

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

Name of Manufacturer	Mylan Laboratories Ltd (during inspection the site name was Matrix)
Unit number	Unit III
Production Block	APIMF 071 Efavirenz Block MB-02
Production Block	APIMF 050 Lopinavir Block MB-04
Production Block	APIMF 039 Emtricitabine Block MB-02 & Block MB-05
Physical address	Plot Nos. 38 to 40, 49 to 51, Phase IV IDA, Jeedimetla, 500055 Hyderabad, Andhra Pradesh, India
Date of inspection	22 - 26 August 2011
Type of inspection	Routine
Active Pharmaceutical Ingredients included in the inspection	Efavirenz Emtricitabine Lopinavir
Summary of the activities performed by the manufacturer	Production, quality control, packaging, storage and distribution of APIs.

Part 2: Summary
General information about the company and site

The site was established in 1984 by the company Herren Drugs.

Matrix Laboratories Ltd (hereafter: Matrix) had the following manufacturing facilities:

1. Matrix Unit I/Unit II, Kazipally
2. Matrix Unit III, Jeedimetla
3. Matrix Unit VII, Pashamylaram
4. Matrix Unit VIII, Vishakhapatnam
5. Matrix Unit IX, Vishakhapatnam

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6. Matrix Unit XI, Mumbai, Maharashtra
7. Matrix Xiamen, China
8. Matrix FDF, Nashik, Maharashtra
9. Matrix FDF, Aurangabad, Maharashtra

Matrix was engaged in the manufacture of active pharmaceutical ingredients (APIs), intermediates and finished dosage forms. Neither high pharmacological activity substance nor highly sensitizing materials such as penicillin or cephalosporin were manufactured in the Unit III.

Inspected Matrix Unit III had 5 Manufacturing Blocks (MB) and 1 Solvent Recovery Plant.

Total number of employees was about 499; 35 employees were involved in Quality Assurance (QA) activities, 223 in production activities and 71 in Quality Control (QC) activities.

Matrix Laboratories Ltd (Matrix) is an Indian subsidiary of Mylan Laboratories Inc.

History of WHO and/or regulatory agency inspections

The Matrix Unit III facility has never been inspected the WHO team.

Focus of the inspection

The inspection focused on the production and control of three APIs: Efavirenz, Emtricitabine and Lopinavir. The inspection covered all the sections of the WHO good manufacturing practices for active pharmaceutical ingredients, including premises, equipment, documentation, materials, validation, sanitation and hygiene, production, quality control and utilities. None of the three APIs were in production during the inspection.

Inspected Areas

- Documentation, including SOPs, Batch Manufacturing Records (BMRs) and Master documents
- Warehouses
- Production
- Waste management
- Recovery of solvents
- Quality control laboratories

2. QUALITY MANAGEMENT

Quality management system in general was well established, documented and implemented. The site organizational structure was presented and was acceptable. Quality-related activities were defined and documented. The Quality Unit was independent from production. The persons authorized to release intermediates and APIs were specified. Deviations from established procedures were documented and explained.

Deviations

SOP "Handling and investigation of deviations" was reviewed. This SOP was applicable for all deviations from approved procedures related to testing, manufacturing, packaging, storage, issuance of materials, related to raw materials, intermediates, APIs and equipment performance.

Deviations were recorded in Batch Manufacturing Records (BMRs). Deviation log registers for 2010 and 2011 were reviewed.

Responsibilities of Quality Unit(s)

The quality unit (QU) was involved in all quality-related matters. The QU responsibilities were described in writing.

- SOP "Quality unit responsibilities" was reviewed, no remarks.

Responsibilities of production activities

The responsibility for production activities was not described in writing.

Internal audits, self inspection

Regular internal audits were performed in accordance with an approved schedule.

- SOP "Internal quality audit" was reviewed. Responsible person for internal audits was Head QAD and or Management representative. Audit was carried out once in six months or earlier on need basis, according to the check list. Audit report was written indicating observations and observation category. Observations were categorized as:

- Critical
- Major
- Minor

Non conformance report was also prepared by the auditors and approved by the Head QAD. The report indicated the following:

- Non conformance
- Root cause analysis
- Corrective action (CA)
- Preventive action (PA)

Product quality review

Regular quality reviews of APIs were conducted. The results of this review were evaluated and an assessment made of whether corrective action or any revalidation should be undertaken.

