Los Angeles County Department of Public Health Institutional Review Board (IRB)
313 N. Figueroa St., Room 127
Los Angeles, CA 90012
Phone:(213) 288-8675
Email: irb@ph.lacounty.gov
http://publichealth.lacounty.gov/irb/

Los Angeles County Department of Public Health Institutional Review Board (IRB) Policy Regarding Events that Must be Reported to the IRB

PURPOSE:

To set forth procedures through which the Office of the Institutional Review Board (IRB) for the Los Angeles County Department of Public Health, whose IRB serves as the IRB of record for the Department of Health Services (DHS) Ambulatory Care Network (ACN), Correctional Health Services (CHS) and Health Services Administration (HSA), and select community-based organizations (CBOs), reviews reportable events, including adverse and unanticipated events during the course of a project. This policy applies to all research and related activities that are sponsored by, or involve, DPH including staff, and individuals who receive clinical care and community-based services. [1]

SCOPE:

This policy ensures that Principal Investigators (PI) or project leads for research and related activities that are sponsored by, or involve, ACN, CHS, HSA, and select CBOs meet the requirements stated in the Code of Federal Regulations 45 CFR 46 Protection of Human Subjects ("Revised Common Rule").

DEFINITIONS:

"**Research**" is (1) a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge, or (2) a systematic collection or analysis of data with the intent to generate new knowledge.

"**Related activities**" means any process that involves collecting, accessing, or analyzing data from or about human subjects other than those activities meeting the regulatory definition of "research." "Related activities" include but are not limited to activities that may not be considered research such as 1) program evaluation for external use and/or publication; 2) certain quality assurance and improvement projects; 3) certain non-legally mandated surveillance;[2] and 4) needs assessments. The activities listed below are excluded from the above definition of "related activities", and thus would not require IRB review. However, the IRB reserves the right to make the final determination whether an activity falls under one of the exclusions listed

[1] Los Angeles County Department of Public Health IRB Policy Regarding IRB Review of Research and Related Activities Involving Human Subjects sets forth the procedures for which the IRB reviews research and related activities that are sponsored by, or involve, CAN, CHS, HAS, and select CBOs, including subjects who receive clinical care and community-based services.
[2] This may include surveillance data used for other than its original purpose.

below, and Principal Investigators (PIs)/project leads should consult with the IRB before assuming a project is excluded from IRB review requirements.
Exclusions: 1) anonymous meeting evaluations; 2) customer satisfaction surveys that do not collect/access data about persons belonging to vulnerable populations such as minors; 3) customer satisfaction surveys that do not collect/access data that involve sensitive topics such as substance use/disorder; 4) customer satisfaction surveys that do not collect/access personally identifiable information (PII) or protected health information (PHI); 5) staff assessments or other internal queries that pertain to core job duties and skills; 6) program evaluation for internal use with no intention to publish; 7) evaluations for internal use for trainings that are linked to receiving CE units or certificates of completion or that do not involve vulnerable populations and/or where the IRB determines that informed consent is not required for participation in the trainings; 8) listening sessions that do not involve sensitive topics such as substance use/disorder or that do not involve vulnerable populations; and 9) small-scale staff needs assessments that do not involve PII/PHI, vulnerable populations or sensitive topics.

A "**principal investigator**" (PI) is the person responsible for all aspects of research and related activities, including methodology, recruitment, data collection, data analysis, ethical conduct, and compliance with all federal, state and local regulations as well as the policies of the IRB. For related activities, the term "**project lead**" can be used to refer to the person with the same responsibilities as a PI.

"**Minimal risk**" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

An "**adverse event**" is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (e.g., abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in research or related activity, whether or not it is considered related to the subject's participation in the research or related activity. Adverse events encompass both physical and psychological harms. Adverse events occur most commonly in the context of biomedical research, although on occasion, they can occur in the context of social and behavioral research.[3, 4]

The following adverse events must be reported to the IRB:

- Internal adverse events that are unexpected, involve new or increased risks, and are related to the research
- External adverse events that are unanticipated problems involving risks to subjects or others
- Projects involving changes made to the research without prior IRB approval in order to eliminate apparent immediate harm
- Other unanticipated information that is related to the research and indicates that subjects or others might be at increased risk of harm

An "**unanticipated problem involving risks to subjects or others**" is any incident, experience, or outcome that meets the following criteria:

---

[3] Please see Health and Human Services (HHS) Office for Human Research Protection (OHRP) Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events for a comprehensive definition. Since our IRB mainly reviews social-behavioral research and not biomedical research, we are not highlighting the definition that relates to biomedical research.

