

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

Policy for Verbal Notification of New High-Risk Adverse Events

Purpose

The purpose of this Helen Diller Family Comprehensive Cancer Center (HDFCCC) policy is to detail the verbal notification process of new high-risk adverse events (AEs) to participants on study treatment for interventional studies, both internally and externally sponsored, prior to re-consent with an updated informed consent form (ICF).

Background

Per FDA guidelines, study participants must be provided, when appropriate, with *“significant new findings developed during the course of the research which may relate to the subject’s willingness to continue participation”* (21 CFR 50.25 (b) (5) and 45 CFR 46.116(b) (5)). Study participants are considered on study treatment from the time of initiation of study therapy until completion of the treatment portion of the study, as defined in the protocol.

Procedures

Notification of New Risk AEs

It is the responsibility of the sponsor to identify all new risks and distribute it to all participating study sites and investigators. Refer to the [HDFCCC External Adverse Event Report Management Policy](#) for requirements, sponsor responsibilities, and procedures for retrieving and processing external new risk information.

Determination of New Risk AEs as High-Risk

Determinations of “high risk” is made the by Principal Investigators (PI) at their discretion and best judgement. “High risk” changes the risk/benefit ratio or are significant/immediate.

Examples of high risks requiring verbal notification may include, but are not limited to, life threatening and/or requiring immediate medical attention such as grade 4 neutropenia, grade 4 thrombocytopenia, liver/kidney failure and pancreatic failure.

All new risk is not considered “high risk,” including PI non-response, until determined otherwise by the study principal investigator (PI). Sub-investigators are permitted to determine high risk in the absence of the study PI, when needed.

Verbal Notification of On-Treatment Participants

To ensure participants are provided adequate information to determine whether they want to continue participating or not, the PI or authorized member(s) of the study team must verbally notify each participant on the study treatment impacted by that new high risk prior to his/her next treatment for all newly identified high-risk AEs, unless the updated institutional review board (IRB) approved ICF is ready first to use for re-consent. For participants on self-administered oral agents, participants must be notified within 10 business days from the date of determination of high risk. If the participant cannot be reached, appropriate attempts to contact must be made and documented. For non-English speaking participants, a translator is required during verbal notification of new high-risk AEs.

Participant Reconsent

Once the revised ICF containing new risk is approved by the IRB of record, all participants impacted by the new risk change must be reconsented (regardless if notification has taken place or not). If the IRB approved ICF is ready prior to verbal notification, then reconsent is needed instead of verbal notification. Refer to the [HDFCCC Policy for Obtaining Informed Consent of Potential Patients for Therapeutic and Non-Therapeutic Oncology Clinical Trials](#).

Participant Withdrawal

If a participant is verbally notified of new high-risk(s) per this policy and subsequently withdraws from the study prior to IRB approval of the updated ICF, the participant does not need to be reconsented. The verbal notification, as a continuation of the consent process, will satisfy the requirement to notify the participant.

Off-Treatment Participants

PIs must evaluate newly identified high-risk AEs to determine whether off-treatment participants (participants who completed the treatment portion of the study, as defined in the protocol) need to be verbally notified. Participants who are off treatment must be verbally notified of the risk when determined appropriate by the study PI. Participants on long-term or survival follow-up are not verbally notified, unless otherwise indicated by the PI and/or the IRB.

Documentation of Verbal Notification

After each verbal notification, regardless of participant treatment or study status, the PI or authorized member(s) must document the conversation in the UCSF medical record or research chart and indicate the participant's willingness to continue in the study.

References

FDA Guidelines

- 21 CFR 50.25 (b) (5) and 45 CFR 46.116(b) (5)

HDFCCC Policies

- [HDFCCC External Safety Policy](#)
- [HDFCCC Policy for Obtaining Informed Consent of Potential Patients for Therapeutic and Non-Therapeutic Oncology Clinical Trials.](#)

Alternate Procedure

None.

