

CLINICAL LABORATORY TESTING IN HUMAN SUBJECTS RESEARCH

This guidance document is intended for investigators planning to conduct human research that involves clinical laboratory testing. Should you need additional assistance, please contact OPHS at 510-642-7461 or ophs@berkeley.edu.

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A. Background and Introduction

The U.S. Congress passed the Clinical Laboratory Improvement Amendments (CLIA) in 1988. CLIA established quality standards for all laboratory tests to ensure the accuracy, reliability, and timeliness of patient test results, regardless of where the test was performed. CLIA defines a “clinical laboratory” as any facility which performs testing on specimens derived from humans for the purpose of providing data for the diagnosis, prevention, or treatment of disease in an individual, or for the purpose of health assessment.

CLIA states that laboratories which perform tests on human specimens and report patient-specific results must be certified under the CLIA provisions. CLIA applies only to those tests that are performed on human specimens collected within the United States and its territories. However, should specimens be transported outside of the United States and its territories for testing by international laboratories, those laboratories are also subject to CLIA (in addition to any local laboratory requirements).

Federal and state governments have adopted *academic exceptions* to CLIA. These aim to protect academic activities from the administrative burdens associated with complying with CLIA laboratory and testing rules. In California, CLIA should therefore not apply when tests will be performed for research and/or teaching purposes only, “and do not report results or use subject-specific results for the diagnosis, prevention or treatment of any disease or impairment of, or for the assessment of the health of, an individual” (Cal. Bus. & Prof. Code § 1241[b]((44)). Federal and state regulators have broadly defined the purpose statement in the definition of a laboratory test, and narrowly defined the interpretation of the academic exception.

In general terms, researchers should use CLIA-certified laboratories when the results will be shared with subjects or their physicians, or used as described above. Conversely, if researchers do not plan to share results with subjects or their physicians, testing may be performed via any appropriate laboratory.

In addition to evaluating whether or not CLIA applies, researchers should consider, on a case-by-case basis, whether or not sharing results with subjects is appropriate. The Committee for Protection of Human Subjects (CPHS) will also take these factors into consideration when it reviews each protocol that includes such testing.

B. Ethical Considerations

In determining whether or not to share results with subjects, researchers should consider the following:

1. *Risk/Benefit ratio.* The benefits of providing test results to individual subjects or their physicians must be weighed against risks such as false positives/negatives, diagnoses in the absence of available treatment, and loss of insurability.
2. *Right to be informed.* Individuals generally have a right to be informed about research in which they participate, including receiving study results that may be useful or of interest. However, the merit of reporting some test results is unknown. Reporting test results may lead to negative consequences such as creating subject anxiety, misunderstanding, and the pursuit of unnecessary treatment.

C. Specific Guidance

1. *When results will be reported to individual subjects or their physicians.* For diagnostic or health-related uses¹, the tests must be physician-ordered and performed at a CLIA-certified laboratory. The CPHS application should include the fact that testing will be conducted in a manner consistent with CLIA requirements. Additionally, the Risks and Benefits sections of the protocol should discuss how the benefits of providing the results outweigh the associated risks, and what efforts will be taken to minimize such risks.

Examples. CLIA requirements are generally triggered when test results will/may be:

- a. Used to identify potential study subjects (e.g., those individuals who will receive a study drug, device, or procedure).
- b. Used to determine assignment of research interventions (e.g., to assign subjects to the treatment arm of a clinical trial).
- c. Returned to study subjects.
- d. Passed on to a health care provider/other researcher (e.g., when the results may be used for determining a course of treatment/intervention).
- e. Involved in the development of genetically guided therapies.
- f. Used to research the effect of genetic information (or information about other biomarkers) on behavior change (e.g., study involves performing a test, sharing results with subjects, and determining whether knowledge of the results is associated with positive behavior change).
- g. Performed on behalf of another research site (e.g., a collaborating institution) if it is known that other site will report results to participants or otherwise use as outlined above.

¹ *Diagnostic or health-related uses* would include the use of subject-specific results for the diagnosis, prevention or treatment of any disease or impairment of, or for the assessment of the health of, an individual.

2. *When results will be withheld from individual subjects.* When research subjects are asked to take laboratory tests, they frequently expect that test results will be provided to them. It is important to clarify with subjects from the outset that the tests are *research*-related tests, and that the results will not be shared. Accordingly, the consent documents should include language such as: “The requested laboratory tests are research-related tests only. We will not pass the results of the test on to you, as the results may not be clinically meaningful.”

HIPAA Considerations for Covered Entities (at UCB, this includes the Tang Health Center, Optometry Clinic, Human Resources Health Plan, and Athletics and Recreational Sports). When test results are recorded in a subject’s medical chart, the results constitute Protected Health Information (PHI) under the Health Information Portability and Accountability Act (HIPAA). Accordingly, an appropriately worded, signed HIPAA Authorization for Release of Personal Information for Research must be obtained from each research subject. For more information, see <http://cphs.berkeley.edu/hipaa/hipaa.html>.

- a. Wherever possible/appropriate, subjects should be permitted to choose what test results will become part of their medical records.
 - b. If test results reveal condition(s) not already documented in a subject/patient’s medical record, the consent documents should discuss the potential for loss of insurability, should the test results become known to insurance carriers.
4. *Consultation.* University of California Berkeley (UCB) researchers who are uncertain whether or not CLIA applies to particular situations should contact the UCB Office for Protection of Human Subjects at ophs@berkeley.edu or 510-642-7461 for assistance.