CTSI Lost to Follow-Up Guidance

**Overview:**

All study visits and procedures must be completed as outlined in the protocol and the specified timeframes to ensure subject/participant safety and validity of the data analysis.

Actively enrolled subjects who are unable to be located/contacted may be considered “**lost to follow-up**”. Research protocols should include:

* the specific requirements/actions needed before a subject can be considered “lost to follow-up.”
* what will happen to the lost to follow-up subject’s data and whether the data will be included in the data analysis. (**NOTE:** <5% loss leads to little bias, while >20% poses serious threats to validity). These issues should be included in the Data Safety and Monitoring Plan (DSMP).
	+ case-wise deletions (subjects lost to follow-up not included in analyses
	+ multiple imputation (missing follow-up values are imputed)
	+ partial information included in the analyses (example with repeated measures, you can use the data you have available for analysis)

Protocols that do not include guidance for lost to follow up qualifications may utilize:

* an established team policy/process
* [“Alliance 8 Data Management v Jan 1, 2018: (section 8.1.2.5 Confirmation of lost to follow-up status)”](https://www.allianceforclinicaltrialsinoncology.org/main/cmsfile?cmsPath=/Public/Governance/files/Alliance%208%20Data%20Management%20clean%20January%201%202018.pdf) (has a 2-year contact requirement)
* other reference materials identified by the study team/study sponsor

Study subjects who have refused to partake in certain aspects of study participation or who have withdrawn consent from further participation **are not considered** “lost to follow-up".

NOTE: [ICH E9 "Statistical Principals for Clinical Trials"](https://database.ich.org/sites/default/files/E9_Guideline.pdf) suggests that the effect of losses of subjects or data, withdrawals from treatment, and major protocol violations on the main analyses of the primary variable(s) should be considered carefully, and that any subjects lost to follow-up, withdrawn from treatment, or with severe protocol violation should be identified, and a descriptive analysis of them provided, including the reasons for their loss and its relationship to treatment outcome.

**Contact Actions:**

Each attempt to contact the patient needs to be documented. Contact attempts may include:

* Phone calls
* Email, if permissible (template must be IRB approved)
* Mailing certified letter to the subject’s last known address (template must be IRB approved)
* Contacting the primary care physician (PCP) – if permitted in the consent form
* Contact people listed for the subject, if permitted in the Informed Consent Form (I.e., family member(s) and/or next of kin)

**NOTE:** Any written materials (written letters, emails, MyChart messages, etc.) that are distributed to the subject must be IRB approved prior to distribution.

**Due Diligence Actions:**

Each due diligence attempt to locate a participant or verify their living status needs to be documented. Due Diligence attempts may include:

* EMR review
* Reviewing public records (internet search, newspaper articles) such as obituaries or the “Office of Vital Statistics” for death records

**Duration of Contact and Due Diligence Actions**

In most cases, three attempts to contact the subject with one including a certified letter, may be considered reasonable to identify the participant as lost to follow-up.

Contact actions and due diligence actions may need to be completed until the participants anticipated study participation end date.

**Coming into Contact with a Lost to Follow-up Participant**

If the research team comes into contact with a lost to follow up participant, the research team should document the following:

* The type of contact made and how the contact came about (example: the participant called the study team, or the participant came into clinic for an alternative treatment plan)
* The reason the participant was unable to be contacted (the participant was hospitalized, the participant passed away on MMDDYYYY)
* If participant is still living, whether the participant wants to continue participation in the study or if they would like to withdraw from the study or study treatment and the reasons why. If the participant doesn’t want to provide a reason for early withdraw document that the participant does not wish to disclose their reasons for withdrawing.

*Example Letter Template (Must be IRB Approved Prior to Use):*

Dear Mr./Mrs. (Last Name),

I hope you are doing well. I am reaching out to you on behalf of Dr. XXX’s , [Study Protocol Title], study.

I have been trying to reach you to schedule your [study visit information, i.e., 1 year telephone follow-up call, MRI for your 6-month follow-up etc.], but have not been successful in contacting you.

Please give me a call at XXX-XXX-XXXX, email me at [coordinator email], or reply via mail to the address below so that we can schedule your appointment or discuss any concerns you are having at this time.

I look forward to hearing from you.

Do Not Use without IRB Approval

Thank you,

[Coordinator First Name Last Name]

[Coordinator Mailing Address]

[Coordinator e-mail]

[Coordinator Phone Number]