SOP "Annual Product review" was reviewed. PQR was applied for all batches of API starting materials (manufactured/procured), intermediates and APIs manufactured including those reprocessed and reworked batches.

Emtricitabine (EMT) Annual product review (APR-2009) was reviewed in details, no remarks.

PQRs were spot-checked for:

- Emtricitabine 2010
- Efavirenz 2007, 2008

3. PERSONNEL

Personnel qualifications

There were adequate numbers of personnel qualified by appropriate education, training and/or experience available on the site. Responsibilities of personnel engaged in the manufacture of intermediates and APIs were specified in writing.

- The following Job descriptions were reviewed:
 - Associated Vice President - Production
 - Assistant General Manager - Production
 - Senior General manager - Quality

- Senior Manager - QC

Data about personnel was systematically maintained; signature lists were kept. On spot-checks no discrepancies were noticed in terms of batch records and attendance in production processes.

Training of production and laboratory personnel was systematically conducted; on spot-checks the records were available. Training SOP was a corporate level document, analyst evaluation SOP was a site level document; no remarks.

Personnel from other private companies were used for material shifting and housekeeping duties. Records were kept.

Personnel Hygiene

Direct contact with intermediates or APIs was avoided. Smoking, eating, drinking, chewing and the storage of food were restricted in production and storage areas. Personnel with an infectious disease or open lesions on the exposed surface of the body were not engaged in manufacturing activities.

- SOP "Hygiene practice in manufacturing and laboratory areas" was reviewed, no remarks.
- SOP "Procedure for medical check up of employees" was reviewed. All personnel undergone medical examinations once in six months.
- SOP "Procedure for medical check up of employees" was reviewed, no remarks.

4. BUILDINGS AND FACILITIES

Design and construction

Buildings and facilities used in the manufacture of intermediates and APIs were located, designed, and constructed to facilitate cleaning, maintenance and operations as appropriate to the type and stage of manufacture. Buildings and facilities had adequate space for the orderly placement of equipment and materials to prevent mix-ups and contamination. QC areas and operations were separated from production areas.

The four plots named in the administrative address of the company did not have relevance to separate manufacturing blocks, the site used the whole area as one entity. Manufacturing blocks were identified as MB-1 to MB-05.

Unit III consisted of five manufacturing blocks (MB) for API synthesis. MB-02 was divided into Bay 1 and Bay 2.

Unit III had common systems and functions:

- Utilities: processed water, compressed air, nitrogen, solvents, solvent recovery in high distillers/columns, and respective delivery systems;
- Warehouses
- QC including in-process QC, QA.

Each MB had a Production Head.

Utilities

The company explained that utilities, as heating, ventilation and air conditioning were qualified; however qualification documents were not checked. Drawings for these utility systems were available. Adequate ventilation, air filtration and exhaust systems were provided for "clean rooms".

- Re-validation report of specific AHU serving compaction room in the manufacturing bloc No 3 was reviewed. The tests were carried out as per ISO 14644 standard, and reports were reviewed.

In general, permanently installed pipe-work was appropriately identified.

Water

Potable water samples were sent once in 4 months to an outside laboratory for a wider scope of chemical testing.

SOP "Procedure for sanitization of purified water loop system and storage tanks" was reviewed, no remarks.

Lighting

Adequate lighting was provided in all areas to facilitate cleaning, maintenance and proper operations.

Sewage and refuse

Solid waste was stored outside, in a separate area of the Unit III grounds. Other waste was not inspected. SOP "Collection; classification; packaging, labelling, storage and disposal of hazardous wastes" was reviewed.

Sanitisation and maintenance

Buildings used in the manufacture of intermediates and APIs were properly maintained and repaired and kept in a clean condition. Written cleaning procedures were available and checked.

- SOP "Procedure for cleaning underground and overhead tanks (PO)" was reviewed.
- SOP "Procedure for cleaning of transfer lines and SS flexible hosepipes/HDPE and nylon hosepipes" was reviewed.

5. PROCESS EQUIPMENT

Design and construction

Equipment used in the manufacture of intermediates and APIs was of appropriate design, adequate size, and suitably located. Construction material was chosen with the aim not to alter the quality of intermediates. Stainless steel (SS) was used for production equipment. Processing was mainly conducted in closed equipment. Manual unloading of solid intermediates was an open step.

