U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Notification to Pharmaceutical Companies: Clinical and Bioanalytical Studies Conducted by Semler Research Are Unacceptable

[4/20/2016] FDA is notifying sponsors of New Drug Applications (NDAs) and Abbreviated New Drug Applications (ANDAs) that clinical and bioanalytical studies conducted by Semler Research Private Limited (Semler) located in Bangalore, India, are not acceptable as a result of data integrity concerns, and need to be repeated. Semler is a contract research organization that conducts bioequivalence and bioavailability studies for a number of pharmaceutical companies.

FDA is taking this action as a result of an inspection of Semler's bioanalytical facility in Bangalore, India, conducted between September 29, 2015, and October 9, 2015. The inspection found significant instances of misconduct and violations of federal regulations, including the substitution and manipulation of study subject samples. Yesterday, FDA issued an "Untitled Letter" to Semler detailing our findings related to the facility. A copy of this letter is available below.

FDA has evaluated drugs that were approved based on data from Semler that supported approval during the regulatory review process. FDA has conducted a thorough review of postmarket serious adverse events for all drug products which had studies conducted at Semler facilities. To date, the agency has not identified reports that raise serious safety concerns with these products. However, FDA is requiring that sponsors of approved applications repeat the bioequivalence/bioavailability studies using an entity other than Semler. FDA is also changing the therapeutic equivalence (TE) rating in FDA's Approved Drug Product with Therapeutic Equivalence Evaluations (the Orange Book) for any approved ANDA that relied on data from Semler to "BX." A BX rating indicates that data reviewed by the agency are insufficient to determine therapeutic equivalence, i.e., substitutability, of the generic product to the drug it references.

FDA is sending letters to sponsors of applications that are currently under review that include data from studies conducted at Semler. The letter informs the sponsor that it must repeat the bioequivalence/bioavailability studies using an entity other than Semler at an acceptable alternate study site.

Affected sponsors are encouraged to review the documents below, and contact the relevant FDA review division in the Office of Generic Drugs or the Office of New Drugs for further information.

Additional Information

- **Sample Information Request to Sponsors (PDF - 30KB) (/downloads/Drugs/DrugSafety/UCM496783.pdf)**
- **483: Semler Bangalore, India, issued 10/09/15 (PDF - 1.5MB) (/downloads/Drugs/DrugSafety/UCM496785.pdf)**
- **Semler Untitled Letter (PDF - 1.8MB) (/downloads/Drugs/DrugSafety/UCM496790.pdf)**

More in Drug Safety and Availability (/Drugs/DrugSafety/default.htm)

Drug Alerts and Statements (/Drugs/DrugSafety/ucm215175.htm)

Medication Guides (/Drugs/DrugSafety/ucm085729.htm)

Drug Safety Communications (/Drugs/DrugSafety/ucm199082.htm)

Drug Shortages (/Drugs/DrugSafety/DrugShortages/default.htm)

Postmarket Drug Safety Information for Patients and Providers (/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/default.htm)

Information by Drug Class (/Drugs/DrugSafety/InformationbyDrugClass/default.htm)

Medication Errors (/Drugs/DrugSafety/MedicationErrors/default.htm)

Drug Safety Podcasts (/Drugs/DrugSafety/DrugSafetyPodcasts/default.htm)

Safe Use Initiative (/Drugs/DrugSafety/SafeUseInitiative/default.htm)

Drug Recalls (/Drugs/DrugSafety/DrugRecalls/default.htm)

Drug Supply Chain Integrity (/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/default.htm)