

**UNIVERSITY OF COLORADO
DEPARTMENT OF OTOLARYNGOLOGY
STANDARD OPERATING POLICY AND PROCEDURE**

Title	Recognizing, Documenting and Reporting Adverse Events
SOP #:	OTO 102
Version #:	3
Effective Date:	July 17, 2019
Supersedes:	OTO 102 Recognizing, Documenting, and Reporting Adverse Events

1. POLICY

Investigators and their key study personnel must properly identify and report adverse events (AEs) in accordance with Food and Drug Administration (FDA) regulations, International Conference on Harmonization (ICH) Good Clinical Practices (GCP) Guidelines, Institutional Review Board (IRB) policies, and protocol requirements.

2. SCOPE

These policies and procedures apply to all personnel who conduct or are involved in research involving human subjects.

3. RESPONSIBILITY

The Principal Investigator is responsible for the timely identification and reporting of all untoward events or effects (hereinafter collectively referred to as “adverse events” or “AEs”). The Principal Investigator is responsible for training co-investigators and study personnel to identify, classify, and communicate adverse events as they relate to the study protocol.

4. DEFINITIONS

- **Adverse Event (Effect):** any untoward change from baseline (pre-treatment or pre-participation) condition; any intercurrent illness that occurs during the course of a clinical study after treatment with the investigational product/treatment has started, whether considered related to the investigational product/ treatment/ processes or not, or any effect that is unintended and/or unfavorable, such as a sign, a symptom, a laboratory abnormality, or a disease.
- **Serious Adverse Event (Effect) or Serious Adverse Reaction:** an adverse event that results in death, is life-threatening, requires inpatient hospitalization (or prolonged stay), significantly incapacitates or disrupts the subject’s ability to lead a normal life, results in a congenital anomaly/birth defect or if intervention is required to prevent one of the above outcomes.
- **Unanticipated Adverse Event (Effect):** a problem not previously identified in nature, severity, or degree of incidence in the investigational plan, informed consent or application (including a supplementary plan, consent or application), or any other unanticipated serious problem associated with an investigation that relates to the rights, safety, or welfare of subjects.
- **Suspected Adverse Reaction:** reasonable possibility that an adverse event was caused by drug or treatment.

5. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.32	IND Safety Reporting
21 CFR 312.3	Definitions
21 CFR 812.150	Reports
ICH E6, 2.7	The Principles of ICH GCP
ICH E6, 4.3	Medical Care of Trial Subjects

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ICH E6, 4.7	Randomization Procedures and Unblinding
ICH E6, 4.11	Safety Reporting
ICH E6, 5.3	Medical Expertise
ICH E6, 5.5	Trial Management, Data Handling and Record Keeping
ICH E6, 5.16	Safety Information

6. REFERENCES TO OTHER APPLICABLE SOPS

- OTO 100 Institutional Review Board (IRB) Oversight
- OTO 104 Records Management and Retention
- OTO 200 Investigational Device Inventory Management
- OTO 202 Subject Management While On Study

7. ATTACHMENTS

None

8. PROCESS OVERVIEW

- A. Identifying Adverse Events
- B. Reporting Procedures for Adverse Events
- C. Clinical Management and Documentation of Adverse Events

9. SPECIFIC PROCEDURES

A. Identifying Adverse Events

#	Who	Task
1.	Principal Investigator and Study Personnel	The investigator and study personnel recognize an adverse event from study results, subject observation, reports from professionals and family members, questionnaires, dialog or written correspondence with subjects, and/or medical record notes
2.		Additionally, the investigator and site staff should monitor for serious and/or unanticipated adverse events ¹
3.		In the case of differentiating the vague report of "pain" the investigator will incorporate the "pain scale" to evaluate the severity of the report.
<p>Note: ¹Investigators should monitor for serious and/or unexpected AEs by: interviewing subjects, reviewing lab reports, reviewing subjects' medical records for additional information, reviewing (if applicable) subjects' diaries and communicating with subjects' medical providers. This should include: onset date, etiology (known or suspected), nature of the event, severity and duration of the event and possible relationship of the event to the investigational product.</p>		

B. Reporting Procedures for Adverse Events

#	Who	Task

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1.	Investigator	If applicable, report all adverse events to Sponsor and/or Principal Investigator, in the timeframe as specified in the protocol, or as soon as possible in the case of serious and/or unanticipated adverse events.		
2.		If appropriate, report unanticipated and/or serious adverse event to IRB In no more than 10 working days (but potentially sooner per IRB policy) and/or FDA within 7 calendar days for drug trials and 10 working days for device trials. Where available, use forms provided by the IRB and FDA. Access forms directly from the IRB's website to ensure the most updated form is being used.		
3.		If applicable, communicate to the sponsor if the IRB requires revisions to the informed consent form or other measures based on its review of the adverse event. If study is investigator-initiated, amend informed consent and/or protocol if requested by the IRB or is otherwise appropriate		
4.		For terminated studies, cease enrolling any new subjects until approval to restart the study has been received from FDA and IRB (and other regulatory authorities)		
5.		Follow up and assess all AEs until subjects are stabilized and/or resolved ¹		
6.		Update the sponsor, IRB, and FDA (all that apply) as new information becomes available		
7.		Report all AEs as part of the periodic or annual reporting requirements to the IRB(s) of record, if applicable for study		
8.		In the case of a multi-site study, ensure any reports of external adverse events from the sponsor are appropriately reported to the IRB, if required by IRB		
9.		In the case of a multi-site, investigator-initiated study where UC Denver (or affiliated site) is the Lead Site, notify all other sites of internal or external unanticipated and/or serious adverse events within 15 calendar days of determination		
10.	<p>Note:</p> <p>¹The investigator may perform directed or complete physical examination and clinical assessment; appropriate laboratory tests, diagnostic procedures and/or studies; and arrange medical/surgical consultation as needed.</p>			

C. Clinical Management and Documentation of AEs

#	Who	Task	
1.	Investigator	If applicable, complete sponsor Case Report Form (CRF) and submit to sponsor	

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2.		Complete adverse event reporting form(s) required by IRB and/or FDA as appropriate. If sponsor submits report to IRB and/or FDA, ensure timely submission and obtain copy of report for study records	
3.		File copies of reporting forms in the Regulatory Binder and Subject Folder as described in OTO 104 – Records Management and Retention	
4.		Keep originals or photocopies of all relevant documentation and file them in the subject's file	
5.		File copies of all AE correspondence and follow-up with the IRB in the site Regulatory Binder and provide copies to sponsor, if applicable	