

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

Name of Manufacturer	Shasun Pharmaceuticals Ltd
Unit number	NA
Production Block	• Production block No 4 • Packing block No 5
Physical address	A1/B, SIPCOT Industrial Complex, Kudikadu – Village, Cuddalore - 607 005, Tamilnadu, India
Contact person and email address.	Mr. B. Sreedhar Head - Quality Management & RA E-mail: sreedhar@shasun.com MOB: 91-7373736614
Date of inspection	29 November - 01 December 2012
Type of inspection	Follow up inspection of 19 - 21 March 2012
Active Pharmaceutical Ingredient(s) included in the inspection	APIMF177 Cycloserine
Summary of the activities performed by the manufacturer	Production, quality control, packaging, distribution of APIs and intermediates

Part 2: Summary

General information about the company and site

The facility inspected was **Shasun Pharmaceuticals Ltd, A1/B, SIPCOT Industrial Complex, Kudikadu – Village, Cuddalore - 607 005, Tamilnadu, India**, here after referred to **Shasun Cuddalore**. Shasun Pharmaceuticals Ltd was established in 1976 with its first plant at Valechery Chennai, focusing on the manufacturer Analgin API. The second plant was established at Puducherry (*formerly known as Pondicherry*) in 1986 with a focus to manufacture Ibuprofen. The plant under the focus of this inspection was established at Cuddalore in 1991 for the production of Ranitidine Hydrochloride. In 2005 a Contract Research, Manufacturing and Synthesis Centre (CRAMS) was established at Keelakottai, Chennai with a focus as a pilot plant for contract manufacturing and a formulations facility was opened at Puducherry the same year. Shasun acquired an API facility at Dudley in UK in 2006 focusing on contract manufacturing of new chemical entities (NCEs). The company also has a Biotech facility at Puducherry and is constructing an API factory in Vizag.

According to the site master file SMF/CUD/09/2011 effective 02/12/2012 and the presentation made by the company at the opening meeting, Shasun Cuddalore was located on a plot of land 64,000m² with most of it already built currently with 4 multi-product independent production blocks, each with an intermediate zone and Pharma zone (class 100,000).

The site had a licence on Form 25: 703 issued by Drug Control Administration, Tamil Nadu, Chennai, India. The site manufactures various intermediates and non-sterile APIs. The major products were stated to be Gabapentin, Venlafaxine Hydrochloride, Ranitidine Hydrochloride, Nizatidine and Cycloserine. No steroids, beta lactam antibiotics (e.g. penicillins and cephalosporins), hormones, cytotoxics and non-pharmaceutical products are manufactured on the site.

According to the company presentation and SMF, the site operates 24 hours in 3 production shifts and one general day shift. It employed a total of 511 people:

History of WHO and/or regulatory agency inspections

This was a follow up inspection of this site by WHO Prequalification of Medicines Programme (WHO-PQ) to the one conducted March 19 – 21, 2012. According to the company presentation, the site has been inspected by the following agencies, none of which had specifically covered Cycloserine:

1. 1998 – TGA (Ranitidine)
2. 1999 – USFDA (Nizatidine and Ranitidine Hydrochloride)
3. 2002 – USFDA (Methohexital)
4. 2003 – EDQM
5. 2007 – USFDA (Nizatidine, Ranitidine Hydrochloride, Gabapentin, Olanzapine)
6. 2008 – Danish Medicines Authority

7. 2010 – USFDA (Sevelamer HCl, Nizatidine, Ranitidine Hydrochloride, Gabapentin, Olanzapine)
8. 2012 – WHO-PQ (Cycloserine)

Focus of the inspection

The inspection focused on the production and control of **APIMF177: Cycloserine** API with particular focus on the status of implementation of the corrective and preventive actions (CAPAs) to the observations of the previous inspection. The inspection covered all the sections of WHO Good Manufacturing Practice (GMP) for Active Pharmaceutical Ingredients (APIs), including premises, equipment, documentation, materials, validation, sanitation and hygiene, production, quality control and utilities.

