DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food and Drug Administration 10903 New Hampshire Avenue Bldg 51, Room 5346 TEL: 301-796-3865 Silver Spring, MD 20993 Industry Information: www.fda.gov/oc/industry	September 29 - October 9, 2015
	FEI NUMBER 3007675007

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Dr. Krathish Bopanna, President and Chief Executive Officer

FIRM NAME	STREET ADDRESS
Semler Research Center Private Limited	75A, 15th Cross, I Phase
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
J.P. Nagar, Bangalore- 560 078, India	Bioanalytical Laboratory

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS; AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

OBSERVATION 1

During the inspection, FDA investigators found an Excel spreadsheet on Semler's server describing the substitution of plasma samples for studies (b) (4) For example, in Study (b) (4) the spreadsheet indicates that plasma samples from subject 10 who received reference product were substituted for the plasma samples from subject 41 who received test product.

OBSERVATION 2

Not all aqueous humor samples were accurately reported in the study report for Study (b) (4) Specifically, the final report states that 19 aqueous humor samples were excluded from the PK analysis because they were contaminated with blood. However, email communications between Semler and the Sponsor in July 2012 documented that only 2 of 19 aqueous humor samples were contaminated.

OBSERVATION 3

During the PK analysis of study (b) (4) the 3.5 hour concentration for subject 21, period 1 was switched with the 3.5 hour concentration for subject 22, period 1 without any documentation of sample mix-up. An investigation undertaken by Semler at the clinical and analytical sites did not uncover any evidence of sample mix-up.

OBSERVATION 4

Not all study-related documentation was retained to allow reconstruction of the study. Specifically,

1. The location of the plasma samples for subjects 17-32, period 1 of study (b) (4) were incorrectly recorded in the freezer log book for freezer 483.

2. The calibrators and QCs used for study (b) (4) could not be reconciled. Based on the log book for freezer 138, 110 set of calibrators were prepared on June 2, 2014 and 25 sets of calibrators remain in the freezer. However, the calibrators and QCs were unable to be located and the freezer log book was not updated.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (*Print or Type*)	DATE ISSUED
		Dipesh Shah, Investigator Daniel J. Roberts, Investigator Arindam Dasgupta, Pharmacologist Charles R. Bonapace, Pharmacologist	10/09/2015

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3. Instrument audit trails were not captured for archived projects performed from January 2015 through May 28, 2015 for chromatographic LC/MS instruments LCMS-138, LCMS-139, and LCMS-475. For example, LCMS 139 instrument was used for analyzing samples from bioequivalence studies without any corresponding audit trail testing information.

4. Not all study-related correspondences were archived with the study file to allow complete reconstruction of study activities.

OBSERVATION 5

Not all raw data were maintained in the study folder. Specifically, bioanalytical data worksheets were discovered crumpled/torn in a trash pile on the floor or otherwise discarded inside the bioanalytical laboratory. Examples include the following:

1. Sample dilution concentration sheet for (b) (4) with handwritten notes dated September 4, 2015.
2. Batch schedule for bioanalytical injection sequence for (b) (4) Batch (b) (4) dated September 23, 2015.
3. Overview-Area Table Results for (b) (4) testing for Phosphate Analysis study (b) (4) dated September 28, 2015 with the word "Determination" handwritten on the sheet.
4. Chromatographic sample table for sample set (b) (4) dated September 29, 2015.
5. Results table for study (b) (4) subject 10 dated January 26, 2015.

OBSERVATION 6

Laboratory analysts had the ability to delete, copy and rename chromatographic LC/MS raw data folders and run files on the computer system connected to LC/MS instruments. Specifically,

1. On September 30, 2015, we observed that laboratory analysts could delete data for LCMS 241 instrument that was being used to test samples for bioequivalence studies including (b) (4) (b) (4)

2. Laboratory analysts had the ability to delete raw data folders and files during the time period of May 28, 2015

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and September 9, 2015 on instrument LCMS 139 during the upgrade of Analyst Software System from version 1.4.1 to version 1.6.2. This LCMS 139 instrument was used during this time period to test samples for bioequivalence studies that included (b) (4)

OBSERVATION 7

Not all data generated in the in-vitro bioanalytical laboratory are adequately recorded to prevent accidental data loss. Specifically, the continuous temperature monitoring for the laboratory orbital 37C shaker (equipment number EOS 799) used for in-vitro bioanalytical testing is recorded on an uncontrolled portable thumb drive. The electronic temperature data that is downloaded on the thumb drive can be deleted/altered.

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or

2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgement, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."