Equipment maintenance and cleaning

Preventive maintenance (PM) schedule was presented to the inspectors.

- Annual PM Schedule for plant equipments for 2011 was reviewed. On spot-checks the schedule was followed.
- Monthly PM schedule for plant equipments (August) was reviewed. On spot checks the schedule was followed.

Cleaning of equipment was carried out according to written procedures. There were two types of cleaning procedures: batch to batch cleaning and cleaning after campaign production. Unit III stated that their production equipment was not used by other Matrix Units or for contract work for other companies.

Calibration

Control, weighing, measuring, monitoring and test equipment was calibrated according to written procedures and an established schedule. Calibration records were maintained

- Instrument calibration plan/schedule for the year 2011 was reviewed. On spot-checks the schedule was followed.
- Monthly calibration schedule (August) of all QCL equipments was reviewed.
- In-house calibration of some process monitoring temperature sensors was checked.

Computerized systems

GMP-related computerized systems, such as HPLC software, GS software and SAP were validated.

6. DOCUMENTATION AND RECORDS

Documentation system and specifications

All documents related to the manufacture of intermediates or APIs were prepared, reviewed, approved and distributed according to written procedures. The issuance, revision, superseding and withdrawal of all documents were controlled with maintenance of revision histories. All production, control and distribution records were retained 6 years.

Equipment cleaning and use record

Records of major equipment use, cleaning, sanitization and maintenance showed the date, time, product and batch number of each batch processed in the equipment, and the person who performed the cleaning and maintenance.

Records of raw materials, intermediates, API labeling and packaging materials

As mentioned below, all material labels were managed by SAP.

Master production instruction (master production and control records)

Master production instructions for each intermediate and API were available, dated and signed and independently checked, dated and signed by a person in the quality unit.

Batch production records (batch production and control records)

Batch production records were available for each intermediate and API and included complete information relating to the production and control of each batch. These records were numbered with a unique batch number, dated and signed when issued.

From 4th of August a new batch numbering system was in use.

- SOP "Batch numbering system", corporate level SOP, was reviewed, no remarks.

Laboratory control records

Laboratory control records contained complete data derived from all tests conducted. Raw data - chromatograms, spectra, printouts from balances - were retained. Analytical work sheets were signed by the analyst who performed the analysis and checked by a senior analyst.

Batch production record review

Written procedures were established and followed for the review and approval of batch production and laboratory control records, including packaging and labeling, to determine compliance of the intermediate or API before dispatch.

- SOP "Release of intermediates and APIs to market" was reviewed. QA department personnel were responsible to release the intermediates and APIs. List of approved persons for release of finished product to market was annexed to the SOP, no remarks.

7. MATERIALS MANAGEMENT

General controls

Written procedures describing the receipt, identification, quarantine, storage, handling, sampling, testing and approval or rejection of materials were available. From 4th of August 2011 all raw materials in stock, including solvents and recovered solvents, and finished APIs had been re-coded and respectively re-labelled.

Fresh solvents and recovered/reprocessed solvents were assigned different material codes.

- SOP "Assigning of manufacturing, retest and expiry date through SAP" was reviewed as well as SAP validation protocol/report.

Supplier evaluation:

- SOP "Vendor approval" and flow chart for vendor qualification (API starting materials, general raw materials, packaging materials) were reviewed. Key starting material vendor audits was carried out by corporate personnel and site personnel. According to the SOP, suppliers (brokers, agents) were not audited; they were approved on the basis of a questionnaire. Vendors and primary packaging material producers were audited once per 3 years. Vendor audit schedule for API key starting materials and approved vendors' list were presented to the inspectors. Specific vendor audit report was reviewed by inspectors. Observations were listed in the audit report, CAPAs were received from the vendor indicating target date and status, and also supporting documents were presented.

Receipt and quarantine

Receipt and quarantine of all materials was managed by the SAP.

Sampling and testing of incoming production materials

Identity tests using NIR was carried out for all key starting materials containers. Sampling was carried out in two sampling boots, provided with AHUs and HEPA filters. Carbon was sampled in carbon storage room. Containers from which samples were withdrawn were marked to indicate that a sample has been taken.