[4] Please see the FDA's definition in the following guidance: Investigational New Drug Safety Reporting Requirements for Human Drug and Biological Products and Safety Reporting Requirements for Bioavailability and Bioequivalence Studies in Humans.

1. Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document/process; and (b) the characteristics of the subject population being studied;
2. Related or possibly related to a subject's participation in the research; and
3. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized.

An "**unexpected adverse event**" is any adverse event occurring in one or more subjects in a research protocol, the nature, severity, or frequency of which is not consistent with either:

- The known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol–related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document/process, and (b) other relevant sources of information, such as product labeling and package inserts; or
- The expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

A "**serious adverse event**" refers to any adverse event temporally associated with the subject's participation in research that meets any of the following criteria:

- Results in death or is life-threatening (places the subject at immediate risk of death from the event as it occurred)
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in a persistent or significant disability/incapacity (either physical or psychological)
- Results in a congenital anomaly/birth defect in the offspring of the subject
- Results in a breach of confidentiality
- Any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health, and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse)

"**Noncompliance**" is the failure to follow federal, state, or local regulations and policies governing human research, or requirements or determinations of the IRB. This definition may include action(s) taken by a PI/project lead or any research personnel. Noncompliance is a generic term that is used to describe behavior that is not expected or acceptable and may or may not be intentional. Noncompliance may require action by the IRB.

"**Serious noncompliance**" is an action or omission by an individual that any other reasonable individual would have foreseen as compromising the rights and welfare of a subject or others.

"**Continuing noncompliance**" is a pattern of repeated actions or omissions by an individual that 1) indicates a pattern of deficiency in the ability or willingness of an individual to comply with federal regulations or determinations or requirements of the IRB; 2) if allowed to continue could reasonably be expected to develop into serious noncompliance; or 3) recurs after a report of the activity has been evaluated and corrective action has been mandated.

REPORTING OF ADVERSE EVENTS:

Reporting of adverse events to the IRB must occur as soon as possible, but not later than seven working days after the Principal Investigator/project lead or research personnel become aware of the adverse event. The PI/project lead must submit a Reportable Events form using the IRBManager portal.

PIs/project leads will be asked to provide the following information:

- A detailed description of the adverse event
- A description of corrective actions that have been implemented or are proposed in response to the event.
    - Protocol changes and informed consent changes must be submitted through an IRBManager amendment application, which may accompany (but more often follows) the submission of the Reportable Events form

It is the responsibility of the PI/project lead to ensure that, when appropriate, the adverse event is reported to a monitoring entity (such as the research sponsor, a coordinating or statistical center, an independent research monitor, United States Department of Health and Human Services, or a Data Safety Monitoring Board/Data Monitoring Committee) as required under the monitoring provisions described in the IRB-approved application.

For research covered by Department of Health and Human Services (DHHS) regulations, a report of unanticipated problems involving risks to subjects or others must be sent to the Office for Human Research Protections (OHRP). When research is not covered by DHHS regulations, reports of unanticipated problems involving risks to subjects or others do not need to be reported to OHRP.

For research covered by the Food and Drug Administration (FDA) regulations, a report of unanticipated problems involving risks to subjects or others must be sent to the FDA. When research is not covered by FDA regulations, reports of unanticipated problems involving risks to subjects or others do not need to be reported to the FDA.

PRIMARY REVIEW OF ADVERSE EVENTS:

The IRB Chair/Vice Chair/Designee conducts a primary review of the Reportable Events form to determine whether the adverse event is an unanticipated problem involving risks to subjects or others.

