PURPOSE

This standard operating procedure (SOP) describes the steps research personnel must take and the documentation required when the principal investigator (PI) removes a participant from the study, the participant withdraws consent, or when a participant is lost to follow-up.

SCOPE

This SOP applies to the activities involved when the PI removes a participant from the study, a research participant voluntarily withdraws consent to continue participation in the study or continued contact with the participant cannot be maintained for those studies which involve follow-up visits.

RESPONSIBILITY

This SOP applies to the PI and key research personnel involved in the conduct of clinical trials at Beaumont Health System (BHS).

PROCEDURES

Protocol considerations

The study protocol should detail participant withdrawal and removal criteria (i.e., study termination) and specify: reasons for PI removal, study procedures/follow-up for early termination, and whether or not additional participants can be enrolled depending on the timing and number of withdrawals or removals.

If the PI desires to accrue additional participants in response to those removed or withdrawn, he/she must obtain prior approval from the sponsor and HIC, via an Amendment Request submission. Budgetary considerations must be reviewed with RI Accounting. If the PI must remove multiple participants or there are an unexpected number of participants withdrawing continued participation, it may be prudent for the PI to re-evaluate the protocol and determine whether changes may be necessary to facilitate participant retention without weakening the scientific merit of the study.

PI participant removal

The PI may remove a research participant from the study at any time in the event the participant’s safety may be compromised (e.g., serious adverse event(s) or unanticipated problems, the study being closed by the investigator or sponsor related to increased risk to participants, the participant is non-compliant with required study regimens/procedures, or the PI determines it is in the best interest of the participant).

Criteria for participant removal by the PI should be outlined in the protocol and/or HIC application, as noted previously. The criteria should also be listed in the informed consent and authorization document (ICAD) for studies in which consent and/or assent is required.
PARTICIPANTS REMOVED, WITHDRAWN OR LOST TO FOLLOW-UP

Prepared By: Research Administration

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Documentation including the date of removal and rationale should be entered in the participant’s research record. The PI should always inform the participant for the reason of removal. In the event of a research-related injury, the PI should provide the participant with the appropriate referral resources as needed.

**Participants who withdraw consent**

An essential element of the ICAD is the participant’s voluntary participation. Refusal to participate or a decision to discontinue participation involves no penalty or loss of benefits to which the participant is otherwise entitled.

The ICAD should state the participant will provide a written letter to the PI indicating the decision to stop participation. This letter should be filed in the participant’s research record, as well as documentation of any correspondence with the participant regarding their withdrawal (e.g., date first contacted regarding withdrawal, discussion of rationale, etc.). The date of this letter will serve as the date of participant withdrawal unless the participant has already done so verbally. When the participant withdraws consent, all data collected prior to the date of withdrawal remains within the study database and can be included in data analysis. The HIC ICAD template includes a statement regarding written withdrawal and should be used when drafting consent documents.

In the event the participant becomes lost to follow-up after they have verbally withdrawn consent without providing a letter to the PI, thorough documentation should be made in the research record (per the lost to follow-up guidelines below).

**Participants considered lost to follow-up**

Three (3) attempted telephone contacts should be documented by key research personnel in order to consider the participant lost to follow-up. Furthermore, for studies considered greater than minimal risk to participants, key research personnel should mail a certified letter to the participant’s address. If the participant does not respond, the certified letter receipt should be filed in the individual’s research record with a copy of the letter sent. For minimal risk studies, the certified letter is not required.

If the PI would like more stringent procedures to be followed (e.g., six telephone contact attempts over the course of one week), these criteria should be detailed in the study protocol and approved by the HIC.

Research personnel should promptly notify the PI (within one business day) of any participant withdrawal or important update regarding the withdrawal.

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### Continuing Review

Tracking of participant removal, withdrawal or lost to follow-up status should be documented on the Enrollment Log, indicating the date the event occurred. Details of the occurrence must be documented in the individual participant’s research record, as noted above.

At the time of HIC continuing review, the Progress Report Form must indicate the number of participants who withdrew their participation or were removed by the PI with rationale, under the Enrollment Information section. The number of participants who were lost to follow-up is also entered here. The PI is ultimately responsible for thorough, transparent documentation regarding enrollment information throughout the course of the study.

### REFERENCES

- 21 CFR 312.62 Investigator recordkeeping and record retention
- 21 CFR 812.140 Records
- ICH Guideline for Good Clinical Practice 6.5 Selection and Withdrawal of Subjects

### ASSOCIATED POLICIES

- RI Policy # 118 Responsibilities of the Principal Investigator
- HIC Policy # 205 Continuing Review and Renewal of a Protocol
- HIC Policy # 221 Informed Consent and Authorization in Research
- HIC Policy # 232 Research Record Retention
- HIC Policy # 254 Administrative Holds, Suspensions, and Terminations
- RI Clinical SOP # 608 Regulatory Files and Study Subject Records

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**Clinical Research Policies and Procedures**

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