

### WHO Public Inspection Report (WHOPIR) of a Contract Research Organization

The report is the property of the organization responsible for performing the inspection.

#### Part 1: General information

Name of organization	Manipal AcuNova KMC Hospital Clinical Pharmacology Unit
Physical address	5 <sup>th</sup> floor, MCODES Building, KMC Hospital. Attavar, 575001 Mangalore, India.
Postal address	Same as above
Telephone number	00 91 824 244 5858 / 6141
Fax number	00 91 824 242 5092
Summary of activities	Performance of clinical studies, including bioequivalence trials (clinical and bio-analytical parts)
<b>WHO reference number</b> Study	<b>HA 392</b> # 036-07 Study Title : A randomized, open label, balanced, two treatment, two period, two sequence, single dose, crossover, bioequivalence study of lamivudine/zidovudine 150mg/300mg tablet (Matrix Laboratories Ltd, India) with Combivir® (Lamivudine/Zidovudine) 150mg/300mg tablet, (GlaxoSmithKline, Inc. USA, in 44 healthy human adult male subjects under fasting conditions.
Start and stop dates for each phase of the clinical study	Period 1 : 6 February 2007 to 8 February 2007 Period 2 : 17 February 2007 to 19 February 2007
Investigational Products	Lamivudine and Zidovudine 150mg/300mg Tablets Manufactured by : Matrix Laboratories Limited, F-4 & F-12, Malegaon, MIDC, Sinnar- 422 113, Nashik District, Maharashtra State, India. Batch number : LZDA116001 Manufacturing date : May 2006
Reference Products	Combivir® (Lamivudine/Zidovudine) 150mg/300mg tablets Manufactured by : GlaxoSmithKline, USA. Batch number : 6ZP1816
Sponsor	Matrix Laboratories Limited, India
Date of inspection:	21 January 2008
Project (if any):	Prequalification Programme : Priority Essential Medicines

#### Part 2: Summary

The purpose of the inspection was to assess the bioequivalence study performed at Matrix Laboratories Ltd, Clinical Research Centre for the product:

**HA 392** : Lamivudine and Zidovudine 150mg/300mg Tablets, manufactured by Matrix Laboratories Limited

and to evaluate whether the clinical part of the bioequivalence study was conducted in compliance with the submitted and assessed protocol and Good Clinical Practices (GCP) and other relevant WHO or international Good Practices and standards where applicable.

The bio-analytical part of the study was done at :  
Matrix Laboratories Limited, Clinical Research Centre 2<sup>nd</sup> Floor, Crescent Krishna Metropolis, Sainikupuri, A.S. Rao Nagar, 500 062 Hyderabad, India

Manipal AcuNova started its clinical and bio-analytical operations for bioavailability / bioequivalence studies, phase I studies and Clinical trials (phase II to phase IV) in August 2005 in Manipal and in July 2006 in Mangalore. There is a third facility of 60 beds in Bangalore still under construction without activity so far.

The Manipal AcuNova Clinical Pharmacology Unit located in Mangalore is situated in the KMC Hospital and is exclusively performing clinical parts of clinical studies. There are a total of 48 beds spread over 3 wards

There are currently about 20 full time persons employed.

This Prequalification Programme inspection was the first audit conducted by WHO at the Manipal site of Manipal AcuNova.

The site has been authorized by the Indian Regulatory Authority and was inspected in February 2005 and July 2006.

The site as also been previously inspected by the USFDA in September 2007.

Various areas of the clinical facilities were inspected. These included the 3 bedded facilities where two studies can be conducted simultaneously. Emergency room equipped for intensive care medical management, phlebotomy rooms, registration areas, screening areas, sample processing areas, pharmacy\*, washrooms and dining halls.

The facilities in the pharmacy consist of a humidity chamber for study drug storage. During the inspection, the remaining study drug samples were examined in the pharmacy.

Manipal AcuNova has a computerized data base where all of the volunteer are registered and identified with their photograph and thumb print. The subject database is linked to biometric finger print identification software. Each Volunteer Data Sheet also contained a copy of the subject's identification document such as school leaving certificate, passport or driving licence.



A volunteer's consent for registration has to be obtained before he can be considered as a potential study subject. A separate consent is then administered for general screening for study eligibility. The consent documents were available in English, Hindi, and the local language Kannada.

A review of the qualification of the principal investigator who left the company was done. The personal file including job description and training of one of the QA staff was also reviewed.

From the attendance sheet for pre-study meeting it appeared that the study personnel were informed of the study requirements and their roles.

There was a range of SOPs and associated records available and key SOPs and corresponding records were checked as the SOP for dispensing and dosing.

The source data of the study including clinical data, drug accountability records, dosing records etc. and remaining study drug samples at the site were audited to verify the accuracy, consistency, completeness, and reliability of the study reports. Various staff members were interviewed in relation to the conduct of the studies.

In the clinical facility, it appeared that the facilities and resources were adequate for support of the study workload.

Documentation reviewed included:

- Independent ethics committee review procedures
- Screening, and study consent forms
- Source data and results
- Master lists for subjects
- Documentation and SOPs relating to study drugs accountability and dispensing records, and study drug labels
- Randomization schedule
- Study drug administration
- Blood sample collection
- Lists of staff present during the study
- Master list of signatures of volunteers
- QA audit reports

At the time of the inspection the study was already accepted by the assessors.

### **Part 3: Conclusion**

Based on the people met and the documents reviewed, and considering the findings of the inspection, reflected in the observations listed in the inspection report, the studies, clinical part, inspected can be considered to have been conducted at an acceptable level of compliance with WHO Good Clinical Practices (GCP) and Good Laboratory Practices



(GLP), by Manipal AcuNova KMC Clinical Pharmacology Unit located in Mangalore, India.