Inspected Areas

Day 1: 29 November 2012

The first day of inspection covered the following:

1. Opening meeting which covered the following:
 - Introduction of the inspectors and the WHO-PQ.
 - Scope of the inspection and confirmation of the inspection schedule.
 - Introduction of the company staff.
 - Company presentation highlighting the company overview, site description, production and quality control (QC) capacities, quality management and assurance systems, summary of manufacturing processes, major equipment and product range, inspection history.
2. Presentation of the manufacturing process for Cycloserine (4 stages and respective scale of inputs and outputs).

Several changes had been implemented in the manufacturing process of Cycloserine, related equipment and methods of analysis; most of which had been closed but a few were still open.

3. Status of implementation of the CAPAs to the observations: Most of the CAPAs had been implemented but a few similar issues were noted as follows:
 - Pipes painted before adequate de-rusting and priming.
 - Inadequate installations and maintenance of pipe work and joints.
4. Documents Reviewed:
 - Qualification of new reactor
 - Process Validation

Issues with documentation were observed but these were subsequently adequately addressed.
5. Visited and inspected the Quality Assurance (QA) department offices and archives. Issues of organisation were observed but there were subsequently adequately addressed.

6. The following areas and aspects of the QA department were reviewed:
 - Change control standard Operating Procedure (SOP).
 - SOP for control of documents.
 - Recovery of methylene dichloride (MDC): specifications and standard testing procedures. 16 batches had been recovered, tested and used.
 Observations of this assessment are discussed in section 2.1 below.

7. Organograms:
 - Site organisation chart with names of current position holders.
 - Organisation chart for the Quality Unit of Shasun.
 - Organisation charts for:
 - i. Block IV.
 - ii. QA department
 - iii. QC department
 See section 2.2 below for further discussion of personnel issues.

8. Job descriptions of selected personnel:
 - Manager (probation)/Head of Block IV.
 - Two persons designated as Shift Head
 - Head of Site QA.
 - Batch Release:
 - i. Executive QA.
 - ii. Management Trainee QA.
 - iii. Senior Executive QA.
 - Head of Site QC.
 - Senior Executive/Section Head – Raw Materials (RM)
 - Signing of Certificates of Analysis (CoAs):
 - i. Manager - QC/Shift Supervisor
 - ii. Senior Manager - QC/Shift Supervisor.
 - iii. Three Senior Executives - QC/Shift Supervisors.
 - iv. Executive- QC/Shift Supervisor.
 The deputies of the key personnel were not specified and the title used were not consistent within the organograms and in comparison with the job descriptions. This and other minor issues were subsequently adequately addressed.

9. Recall SOP and Mock Recall. See section 2.14 for more discussion of this aspect.

10. Complaints SOP and Complaints register for 2012: there had been 14 complaints and 9 had been closed. See section 2.14 for more discussion of this aspect.

Day 2: 30 November 2012

Feedback was given on the previous day's inspection and the company was given an opportunity to provide any preliminary response.

The inspection of the following issues and areas followed:

1. Supplier qualification: There was an SOP for qualification of suppliers of raw materials, packaging materials, intermediates and printed labels. For critical raw

materials [API Starting Material (APISM) and Intermediates] this involved a screening questionnaire; confirmation of ability to meet Shasun's specifications; analysis of a sample by QC/R&D; declaration of absence of melamine and freedom from TSE/BSE and Genetic Modified Organisms (GMO); disclosure of critical materials, residual solvents and metal catalysts; and evaluation of the manufacturer's questionnaire before provisional approval to purchase 1 - 2 qualification batches for performance qualification (PQ) or R&D. Suppliers were exempted from supplying sample in case of hazardous materials, narcotics or if out of stock on the domestic market. A quality agreement was then signed which covered the need to be notified of all significant changes and a declaration of willingness to be audited. For domestic suppliers a site audit had to be conducted before validation while for overseas suppliers the need depended on the outcome of the evaluation of the manufacturers' questionnaire. Approval was by Senior Corporate QA for 3 years and a supplier was removed from the register if there were no supplies for 3 years, 3 consignments rejected for quality reasons or a score of <85% based on a standard evaluation criteria.

One of the vendors for the APISM had been evaluated and approved in 2005 based on the manufacturer questionnaire. Review of the evaluation documents indicated that issues cleaning validation and risk of cross-contamination had not been adequately evaluated and the site had never been audited. These issues were subsequently adequately addressed through CAPAs. The other suppliers mentioned in the APIMF had been removed from the approved vendor list (AVL) because they had not supplied for the last 3 years.