- SOP "Procedure for handling of raw materials" was reviewed. Dedicated scoops and rods were used for sampling of solid raw materials.

Storage

Materials stored in fiber drums, bags or boxes were stored off the floor; sufficient space was left to permit cleaning and inspection. Rejected materials were identified and stored in separate room.

Re-evaluation

Re-test periods were specified for key starting materials and APIs.

8. PRODUCTION AND IN-PROCESS CONTROLS

Production operations

Raw materials for manufacturing of intermediates and APIs were weighed and measured under appropriate conditions. Critical weighing, measuring or subdividing operations were witnessed. Actual yields were compared with expected yields at designated steps in the

production process. The processing status of major units of equipment was indicated on status labels.

The Unit was operational 24 hours; 3 shifts were arranged.

Solvents were dispensed by volume, visually checking the dispensed volume in the level indicator. Quantities were traceable in batch records.

Time limits

Time limits were specified in the BMRs, deviations were documented and evaluated. For the hold time validation the samples were tested at the 1 month, 2 months, 3 months and 6 months intervals.

In-process sampling and controls

In-process controls and their acceptance criteria were defined. Critical in-process controls including the control points and methods were defined and approved by the quality unit. In-process controls were performed in the QCL.

Blending batches of intermediates or APIs

Blending processes were adequately controlled and documented and the blended batches were tested. The batch record of the blending process allowed tracing back to the individual batches that make up the blend. The expiry or retest date of the blended batches was based on the manufacturing date of the oldest tailings or batch in the blend.

- SOP "Procedure for blending and packing of intermediates/finished products" was reviewed. Blending process was carried out as per Master Batch Manufacturing Record (MBMR).

Contamination control

Production operations were conducted in a manner that was aimed at preventing contamination of intermediates or APIs by other materials.

9. PACKAGING AND IDENTIFICATION LABELLING OF APIs AND INTERMEDIATES

General

The written procedure describing the receipt, identification, quarantine, sampling, examination and/or testing and release and handling of packaging and labeling materials was available and reviewed by the inspectors. As stated above, materials were managed by SAP.

Packaging materials

Containers provided adequate protection against deterioration or contamination of the intermediate or API that may occur during transportation and recommended storage.

Label issuance and control

Labels were printed by SAP.

Packaging and labeling operations

Labels used on containers of intermediates or APIs indicated the product name, manufacturer name and address, the batch number of the product and the storage conditions, manufacturing date and re-test date.

- SOP "Procedure for labelling of finished product" and finished product labels for Emtircitabine were reviewed; no remarks..

10. STORAGE AND DISTRIBUTION

Warehousing procedures

Facilities were provided for storage of raw materials, packaging materials and intermediates. Procedures were in place to maintain traceability and avoid contamination.

- SOP "Procedure for cleaning of warehouse and its accessories" was reviewed; no remarks.

Distribution procedures

APIs and intermediates were released for distribution after they had been released by the Quality Unit. Special transport or storage conditions for an API or intermediate were stated on the label. A system was in place by which the distribution of each batch of intermediate and/or API can be determined to permit its recall.

11. LABORATORY CONTROLS

General controls

There was an independent Quality Unit. Documented procedures describing sampling, testing, approval or rejection of materials and recording and storage of laboratory data were available. Laboratory records as well as production records were stored for 6 years. Specifications and test procedures were available for all product all stages and recovered solvents. Out of Specifications (OOS) results obtained were investigated and documented according to a written SOP. Complete records should also be maintained for Out of Trends (OOT) investigations.

- SOP "Investigations of out of specification results" + flow chart and OOS log register for 2011 were reviewed. The SOP was applicable for raw materials, intermediates, packing materials, finished products, and stability samples. OOS log register for 2011 was reviewed, no remarks.

Reagents and standard solutions were prepared and labeled following written procedures. "Use by" dates were applied as appropriate for analytical reagents or standard solutions.

Working reference standards (WS) were appropriately prepared, labeled, identified, tested, approved and stored. WS were dispensed in amber glass vials. 1 vial was intended to be used within 1 month. The suitability of each batch of secondary reference standards were determined prior use. Shelf-life of WS was defined as 2 years.

Each batch/lot of WS was re-tested/re-qualified annually. Re-testing of specific impurity WS was spot-checked; no remarks.

