SAINT AGNES MEDICAL CENTER

CLINICAL RESEARCH CENTER

Fresno, California

Standard Operating Procedures

Institutional Review Board

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SUBJECT: MANAGING ALLEGATIONS OF NONCOMPLIANCE

1. PURPOSE

To define noncompliance as it relates to complying with federal and state regulations governing clinical research involving human subjects and outline the procedures for handling alleged cases.

2. SCOPE

This applies to all clinical research studies that are not exempt from federal or state regulations governing the conduct of research involving human subjects and are conducted within Saint Agnes Medical Center facilities.

3. POLICY

The Clinical Research Center (CRC) will investigate all allegations of noncompliance and present its findings to the Institutional Review Board (IRB). Depending on the validity of the allegation and degree of seriousness, the IRB, in conjunction with the CRC, will determine how the matter should be resolved. Each allegation will be taken seriously and reviewed in a consistent, prompt and professional manner.

4. PROCEDURE

4.1. Definitions

A. **Noncompliance** is a failure to comply with federal and state regulations, IRB policy or the determinations or the requirements of the IRB.

1. *Non-serious and non-continuing* noncompliance involves isolated incidents, e.g., an unintentional mistake, an oversight or misunderstanding. The issue is not serious or continuing in nature.

2. *Serious noncompliance* is an action or omission not in compliance with federal and state regulations or IRB policy, taken by an Investigator (or the Investigator's staff) that any reasonable Investigator (or reasonable staff member) would have foreseen as increasing risks or compromising the rights and welfare of a participant or other persons. It also includes any activity or omission which compromises the scientific integrity of the clinical data resulting from the research procedures conducted under the protocol.

   Some examples of serious noncompliance may include but are not limited to the following:

   - Failure to obtain proper consent
   - Failure to maintain accurate, complete documentation of informed consent
   - Failure to maintain accurate and complete case histories
   - Failure to conduct the study according to the protocol or federal and state regulations
   - Failure to conduct or personally supervise the investigation
   - Failure to inform current and past participants of new information
   - Failure to protect the rights, welfare and safety of the research subjects

3. *Continuing noncompliance* is a pattern of repeated actions or omissions taken by an Investigator or the investigator's staff that indicates a deficiency in the ability or willingness to comply with either federal or state regulations, or IRB policy or the determinations or requirements of the IRB.

B. **Protocol Deviations/Exceptions** do not fall within these definitions unless they meet the distinction of being serious and/or continuing. Some examples of protocol deviations/variances may include but are not limited to the following:

   - Isolated case of a research subject(s) missing a scheduled visit or a required procedure
   - the Investigator enrolling a subject that doesn't completely fit the inclusion/exclusion criteria but in the Principal Investigator's judgment the action would **not** increase the risks to the subject and there was the possibility of direct benefit to the subject - as long as the decision was approved by the Sponsor's Medical Monitor or the IRB Chair before the decision to enroll or, if there was no time to gain prior approval, the enrollment was reported to the Sponsor and IRB Chair within 5 days of its occurrence. Any further allowance of this exception to the criteria would require submission of a protocol amendment by the Sponsor to the IRB for approval before any additional enrollments could take place. Continuance without approval would constitute serious and continuing noncompliance.

4.2 Reporting Requirements for Suspected Noncompliance

Investigators and research staff are expected to report all suspected noncompliance to the Director of Clinical Research/IRB Administrator. Information regarding noncompliance may come to the attention of the Director of Research/IRB Administrator or the IRB through other means such as:

- New applications
- Continuing reviews
- Internal audits
- FDA, OHRP, CMS, Joint Commission, or Sponsor audits
- Adverse events and safety reports
- Reports from collaborators, employees, participants, family members
- Any other sources

4.3 Inquiry Process

Conditions Leading to a 'Hold for Inquiry' Status:

- Upon receipt of an allegation, the Director of Clinical Research/IRB Administrator will review the allegation. If it appears valid, the Director of Clinical Research/IRB Administrator will undertake a preliminary investigation which may include an onsite audit by a CRC staff member within 5 days of learning of the suspected noncompliance. The purposes of the investigation is fact-finding and may involve examination of study records and discussion with the on-site research team, including the Principal Investigator (PI), Sub-Investigator(s), research participants, witnesses and the person(s) making the allegations.

- Based on the findings, the Chair of the IRB will determine if the study should be 'Held for Inquiry' and request the Investigator to respond to the findings. This condition serves as a temporary time-out to understand the facts and implications of the Investigator's actions/decisions and those of his/her staff [see IRB SOP R-1214].

4.4 Resolution of Inquiry and Resulting Study Status

Upon receipt of the Investigator's response(s) to the preliminary investigation, The IRB will evaluate at judge the situation according to the following criteria:

Non-serious and Non-continuing Noncompliance

The issue is resolved by the PI. The issue and report findings are presented to the convened IRB at the next regularly scheduled IRB meeting. The IRB will document the outcome in a report that outlines any corrective action(s) required on the part of the PI and a timeline for their resolution. A copy of this report will be sent to the PI and any others deemed appropriate.

A written response from the PI acknowledging the report is required within 5 business days from the date of the report. All pertinent reports and correspondence regarding the noncompliance will be retained in the IRB study binder.

Serious and Continuing Noncompliance

The issue and report findings are presented to the convened IRB at the next regularly scheduled time or at an emergency meeting. After discussion and deliberation, the IRB will vote to either 'Suspend' study approval and allow the Investigator to make corrective actions, or 'Terminate' study approval [IRB SOP R-1214].

The IRB will document the corrective actions the PI and research team must comply with within the stated timeframe. The PI will formally be notified by the IRB Chair of these actions and requirements. A written acknowledgment from the PI is required within 5 business days from the date of the report. All pertinent reports and correspondence regarding the noncompliance will be retained in the IRB study binder.

Federal regulatory agencies and institutional officials will be notified if the findings support the IRB's conclusion that the noncompliance is serious and/or continuing and that the IRB has either 'Suspended' and or 'Terminated' the study.

REGULATORY REFERENCES

45 CFR 46	Protection of Human Subjects ("The "Common Rule")
21 CFR 50	Protection of Human Subjects
21 CFR 54	Financial Disclosure By Clinical Investigators
21 CFR 56	Institutional Review Boards
21 CFR 312.60 -312.70	General Responsibilities of Investigators
21 CRF 812.100 -812.150	General Responsibilities of Investigators
ICH E6	Good Clinical Practice: Consolidated Guidance
CA H&S Code 24170-24179.5	Protection of Human Subjects in Medical Experimentation
CA H&S Code 111515-111545	Experimental Use of a Drug
CAMH R1.2.180	Protection of Research Subjects