



**WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Contract Research Organization**

Part 1: General information

WHO product numbers covered by the inspection	• TB304: Cycloserine 250 mg capsules • MA107: Artesunate/Amodiaquine 100 mg/270 mg tablets • HA613: Fluconazole 200 mg Tablets
Study number	Study #:034-14: TB304 Study#C11197: MA107 Study#C13236: HA613
Title of the study	An open-label, balanced, randomized, two-treatment, two-sequence, two-period, cross-over, single dose, oral bioequivalence study of Cycloserine 250 mg capsules (Test, TB304) of Mylan Laboratories Limited, India and Cycloserine capsules USP 250mg (Reference) of The Chao Center for Industrial Pharmacy & Contract Manufacturing., West Lafayette IN 47906, USA in healthy, adult, human subjects under fasting conditions. An open-label, balanced, randomized, two-treatment, two-period, two-sequence, single-dose, crossover oral bioequivalence study of Artesunate / Amodiaquine 100 mg / 270 mg tablets (MA107) of Mylan Laboratories Limited, India with Coarsucam[®] (Artesunate / Amodiaquine) 100 mg / 270 mg tablets of Sanofi Aventis, Casablanca, Morocco in normal healthy adult human subjects under fasting conditions. An open-label, balanced, randomized, two-treatment, two-period, two-sequence, single-dose, crossover oral bioequivalence study of Fluconazole 200 mg Tablets (HA613) of Mylan Laboratories Limited, India with Diflucan[®] 200 mg (fluconazole) Tablets of Roerig Division of Pfizer Inc., U.S.A in normal healthy adult human subjects under fasting conditions.
Clinical Part of the study: Name and address of the organization	Axis Clinicals Limited, (TB304) Clinical Unit 1-121/1, Miyapur Hyderabad-500 049, India

	Aizant Drug Research Solutions Pvt Ltd (MA107 & HA613), Clinical Pharmacology Department, Clinical Development Division, Survey No.: 172 & 173, Apparel Park Road, Dulapally Village, Quthbullapur Mandal, Hyderabad, Andhra Pradesh, India - 500014. Phone No.: +91 40 23792190/91/92, Fax No.: +91 40 23792223
Bio-analytical laboratory: Name and address	TB304, MA107 and HA613: Mylan Laboratories Limited, Clinical Research Centre, Saradhi Chambers, Plot No. 4-A, Beside Poulomi Hospital, Rukminipuri, Dr. A. S. Rao Nagar, Hyderabad, Telengana State, India - 500062. Phone No.: +91 40 30492900, Fax No.: +91 40 27138562.
Date of inspection	20 March 2015 26 and 27 March 2015

Part 2: Summary

General information about the site(s)

Mylan Laboratories Inc., USA was founded in 1961 and with headquarters located in Pittsburgh, Pennsylvania, United States. The company produces generic pharmaceuticals, branded generics, specialty & brand pharmaceuticals and active pharmaceutical ingredients. Mylan Laboratories Inc. had acquired Matrix and renamed it to Mylan, effective from 05 October, 2011. The corporate office of **Mylan Laboratories Limited (India)** is based in Hyderabad, India.

Mylan Clinical Research Centre (CRC) was established in July 2006 in Hyderabad, India, to support the generic drug development program for AIDS and also to support R&D for screening of formulations through pilot Bio-Equivalence (BE) studies.

The in-house bio-analytical facility was commenced in July 2006 with 2 LCMS/MS systems and 25 people in a 5000 Sq. ft. facility. The bio-analytical facility was expanded in the year 2008, to the current facility to suit the growing portfolio and other bioequivalence needs. The existing facility area is 25,000 Sq. ft. spread across 4 levels. Total manpower was 88 (84 + 4 new employees to join) and total strength including contract staff at present is: 84+20= 104.

Bioanalytical Laboratory activities were spread across Levels 1, 2 and 3 which consists of:

- Instrument Labs
- Processing Labs
- Plasma Sample Storage

- IT section:

History of WHO and/or regulatory agency inspections

This is the 7th inspection performed by WHO. The last WHO inspection was performed in October 2011.

From the opening meeting presentation, it was noted that Mylan CRC had been inspected by the following regulatory authorities:

- First regulatory audit was triggered in Sept-07 for an ARV through PEPFAR.
- USFDA inspected the bioanalytical facility in 2008, 2010, 2011, 2013 and 2014
- Thai FDA inspected the facility in 2007, 2010 and 2013
- DCGI, India inspected the facility in October 2014
- EMA inspected the facility in January 2015

Focus of the inspection

The inspection focused on the bio-equivalence studies and in particular the bioanalytical section of three of the studies listed under Part 1 (TB304, MA107 and HA613). The inspection covered most of the sections of the WHO GLP texts, including EMA and FDA guideline on Bioanalytical Method Validation.

Inspected Areas

Days 1, 2 and 3 focussed mostly on the general organization of the Mylan Laboratories Limited, Clinical Research Centre site as well as on the bioanalytical portion of all three studies conducted by Axis Clinicals Limited (TB304) and Aizant Drug Research Solutions Pvt Ltd (MA107&HA613). The remaining points and closing meeting were given on day 3.

2.1. PROVISIONS AND PREREQUISITES FOR A CLINICAL TRIAL

Not applicable

2.2. THE PROTOCOL

Not applicable

2.3. PROTECTION OF TRIAL SUBJECTS

Not applicable

2.4. RESPONSIBILITIES OF THE INVESTIGATOR

Not applicable

2.5. RESPONSIBILITIES OF THE SPONSOR

Not applicable

2.6. RESPONSIBILITIES OF THE MONITOR

Not applicable

2.7. MONITORING OF SAFETY

Not applicable

2.8. RECORD-KEEPING AND HANDLING OF DATA

Not applicable

2.9. STATISTICS AND CALCULATIONS

Not inspected

2.10. HANDLING OF AND ACCOUNTABILITY FOR PHARMACEUTICAL PRODUCTS

Not applicable

2.11. ROLE OF THE DRUG REGULATORY AUTHORITY

Not applicable

2.12. QUALITY ASSURANCE FOR THE CONDUCT OF A CLINICAL TRIAL

Not applicable

2.13. SHIPPING AND HANDLING OF SAMPLES

This section was inspected and found to be satisfactory.

2.14. GENERAL INFO ABOUT THE STUDY

Refer activities inspected during Day 1 to Day 3.

2.15 COMPUTERIZED SYSTEMS AND DATA INTEGRITY

Computer systems were qualified. Backups of data were made. Procedures were generally in place to ensure data integrity.

Part 3: Conclusion

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the deficiencies listed in the Inspection Report, the **bioanalytical section** of **TB304, MA107 and HA613** was considered to have been conducted at an acceptable level of compliance with WHO GLP at ***Mylan Clinical Research Centre, Hyderabad, Telangana, India.***

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 CRO, 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.