Examples of unanticipated problems involving risks to subjects or others:

- A breach in confidentiality that involves risk to that individual or others, such as theft of an investigator's laptop which contains identifiable medical information and/or research data about subjects (if laptop is encrypted, data is not considered "identifiable")
- Subject complaints that cannot be resolved by the research team or which indicate increased or unanticipated risks
- Any accidental or unintentional change to the IRB-approved protocol that increases risk or decreases benefit, affects the subject's rights, safety, welfare, or affects the integrity of the resultant data
- Any publication in the literature, safety monitoring report including a Data and Safety Monitoring Board report, interim result, or other finding that indicates an unanticipated change to the risk/benefit profile of the research

If the Chair/Vice Chair/Designee determines the event is not an unanticipated problem involving risks to subjects or others, the IRB shall issue a letter acknowledging that the risk/benefit ratio remains unchanged as a result of the event.

If the Chair/Vice Chair/Designee determines the event is an unanticipated problem involving risks to subjects or others, they must then decide if the risk is minimal (as defined above). If the risk is deemed minimal, the IRB shall issue a letter acknowledging that the event affects the risk/benefit ratio, but that the risk to subjects is considered minimal.

If the risk is deemed to be greater than minimal risk, or if the Chair/Vice Chair/Designee is unsure of the level of risk, the Chair/Vice Chair/Designee assigns the adverse event to the Full Board for review. The Institutional Official (IO) shall also be notified of the adverse event when the risk is deemed greater than minimal risk. If subjects are at immediate risk of harm and there is insufficient time to wait for review by the convened IRB, the Chair/Vice Chair/Designee may immediately halt further enrollment and/or suspend activities for currently enrolled subjects.

When Full Board review of an adverse event is required, IRB staff assigns the item to the next Full Board meeting agenda. All board members shall have, no less than 1 week prior to the meeting, access to the following materials:

- Reportable Events form
- Data Safety Monitoring Board (DSMB) or safety report, if applicable
- Any attached supplemental material submitted with the form
- The current IRB approved application, which may include the informed consent documents, protocol, data-collection instruments, and any other pertinent materials such as recruitment materials or data-sharing agreements

IRB COMMITTEE REVIEW OF ADVERSE EVENTS:

During its review of the adverse event, the Full Board is required to consider the following actions:

- Suspension of IRB approval the research
- Termination of IRB approval the research
- Notification of current subjects when such information might relate to subjects' willingness to continue to take part in the research

In addition to the required actions, the Full Board may consider the following possible actions:

- Modification of the protocol
- Modification of the information disclosed during the consent process
- Providing additional information to past subjects
- Requiring current subjects to re-consent to participation
- Modification of the continuing review schedule
- Monitoring of the research
- Monitoring of the consent process
- Referral to other organizational entities

The IRB will issue a letter to the Principal Investigator/project lead describing the Full Board’s determination regarding the adverse event including any required modifications or actions.

REPORTING OF ALLEGED NONCOMPLIANCE:

Reports of alleged noncompliance may involve PIs/project leads and their staff as well as IRB board members and Office of the IRB staff, and they may come to the attention of the IRB from different sources. The IRB investigates all reports of alleged noncompliance that it receives.

IRB members, Office of the IRB staff, PI/project leads, project personnel, and County employees must report alleged instances of noncompliance by submitting a Noncompliance Report form using the IRBManager portal. Reporting of adverse events to the IRB must occur as soon as possible, but not later than seven working days after becoming aware of the instance of noncompliance.

Subjects in research and related activities, their family members or guardians, and the general public can report instances of noncompliance to the IRB using the contact form available on the IRB's public website. If anonymity is preferred, instances of noncompliance can be reported via the participant telephone hotline (213-288-7680).

IRB REVIEW OF ALLEGED NONCOMPLIANCE:

When the IRB is notified of an alleged instance of noncompliance, a primary review of the Noncompliance Report is conducted by the Chair/Vice Chair/Designee. The Chair/Vice Chair/Designee makes the determination of serious and/or continuing noncompliance based on a description of the allegation, the entire research file, interviews with research personnel/PI/project lead, and any complaints submitted by subjects. Instances of noncompliance can also be identified during routine IRB audits.

If it is determined the instance of noncompliance is neither serious nor continuous, the matter will be closed and documentation of the determination shall be added to the project materials in IRBManager.

