TABLE OF CONTENTS

Purpose
Policy
Procedures
I. Investigational Site PI Responsibilities
II. Research Protocol Study Chair Responsibilities
III. NACHO Operations Center Responsibilities
Maintenance Responsibility
Authorization
Version/Revision History

PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to establish an efficient process for the monitoring, recording, and reporting of safety data for research participants. Adherence to these standards will ensure timely and accurate monitoring and reporting of study subject safety data in compliance with Good Clinical Practices and regulations of governing authorities.

POLICY

Adverse Event (AE) and Serious Adverse Event (SAE) reporting is a routine part of every research protocol. Reporting of adverse events will be based on the research protocol's risk, the sponsor's requirements, and each investigational institution's (site's) policies.

All NACHO research protocols will have clearly defined reporting criteria for AEs, SAEs, and procedures for monitoring, recording, and reporting AEs and SAEs (toxicity) in the protocol.
The NACHO Operations Center recommends the use of the National Cancer Institute's (NCI) Common Terminology Criteria for Adverse Events (CTCAE).
http://www.hrc.govt.nz/sites/default/files/CTCAE%20manual%20-%20DMCC.pdf
Each research protocol will specify which version of the CTCAE will be used for describing and grading of AEs.

PROCEDURES

For NACHO research protocols, AEs will include those untoward medical occurrences that transpire during participation on the research protocol. The time point for initiating data collection regarding AEs will be specified in the research protocol. All medical events that occur prior to these time points are considered part of the participant's medical status/medical history. Investigational sites will record all AEs in each protocol specific database per the specified protocol timelines and guidelines, using the NCI CTCAE for grading.

During clinical investigations, adverse events may occur which might be significant enough to lead to important changes in the way the therapy or investigational product is developed (SAEs). This is particularly true for reactions that, in their most severe forms, threaten life or function. In this case, the research protocol may require a temporary hold on enrollment or a complete cessation of the protocol. It is required that such reactions be reported promptly by the investigational institution's Principal Investigator (Site PI) per the research protocol, to the research protocol Study Chair (SC), sponsor, Institutional Review Board (IRB), and the NACHO Operations Center.

Responsibility for reporting all serious or unexpected adverse events that impact the safety of or risk to study participants lies with the research protocol Site PI.

The NACHO research protocol will clearly delineate reporting requirements to the IRB, research protocol Study Chair, Data Safety Monitoring Board, Federal Drug Administration, and sponsor.

An important part of adverse event reporting is the determination of the expectedness of the event. An "unexpected" adverse event is one where the nature or severity of the event is not consistent with information in the relevant source document(s). The research protocol Site PI will determine whether there is a reasonable

possibility that the investigational treatment is etiologically related to the adverse event, and report per the research protocol requirements.

In addition to protocol-required reporting, all NACHO institutions will report Unexpected Serious Adverse Events to the NACHO Operations Center at NACHO.ExpeditedReport@stjude.org . The NACHO CRA will ensure that the SAEs have been reviewed by the Director of NACHO Operations.

Summary of Responsibilities:

I. Investigational Site PI responsibilities

- Report all serious or unexpected adverse events that impact the safety of or risk to protocol participants
- Determine whether there is a reasonable possibility that the investigational treatment is etiologically related to the adverse event. (attribution)
- Indicate if the event was also a Dose Limiting Toxicity (DLT)
- Follow the sponsor's requirements for reporting a Serious Adverse Event according to the protocol-specific instructions for classifying an SAE within the specific protocol. SAE's must be reported to the sponsor as soon as they are identified utilizing the sponsor contact and means of communication.
- If an adverse event occurs on an IND study, please refer to "IND Safety Reporting Procedures" NACHO SOP
- Record the details of all adverse events in the source documentation and complete the appropriate Case Report Forms (CRFs) or data collection forms.
- Keep originals or photocopies of all AE related documentation and correspondence, including sponsor notification (e.g., facsimile confirmations, e-mail notifications) and file in the protocol specific regulatory file.

II. Research Protocol Study Chair responsibilities

- Review all serious or unexpected adverse events reported.
- Make final determination of attribution.
- Review events that require reporting to the FDA or other governing federal regulatory agencies.

III. NACHO Operations Center Responsibilities

- Determine (with SC) whether the SAE requires further reporting to all other research protocol participating sites
- Review all SAEs with the Executive Committee during monthly meeting
- Disseminate Safety Reports to all participating sites
- Safety Reports will be made available on the NACHO website under each research protocol webpage.

MAINTENANCE RESPONSIBILITY

The NACHO SOP Ad Hoc Committee is responsible for the annual review of this SOP. Suggested changes must be proposed to and approved by the NACHO Executive Committee.

AUTHORIZATION

This SOP was developed by the SOP Ad Hoc Committee and reviewed and approved by the NACHO Executive Committee.

VERSION/REVISION HISTORY

Approval Date	Version	Version/Revision Summary
12/11/2017	V 1.0	Original documentation/publication.