2. Documents reviewed: Cycloserine Crude specification. These were found not to be comprehensive but revised specifications have since been submitted to the assessors for evaluation.
3. Inspection of the storage facilities (including outdoor storages):
 - For bulk solvents: There was no shade for sampling transport tankers during adverse weather. There were dedicated discharge hoses and underground tankers were identified with the letter and colour codes. The levels of tankers had been calibrated for quantification and the analytical report (A.R.) number of the composite sample of the solvent after recirculation was always indicated – several examples were sited. Some sampling points were not in good sanitation condition, but this was subsequently adequately addressed. The solvent were pumped via flow meters to day tanks near the production blocks.
 - For liquid raw materials in drums. These were labelled, sampled and tested before use and others were approved based on supplier certificate of analysis. Records of receipt, storage and use could facilitate traceability of the individual batches. Concerns about investigation and handling of a few drums of a solvent that had been received without seals were subsequently adequately.

- For starting materials / intermediate products: reception, sampling, storage procedures and records were reviewed and no issues of concern were noted.
 - Packaging materials: Suppliers of LDPE bags (black and white) were approved. A case of tighter sampling size for black bags, which are not in direct contact with the materials, than for white bags was noted without justification but in each case, the sample size was adequate.
 - SAP: was in place but not validated and hence not used for regulatory control. For example, it could not provide adequate audit trail for a batch of material whose dispensed was reviewed.
 - Dispensing area was fitted with reverse laminar airflow (RLAF) cabinet. The balances had been calibrated and records of daily check were available. The Nitrogen cylinder did not have an identification number and no evidence of QC/QA approval. Adequate preventive and corrective action was subsequently implemented. One of the hazardous materials was not dispensed, but was sent to production in the suppliers containers for direct charging via dedicated pump with flow meter.
 - For finished products (APIs): packaging, labelling, storage procedures and records were reviewed and found adequate.
4. Inspection of production activities in Block IV: The major pieces of equipment were identified and log books were well maintained, indicating that the equipment was used at different stages and also for several products.

In the intermediate section, production of batch and solvent recovery were on going. Several issues related to pipework and filter installation, identification of pipework, maintenance of pipes, equipment and doors, calibration of gauges and cleaning were noted. These were subsequently adequately addressed and confirmed through CAPAs.

In the clean area crystallization of a batch was on going. The log books were in place. Cycloserine was purged with N₂ between drying, sifting and final packaging including silica gel. The issues noted related to inadequate maintenance, labelling, differential pressure monitoring, and installation of pressure gauges and malfunctioning of a temperature gauge. These were subsequently adequately addressed and confirmed through CAPAs.

Day 3: 01 December 2012

Feedback was given on the previous day's inspection and the company was given an opportunity to provide any preliminary response.

The inspection of the following issues and areas followed:

1. Records of receipt, sampling and testing of selected consignments of solvents.
2. Equipment log for one Rotor-Cone Dryer (RCD).
3. Specimen signatures of operators and supervisors in Block IV.
4. Records of calibration of one of the temperature sensors for 2 consecutive intervals. Two master calibration gauges were indicated on the calibration

certificate but the one actually used was not specified and only one had a valid calibration certificate. Measures were put in place to avoid future re-occurrence of the same.

5. Use and cleaning log book for Micron Filter for one of the solvents. It was cleaned and integrity checked every 15 days.
6. SOP on “Checking of secondary weights against primary weights” and calibration certificate of secondary weight of 50kg (labelled 50.05kg). It was calibrated against a Master Weight with valid certificate.
7. SOP on “Cleaning procedure – validation and routine evaluation”. It categorised cleaning procedures for process equipment disassembled and not disassembled. Product change cleaning procedure required validation but batch to batch cleaning procedures did not. Cleaning validations included 3 consecutive batches using rinse (mg/litre) and swab ($\mu\text{g}/100\text{cm}^2$) samples with consideration of the recovery factor and acceptance criteria of 10ppm and visually clean. The results and report covering one of the crystallizers were reviewed. This was cleaned using 15 litres of water for the next batch. The limits for rinse and swab tested were calculated. The raw data for calculation of the standard concentration was not available and the calculation of results was not performed according to the SOP on “Preparation and analysis of swab and rinse samples”. Results of several pieces of process equipment were also reviewed with similar observations. These were subsequently adequately addressed and confirmed through CAPAs.
8. SOP on “Reprocessing and Reworking”. Examples were selected from the register and reviewed, with not serious issues noted.
9. Other documents reviewed:
 - Specifications of new and recovered dichloromethane
 - Specification of one of the reactors
 - Specification of one of the centrifuges
 - Stability data

These were generally found to be adequate, save for minor deficiencies that were subsequently adequately addressed.