If the Chair/Vice Chair/Designee determines the instance of noncompliance is serious and/or continuous, the matter is assigned to the Full Board for review. If more information is needed, the Chair/Vice Chair/Designee can request the initiation of a for-cause audit by Office of the IRB staff. The PI/project lead is promptly notified in writing of the "for cause" audit. The completed audit report is presented to the IRB Chair and reviewed at the next convened Full Board meeting.

The Full Board shall review the following materials in advance of the meeting:

- Audit report, if applicable
- Notification of noncompliance
- Pertinent IRB correspondence (such as IRB applications, IRB approval letters, IRB approved informed consent)

During its review of the alleged instance of noncompliance, the Full Board is required to consider the following actions:

- Suspension of IRB approval of the research
- Termination of IRB approval of the research
- Notification of current subjects when such information might relate to subjects' willingness to continue to take part in the research

In addition to the required actions, the Full Board may consider the following possible actions:

- Modification of the protocol
- Modification of the information disclosed during the consent process

- Providing additional information to past subjects
- Requiring current subjects to re-consent to participation
- Modification of the continuing review schedule
- Monitoring of the research
- Monitoring of the consent process
- Referral to other organizational entities

The discussion, actions, and determinations made by the Full Board during the convened meeting shall be noted in the minutes. When applicable, the Office of the IRB shall promptly notify the PI/project lead of a determination of serious and/or continuing noncompliance including any required corrective actions imposed by the Full Board. When applicable, the IRB may impose additional training or educational requirements on IRB members or Office of the IRB staff if implicated in determinations of serious and/or continuous noncompliance. The IRB shall promptly notify the Institutional Official (IO) of any determination of serious or continuing noncompliance.

When applicable, it is the responsibility of the Principal Investigator/project lead to notify regulatory agencies of the IRB's determination of serious or continuing noncompliance related to research overseen by those agencies.

For research covered by Department of Health and Human Services (DHHS) regulations, the Principal Investigator/project must promptly notify the Office for Human Research Protections (OHRP) of the IRB's determination of serious or continuing noncompliance.

For research covered by the Food and Drug Administration (FDA) regulations, the Principal Investigator/project must promptly notify the FDA of the IRB's determination of serious or continuing noncompliance.

SUSPENSION AND TERMINATION OF RESEARCH:

The IRB may suspend or terminate any project approved by the IRB when the IRB has an indication that circumstances warrant and there is cause (such as serious and continuing noncompliance, increased or undue risk, or unanticipated serious harm to subjects).

Examples of actions that may cause suspensions or terminations include, but are not limited to:

- Inappropriate involvement of human subjects in research
- Impairment of the rights or welfare of subjects
- Serious or continuing noncompliance with federal regulations or IRB policies
- New information indicating increased risk to human subjects

The regulatory difference between suspension and termination is described below:

A **suspension** exists when the IRB temporarily or permanently withdraws approval of some or all research activities in a protocol. While suspended, the research remains under the jurisdiction of the IRB.

Termination takes place when the IRB permanently withdraws approval of ALL research activities in a protocol. Terminated research is no longer required to undergo continuing review and does not remain under the jurisdiction of the IRB.

The Full Board and IRB Chair are authorized to suspend or terminate research. The IRB Chair can suspend or terminate a project outside of a convened Full Board meeting if the circumstances warrant, such as for

reasons related to participant safety. Suspension or termination that occurs outside of a convened Full Board meeting shall be reported to the convened Full Board at the next meeting and any resulting discussion must be summarized in the minutes.

RESPONSIBILITIES OF THE IRB WHEN SUSPENDING OR TERMINATING A PROJECT:

Before suspending or terminating IRB approval, the Full Board or IRB Chair must consider whether:

- Actions are necessary to protect the rights and welfare of currently enrolled subjects
- Procedures for withdrawal of enrolled subjects take into account their rights and welfare (e.g., making arrangements for medical care outside of a research study, transfer subjects to another researcher, and continuation in the research under independent monitoring)
- Current subjects should be informed of the termination or suspension
- Any adverse events or outcomes have been reported to the IRB

The Full Board or IRB Chair may request an ad hoc review from an independent source with expertise in the type of research being conducted or expertise in the specific area of concern. The Full Board or IRB Chair may also request the initiation of a for-cause audit to assist in their determination.

