

WHO PUBLIC INSPECTION REPORT API Manufacturer
**WHO PUBLIC INSPECTION REPORT
(WHOPIR)
API Manufacturer**
Part 1: General information

Name of Manufacturer	Acebright (India) Pharma Pvt. Ltd
Unit number	77D & 116/117
Production Block	Production block 1 (Line 1 and Line 2)
Physical address	KIADB Industrial area, Jigani, Bangalore – 560 105, Karnataka, India
Contact person and email address.	Ms Manorama Avinash, Executive Director manorama@acebright.in Mr. S. Padmanabha GM Quality, padmanabha@acebright.in Mr. Rajeev V. Jahagirdar Vice President, Operations rajeev.jahagirdar@acebright.in
Date of inspection	23-26 February 2015
Type of inspection	Follow up inspection
Active Pharmaceutical Ingredient(s) included in the inspection	Efavirenz (APIMF173) Tenofovir Disoproxil Fumarate (APIMF 219, under assessment) Lopinavir APIMF 258 (Under assessment)
Summary of the activities performed by the manufacturer	Production and control of APIs

Part 2: Summary

General information about the company and site

Acebright (India) Pharma Pvt Ltd Bangalore (formerly Cdymax India and Intermed Labs Pvt Ltd) was established in the year 1991 for manufacturing drug intermediates and APIs. There were 2 multi-product productions blocks (PB) in the site.

PB 1 for “general” APIs:

- Efavirenz, USP/ Ph. Int
- Tenofovir Disoproxil Fumarate, Ph.Int/IP
- Oseltamivir Phosphate USP/Ph.Eur
- Ritonavir USP
- Lopinavir USP/Ph.Int

PB 2 for oncology APIs (out of the inspection scope)

The main changes at the site since last inspection:

- Underground storage tanks-4 for both PB-1 & 2
- Charcoal storage changed from PB-1 to drum shed
- Walk in cooling chamber 1 for reference sample storage
- HPLC & GC (Agilent)
- New products introduced (Atazanavir sulfate and Abacavir sulphate)
- Efavirenz APIMF173 amendment approved by WHO-PQ

History of WHO and/or regulatory agency inspections

This was the 4th WHO at the site after years 2012, 2013 and 2014.

Focus of the inspection

The inspection focused on the production and control of Efavirenz (APIMF173), Tenofovir Disoproxil Fumarate (APIMF 219) and Lopinavir (APIMF 258). The inspection covered all the sections of ICH Q7, including premises, equipment, documentation, materials, validation, sanitation and hygiene, production, quality control and utilities.

Inspected Areas

The inspection covered most of the sections of WHO GMP for Active Pharmaceutical Ingredients (ICH Q7), including Quality Management; Personnel; Buildings and Facilities; Process Equipment; Documentation and Records; Materials Management; Production and In-Process Controls; Packaging and Identification Labelling of APIs and Intermediates; Storage and Distribution; Laboratory Controls; Validation; Change Control; Rejection and Reuse of Materials and Complaints and Recalls.

2.1 QUALITY MANAGEMENT

The quality management system did not change since the last WHO inspection in general.

In general, all required quality management systems and elements were established, documented and implemented. The QMS is generally mature with a strong corporate element. The organizational structure, procedures, processes and resources provided were generally satisfactory. Quality-related activities were defined, documented and were seen to be recorded at the time they were performed.

Responsibilities of the quality unit (personnel) and the responsibility of the production unit (personnel) activities were available for inspection. The responsibilities of the quality Unit are independent of production Unit. Appropriate job descriptions and role definitions were documented.

The observations raised from this section have been addressed satisfactorily and will be verified during future inspections.

2.2 PERSONNEL

There was adequate number of personnel qualified to perform and supervise the manufacture of intermediates and APIs. The responsibilities of personnel engaged in the manufacture of intermediates and APIs were documented in written job descriptions.

2.3 BUILDINGS AND FACILITIES

The manufacturing facilities did not change since the last WHO inspection. The tour at the manufacturing facilities covered the synthesis workshops and the powder processing areas (Line 1 and Line 2).

The final processing steps were performed in facilities with environmental control, claimed meeting the requirements of “ISO 8”.

2.4 PROCESS EQUIPMENT

The manufacturing process equipment (multi product in the most sections of production areas) did not change since the previous WHO inspection.

The manufacturing process parameters were controlled manually, the status of equipment was indicated on labels and the usage of equipment was recorded in logbooks.

The observations raised from this section have been addressed satisfactorily and will be verified during future inspections.

2.5 DOCUMENTATION AND RECORDS

Documents related to the manufacture of APIs were sampled and reviewed throughout the inspection and were found to have been prepared, reviewed, approved and distributed according to SOP and effectively handled.

2.6 MATERIALS MANAGEMENT

The material management was controlled by means of an ERP software with the following functions: Purchase requisition, Purchase order, Material receipt, Storage, Labelling, Dispensing/issuance.

The observations raised from this section have been addressed satisfactorily and will be verified during future inspections.

2.7 PRODUCTION AND IN-PROCESS CONTROLS

Examination of the flow of the manufacturing process and relevant equipment was in line with the BPR examined in general compliance with the details in the submissions to WHO PQT. That equipment used in different steps of the manufacturing process that was inspected was satisfactory. Majority of the equipment used for production of the APIs in focus were not dedicated.

Production flows were generally well laid out and logical. The production areas were in good condition and appropriate to their application.

The observations raised from this section have been addressed satisfactorily and will be verified during future inspections.

2.8 PACKAGING AND IDENTIFICATION LABELLING OF APIs AND INTERMEDIATES

The procedures belonging to this section did not change since the last WHO inspection.

2.9 STORAGE AND DISTRIBUTION

See section 2.6, Material management.

2.10 LABORATORY CONTROLS

Basically, the quality control laboratories for PB1 and PB2 products were separated by organization and facilities. Despite, some of the functions (storage of stability samples and occasional quality control testing) were performed by PB2 quality control laboratory for PB1.

Inspection of PB1 laboratory was performed with an objective to verify analysis done in accordance to WHO Good Control Laboratory Practices, Principles.

The observations raised from this section have been addressed satisfactorily and will be verified during future inspections.

2.11 VALIDATION

The company's overall validation policy had not been changed since last inspection. The system is comprehensive and adequate. Written validation protocols specifying critical processes steps and acceptance criteria were established and available where requested.

In general appropriate qualification of critical equipment and ancillary systems were carried out. The cleaning validation was performed with worst case approach. Records and performance of the studies reviewed were satisfactory.

The observations raised from this section have been addressed satisfactorily and will be verified during future inspections.

2.12 CHANGE CONTROL

The system for management of changes was described in the procedure. The changes are events which are planned and classified and handled as "permanent" or "temporary". The investigated cases were given a unique identification code and listed in a register.

The observations raised from this section have been addressed satisfactorily and will be verified during future inspections.

2.13 REJECTION AND RE-USE OF MATERIALS

The reprocess, rework and solvent recovery procedures and practices did not change since the last inspection.

2.14 COMPLAINTS AND RECALLS

The procedure on handling of complaints was described in the SOP.

2.15 CONTRACT MANUFACTURERS (INCLUDING LABORATORIES)

There was no contract manufacturing carried out on site and no manufacturing activity contracted out.

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, APIs (Efavirenz, Tenofovir Disoproxil Fumarate and Lopinavir) manufactured at *Acebright (India) Pharma Private Limited, India* were considered to be manufactured in compliance with WHO GMP for Active Pharmaceutical Ingredients.

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.