World Health Organization
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# WHO PUBLIC INSPECTION REPORT

# (WHOPIR)

## Quality Control Laboratory

**Part 1: General information**

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|---|---|
| Name of QC Laboratory | Vimta Labs Ltd. |
| Physical address | Life Sciences Facility,<br>Plot No. 5, Alexandria Knowledge Park,<br>(Formerly S.P. Biotech Park),<br>Genome Valley, Hyderabad, 500 078<br>India |
| Contact person and email address. | Mrs Harita Vasireddi<br>Managing Director<br>harita@vimta.com |
| Date of inspection | 21, 22 and 23 August 2013 |
| Type of inspection | Routine inspection |
| Type(s) of testing included in the inspection | Physical, chemical and microbiology testing |
| Summary of the testing activities performed by the QC Laboratory | |

| *Type of analysis* | *Finished products* | *Active pharmaceutical ingredients* |
|---|---|---|
| Physical/Chemical analysis | pH, density, refractometry, viscosity, loss on drying, water content, disintegration, dissolution, uniformity of dosage units (mass, content), friability, tablet hardness, particulate matter test, dimensions, limit tests | pH, density, refractometry, 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, saponification value, nitrogen, limit tests, neutralizing capacity |
| Identification | HPLC (UV-Vis, PDA, RI, Fluorescence detection), GC (FID, ECD), | HPLC (UV-Vis, PDA, RI, Fluorescence detection), GC (FID, ECD), TLC, HPTLC, UV-VIS |

| | | | |
|---|---|---|---|
| | | GC/MS, TLC, HPTLC, UV-VIS spectrophotometry, IR, AAS | spectrophotometry, IR, FTIR, AAS,chemical reaction |
| | Assay, impurities and related substances | HPLC (UV-Vis, PDA, RI fluorescence, light scattering detection), GC (FID, ECD, HRGC-MS, GC-MS), TLC, HPTLC, UV-VIS spectrophotometry, AAS, fluorimetry, volumetric titrations, amperometry, potentiometry, nitrogen assay, Polarimetry, ICP-MS | HPLC (UV-Vis, PDA, RI fluorescence, light scattering detection), GC (FID, ECD, HRGC-MS, GC-MS), TLC, HPTLC, UV-VIS spectrophotometry, AAS, fluorimetry, volumetric titrations, amperometry, potentiometry, nitrogen assay, thermal analysis (DSC), Polarimetry, ICP-MS, Flame photometry |
| | Microbiological tests | Sterility test, microbial purity, bacterial endotoxins test (LAL), microbial assay, antimicrobial effectiveness | Sterility test, microbial purity, bacterial endotoxins test (LAL), Microbial assay, antimicrobial effectiveness |
| | Stability studies | Storage and testing as per ICH guidelines and client protocol | Storage and testing as per ICH guidelines and client protocol |

## Part 2: Summary

### *General information about the company and site*

Vimta Labs Limited (hereafter Vimta) was established in 1984 as a Partnership Firm and then converted to a Limited Company in 1991. The registered office is located in Cherlapally, Hyderabad, India. Vimta has two laboratories located around Hyderabad, India, one is located in Cherlapally (also headquarter) whereas another one in Alexandria Knowledge Park. From the opening meeting presentation, it was noted that total Alexandria Knowledge Park, Genome Valley site employed around 345 employees.

### *History of WHO and/or regulatory agency inspections*

- The last WHO inspection was conducted in December 2010, and was found to be compliant.
- The laboratory had been recently inspected by the Drug Control Administration, Andhra Pradesh, India in June 2012 and licence had been renewed upto June 2017
- The laboratory had been inspected by the National Accreditation Board for Testing and Calibration Laboratories/NABL in November 2012 (once in 2 year). The accreditation had been renewed upto March 2015.

The inspection focussed on the quality management system and on physical/chemical analysis, identification, assay, impurities and related substances, residual solvents as well as microbiological tests (sterility, microbial count and bacterial endotoxin test), as the areas of quality control testing prequalified by the WHO.