- SOP "Preparation, qualifications, handling and storage of working standards and reference standards for drug substances" was reviewed; no remarks.
- SOP "STP Purified water" was reviewed; no remarks. The following microbiological tests were carried out:
 - Total Aerobic Microbial count
 - Tests for pathogens
 - PW trends for July 2011 were presented to the inspectors upon request. All results were within specified limits.
- An R2A media preparation records was reviewed. Media was prepared and sterilized according to manufactures instructions.

The analytical balance verification schedule was the following:

- Daily using maximum and minimum standard weights
- Weekly using 3 different standard weights
- Monthly covering total range

Laboratory instruments were calibrated according to written procedures. Calibration schedules were following:

- HPLC, calibrated every 6 months, every months flow rate was checked
- GC, calibrated every 6 months
- UV, calibrated every 3 month
- IR, calibrated every 1 month

Log books were available for all laboratory instruments.

Class A volumetric glassware was used in the laboratory. Glassware was washed in washing machines and dried at 60 °C.

IR grade KBr was stored in a dry box at 62 °C temperature. CoA of polysterine film used for IR calibration polysterine film was showed to the inspectors; expiry date was given by the film manufacturer.

Testing of intermediates and APIs

For each batch of intermediate and API, appropriate laboratory tests were conducted to determine conformance to specifications.

Validation of analytical procedures

Analytical procedures were validated at R&D. Also R&D carried out verification of Pharmacopoeial methods.

SOP “Operation and calibration of NIR” and validation of identification method of specific raw material were reviewed.

Certificates of analysis

Certificates of analysis were issued for each batch of intermediate or API. Information on the name of the intermediate or API, the batch number and the date of release, was provided on the certificate of analysis. For intermediates or APIs with an expiry date, the expiry date was provided on the label and certificate of analysis. For intermediates or APIs with a retest date, the retest date was indicated on the label and/or certificate of analysis. Certificate listed each test performed. Certificates were dated and signed by authorized personnel from the quality unit.

Stability monitoring of APIs

A documented, ongoing testing programme was provided to monitor the stability characteristics of APIs. Stability samples were stored in containers that simulated the market container. One batch per year of API manufactured was added to the stability monitoring programme and tested at least at regular intervals to confirm the stability. Stability chambers were equipped with sound alarm system. T and RH was monitored and recorded daily, every hour.

Stability chambers were equipped with alarm system. T mapping was carried out for all stability chambers, T was monitored regularly. On going stability samples were stored in

chamber with T 30 °C and RH 65%. Re-validated batches and other batches with critical changes/deviations were placed for on going stability studies.

Expiry and retest dating

An API expiry or retest date was based on an evaluation of data derived from stability studies.

Reserve/retention samples

Appropriately identified reserve samples of each batch of API were retained for one year after the expiry date. The reserve samples were stored in the same packaging system in which the API was stored.

12. VALIDATION

Validation policy

The company's overall policy, intentions and approach to validation, including the validation of production processes, cleaning procedures, analytical methods, in-process control test procedures, computerized systems and personnel responsible for design, review, approval and documentation of each validation phase, were specified in Validation Master Plan.

- Validation master plan was reviewed. The following systems/procedures were intended to be validated:
 - HVAC system
 - PW system
 - Process validation
 - Qualification of analytical instruments
 - Blending validation
 - Cleaning validation
 - Analytical methods validation
 - Vendor evaluation
 - Computer system validation

Re-qualification for equipments were carried out once in 5 years

Re-validation - had to be carried out when there were changes in equipment/analytical instruments/methods, key starting materials, processes, location, batch size. Cleaning re-validation was carried out when a new product was introduced.

Validation documentation

Written validation protocols were established that specified how validation of a particular process will be conducted. The protocols were reviewed and approved by the quality unit and other designated units. Validation reports that cross-referenced the validation protocol were prepared, and summarized the results obtained.

- SOP "Computer system validation" was spot-checked.
- Re-validation report for specific AHU serving compaction room in MB-03 was reviewed. The following tests were carried out and reports were reviewed:
 - Airborne particle count test
 - Differential pressure test
 - T and RH
 - HEPA filter leakage test

Qualification

Appropriate qualification of critical equipment and ancillary systems were carried out. The company stated that IQ, OQ and PQ were carried out for all critical production equipment, QCL instruments and stability chambers. IQ, OQ and PQ protocols/reports were not reviewed.

