Establishment Inspection Report
Semler Research Center Pvt. Ltd.
Bangalore, India

FEI: 3009591191
EI Start: 12/09/2013
EI End: 12/13/2013

SUMMARY

The current, FY '14, High Priority CDER [redacted] Pre-Approval Data Validation Inspection for the President's Emergency Plan for AIDS Relief [redacted] at this Contract Research Organization (CRO) was conducted in response to assignment memo (attached) dated July 25, 2013 from Sam H. Haidar, R.Ph., Ph.D., Chief Bioequivalence Branch DBGC/OSI, HFD-45. Assigned coverage was the clinical and analytical portions of studies conducted by Semler Research Center Pvt. Ltd. Bangalore, India, in support of [redacted] Coverage was provided to two protocols: [redacted] "A randomized, open label, balanced, single center, two treatment, two-period, two-sequence, single dose, crossover bioequivalence study of fixed dose combination of [redacted] subjects, under fasting conditions". The second study covered was **Study** [redacted] which is the associated fed study; the title of the [redacted] study is identical to the [redacted] with the last three words "under fed conditions". The analysis of the associated samples from both studies was performed via LC-MS/MS methodology at a separate Semler facility located in Bangalore, India. The study sponsor was [redacted] The current inspection was conducted in accordance with C/P 7348.001 – In Vivo Bioequivalence and C/P 7348.810 – Sponsors, Contract Research Organizations (CROs) and Monitors.

The current inspection covered two Semler facilities as described in detail below. The clinical studies were conducted at the firm's "**Sahakarnagar**" location (FEI: 3009591191). The previous FDA inspection at that facility occurred Sept. 17-21, 2012. At the conclusion of that inspection, no FDA 483 Inspectional Observations form was issued; discussion items were administrative in nature. The previous inspection was classified by the Center as No Action Indicated. The associated bioanalytical studies were conducted at the firm's "**J.P. Nagar**" location (FEI: 3007675007). The previous FDA inspection at that facility occurred July 29-31, 2013. Due to the fact this inspection was relatively recent, no information was available in [redacted] As of the beginning of the current inspection, no information, outcomes, findings or observations were available regarding the previous inspection.

The current inspection covered the clinical and analytical portions of the aforementioned protocols; Semler Studies [redacted] Inspectional coverage included: firm history, clinical study performance, informed consent process, ethics committee approvals and correspondence, test article accountability, dispensation and storage, processing and handling of biological (plasma) samples collected during the study, equipment calibration, employee training, computer controls, and a tour of the facility. Regarding the analytical facility and operations, coverage was provided to firm practices, qualifications of personnel, and procedures utilized during the method validations and analytical testing. A review of the clinical study data, analytical method validation, and analytical study data was accomplished. Raw data were compared to reports submitted by the CRO and

sponsor. The current inspections at both facilities did not reveal any significant objectionable conditions or practices; no FDA 483 Inspectional Observations form was issued. The following items were discussed with those present: Clinical - Review the informed consent process to determine if the clinical investigators involvement and interaction with the subjects/volunteers should be longer than two minutes in duration. Bioanalytical - Athough the AZT glucoronides were separated during the zidovudine assay, AZT glucoronides were not identified positively. Because the 5'-O glucoronide is available commercially, it was suggested that the glucoronide could be identified with certainty using the standard.

Bioequivalence retention samples were collected and submitted to CDER-DPA, St. Louis, MO for analysis. Sample # 829524 contains the "Test" product, [redacted] manufactured by: [redacted] Sample # 829525 contains two "Reference" products: [redacted]

ADMINISTRATIVE DATA

Inspected firm:	Semler Research Center Pvt. Ltd.
Location:	PA Arcade, No. 21, 22, 23 Kodigehalli Main Road, Sahakarnagar Bangalore, India
Phone:	+9180 43027100
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Mailing address:	PA Arcade, No. 21, 22, 23 Kodigehalli Main Road, Sahakarnagar Bangalore, India
Dates of inspection:	12/9/2013, 12/10/2013, 12/11/2013, 12/12/2013, 12/13/2013
Days in the facility:	5
Participants:	Scott B Laufenberg, Investigator Arindam Dasgupta, Ph.D., Pharmacologist, CDER/OSI/OC