10. QC Laboratories:

The following aspects were reviewed:

- a) Results of specific optical rotation (SOR) for one batch of an intermediate. All raw data was available and in order.
- b) Performance checks on an Automatic Polarimeter. The frequency was adhered to and records were available and in order.
- c) IR tests: The ratio of KBr:Sample (300:10) used was not consistent with the pharmacopoeial recommendation and there was no justification for the ratio used. The finger print region was not known by the analysts and no acceptance criteria for the quality of spectra had been set (e.g. absorbance at 2000cm^{-1}). The evaluation of concordance was only visual and did not include correlation coefficient, slope, intercept and comparison of main peaks. Adequate explanation and corrective actions were confirmed through CAPAs.
- d) Test for benzene by GC in batches of methanol and isopropyl alcohol (IPA) with none detected.

e) Records of qualification, calibration and maintenance of the following QC equipment:

- High performance Liquid Chromatography (HPLC)
- Gas Chromatography (GC)
- Infra-Red Spectrophotometer (IR)

These were generally found to be adequate.

11. Stability samples and reserve samples were found to be adequately handled.
12. Purified Water system: sampling and testing was found to in line with set procedure.
13. HVAC: inspected the AHU-6 serving Crystallizer and Centrifuge area 3. The filtration system included Primary filters (20µ and 10µ), secondary filters (5µ and 2µ) and HEPA filters (0.3µ) one in the plenum and one terminal. The primary filters were washed with water while the 5µ was cleaned with compressed air. No major issues were noted.
14. Compressed air: Compressed air was not adequately filtered. The final filter used was claimed to be 0.2µ, during inspection compressed air sprayed on a paper left it very wet. This was subsequently investigated and found that the solenoid valve installed in the air dryer was malfunctioning. This was subsequently replaced.

At the closing meeting, the inspectors gave feedback on the inspection observations of the day and the entire inspection. The company was informed about the procedures and timelines for the report, Corrective and Preventive Actions (CAPAs) and WHO Public Inspection report (WHOPIR).

2.1 QUALITY MANAGEMENT

Quality management system of the company was established in form of the organisational structure, standard operational procedures and related resources. There was a quality unit composed of the quality assurance and Quality control departments which were independent of production.

Most of the CAPAs had been implemented but a few similar issues were noted related to pipes painted before adequate de-rusting and priming and inadequate installations and maintenance of pipe work and joints. These were subsequently adequately addressed and confirmed through CAPAs.

There was a system for self-inspection but its effectiveness was in question given the observation of the inspection. No product quality review had been prepared since the last inspection, so this area was not inspected. More vigilance was needed in the management of the quality system and there were issues noted with documentation of the responsibilities for production activities, quality unit and particularly the responsibilities for batch release and signing of certificates of analysis. These were subsequently adequately addressed and confirmed through CAPAs.

2.2 PERSONNEL

The site had an adequate number of personnel to perform the site operations. They were supported by job descriptions although there was need to clearly designate the deputies for key responsibilities. Training programmes were in place but the observations of the inspection put in question its effectiveness. These were subsequently adequately addressed and confirmed through CAPAs.

There were facilities to ensure personnel hygiene and they were provided with appropriate clothing suitable for the manufacturing activities. There were separate dining for use by staff for eating and drinking.

2.3 BUILDINGS AND FACILITIES

Cycloserine was produced in Block IV with two sections, one for intermediates and the clean area for purification and powder processing. The premises were not dedicated to Cycloserine but were used to produce several products. Overall, buildings were suitable for the tasks being carried out. Construction was of masonry with painted exterior and suitable internal finishes, such as tiles or paint, depending upon the application. Floors were of sealed concrete, or brick or Kota stone slabs. In controlled areas, joints between walls and floors and walls and ceilings were coved. There were several examples of inadequate installation, maintenance and housekeeping. These were subsequently adequately addressed and confirmed through CAPAs.

