INSTRUCTIONS FOR THE ADVERSE EVENTS FORM (AER)

I. General Instructions

The Adverse Events form is designed to track any adverse event that affects a study participant in the ACHIEVE study. The form must be completed in CDART within 48 hours of an adverse event.

See the ACHIEVE Manual, Section 11.2 for a definition of adverse events and unanticipated problems and their classification. Once the study participant's safety and comfort have been addressed following an adverse event, the AER is entered into CDART.

Given that the ACHIEVE study does not involve any major risks to participants and that the age of participants may naturally lead to numerous adverse health outcomes (e.g., falls, death), the approved ACHIEVE Data and Safety Monitoring Plan specifies that only a limited, pre-specified set of adverse events will be collected and evaluated in this trial. Other adverse events may be captured if desired (particularly if there is concern that it may be related to the study) but are not required.

Only the following adverse events and serious adverse events are required to be recorded and reported:

Adverse Events	**Serious Adverse Events**
Otitis externa	Death from any cause
Cerumen impaction or ear foreign body requiring removal by a physician	

This form may be accessed more than once, since information may not be complete at the time of initial entry about actions taken by the field center concerning the adverse event. Similarly, updates may be needed once more information related to the adverse event becomes available.

II. Specific Instructions

Obtain as much information about the adverse event as possible before beginning to enter the AER into CDART.

Item 1. Select the correct drop-down menu choice for the adverse event.

- Otitis externa is an infection or inflammation of the outer ear, and the field site audiologist or another clinician can advise if this event has occurred.
- Cerumen impaction or an ear foreign body (e.g., the hearing aid dome) is considered an adverse event only if removal requires consultation with a physician (i.e., not if the audiologist is able to manage this independently)
- Death from any cause

- Other – select this option if there is another adverse event (see definition in ACHIEVE Manual, Section 11.2) that you feel needs to be captured after consultation with other field center staff and the PI. Other adverse events are **not required** to be captured per the ACHIEVE safety protocol.

Item 2. Select the source of information about the adverse event. If more than one option applies, select the one from which the most information was gathered.

Item 3. Record the start date of the adverse event. If the adverse event is "death from any cause", record the date of death.

Item 4 Classify the severity of the adverse event:

- For otitis externa (to be completed by the study audiologist):
    - **Mild** if the symptoms are self-limited and resolve with interventions such as transiently limiting hearing aid use and/or the use of over-the-counter pharmacological therapies such as hydrocortisone cream or swimmer's ear drops.
    - **Moderate** if the symptoms require evaluation and management by a physician *and* the use of topical prescription pharmacological therapies such as antibiotic ear drops.
    - **Severe** if the symptoms require evaluation and management by a physician and the use of oral or parenteral antibiotics.
- For cerumen impaction or an ear foreign body requiring removal by a physician:
    - **Mild** if the cerumen impaction or foreign body is resolved without further need for therapy besides over-the-counter pharmacological therapies such as cerumenlytic drops.
    - **Moderate** if there is an associated otitis externa requiring the use of topical prescription pharmacological therapies such as antibiotic ear drops.
    - **Severe** if the cerumen impaction or ear foreign body results in a perforation of the tympanic membrane or an associated otitis externa requiring the use of oral or parenteral antibiotics.
- For death from any cause, always classify as "Severe"
- For other adverse events which field site staff elect to record, classify severity according to:
    - **Mild**: Awareness of signs or symptoms, but easily tolerated and are of minor irritant type causing no loss of time from normal activities. Symptoms do not require therapy or a medical evaluation; signs and symptoms are transient.
    - **Moderate**: Events introduce a low level of inconvenience or concern to the participant and may interfere with daily activities, but are usually improved by simple therapeutic measures; moderate experiences may cause some interference with functioning
    - **Severe**: Events interrupt the participant's normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating

Item 5. Record the relationship of the adverse event to ACHIEVE study procedures. Study-relatedness of AEs or SAEs will be based on the judgement of the field site PI in consultation as needed with the study audiologist and/or study PI Lin based on the following guidelines:

- **Definitely Related:** The adverse event is clearly related to the investigational intervention – i.e., an event that follows a reasonable temporal sequence from administration of the study intervention, follows a known or expected response pattern to

the suspected intervention, that is confirmed by improvement on stopping and reappearance of the event on repeated exposure and that could not be reasonably explained by the known characteristics of the subject's clinical state.

- **Possibly Related**: An adverse event that follows a reasonable temporal sequence from administration of the study intervention follows a known or expected response pattern to the suspected intervention, but that could readily have been produced by a number of other factors.
- **Not Related**: The adverse event is clearly not related to the investigational agent/procedure - i.e., another cause of the event is most plausible; and/or a clinically plausible temporal sequence is inconsistent with the onset of the event and the study intervention and/or a causal relationship is considered biologically implausible.

Item 6. Indicate whether the participant discontinued the study due to the adverse event.

For 'Death from any cause' always select 'Yes'

Item 7 Indicate the adverse event resolution status. This field can be updated later. For

"Death from any cause" always select "Fatal"

Item 8. If the answer to item 7 was "Resolved" then indicate the date the adverse event was resolved. If the answer to item 7 was NOT "Resolved" then no response is required to item 8 so proceed to item 9.

Item 9. Specify whether the adverse event meets the criteria for a SERIOUS adverse event. This should generally be 'no' unless in the case of "death from any cause" which is always considered SERIOUS. If 'Yes' to Item 9, complete items 9a-9f to specify which criterion apply to the serious adverse event. See the ACHIEVE manual, Section 11.2 for further definition of a SERIOUS adverse event.

Items 9a-9f: Select "Yes" to the item which best describes the adverse event and select "No" for all other items within 9a-9f. For "Death from any cause" Item 9e ("Was the adverse event fatal") should always be "Yes".

Item 10. Indicate whether the adverse event was unexpected.

- An adverse event is considered unexpected if the nature, severity, or frequency of the event is not consistent with information about the condition (e.g., older adults, aging, hearing loss) under study or intervention in the ACHIEVE protocol and consent form. **Any death that occurs during the trial should be marked as unexpected.**
- An event is expected if the event is known to be associated with the intervention or condition under study (e.g., aging, older adults, treatment of hearing loss).

Item 11. Provide additional details above the adverse event if the event meets the following criteria:

- Unexpected
- **Possibly or Definitely Related to the Study** (likely all deaths in ACHIEVE will be unrelated to the study, therefore, not reportable within 48 hours)
- Serious Adverse Event