Policy Approval

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

DocuSigned by:
Eric Small
7FCB32D327E3438...
Eric Small, MD
Chief Scientific Officer
Helen Diller Family Comprehensive Cancer Center

10/21/2019

Date

DocuSigned by:
Thierry Jahan
F67EAB476220482...
Thierry Jahan, MD
Chair, Data and Safety Monitoring Committee
Helen Diller Family Comprehensive Cancer Center

10/24/2019

Date

DocuSigned by:
Charalambos Andreadis
6F7C7F62042E47D...
Charalambos Andreadis, MD
Medical Director, Clinical Research Support Office
Helen Diller Family Comprehensive Cancer Center

10/21/2019

Date

DocuSigned by:
Kate Shumate
80D38159E89D41E...
Kate Shumate, MPA, CCRP
Chief of Staff
Helen Diller Family Comprehensive Cancer Center

10/21/2019

Date

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

Summary of Changes

Policy Title: Policy for Verbal Notification of New High-Risk Adverse Events

Version Date: 08/12/2019

Version Number: 1.0

New Text	This policy replaces the previous policy, which has been decommissioned.
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Version Date: 10/21/2019

Version Number: 2.0

Page No.: All		Section: Footer
Original Text	Version 1 8/12/2019	
New Text	Version 2 10/12/2019	
Reason for Change	Updated text to reflect revised version number and date	

Page No.: 1		Section: Determination of New Risk AEs as High-Risk
Original Text	<p>All new risk is not considered “high risk,” including PI non-response, until determined otherwise by the study principal investigator (PI).</p> <p>Sub-investigators are permitted to determine high risk in the absence of the study PI, when needed.</p> <p>Examples of high risks (i.e. changing the risk/benefit ratio) requiring verbal notification include, but are not limited to, life threatening and/or requiring immediate medical attention such as grade 4 neutropenia, grade 4 thrombocytopenia, liver/kidney failure and pancreatic failure.</p>	
New Text	<p>Determinations of “high risk” is made the by Principal Investigators (PI) at their discretion and best judgement. “High risk” changes the risk/benefit ratio or are significant/immediate.</p> <p>Examples of high risks requiring verbal notification may include, but are not limited to, life threatening and/or requiring immediate medical attention such as grade 4 neutropenia, grade 4 thrombocytopenia, liver/kidney failure and pancreatic failure.</p> <p>All new risk is not considered “high risk,” including PI non-response, until determined otherwise by the study principal investigator (PI). Sub-investigators are permitted to determine high risk in the absence of the study PI, when needed.</p>	
Reason for Change	Added clarifications about the definition of high risk	

Page No.: 2		Section: Verbal Notification of On-Treatment Participants
Original Text	To ensure participants are provided adequate information to determine whether they want to continue participating or not, the PI or authorized member(s) of the study team must verbally notify each participant on the study treatment impacted by that new high risk prior to his/her next treatment for all newly identified high-risk AEs, unless the updated institutional review board (IRB) approved ICF is ready first to use for re-consent. For non-English speaking participants, a translator is required during verbal notification of new high-risk AEs.	
New Text	To ensure participants are provided adequate information to determine whether they want to continue participating or not, the PI or authorized member(s) of the study team must verbally notify each participant on the study treatment impacted by that new high risk prior to his/her next treatment for all newly identified high-risk AEs, unless the updated institutional review board (IRB) approved ICF is ready first to use for re-consent. For participants on self-administered oral agents, participants must be notified within 10 business days from the date of determination of high risk. If the participant cannot be reached, appropriate attempts to contact must be made and documented. For non-English speaking participants, a translator is required during verbal notification of new high-risk AEs.	
Reason for Change	Added window for notification of participants on oral investigational agents taken at home	

Page No.: 2		Section: Off-Treatment Participants
Original Text	PIs must evaluate newly identified high-risk AEs to determine whether off-treatment participants (participants who completed the treatment portion of the study, as defined in the protocol) need to be verbally notified. Participants who are off treatment must be verbally notified of the risk when determined appropriate by the study PI.	
New Text	PIs must evaluate newly identified high-risk AEs to determine whether off-treatment participants (participants who completed the treatment portion of the study, as defined in the protocol) need to be verbally notified. Participants who are off treatment must be verbally notified of the risk when determined appropriate by the study PI. Participants on long-term or survival follow-up are not verbally notified, unless otherwise indicated by the PI and/or the IRB.	
Reason for Change	Added clarification of process for participants on long-term or survival follow-up that was implied in previous policy but not explicitly stated	

Page No.: 2		Section: Documentation of Verbal Notification
Original Text	After each verbal notification, regardless of participant treatment or study status, the PI or authorized member(s) must document the conversation in the UCSF medical record and indicate the participant's willingness to continue in the study.	
New Text	After each verbal notification, regardless of participant treatment or study status, the PI or authorized member(s) must document the conversation in the UCSF medical record or research chart and indicate the participant's willingness to continue in the study.	
Reason for Change	Added clarification that paper documentation is also acceptable	