The Purified Water system was satisfactory. Materials used, electro-polished stainless steel, was adequate.

2.4 PROCESS EQUIPMENT

The inspection of production facilities was limited to Block IV, concerned with the production of Cycloserine. The equipment was not dedicated but was used to produce multiple products on campaign basis followed by cleaning. Overall, the design and construction of equipment was adequate but deficiencies were observed in some areas. These include details regarding installation and identification of pipework and the material of construction of one centrifuge in particular. Other concerns were related to the poor location of filters on solvent supply pipelines and aspects of inadequate recording cleaning status. These were subsequently adequately addressed and confirmed through CAPAs.

2.5 DOCUMENTATION AND RECORDS

There was an extensive documentation in form of batch production instruction and records, specifications, standard operating procedures, records of materials at different stages of processing and storage and quality control methods and records. Several examples were observed of inadequate documentation control and practices. These include uncontrolled logbooks, unclear details in reports and SOPs and incomplete

documents. These were subsequently adequately addressed and confirmed through CAPAs.

2.6 MATERIALS MANAGEMENT

Flammable solvents were stored in the Explosive Yard in underground tanks. Access was via a gateway, usually kept locked. Hoses were stored in a masonry shed at the centre of the area. Overall, standards were satisfactory but there were some deficiencies which were subsequently adequately addressed.

Solids and 200L drums of materials were stored in the Raw Materials Warehouse. Some were approved based upon the supplier's Certificate of Analysis. Information on their approved suppliers was available. Records of sampling and testing were reviewed.

Deficiencies were observed, particularly regarding documentation. These were subsequently adequately addressed and confirmed through CAPAs.

2.7 PRODUCTION AND IN-PROCESS CONTROLS

Cycloserine was manufactured in 4 stages starting with esterification of D-Serine followed by chlorination, cyclization, purification and powder processing with an output 75kg Cycloserine. The batch size was continuous for all stages and there was no blending of batches.

In general, controls were adequate with the exception of some note deficiencies which were subsequently adequately addressed and this confirmed through CAPAs.

2.8 PACKAGING AND IDENTIFICATION LABELLING OF APIs AND INTERMEDIATES

Packing Materials were stored in the Raw Materials Warehouse. Cycloserine was packed in a white translucent LDPE bag, then into another white translucent LDPE bag purged with nitrogen, with a silica gel sachet between the two bags and then into a lacquered steel drum with silica gel pack with a lid.

Some issues were note in the packing operations of Cycloserine API. These were, however, subsequently adequately addressed and confirmed through CAPAs.

2.9 STORAGE AND DISTRIBUTION

There were separate storage facilities for raw materials, packaging materials, returned and rejected materials, intermediates and finished goods/APIs. The digital hygrometer to monitor storage conditions for the finished API had malfunctioned at the time of the inspection. This was subsequently replaced with a new instrument and calibration frequency was increased to once in a month from once in three months.

Records of storage and distribution could facilitate traceability.

2.10 LABORATORY CONTROLS

The QC Laboratories were adequately equipped for the work being carried out. The building was approximately 9 years old at the time of the inspection and several aspects of inadequate building maintenance were noticed. These were, however, subsequently adequately addressed and confirmed through CAPAs.

The GC used to conduct residual solvents test for the release of Cycloserine was approximately 6 years old and had previously been used in the R&D Department. The design qualification was adequate but the performance qualification deficient. It was subsequently requalified, the report submitted and found generally adequate.

There was an SOP for performance check of GC instruments. The register for one of the GC instruments was checked. The annexures did not make reference to the SOP on the title page but otherwise were satisfactory.

Documentation relating to HPLC instrumentation was generally satisfactory. When not in use, columns were correctly stored. Related logbooks included those for column use and, a register of those approved for use in the laboratory. Logbooks were not numbered by QA.

Deficiencies were observed regarding the control of the external party maintaining the instruments. These were subsequently adequately addressed and confirmed through CAPAs.

