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# WHO PUBLIC INSPECTION REPORT (WHOPIR) Contract Research Organization

## Part 1: General information

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| WHO product numbers covered by the inspection | • MA107:Artesunate/Amodiaquine 100 mg/270 mg tablets (Clinical by Aizant)<br>• HA613: Fluconazole 200mg Tablets (Clinical by Aizant)<br>• HA614: Clarithromycin 500 mg Tablets (Clinical and Bioanalytical by Aizant) |
| Study number | **Study#C11197 (MA107)**<br>**Study#C13236 (HA613)**<br>**Study#C13239 (HA614)** |
| Title of the study | 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) 100mg / 270 mg tablets of Sanofi Aventis, Casablanca, Morocco in normal healthy adult human subjects under fasting conditions.<br><br>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® 200mg (fluconazole) Tablets of Roerig Division of Pfizer Inc., U.S.A in normal healthy adult human subjects under fasting conditions.<br><br>An open-label, balanced, randomized, two-treatment, two-period, two-sequence, single-dose, crossover oral bioequivalence study of **Clarithromycin 500mg Tablets (HA614)** of Mylan Laboratories Limited, India with BIAXIN®FILMTAB® (Clarithromycin USP 500 mg) Tablets of Abbott Laboratories, U.S.A in normal healthy adult human subjects under fasting conditions. |
| Clinical Part of the study:<br>Name and address of the organization | For MA107, HA613 and HA614:<br>Clinical Pharmacology Department,<br>Clinical Development Division,<br>**Aizant Drug Research Solutions Pvt Ltd.,** |

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| | Survey No.: 172 &173, Apparel Park Road,<br>Dulapally Village, Quthbullapur Mandal,<br>Hyderabad, Andhra Pradesh, India - 500014.<br>Phone No.: +91 40 23792190/91/92,<br>Fax No.: +91 40 23792223 |
| Bio-analytical laboratory:<br>Name and address | For HA614 only:<br>Bioanalytical Department,<br>**Aizant Drug Research Solutions Pvt Ltd.,**<br>Survey No.: 172 &173, Apparel Park Road,<br>Dulapally Village, Quthbullapur Mandal,<br>Hyderabad, Andhra Pradesh, India-500014<br>Phone No.: +91 40 23792190/91/92,<br>Fax No.: +91 40 23792223. |
| Date of inspection | 23, 24 and 25 March 2015 |

**Part 2: Summary**

***General information about the site(s)***

Aizant Drug Research Solutions was incorporated in the year 2005.

The facility has 80 beds (2 Clinics of 40 bed each) with 60 + full time employees and 30+ on contract. The facility is spread across a 28,000 Sq. ft. area which has a dedicated registration /medical screening area, with uni-flow process, well equipped ICU's, Bed lift and a ramp and ambulance to take of care of emergencies. The CRO is associated with two tertiary care hospitals within 10 min drive from the facility and has an in-house diagnostics section. The facility has access to an Independent Ethics Committee (IEC)/ Institutional Review Board (IRB).

The bioanalytical facility is equipment with 8 LC-MS/MS and has 40+ full time employees. The laboratory was spread over 7,000 Sq. ft. area.

***History of WHO and/or regulatory agency inspections***

This is the second WHO inspection of Aizant. The CRO was last inspected in October 2011 for the clinical part of a study. The CRO had also been inspected by the USFDA in April 2010 and June 2013. In addition, the CRO was inspected by CDSCO India, Turkey MOH, and ANSM France for various studies and had been declared compliant.

***Focus of the inspection***

The inspection focused on the bio-equivalence study conducted for the products listed under Part 1 (Clinical part for MA107, HA613 and HA614 and bio-analytical for HA614 only). The inspection covered most of the sections of the WHO GCP and GLP texts, including the WHO guidance for organizations performing in vivo bioequivalence studies.

***Inspected Areas***

Days 1 and 2 focussed mostly on the general organization of the Aizant Drug Research Solutions Pvt Ltd site as well as on the clinical portion of all three studies, while day 3 was focussed mostly on the bioanalytical portion of one study conducted by Aizant Drug Research Solutions Pvt Ltd. The remaining points and closing meeting were given on day 3.

## 2.1. PROVISIONS AND PREREQUISITES FOR A CLINICAL TRIAL

All of the provisions and prerequisites for a clinical trial were met in general for the studies that were seen. The clinics were found to be in generally acceptable condition.

## 2.2. THE PROTOCOL

Protocols were found to be acceptable in general for the studies reviewed.

## 2.3. PROTECTION OF TRIAL SUBJECTS

The clauses from the Declaration of Helsinki were given during informed consent according to the documentation that was seen and these were displayed in the screening area.

The Independent Ethics Committee composition and organization followed the necessary requirements.

## 2.4. RESPONSIBILITIES OF THE INVESTIGATOR

The responsibilities of the investigator were considered to be fulfilled in general.

## 2.5. RESPONSIBILITIES OF THE SPONSOR

The sponsor for these studies was Mylan. The applicable responsibilities were in general fulfilled.

## 2.6. RESPONSIBILITIES OF THE MONITOR

The sponsor performed monitoring of both the studies including assessment of CRO prior to signing the contract with the CRO.

## 2.7. MONITORING OF SAFETY

No issues were found regarding the handling, recording and reporting of adverse events.

## 2.8. RECORD-KEEPING AND HANDLING OF DATA

The responsibilities of the investigator and sponsor were generally fulfilled with regards to record keeping and data handling. The on-site archive was equipped with a fire extinguishing system and a steel door. Documents were tracked using a logbook for the removal and return of documents and personnel entry was also entered in a logbook. The documents were found to be in adequate order.

## 2.9. STATISTICS AND CALCULATIONS

Randomization was inspected but not statistical analysis due to time constraints. Product and bioanalytical samples were named “T” and “R” for Test and Reference.

Statistical analyses were performed using the SAS program. No issues of concern were found upon examination of the statistical data for all of the studies.

## 2.10. HANDLING OF AND ACCOUNTABILITY FOR PHARMACEUTICAL PRODUCTS

The CRO had received test and reference products from Mylan, according to the forms that were reviewed. The batch numbers of the products received matched those reported in the trial report. The SOPs and associated forms on dispensing were reviewed and found satisfactory.

## 2.11. ROLE OF THE DRUG REGULATORY AUTHORITY

The trials carried out by Aizant had been authorized by the CDSCO. Two of the CDSCO inspectors (one from central and another from the zonal office) were present during the WHO inspection. The CRO was previously inspected by several other regulatory authorities. This was not verified during the inspection.

## 2.12. QUALITY ASSURANCE FOR THE CONDUCT OF A CLINICAL TRIAL

A system of quality assurance covering both clinical and bioanalytical aspects was generally in place. Quality control procedures were applied to each stage of data handling.

**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 Clinical part of the studies (MA107 #C11197, HA613 #C13236 and HA614 #C13239) were considered to have been conducted at an acceptable level of compliance with WHO GCP at Aizant Drug Research Solutions Pvt Ltd,*** Survey No.: 172 &173, Apparel Park Road, Dulapally Village, Quthbullapur Mandal, Hyderabad, Andhra Pradesh, India - 500014.

Furthermore, ***the bioanalytical part of the studies*** (***HA614 #C13239) was considered to have been conducted at an acceptable level of compliance with WHO GLP at Aizant Drug Research Solutions Pvt Ltd,*** Survey No. 172 &173, Apparel Park Road, Dulapally Village, Quthbullapur Mandal, Hyderabad, Andhra Pradesh, India - 500014.

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.