### *Inspected Areas*

The following areas of the WHO good practices for the pharmaceutical quality control laboratories were covered in this inspection:

- Organization and management
- Quality management system
- Control of documentation
- Records
- Data-processing equipment
- Personnel
- Equipment, instruments and other devices
- Contracts
- Reagents
- Calibration, verification of performance and qualification of equipment, instruments and other devices
- Traceability
- Incoming samples
- Analytical worksheet
- Validation of analytical procedures
- Testing

- Evaluation of test results
- Certificate of analysis
- Retained samples
- Safety

***List of persons (and their positions) met during the opening/closing meeting***

- Ms Harita Vasireddi, Managing Director
- Mr Harriman Vungal, Executive Director, Operations
- Ms V Anuradha, Senior Manager Quality Assurance
- Mr B.V. Ramakrishna, Senior Manager, Analytical (Drugs & Pharma)
- Mr Sireesh Chandra Vungal, Manager IT (present at opening meeting only)
- Ms Prasanna Bharathi, Group Leader, Quality Assurance
- Mr Dharma Raju, Manager Drugs & Pharma

## 2.1 Organization and management

A management structure was in place to manage a wide variety of tests being conducted at the site (the testing of medicines as well as the testing of food, water, and trace analysis). The current organization chart was updated in January 2013. It was noted that there was a change in the organization management wherein Ms Harita had been promoted to the Managing Director position (who used be the Director Quality), Director Quality position had been vacant since then.

The issues highlighted were subsequently addressed, and the same will be verified during next inspection.

## 2.2 Quality management system

A quality management system was in place which included quality policy, management system documents (MSD), management system procedures (MSP), and standard operating procedures (SOPs). Vimta has implemented the quality system as per ISO/IEC 17025:2005 and cGMP (USFDA GMP 21 CFR parts 210, 211, WHO GPCL, ICH Q7, EudraLex Volume 4 and The Drugs and Cosmetics Act 1940) for its testing activities. The quality system was laid down in their quality manual covering quality policy, management and technical requirements.

The quality system was common for Water, Food, Drugs & Pharma, as well as laboratory based at Cherlapally and also applicable to the pre- clinical research activities carried out at the same site on a separate building.

## 2.3 Control of documents

An updated (20 Aug 2013) master list of SOPs was available for various departments such as quality assurance, information technology (IT), trace analysis (TAL), microbiology, water, drugs & pharma, stores & purchase, facility & administration, customer relation management (CRM), contract lab 1 and contract lab 3.
An SOP on SOP was available which provided clear instructions on the management of documents including numbering system, issuance, and retrieval of documents at

defined intervals. The documents were reviewed every 2 year. Also, document change history was maintained with each procedure.

The SOP Empower Administration and SOP on General Procedures for Chromatographic Analysis were reviewed.

The issues highlighted were subsequently addressed, and the same will be verified during next inspection.

**2.4 Records**

In general, the records were maintained e.g. training records, validation reports, and analytical worksheets including test reports. The analytical reports were supported with relevant printouts and chromatograms. The issues highlighted were subsequently addressed, and the same will be verified during next inspection.

**2.5 Data-processing equipment**

Drugs & Pharma laboratories had number of HPLC which were equipped with Empower software. Although LIMS was used for the sample management, the same was not extended to HPLC and other computer based equipment. A project on the validation of excel Spreadsheets was on-going at the time of inspection. The issues highlighted were subsequently addressed, and the same will be verified during next inspection.

**2.6 Personnel**

An organization chart showing the hierarchical arrangements, responsibilities and reporting lines in the laboratory was available in quality manual. An adequate number of personnel were working in both Drugs & Pharma and Microbiology laboratories. In general, personnel were found to be experienced, competent and knowledgeable in their area of work. Training at Vimta Labs was performed according to SOP.

**2.7 Premises**

The main laboratory building consists of four levels and each level was further divided into four quadrants. One floor of the building had support services, and three quarter of the space was assigned for various laboratories. Following was the breakup of the laboratory:

| | | |
|---|---|---|
| Level 1 | South West block | sample receipt and archives |
| Level 1 | South East block | sample accession for analytical department |
| Level 2 | North West block | drugs & pharma (routine testing lab) |
| Level 3 | North East block | drugs & pharma validation lab |
| Level 4 | North East block | microbiology laboratory |

Generally, the facility was of adequate space and design for the intended purpose. These laboratories appeared to be cleaned and maintained appropriately. The issues highlighted were subsequently addressed, and the same will be verified during next inspection.

## 2.8 Equipment, instruments and other devices

The laboratories were equipped with instruments and equipment used to perform the analytical work. In general, logbooks were available for every piece of equipment and instruments. Some of the logbooks were briefly reviewed during the inspection and were found to be satisfactory.

## 2.9 Contracts

In general, the contracts were available. The issues highlighted were subsequently addressed, and the same will be verified during next inspection.

## 2.10 Reagents

The shelf life criteria for chemicals and reagents were in accordance to SOP. The reagents were generally labelled appropriately and expiry dates were defined according to the type of reagents e.g. volumetric solutions, general reagents and reference substances.