The IR Spectrometer was located in the Wet Laboratory. Calibration records were checked. The catalogue number of the standard and not the serial number was recorded in the calibration log. Spectra recorded in the instrument's database could not be edited. Spectra absorbances were assigned wavenumber readings by the instrument and these were compared with those from the approved reference standard by the analyst, although from the examples reviewed this was not routinely done. Aspects of the potassium bromide (KBr) pellet die were unsatisfactory. Pre-approved batches were selected for working standards. Additional spectroscopic data was obtained but the qualification was not adequate. These deficiencies were subsequently adequately addressed and confirmed through CAPAs.

Reserve samples were stored in an access-controlled room. Samples of released batch CLN1107003 were checked. Of the three samples, only one was obviously sealed with an atmosphere of nitrogen under a low pressure.

2.11 VALIDATION

Process Validation was described in an approved standard operating procedure. A case of process validation of Cycloserine Stage I and stage II was noted to have been initiated via change requests and respective protocols was in place. The details of the three batches used in each validation were available and the analytical data was satisfactory and yields were in the expected ranges.

An increase in batch size of Stage II was initiated via change request and a protocol to introduce the increase input of Stage I was in place and the details of the bathes used were available. A recovered solvent was used in the last batch. Yields were within the expected range.

Validation of recovery process for one of the solvents was initiated by change request and a protocol was in place. Three batches were used and all were with 300kg input of Stage I. Yields were as expected.

2.12 CHANGE CONTROL

Examples of change requests were reviewed. One related to installation of a reactor in Block IV. Another change request was concerned with adding ethanol, and its denaturant ethyl acetate to the release specification of Cycloserine Ph.Int.

Process Validation studies are initiated by Change Requests. Details are given above in 2.11.

2.13 REJECTION AND RE-USE OF MATERIALS

SOP on “Reprocessing and Reworking” was reviewed and a new batch number was assigned to the reprocessed or reworked batch. Examples were selected from the register and reviewed. Most related batched were reprocessed after failing tests on specific optical rotation (SOR) and purity. The reprocessed batches were adequately tested and the results were available. A few issues were noted but these were subsequently adequately addressed through CAPAs.

One of the solvents used in Cycloserine Stage II was recovered in a reactor in Block IV. The recovered solvent was identified by a material code distinct from the fresh solvent and its specifications were found to be adequate. Results reviewed indicated that the purity of the recovered solvent was similar to that of the fresh solvent. The use of the recovered solvent had been validated. Details are given in 2.11, above.

2.14 COMPLAINTS AND RECALLS

The SOP on the “Handling Recalls” was reviewed. “Recall” was restricted to those initiated by Regulatory Authorities and “Withdrawal” when voluntary by the company following minor deficiencies. It provided for notifying the authorities within 2 – 4 weeks. There was no classification of recalls, means communication and timelines were specified.

A Mock Recall had been performed to evaluate the effectiveness of the procedure but the choice of the market and product did not provide a worst case scenario. The choice of the acceptance criteria was not justified. These issues were subsequently adequately addressed and this was confirmed through CAPAs.

Complaints were managed under an approved SOP. It provided for acknowledgement of the complaint within 2 days and a report within 30 days. It also provided for

registration, investigation by a team, request for samples and classification into manufacturing, packaging, quality and repetitive complaints. In 2012, there had been 14 complaint and 9 had been closed. Several related to observation of black particles. An example was reviewed which related to black particles seen during sieving of one for the batches of another API. Investigation revealed that a Viton O-ring was used on the solvent Micro-filter over a period of 3 – 4 months instead of the Teflon O-ring. Investigation did not refer to similar complaints received in the past. There was no discussion of post operation filter integrity test and there was no record of review of the BMR. Although samples of particles were available, there was no evaluation for comparison and confirmation that they were indeed from the Viton O-ring. The measures that were subsequently taken by the company to address these deficiencies were found to be adequate.

2.15 CONTRACT MANUFACTURERS (INCLUDING LABORATORIES)

The company stated that production operations were not contracted out but some analytical tests were contracted out to contract laboratories. This area was not inspected in detail.

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, **APIMF177: Cycloserine** API manufactured at **Shasun Pharmaceuticals Ltd, A1/B, SIPCOT Industrial Complex, Kudikadu – Village, Cuddalore - 607 005, Tamilnadu, India** was 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.