After reviewing the pertinent details, the Full Board or Chair must determine if suspension or termination is warranted. Some examples of situations that may warrant suspension or termination are:

- Falsification of study safety data
- Failure to comply with prior conditions imposed in writing by the IRB
- Repeated or deliberate failure to obtain or document informed consent from human subjects, which may include:
    - Repeated or deliberate omission of a description of serious risks of the research intervention when obtaining informed consent
    - Repeated or deliberate failure to provide informed consent in a language understandable to the subject
- Repeated or deliberate failure to comply with conditions placed on the study by the County, IRB, sponsor, FDA, or other governmental agency
- Repeated or deliberate failure to obtain prior review and approval of new protocols and on-going human subjects research by the IRB
- Repeated or deliberate failure to follow the IRB-approved protocol, for example, by enrolling subjects who do not meet inclusion criteria
- Repeated or deliberate failure to maintain accurate study records or submit required adverse event reports to the IRB
- Repeated or deliberate falsification, fabrication, or concealment of study records; for example, by substituting the results of biological samples from subjects who met the inclusion criteria for samples of subjects who do not meet the inclusion criteria, or by fabricating subjects

The Office of the IRB shall promptly notify the PI/project lead, in writing, of all suspensions or terminations of IRB approval. The notification letter shall include the following:

- Identifies the suspended or terminated research
- Includes a statement of the reasons for the IRB's action
- Requires the PI/project lead to submit proposed procedures for withdrawal of currently enrolled subjects with consideration of subject rights and welfare. The IRB reviews the proposed procedures. The IRB may transfer this responsibility to another PI/project lead to ensure implementation of these procedures

- Requires the PI/project lead to submit a proposed script or letter notifying all currently enrolled subjects that are impacted by the suspension or termination. The IRB reviews the proposed script or letter. If follow up with subjects for safety reasons is permitted/required by the IRB, subjects should be so informed. The IRB may directly contact subjects with notification.
- As a condition of ending suspension or termination, the IRB may require oversight by IRB staff, or a designee, and/or require the study to be transferred to another PI/project lead who will serve as the new PI/project lead and will be responsible for ensuring that IRB requirements are being implemented

The IRB shall promptly notify the Institutional Official (IO) of any suspension or termination.

INVESTIGATOR RESPONSIBILITIES FOR SUSPENDED OR TERMINATED PROJECTS:

When the IRB has suspended, terminated, or reinstated a project, the PI/project lead must notify the sponsor. When applicable, it is the responsibility of the Principal Investigator/project lead to notify regulatory agencies of any suspensions or terminations of research overseen by those agencies.

For research covered by Department of Health and Human Services (DHHS) regulations, the Principal Investigator/project lead must promptly notify the Office for Human Research Protections (OHRP) of suspensions or terminations of any such research.

For research covered by the Food and Drug Administration (FDA) regulations, the Principal Investigator/project lead must promptly notify the FDA of suspensions or terminations of any such research.

The PI/project lead is responsible for notifying all affected subjects of the suspension, termination, or reinstatement of the research project (by phone, email, letter, or in person). The subject letter or script must be submitted by the PI/project lead to the IRB for review and approval. The PI/project lead must continue to report adverse events, unanticipated problems involving risks to subjects or others, and serious or continuing noncompliance with federal regulations to the IRB during the period of suspension or termination.

PIs/project leads who fail to comply with IRB directives or federal or state law or regulations may be subject to administrative and/or legal action by the County.

REINSTATEMENT OF SUSPENDED RESEARCH:

IRB staff shall communicate corrective actions to be taken by the investigator, as applicable. Research activities must cease as specified in the suspension criteria, until the IRB has granted approval for the study to resume. Suspensions are within the authority of the IRB and remain in effect until the PI/project lead complies with all corrective actions required by the IRB. Reinstatement of suspended research occurs after corrective actions are completed to the IRB's satisfaction. The Full Board may approve the project with or without additional restrictions (such as mandating a data and safety monitoring committee to oversee the research at designated intervals, increasing the frequency of IRB review, or observing the consent process). Any action taken by the Full Board to lift the suspension or termination must also be documented in the convened meeting minutes.