

**University of California, San Francisco
Helen Diller Family Comprehensive Cancer Center**

Policy for External Adverse Event Report Management

Purpose

The purpose of this Helen Diller Family Comprehensive Cancer Center (HDFCCC) policy is to outline the procedures for processing external adverse event (AE) reports for externally and internally sponsored multi-center studies, internally sponsored single center trials, and consortium trials conducted within the HDFCCC at the University of California, San Francisco (UCSF).

Scope

This policy applies to all external AE reports, regardless of distribution method (i.e., web portals, mailing list, etc.) or medium (electronic or hard copy). External AE reports include, but are not limited to, Medwatch, Council for International Organizations of Medical Sciences form (CIOMS), suspected unexpected serious adverse reaction (SUSAR), Action Letters, IND Safety Reports (INDSR), and other reports and narratives for an adverse event (AE).

Background

The Office of Human Research Protections (OHRP) issued guidance in 2007 on [Unanticipated Problems Involving Risks & Adverse Events](#) that clarifies that “it is neither useful nor necessary under the HHS regulations at 45 CFR part 46 for reports of individual adverse events occurring in subjects enrolled in multicenter studies to be distributed routinely to investigators or Institutional Review Boards (IRBs) at all participating institutions conducting the research.”

The [2012 FDA Guidance on Safety Reporting](#) outlines that there must be a “reasonable possibility” that a drug caused an AE. Furthermore, “the sponsor is better positioned than the individual investigator to assess the overall safety of the investigational drug because the sponsor has access to serious adverse event reports from multiple study sites and multiple studies and is able to aggregate and analyze these reports.”

Procedures

Defining Reportable External AEs

Per federal and institutional guidelines, a reportable AE is defined as an “unanticipated problem involving risk to participants or others” or “serious or continuing noncompliance.”

Criteria for Processing External AEs

HDFCCC will process external safety reports 1) after a study obtains IRB approval, and continue until 2) all three criteria are met:

- The study is closed to accrual
- There are no subjects on active treatment (\leq 30 days from last dose)
- There are no subjects in long term or survival follow-up

The HDFCCC and its affiliates will not review, acknowledge, or retain reports that do not meet the reporting criteria for the IRB of record. This applies to reports disseminated via web portals, email, hardcopies, etc

Processing a Reportable External AE

Upon receipt of a reportable external safety report, the Principal Investigator (PI) or designee will review and submit the report to the IRB of Record per its reporting policy.

After the above criteria for processing an external AE has been met, all reportable external safety reports will be stored without acknowledgement in the study file until IRB closure. Any external safety reports received after IRB closure will not be reviewed, acknowledged, or retained by the site.

Sponsor Responsibility for Reporting External AEs

UCSF-Sponsored Studies

For UCSF-Sponsored, investigator-initiated studies where UCSF holds the Investigational New Drug Application (IND), it is the Sponsor-Investigator's responsibility to review external AEs (provided by participating sites or by industry partners/manufacturers) related to the investigational product(s) and determine whether the event meets the reporting criteria for the IRB of record. If the event meets reporting criteria, then the Sponsor-Investigator will store and disseminate the event information to the IRB of record and all participating sites (for multi-center studies). If the external event occurred at a participating site and is related to a study, then the Sponsor-Investigator must determine if the event meets reportable criteria to the FDA ([21 CFR 312.32](#)).

Note: If the Sponsor and PI are separate individuals, then it is suggested that the Sponsor and PI consult with each other to determine if the event represents a significant change in study risk. The Sponsor (not the PI) is responsible for reporting information to the FDA ([21 CFR 312.32](#)).

Externally-Sponsored Studies

For multi-centered studies where an external sponsor holds the IND, the study sponsor or sponsor designee is responsible for notifying the UCSF site PI or PI designee of any external safety reports that meet IRB reporting criteria. External sponsors or industry partners must provide written notification in the form of a memo or Dear Investigator Letter (DIL) to accompany the corresponding safety documents. The memo and/or DIL must include a clear explanation of why the event has been determined to be an unanticipated problem.

To ensure proper reporting, both should be included with the external safety reports:

- Copy of updated study documents (i.e., a revised protocol, informed consent form, and/or investigator's brochure), and
- Summary of the changes specifying changes for the updated documents to help quickly identify new risks and procedure changes.

References

FDA Guidelines

- [21 CFR 312.32](#)
- [45 CFR 46.103](#)

FDA Guidance

- [Safety Reporting Requirements for INDs and BA/BE Studies](#)
- [Safety Assessment for IND Safety Reporting](#)

ICH

- [ICH 5.16.2](#)
- [ICH 8.3.18](#)

UCSF IRB:

- [Protocol Violations or Incident Page](#) (Reporting Requirements Chart for Immediate Protocol Change to Protect Participant Safety)
- [IRB Review Requirements](#) and [Submissions](#)

Alternate Procedure

None

Policy Approval

This policy was approved by the following personnel on the following dates:

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Summary of Changes

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