

Prequalification of Medicines Programme
WHO PUBLIC INSPECTION REPORT
Contract Research Organization

Part 1: General information

WHO product numbers covered by the inspection	IN001
Study number	05-012-042
Title of the study	Bioequivalence study comparing Oseltamivir 75 mg capsule (containing Oseltamivir phosphate equivalent to Oseltamivir 75 mg) of Cipla Ltd., India with Tamiflu [®] capsule (containing Oseltamivir phosphate equivalent to Oseltamivir 75 mg) of Roche, UK in healthy male human subjects.
Clinical Part of the study: Name and address of the organization	Sitec Labs Pvt. 2nd Floor, Bldg No. 14, CTS No. 82, 82 (1-17), Village Hariyali, LBS Marg, Vikhroli (W), 400 083 Mumbai - Maharashtra India
Bio-analytical laboratory: Name and address	Sitec Labs Pvt. 2nd Floor, Bldg No. 14, CTS No. 82, 82 (1-17), Village Hariyali, LBS Marg, Vikhroli (W), 400 083 Mumbai - Maharashtra India
Name and address of the Sponsor	Cipla Ltd. 3rd floor, Raj Plaza, LBS Road, Vikhroli. 400 083 Mumbai Maharashtra India
Date of inspection	23 and 24 February 2009

This inspection report is the property of the WHO
Contact: prequalinspection@who.int

Part 2: Summary

General information about the site, history of WHO and/or regulatory agency inspections and focus of the inspection

The inspection focused on the bio-equivalence study conducted for the product Oseltamivir 75mg capsules. The inspection covered all the sections of the WHO GCP and GLP texts, including the WHO guidance for organizations performing in vivo bioequivalence studies.

Inspected Areas

After a brief opening meeting, the CRO representatives briefed the inspectors of some of the changes in Sitec, including the change of location for the clinical part of the studies. Present in the meeting were Dr M Garg (Principle Investigator), Mr K A Iyer (Director), Mr R Jadhav (Head Operation Bio Clinical Division), and Mrs M Campos (Director QA).

The inspection was conducted at Sitec Labs Pvt Ltd 1st floor, Jayshree Plaza, Near Dreams Mall LBS Marg, Bhandup (W) Mumbai, 400 078 India. The CRO employed (at the time of inspection) 29 persons in the clinical unit, 43 in bio-analytical unit and 13 in QA. The study was however done at the site mentioned in the table above (Vikhroli). Sitec moved its site for clinical studies in September 2007 to the Bhandup location.

The study records were archived at a contracted party (Shell) and were retrieved for the purposes of the inspection prior to the inspection.

At the time of the study, the PI (Dr L Anande) was contracted. He left the CRO in 2006.

On the first day, the inspection focused on the clinical part of the study. Various documents were inspected including:

- Organization chart (current and at the time of inspection)
- SOP for training
- Training calendar 2006
- Training records for Dr J Khan (Head Operations Bio-Clinical) at the time of the study.
- Monitor reports (Dr CH Bowker)
- Contract with the sponsor (Cipla Ltd)
- Project contract
- Master binder contents
- DCGI approval for the manufacture of Oseltamivir
- Form 11 for importation of the Oseltamivir (500 caps from UK and 300 from Germany)
- Proof of purchase of reference product on 5 January 2006 (Tiefenbacher, Germany, stated source as UK)
- All remaining samples of product (test and reference were destroyed on recommendation by the sponsor on 24 July 2007)
- Randomization

- Dispensing
- Contract, audit report and letter of communication with archiving facility (Shell Information Systems - 2005 - 2008)
- Email requesting retrieval of study documents prior to the inspection (December 2008)
- Correspondence between the sponsor and the CRO
- Correspondence and submission of documentation to the IRB
- Study attendance sheet for protocol meeting
- Training of nursing staff
- Record of protocol deviations
- Subject inward - outward record
- Setting of the digital clock
- Subject catering record
- Subject identification code list
- Study personnel inward record
- Checklist for line clearance
- Results for checks of drug abuse
- ICF (subject 21, 27, 34)
- Audit report (sponsor) - clinical and bio-analytical
- Dosing records (against randomization)
- CRFs (subject 2, 3, 9, 19, 21, 27)
- Sample preparation and storage records
- Adverse event form subject 27
- Screening forms and results / raw data
- Consent for screening
- Register for payment (compensation)
- Visitors' register

In general, the following aspects of Good Clinical Practices were considered to have been complied with, excluding some minor deficiencies as referred to in the inspection report. (These were satisfactorily addressed by the CRO after the inspection)

- 2.1 PROVISIONS AND PREREQUISITES FOR A CLINICAL TRIAL**
- 2.2 THE PROTOCOL**
- 2.3 PROTECTION OF TRIAL SUBJECTS**
- 2.4 RESPONSIBILITIES OF THE INVESTIGATOR**
- 2.5 RESPONSIBILITIES OF THE SPONSOR**
- 2.6 RESPONSIBILITIES OF THE MONITOR**
- 2.7 MONITORING OF SAFETY**
- 2.8 RECORD-KEEPING AND HANDLING OF DATA**
- 2.9 STATISTICS AND CALCULATIONS**
- 2.10 HANDLING OF AND ACCOUNTABILITY FOR PHARMACEUTICAL PRODUCTS**
- 2.11 ROLE OF THE DRUG REGULATORY AUTHORITY**
- 2.12 QUALITY ASSURANCE FOR THE CONDUCT OF A CLINICAL TRIAL**

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, the Bioequivalence study comparing Oseltamivir 75 mg capsule (containing Oseltamivir phosphate equivalent to Oseltamivir 75 mg) of Cipla Ltd., India with Tamiflu[®] capsule (containing Oseltamivir phosphate equivalent to Oseltamivir 75 mg) of Roche, UK in healthy male human subjects was considered to have been conducted at an acceptable level of compliance with WHO GCP and GLP at Sitec Labs Pvt. Vikhroli (W), 400 083 Mumbai - Maharashtra, India

Part 4: Reference documents

1. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products. *WHO Expert Committee on the Use of Essential Drugs. Sixth Report.* Geneva, World Health Organization, 1995 (WHO Technical Report Series, No. 850), Annex 3
http://whqlibdoc.who.int/trs/WHO_TRS_850.pdf
2. OECD Principles of Good Laboratory Practice (GLP). [C(97)186/Final], 1997
http://www.oecd.org/document/63/0,2340,en_2649_34381_2346175_1_1_1_1,00.htm
1
3. Additional guidance for organizations performing in vivo bioequivalence studies. WHO Technical Report Series, No. 937, 2006, Annex 9
www.who.int/prequal