Approaches to process validation

Process validation was carried out for all stages of production.

Process validation programme

Written process validation programme was established.

Periodic review of validated systems

Systems and processes were periodically evaluated to verify that they were still operating in a valid manner.

Cleaning validation

The company stated that cleaning procedures were validated. Cleaning validation was not covered during the inspection due to time constraints.

Validation of analytical methods

Analytical methods were validated by R&D.

SOP "Procedure for operation and validation of NIR spectrometer" was reviewed.

13. CHANGE CONTROL

A formal change control (CC) system was established to evaluate changes that may affect the production and control of the intermediate or API. The potential impact of the proposed change on the quality of the intermediate or API was evaluated. After the change had been implemented, the first batch manufactured was placed on stability studies. Manufacturers of the current dosage form were notified of changes from established production and process control procedures that can impact the quality of the API.

- SOP "Change control" was reviewed. Changes were classified as:
 - Major
 - Minor

The SOP was applicable to "all changes affecting product quality of APIs manufactured and affecting the quality system". On spot-checks, change control cases were traceable.

A number of CC forms were reviewed.

14. REJECTION AND RE-USE OF MATERIALS

Rejection

Intermediates and APIs failing to meet established specifications were identified and if applicable, were reprocessed or reworked as per SOP.

Reprocessing

Reprocessing was carried out according to a written SOP.

- SOP "Reprocess and rework" was reviewed. Reprocessed and reworked product batches were recorded in BPRs issuance and retrieval record log book, no remarks

Reworking

Reworking was carried out following the written SOP as above.

Recovery of materials and solvents

Specifications for fresh and recovered solvents were established.

- SOP "Recovery solvent management" was reviewed. Recovered solvent were intended to be used at the same stage or at a previous stage as per validated process. According to the SOP, solvent recovery operations could be contracted out.

Fresh solvents were stored in dedicated tanks; fixed pipelines were dedicated. Solvent recovery was batch-wise (not continuous). Recovery and storage of recovered solvents was done in non-dedicated tanks/distillers (not solvent- or material-specific).

Smaller distillers were installed next to MBs and connected to a particular MB, higher columns were located centrally for the Recovered solvents were allowed to be used in the same process for the same material; labelling was introduced. As stated by the company, final crystallisation is done with fresh solvents.

Returns

Returned intermediates and APIs were identified as such and quarantined. Records of returned intermediates and APIs were maintained.

- SOP "Handling of returned goods" and returned goods register 2010 and 2011 were reviewed; no remarks.

15. COMPLAINTS AND RECALLS

Complaints were recorded and investigated according to a written procedure. A written procedure that defined the circumstances under which a recall of an intermediate or API should be considered was not available

- SOP "Handling customer complaints" was reviewed. Responsible person for dealing with complaints was site Quality Head, deputized by QA Head. Complaints were classified as:
 - Critical
 - Major
 - Minor

Complaints were trended. Product-wise trends for 2010 were presented to inspectors.

- SOP "Product recall" was reviewed. Responsible person for dealing with recalls was site Quality Head, deputized by QA Head. There were no product recalls in the history of Unit III. Details of product recall (if any) should be reviewed as a part of PQR; no other remarks.

16. CONTRACT MANUFACTURERS (INCLUDING LABORATORIES)

Written and approved contracts/quality agreements between the contract giver and the contract acceptor were available. On spot-checks, areas of responsibility were specified. The contract permitted the contract giver to audit the contract acceptor's facilities for compliance with GMP.

- SOP "Procedure on contract manufactured of APIs, Intermediated, starting materials and solvent recovery for Matrix laboratories" was reviewed. Before approving a contract

manufacturer, it should be audited and approved by the Matrix team. Audit report was prepared and sent to the audited site in 15 working days. Audits were carried out once per year.

- Quality agreement for manufacture of specific API was reviewed, no remarks.

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, Matrix Laboratories Ltd, Unit III, located at Plot Nos.38 to 40, 49 to 51, Phase IV IDA, Jeedimetla, 500055 Hyderabad, Andhra Pradesh, India *was* considered to be operating at an acceptable level of 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.