## 2.11 Reference substances and reference materials

All reference and impurity standards required for analysis were supplied by either applicants or manufacturers. Each reference material was supplied with certificate of analysis. On receipt, reference materials were stored at appropriate storage conditions till required by analysts.

## 2.12 Calibration, verification of performance and qualification of equipment, instruments and other devices

The documentation of the HPLC qualification was reviewed in detail during the inspection. The qualification was performed by the vendor and checked by the responsible user. QA review of the documentation was performed at a later time point and documented separately. IQ and OQ were performed for the detector and the separation module including tests for wavelength accuracy and linearity of the detector and flow rate accuracy, gradient proportioning valve, injection accuracy, sample heater/cooler, and tests for the column heater. PQ testing was performed by determination of reproducibility and linearity tests.

The documentation of the qualification of incubator was reviewed during inspection. The qualification (annual re-qualification) was performed by an external company, SIMCO Calibration laboratories by measuring temperature distribution in the chamber using 8 channels over 24 hours. The qualification met the predefined acceptance criteria and was finalized and approved.

The issues highlighted were subsequently addressed, and the same will be verified during next inspection.

## 2.13 Traceability

Test results were traceable to analyst, analytical instruments, equipment, reagents, reference substances and test procedures. The primary & secondary chemical reference standards and pH buffers were traceable to respective USP/EPCRS and NIST.

## 2.14 Incoming samples

Incoming samples were received in the reception area (level 1) and checked for physical intactness and correctness of quantities before being registered in the LIMS system. Samples were then distributed to the respective departments (Drugs & Pharma and Microbiology) for analysis as per the test request.

## 2.15 Analytical sheet

Analysts recorded tests performed, raw data, calculations and results in analytical worksheets. Sufficient details were recorded in analytical worksheets to establish traceability.

Analytical worksheets for Artemether injection and Lamivudine/Zidovudine tablets were reviewed. The worksheets captured complete activities of testing including dilutions, column information, equipment number, reference standards etc. After the completion of testing, these worksheets were reviewed by the next level and signed & dated. The protocols of these products were also reviewed concurrently and compared with the analytical worksheets and were found satisfactory. The issues highlighted were subsequently addressed, and the same will be verified during next inspection.

## 2.16 Validation of analytical procedures

A full analytical method validation according to the provisions of SOP was only performed for customized analytical methods or on specific request by the customer. The SOP was reviewed during the inspection and the required validation parameters were checked against the provisions of the WHO guideline and were found to be acceptable. In the scope of the SOP were chromatography methods including related substances, assay, potency, dissolution, content uniformity and residual solvents. Robustness testing included the variations of the temperature of the column oven, the composition of the mobile phase, the flow rate and the wavelength.

## 2.17 Testing

The samples were tested in accordance with the work plan. There was no competency matrix maintained to ensure samples were allocated to the analyst based on their expertise and training.

Test results were recorded in analytical worksheets as discussed earlier and print outs from instruments were stored with sample information and test reports. System suitability criteria were fulfilled when defined in the method.

At the time of the inspection, sterility test and microbial limit test were not performed. In general, the microbiology laboratory was found to be clean and tidy.

The issues highlighted were subsequently addressed, and the same will be verified during next inspection.

**2.18 Evaluation of results**

During the inspection, three of the analytical worksheets were reviewed and found to be satisfactory in general. These worksheets were completed by the respective analyst before it was reviewed by the group leader. Once the analytical worksheets were reviewed, test reports were prepared and printed (one original and one copy to customer and one copy for retention) accordingly.

The issues pertaining to out of specification procedure were addressed satisfactorily and will be verified during the future inspections.

**2.19 Certificate of analysis**

Certificate of analysis in the form of test results were prepared following the completion of analysis. It was learnt that total 3 sets (one original & one duplicate for customer and one triplicate for retention with Vimta Labs) were prepared. In general, test results covered the essential details as recommended in WHO Guide.

**2.20 Retained samples**

Not inspected.

**2.21 Safety**

In general, the laboratories seem to be well maintained and cleaned. Training of the housekeeping staff on respective cleaning procedures was reviewed and found satisfactory.

**Part 3: Conclusion**

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, as well as the corrective actions taken and planned, *Vimta Laboratories Limited, Genome Valley, Hyderabad, India* was considered to be operating at an acceptable level of compliance with in compliance with WHO Good Practices for Pharmaceutical Quality Control Laboratories.

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 laboratory, 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.