annually along with calibration and maintenance records to determine the status of the equipment.

The procedures and relevant acceptance criteria have been documented in instrument/equipment specific standard operating procedures.

Autoclave validation :
A new autoclave was installed in December 2021. Most of the parameters indicated in the IQ report, were verified by means of a certificate.

HPLC:
Access and privileges SOP was available for Empower 3 systems. System and project audit trails were enabled upon installation of the software.

Backup and restoration of data:
Daily and weekly backups were made as described in the relevant SOP. Once a year, data were restored and verified according to the company SOP.

13. Traceability

The laboratory had an adequate process in place to ensure traceability.

14. Incoming samples

The laboratory had a process in place for sample management. The laboratory was not responsible for the sampling of materials or products. All samples were provided by clients for testing. Sample information was maintained on the Laboratory Information Management System (LIMS). Quantity was entered and the number of labels printed was determined by this quantity.

15. Analytical worksheet

The analysts recorded information about samples, test procedures, calculations, and results in analytical worksheets. Analytical worksheets from different units related to the same sample were assembled together.

All values obtained from each test, including blank results, were entered on the analytical worksheet and all graphical data, whether obtained from recording instruments or plotted by hand, were attached or were traceable to the electronic record file or document where the data was available.

The completed analytical worksheets were signed by the responsible analyst and verified, approved and signed by the supervisor. For corrections, the old information was observed to have been deleted by putting a single line through it. Alterations were signed by the person making the corrections with the date for the changes inserted.

16. Validation of analytical procedures

The laboratory had validation reports available for the disinfectant solutions that were rotated within the facility. The validated contact time was available within the procedure. The cleaning validation for the microbiological facility was reviewed.

17. Testing

Test procedures were described in detail and allowed analysts to perform the analysis in a reliable manner.

18. Evaluation of test results

The SOP for the OOS investigation was available, with a flow chart on the process to be followed.

19. Certificate of analysis

The Certificate of analysis was not reviewed in detail at the time of inspection.

20. Retained samples

The laboratory had a separate facility for the retained samples that was well maintained.

21. Safety

At the time of inspection, staff were observed wearing laboratory coats, appropriate footwear, and suitable eye protection. Special care was taken in handling highly potent, infectious, or volatile substances. The facility was clean and orderly.

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, *of* ***Vimta Labs Ltd, Life Sciences Facility****, located at* ***MN Park (Formerly Alexandria Knowledge Park), Plot No 5, Genome Valley, Shamirpet Mandal, Hyderabad, Medchal-Malkajgiri District, Telangana 500 101, India*** was considered to be operating at an acceptable level of compliance with WHO GPPQCL Guidelines.

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 5	List of WHO Guidelines referenced in the inspection report

1. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1. ***Short name: WHO TRS No. 957, Annex 1***
   http://www.who.int/medicines/publications/44threport/en/

2. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2. ***Short name: WHO TRS No. 961, Annex 2***
   http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

3. 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
   http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

4. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4. ***Short name: WHO TRS No. 937, Annex 4***
   http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1

5. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-first Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. ***Short name: WHO TRS No. 943, Annex 3***
   http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1

6. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7. ***Short name: WHO TRS No. 961, Annex 7***
   http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

7. WHO Guidelines for preparing a laboratory information file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report. Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 2011), Annex 13. ***Short name: WHO TRS 961, Annex 13***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/GuidelinesPreparingLaboratoryInformationFileTRS961Annex13.pdf?ua=1TRS%20961:%20Annex%2013:%20WHO%20guidelines%20for%20preparing%20a%20laboratory%20information%20file

8. Stability testing of active pharmaceutical ingredients and finished 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 10. ***Short name: WHO TRS No. 1010, Annex 10***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

9. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4. ***Short name: WHO TRS No. 1025, Annex 4***
https://www.who.int/publications-detail/978-92-4-000182-4

10. 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 1033, Annex 3***
https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations

11. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4. ***Short name: WHO TRS 1033, Annex 4***
https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations