Standard Operating Procedures (SOPs) are uniformly written procedures, with detailed instructions to record routine operations, processes and practices followed within a business organization. The Campbell Foundation’s SOPs help define the clinical research group’s standard practices and daily processes conducted to assure execution of research tasks in accordance with institutional, state and federal guidances.

Our SOPs contain enough detail to clearly guide research staff through a particular procedure and thereby establish uniformity in the everyday functions of the department. By laying out defined processes, the primary function of a SOP is to specifically avert procedural deviations.

Our SOPs are designed to ensure adherence with applicable guidances and regulations, such as ICH E6 Good Clinical Practice and 21 CFR 50. Campbell Foundation SOPs will be reviewed at regular (annual) intervals, and distribution, education, and training on SOPs will be consistent and documented, and monitored consistently to ensure compliance.

These SOPs were reviewed and approved on May 30, 2017 by:

**James H. Beaty, M.D.,** UT-Campbell Clinic Department of Orthopaedic Surgery and Biomedical Engineering for UT Health Science Center Department Chair

**Frederick M. Azar, M.D.,** Campbell Clinic Chief of Staff

**Thomas W. Throckmorton, M.D.,** Campbell Clinic, Campbell Foundation Research Chairman

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**Appendices**

1. Face Sheet
2. Research Flow
3. Consent Process Check Off List

Approval Date: May 30, 2017
1. **PURPOSE**

Since our founding in 1946, The Campbell Foundation has remained committed to advancing orthopaedic medicine throughout the world, through surgeon education, musculoskeletal research, and community healthcare. The Campbell Foundation Research Committee (CFRC) was founded to oversee all clinical and research investigations conducted at Campbell Clinic. The clinical investigations may be investigator initiated, multi-center, or industry sponsored regardless of funding needs.

2. **SCOPE**

Applies to all clinical investigations conducted at Campbell Clinic in affiliation with Campbell Foundation.

3. **BACKGROUND**

The CFRC is comprised of a representation of sub-specialties at Campbell Clinic to review proposed clinical investigations and determine if any modifications are needed in the following areas:

- Research design
- Scientific merit
- Risk mitigation
- Subject selection
- Data collection
- Study procedure(s)
- Feasibility of study implementation
- Outcome measures

4. **PROCEDURES**

4.1 CFRC Membership

4.1.1 Voting Members

4.1.1.1 The CFRC membership list is updated annually as part of the committee appointment by the Campbell Clinic Chief of Staff.

4.1.1.2 Only CC Surgeons/Physicians are eligible to be voting members of CFRC.

4.1.2 Non-voting Members

4.1.2.1 The CFRC Chair updates this CFRC membership annually
4.1.2.2 These members are chosen based upon their ability to provide information regarding clinical investigation design and implementation.

4.2 Responsibilities

4.2.1 CFRC Chair (CFRC-C):

4.2.1.1 Oversight of meeting discussions/proceedings

4.2.1.2 Approval of agenda items and meeting schedules

4.2.1.3 Review/correct meeting minutes before CFRC review

4.2.1.4 Determination of agenda items appropriate for electronic votes

4.2.1.5 Contribution of expert opinion/knowledge to project evaluation

4.2.1.6 Appointment of non-voting CFRC members

4.2.2 CFRC member

4.2.2.1 Review of meeting materials prior to meeting

4.2.2.2 Meeting minutes review and correction(s)

4.2.2.3 Contribution of expert opinion/knowledge in evaluation of agenda items

4.2.3 Campbell Foundation Clinical Research Coordinator (CF-CRC)

4.2.3.1 Distribution of meeting notices

4.2.3.2 Distribution of call for agenda items at least 6 weeks and again at 2 weeks in advance of the next CFRC meeting

4.2.3.3 Organize agenda and supporting materials for CFRC-C review

4.2.3.4 Finalize meeting packets of materials

4.2.3.5 Distribution of meeting packet

4.2.3.6 Record CFRC meeting proceedings

4.2.3.7 Compile meeting minutes for CFRC-C review
4.2.3.8 Finalize meeting minutes

4.2.3.9 Distribution of agenda items for electronic vote as directed by CFRC-C

4.3 Meeting Details

4.3.1 The CFRC meets bi-monthly on a designated Monday (alternate date if directed by CFRC-C) at 5 PM in the Foundation Library at 1211 Union Avenue, Suite 500.

4.3.2 Meeting dates are set one year in advance for the following year at the November CFRC meeting.

4.3.3 A reminder meeting notice is sent electronically 6 weeks prior to the meeting date and again at 2 weeks prior to the meeting date to all CFRC members (voting and non-voting).

4.4 Agenda Items

4.4.1 Agenda items are submitted electronically to the CFRC-C or CF-CRC.

4.4.1.1 An agenda item may be a new clinical investigation for the CFRC to review. Completion of a face sheet (Appendix 1) serves as a description of the clinical investigation for CFRC review.

If funding for a clinical investigation will be requested as part of the CFRC review, a detailed budget must accompany the face sheet.

4.4.1.2 Miscellaneous agenda items can also be submitted electronically to either the CFRC-C or CF-CRC with a summary of the information for consideration by the CFRC.

4.4.2 Agenda items are requested electronically by the CFRC-C or CF-CRC at least 6 weeks prior to the next meeting date and again at least 2 weeks prior to the next meeting date.

4.4.3 A representative from the clinical investigation or the miscellaneous agenda item is required to attend the CFRC meeting to discuss and answer any questions or concerns from the CFRC.

4.5 CFRC Review and IRB Review

4.5.1 The review/approval by the CFRM is not a prerequisite for IRB submission. A clinical investigation may be submitted to the IRB of record (see Standard Operating Procedure 100) before or after the study is reviewed/approved by the CFCM.
However, the IRB application may need to be amended, suspended or withdrawn pending CFCM action(s).

4.6 Meeting Materials

4.6.1 A packet of meeting materials will be sent electronically at least 3 days prior to the next meeting.

4.6.2 The packet will include an agenda, previous meeting minutes, notification of recent publication(s) and/or presentation(s), face sheets for new clinical investigations to be discussed, and any other materials requested for inclusion by the CFRC-C.

4.7 Meeting Minutes

4.7.1 The CF-CRC will record proceedings from the meeting, transcribe the notes and then review with the CFRC-C. The written record of the meeting minutes will be reviewed by the CFRC and voted on at the next CFRC meeting.

4.7.2 The approved CFRC meeting minutes will be utilized to document and record approval(s) and recommendation(s) of the CFRC.

4.8 Voting Quorums

4.8.1 A voting quorum is required for items that have a funding expenditure and/or actions that impact policy for Campbell Clinic and/or Campbell Foundation.

4.8.2 A voting quorum is defined as 50% plus one of the CFRC membership list per Section 4.1.1.1.

4.8.3 If a voting member is unable to attend a meeting, he/she is responsible for assigning a proxy representative.

Approval Date: May 30, 2017
1. **PURPOSE**

To establish a standard operating procedure (SOP) for a study protocol/design to guide clinical investigations at Campbell Clinic in affiliation with Campbell Foundation. A summary of this SOP can be found in Appendix 2-Research Flow.

2. **SCOPE**

Applies to all site personnel involved in the implementation and coordination of clinical investigation at Campbell Clinic/Campbell Foundation.

Personnel responsible: Principal Investigator (PI), Co-PI(s) and, when delegated by the investigator, Sub-investigator(s), Clinical Research Coordinator(s) [CRC(s)].

3. **BACKGROUND**

A clinical investigation must be designed so that it is scientifically sound and likely to yield valid results. There are many factors to be considered in formulating a clinical investigation that can be impactful on issues regarding musculoskeletal health. Above all, the study protocol/design of the clinical investigation must protect the rights, safety, and welfare of Campbell Clinic patients.

This SOP establishes the expectation that the conduct, oversight, and management of clinical investigations at Campbell Clinic/Campbell Foundation comply with the principles of Good Clinical Practice (GCP), consistent with International Conference on Harmonization (ICH). The principles of GCP help assure the safety, integrity, and quality of clinical investigations. GCP provides a standard for ensuring sound study design/protocol, implementation, data collection, monitoring, and reporting of clinical investigations.

In accordance with:

- 45 CFR 46 Subparts A, B, C, and D – Protection of Human Subjects
- ICH GCP Consolidated Guidelines E6
- U.S. Department of Health and Human Services (HHS) and Food and Drug Administration (FDA) Guidance for Industry, Investigator Responsibilities – Protecting the Rights, Safety, and Welfare of Study Subject, October 2009

4. **PROCEDURE**

4.1 A review of all clinical investigations is completed by the Campbell Foundation Research Committee (CFRC) (see SOP 100). A face sheet (Appendix 1) will be completed by the PI
SOP 101 STUDY PROTOCOL/DESIGN

or designee and sent to the Campbell Foundation CRC to schedule review by the CFRC.

4.2 A literature review is completed by one of the study PI to assess the current body of knowledge and define the details of the clinical investigation on the face sheet.

4.3 The face sheet will detail the study protocol/design for the clinical investigation and be a reference tool for completion of an Institutional Review Board (IRB) application. The face sheet will include the following details about the clinical investigation:

4.3.1 Title of clinical investigation

4.3.2 Investigator(s) and Key Study Personnel (KSP) involved

4.3.2.1 Qualified by education and/or training

4.3.2.2 Current ethics training [Collaborative Institutional Training Initiative (CITI)], National Health Institute (NIH), and/or specific requests by the study sponsor or IRB

4.3.2.3 Current IRB user registration

4.3.3 Purpose of clinical investigation

4.3.4 Hypothesis of clinical investigation

4.3.5 Subject details/selection

4.3.5.1 Inclusion/Exclusion criteria

4.3.5.1.1 Identify CPT or ICD 9/10 codes

4.3.5.1.2 Location of subject population

4.3.5.1.2.1 Campbell Clinic patients only-identify specific office(s) and/or Campbell Clinic Surgery Centers

4.3.5.1.2.2 Hospital(s) and/or affiliated surgery centers

4.3.5.1.2.3 Independent Surgery Center(s)

4.3.5.1.2.4 Campbell Clinic patients with subjects from other clinical investigative sites
4.3.5.1.3 Dates for study inclusion/exclusion

4.3.5.1.3.1 Retrospective review of records (all records in existence)

4.3.5.1.3.2 Retrospective review of record with prospective data collection

4.3.5.1.3.3 Prospective data collection

4.3.5.2 Risks to subjects

4.3.5.3 Benefits to subjects

4.3.5.4 Sample size consideration

4.3.6 Identification of research study procedure(s) [NOTE: consider if the procedures are standard of care or beyond standard of care]

4.3.6.1 Medical record abstraction from Electronic Medical Record (EMR)

4.3.6.2 Medical record abstraction from Athena

4.3.6.3 Medical radiographic abstraction from MedStrat

4.3.6.4 Patient Reported Outcomes (PRO) Tools(s) [i.e. KOOS Jr, WOMAC, ASES,…]

4.3.6.5 Therapeutic intervention(s)

4.3.6.6 Randomization process

4.3.6.7 Blinding process (single vs. double vs. triple)

4.3.6.8 Unblinding process

4.3.7 Consent process

4.3.7.1 Signed consent form (long form or short form)

4.3.7.2 Alteration of consent
4.3.7.3 Waiver of consent

4.3.7.4 Documentation of consent (if applicable)

4.3.8 Budget considerations

4.3.8.1 Research costs of study procedures (procedures beyond standard of care)
   4.3.8.1.1 Who will reimburse Campbell Clinic for these costs?
   4.3.8.1.2 How will these be reimbursed to Campbell Clinic?
   4.3.8.1.3 Will the subject’s insurance payer reimburse for research related injuries/expenses?

4.3.8.2 Patient stipends
   4.3.8.2.1 Commensurate with burden of research procedures to subject
   4.3.8.2.2 Distributed per IRB approval and as specified in the consent form

4.3.8.3 Research costs to Campbell Clinic/Campbell Foundation
   4.3.8.3.1 Who will reimburse Campbell Clinic/Campbell Foundation for these costs?
   4.3.8.3.2 How will these be reimbursed to Campbell Clinic/Campbell Foundation?

4.3.9 Outcome measure(s)

4.3.10 Statistical considerations
   4.3.10.1 Identify appropriate statistical method(s)
   4.3.10.2 Identify resource to execute appropriate statistical method(s)

4.3.11 Data management
4.3.11.1 Electronic records stored in an encrypted file on password protected computer

4.3.11.2 Paper records stored with regulatory records in research office

4.3.11.3 Minimum necessary protected health information (PHI) collected

4.3.11.4 Accessible only to authorized KSP

4.3.11.5 If all data collected is standard of care (SOC), consider an IRB for a Registry creation

4.4 An IRB application will be submitted to the designated IRB of record for approval with a description of the study protocol/design for the clinical investigation. See SOP 102 for Obtaining and Maintaining IRB approval.

Approval Date: May 30, 2017
1. **PURPOSE**

To establish standard operating procedures (SOP) for the exploration, negotiation, and execution of sponsored clinical investigations at Campbell Clinic in affiliation with the Campbell Foundation. These clinical investigations may be a multi-center collaborative study, either with or without funding, or an industry sponsored study with funding.

2. **SCOPE**

Applies to all site personnel involved in the implementation and coordination of clinical investigations at Campbell Clinic/Campbell Foundation including multi-center and industry-sponsored studies.

Personnel responsible: Principal Investigator (PI), Co-PI(s) and, when delegated by the investigator, Sub-investigator(s), and Clinical Research Coordinator(s) [CRC(s)] and other designated site personnel (if information collected is standard of care).

3. **BACKGROUND**

The Food and Drug Administration (FDA) conducts a thorough review of drugs, biologics, and medical devices for safety and effectiveness for a given indication prior to granting approval for marketing. Sponsors of Investigational New Drug/Investigational Device Exemption (IND/IDE) are required by the FDA to document the safety of these products through the execution of clinical trials conducted by qualified clinical investigators.

Multi-center studies are collaborative clinical investigations that seek to answer a study question among a common subject population from multiple sites. These studies may either be funded or non-funded but will have documents to guide the study conduct, protect subject data, and data sharing in a confidential manner.

Campbell Clinic/Campbell Foundation are invited to participate in clinical investigations based upon a proven history of excellence and expertise in the field of orthopaedics. These clinical investigations may have a multi-center or an industry sponsor. The consideration of a clinical investigation is carefully weighed by the physicians, staff, and Campbell Foundation members who are taking part in the clinical investigation.

In accordance with:
- 21 CFR 11 – Electronic Records; Electronic Signatures
- 21 CFR 54 – Financial Disclosure by Clinical Investigators
4. PROCEDURES

4.1 The information that follows in this section is intended to guide Campbell Clinic/Campbell Foundation study personnel in completing the appropriate documents in executing clinical investigations that have an external initiator (either multi-center or industry) and may or may not have funding considerations. The specific documents and processes will be completed as appropriate for the individual clinical investigation.

Shared procedural components for multi-center and industry sponsored clinical investigations

4.2 A confidential nondisclosure agreement (NDA) or its equivalent will be signed by the PI and appropriate Campbell Clinic/Campbell Foundation personnel with the sponsoring entity (lead multi-center site or industry sponsor), to define information considered confidential and/or proprietary, and to specify and control the extent and limits of disclosure of same confidential/proprietary information.

4.3 A review of the study protocol and supporting documents will be sent to Campbell Clinic/Campbell Foundation by the sponsor of the clinical investigation (either the lead PI for a multi-center study or the industry sponsor or designee). These documents will outline the investigative plan for the individual clinical investigation.

The supporting documents may include case report forms (CRFs), Investigator Brochure, Instructions for Use, informed consent template, procedures, schedule of study procedures,… The study protocol and supporting documents will be utilized by Campbell Clinic/Campbell Foundation to determine feasibility and interest of participation in the clinical investigation to include:

4.3.1 Campbell Clinic/Campbell Foundation personnel/resources required

4.3.2 Campbell Clinic/Campbell Foundation daily operations required

4.3.3 Risk/benefit ratio to Campbell Clinic patients

4.3.4 Costs to Campbell Clinic patients

4.3.5 Costs to Campbell Clinic, P.C.
4.4 The study protocol will guide the PI in assigning study roles for key study personnel (KSP). The PI will designate a lead CRC to function as the co-contact with him/her when communicating with the sponsor (lead PI or industry sponsor/designee). These assignments will be documented on either a delegation of authority log or note to file in the regulatory binder.

4.5 Approval of the clinical investigation implementation will be reviewed and voted upon by the Campbell Foundation Research Committee (CFRC). See SOP 100-Campbell Foundation Research Committee.

4.6 IRB approval of the clinical investigation must be obtained prior to completion of the site initiation visit (SIV) and/or its equivalent. [IRB of record determined per Campbell Clinic/Campbell Foundation SOP 102 – Obtaining and Maintaining IRB Approval.]

4.7 Training of Campbell Clinic/Campbell Foundation site research personnel will be conducted by the sponsor (either the lead PI for a multi-center study or the industry sponsor or designee) at a mutually agreeable date, time, and modality (webinar, study document review, on-site,…).

4.8 Study materials and subject data will be maintained in a secure designated area/platform (i.e. remote data capture system, encrypted spreadsheet, study binders,…) as directed per study protocol.

4.9 It is expected that the sponsor will ship supporting study materials (binders, electronic/paper CRFs, brochures,…) to the lead CRC in a timely manner and replenish materials as indicated by Campbell Clinic/Campbell Foundation.

4.9.1 The lead CRC will take and inventory of the above materials/supplies and notify the sponsor of any deficiencies.

4.9.2 The lead CRC will order replacement study materials as needed

4.10 A study close out visit will be scheduled at the request of the sponsor (lead PI of multi-center study or industry sponsor or designee). The PI and lead CRC will complete the arrangements for this visit/procedure and ensure that all materials needed to close out the study site will be available for inspection and stored as agreed upon in the Clinical Trial Agreement (CTA), Research Agreement or equivalent.

4.11 A final report will be submitted to the IRB of record to close the clinical investigation.
Applicable to Multi-Center Studies (financial remuneration may or may not be a component)

4.12 A data use agreement (DUA) or equivalent, if applicable, will be signed to verify methods and means for data sharing to the lead PI of the multi-center study. Transmission of study data to the lead PI site will occur through encrypted files or data entry into a remote data platform with de-identified subject data.

4.13 A research agreement between Campbell Clinic/Campbell Foundation and the lead PI site should be negotiated, approved, and executed prior to commencement of the study.

4.14 If relevant, the research agreement should also include a budget. See Section 4.17 for budget considerations.

4.15 The objective of the research agreement and/or study budget is to specify the obligations and responsibilities of Campbell Clinic/Campbell Foundation, and the multi-center study, and often includes language related to publication rights and limitations, among other details.

Applicable to Industry Sponsored Studies (where financial remuneration will be a component)

4.16 A site feasibility assessment may be completed at the request of the sponsor by Campbell Clinic/Campbell Foundation research personnel electronically and/or on site by the Sponsor or designee(s) prior to execution of the CTA, Research Agreement, or equivalent. This agreement will stipulate the terms between Campbell Clinic/Campbell Foundation and the industry sponsor.

4.17 Financial aspects of the clinical trial will be outlined in a study budget and should include (as applicable):

4.17.1 Specific elements for conduct of the clinical trial to include but not be limited to: study start up, participation in monitor or audit visits by study staff, screen failures reimbursement, reimbursement of the costs related to study procedures (i.e., MRI acquisition, strength measures, additional patient reported outcome measures,...), administrative costs, records storage, special equipment needed for procedures or for storage of the investigational product (IP) and/or specimens, and shipping requirements.

4.17.2 Study costs for subject enrollment and study completion to include but not be limited to: patient stipends, costs of study procedures, treatment for research injuries, and travel reimbursement.
4.17.3 Costs related to IRB preparation for initial preparation as well as renewal and/or safety reporting requirements. These costs include the IRB institutional fees (preferably a “pass through” expense from the IRB institution to the Sponsor) and Campbell Clinic/Campbell Foundation research staff preparation time.

4.18 A CTA or its equivalent and study budget must be approved and executed prior to scheduling a SIV (Note that IRB approval must also be completed prior to SIV-see Section 4.6).

4.19 The PI and study staff must complete the requested forms to disclose any conflicts of interests or to verify that there are no conflicts of interests regarding participation in the clinical investigation and report this information to the appropriate authorities. Any financial changes affecting the PI or study staff during the conduct of the clinical and for one year following the closure of the clinical trial must be reported to the appropriate authorities.

4.20 Completion of the SIV and any additional training requirements specified by the sponsor must be completed before receipt of the IP from the sponsor.

4.21 Secure storage of the IP as indicated in the study protocol is the responsibility of the PI or his/her designee.

4.22 Delegation of authority for the study procedures is the responsibility of the PI and should be documented in the regulatory binder per sponsor requirements.

Approval Date: May 30, 2017
1. **PURPOSE**

To establish standard procedures required to obtain and maintain Institutional Review Board (IRB) approval for clinical investigations conducted at Campbell Clinic in affiliation with the Campbell Foundation.

2. **SCOPE**

Applies to all site personnel involved in the implementation and coordination of clinical investigations at Campbell Clinic/Campbell Foundation including investigator initiated, multi-center, and industry sponsored studies.

Personnel responsible: Principal Investigator (PI), Co-PI(s) and, when delegated by the investigator, Sub-investigator(s), and Clinical Research Coordinator(s) [CRC(s)].

3. **BACKGROUND**

All clinical investigations at Campbell Clinic must receive IRB approval prior to implementation. This procedure is to comply with 45 CFR 46.101 and to uphold and protect the rights, safety, and welfare of Campbell Clinic patients.

IRB approval is required for all behavioral or biomedical research on human subjects to assure that the risks to subjects are minimal and reasonable in relation to the expected benefits. The IRB serves to protect the rights, welfare and safety of research subjects.

Except as provided in 21 CFR 56.104 and 56.105, any clinical investigation involving a test article must meet the requirements for prior submission to the Food and Drug Administration (FDA) shall not be initiated unless the investigation has been reviewed and approved by, and remains subject to continuing review by, an IRB meeting the requirements of 21 CFR 56 [21 CFR 56.103]. A test article is an investigational new drug (IND) or investigational device exemption (IDE) that has not been approved by the FDA for marketing.

The IRB of record will notify the PI in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval. If the IRB decides to disapprove the research, it will include in the written notification a statement of the reasons for its decision and give the PI an opportunity to respond in person or in writing [21 CFR 56.109(d)].

The PI should not implement any deviation from, or changes to the investigational protocol without agreement by the sponsor (if applicable) and prior review and documented approval from the IRB of record, except where necessary to eliminate immediate hazard(s) to clinical investigational subjects, or when the change(s) involves only logistical or administrative aspects of the trial [e.g., change in monitor(s), change in telephone number(s)] (ICH GCP 4.5.2).

IRBs conduct continuing review of research covered by federal regulations at intervals appropriate to the degree of risk, but no less than once per year [21 CFR 56.109(e) and 45 CFR 46.110(b)(1)].
Annual IRB renewal excludes those clinical investigations determined by the reviewing IRB to be exempt from this process [45 CFR 46.101(b)(4)].

In accordance with:
- 21 CFR 56.103 - Circumstances in which IRB Review and Required
- 21 CFR 56.109 - IRB Review of Research
- 21 CFR 56.111 - Criteria for IRB Approval of Research
- 45 CFR 46.101 - To What Does This Policy Apply?
- 45 CFR 46.109 - IRB Review of Research
- 45 CFR 46.114 - Cooperative Research
- ICH GCP Consolidated Guidelines E6 - Part 4.4 Communication with IRB/EC
- ICH GCP Consolidated Guidelines E6 - Part 4.5.2 Compliance with Protocol

4. **PROCEDURE**

4.1 The PI or designee(s) will submit all proposed clinical investigations for review to the designated IRB. This decision is made by the Campbell Clinic/Campbell Foundation lead PI of the clinical investigation. His/her decision is based upon the Campbell Clinic personnel involved, the clinical site(s) involved, and the initiator of the clinical investigation. Clinical investigations may be investigator initiated, multi-center studies, or industry sponsored clinical trials.

4.1.1 The University of Tennessee Health Science Center (UTHSC) IRB will be the IRB of record when UTHSC residents or fellows are involved as key study personnel (KSP) in the clinical investigation.

4.1.2 UTHSC will be the IRB of record when an investigation involves any of the following study sites-Methodist Healthcare, Le Bonheur Healthcare, or Regional One Healthcare.

4.1.3 A collaborative agreement for IRB approval is indicated if KSP are employed by either the University of Memphis (UofM) and/or St. Jude Children’s Research Hospital (SJCRH) for studies conducted in collaboration with Campbell Clinic/Campbell Foundation.

4.1.3.1 The UofM IRB will be IRB of record if the lead PI is an employee of UofM. A collaborative agreement for IRB approval will be requested by Campbell Clinic/Campbell Foundation to the UTHSC IRB.

4.1.3.2 If Campbell Clinic/Campbell Foundation is the lead PI site and the UofM is a secondary site, UTHSC will be the IRB of record; a letter of support from
the UofM PI will submitted as a component of the IRB application.

4.1.3.3 The SJCRH IRB will be the IRB of record if the lead PI site is an employee of SJCRH. A collaborative agreement for IRB approval will be requested by Campbell Clinic/Campbell Foundation to the UTHSC IRB.

4.1.3.4 If Campbell Clinic/Campbell Foundation is the lead PI site and SJCRH is a secondary site, UTHSC will be the IRB of record; a letter of support from the SJCRH PI will submitted as a component of the IRB application.

4.1.4 Baptist Memorial Healthcare will be the IRB of record if the only study site is Baptist Memorial Hospital-Collierville outside of the private Campbell Clinic practice.

4.1.5 Baptist Memorial Healthcare will be the secondary IRB of record if Baptist Memorial Hospital-Collierville is an additional site to those listed in 4.1.2.

4.1.6 A Central IRB, as designated by the industry sponsor, will be the IRB of record for industry sponsored studies that involve the private practice of Campbell Clinic staff. These studies will occur only at Campbell Clinic facilities. UTHSC Residents and Fellow will not be involved clinical investigation procedures defined in the approved study protocol.

4.2 The PI will obtain written approval from the IRB(s) before any human subjects are allowed to participate in a clinical investigation except as provided in 21 CFR 56.104 and 56.105.

4.3 The PI is responsible for submitting all records requiring IRB(s) approval to the IRB(s) in a timely manner. The PI may assign the duty of record submission to appropriate clinical site research personnel. Records requiring IRB(s) review may include:

4.3.1 Protocol and any amendments

4.3.2 Investigator’s brochure/Instruction for Use and any amendment(s)

4.3.3 Consent form and any revisions

4.3.4 A report of prior investigations (i.e. a medical device for human use)

4.3.5 Advertisements to be used for subject recruitment

4.3.6 Other written materials to be provided to subjects (i.e. Case Report Forms)

4.3.7 Safety reports and information

4.3.8 Other documents as required by IRB(s)
4.4 The PI is responsible for resolving proviso(s) from the IRB(s) in conjunction with the CRC.

4.5 The PI or designee will follow IRB(s) specific reporting requirements and submit all reports accordingly.

4.6 The PI or designee will maintain records of all submissions, correspondence, and all actions by the IRB(s) regarding the clinical investigation in the investigator regulatory files.

4.7 The PI or designee will provide the sponsor with a copy of all correspondence related to IRB(s) application and record submissions (if applicable).

4.8 The PI or designee will promptly report all adverse/serious adverse events, sponsor IND/IDE safety reports, protocol deviations, and annual FDA reports to the IRB(s) of record (as indicated).

4.9 If directed by the IRB(s), the consent forms will be revised in the event of new safety information that may impact subject willingness to participate in an investigation. Re-consenting of subjects will be under the direction of the IRB(s). Only current, IRB(s) approved, stamped versions of consent forms will be utilized for obtaining informed consent.

4.10 The PI or designee(s) will submit all study/protocol amendments (and related consent form revisions) to the IRB(s) for approval prior to implementation, except whereas to eliminate immediate hazard(s) to clinical investigational subjects.

4.11 Materials required for IRB(s) renewal (if applicable) will be submitted by the PI or designee(s) in a reasonable time frame to allow the IRB(s) to process the renewal of the clinical investigation.

4.12 Proposed revisions in clinical investigations will be submitted to the IRB(s) for approval prior to implementation. These revisions may include a change in KSP, procedure updates/additions, study protocol amendments,…

4.13 All KSP will maintain current ethics training as determined by the review IRB requirement at [www.citiprogram.org](http://www.citiprogram.org) or other training as requested by the sponsor or IRB(s) of record. See SOP 104 – Training and Responsibilities for Key Study Personnel.

4.14 At the conclusion of a clinical investigation, the PI or designee(s) will file a final report to the IRB(s) if record indicating the status of the clinical investigation including any additional information required by the IRB(s).
4.15 Regulatory files pertaining to the clinical investigation will be maintained for at least two years following IRB(s) closure and longer as indicated by the study protocol/design, clinical agreement(s) and/or IRB direction.

Approval Date: May 30, 2017
1. **PURPOSE**

To establish standard research training and responsibilities requirements for Key Study Personnel (KSP) in clinical investigations conducted at Campbell Clinic in affiliation with the Campbell Foundation.

2. **SCOPE**

Applies to all site personnel involved in the implementation and coordination of clinical investigations at Campbell Clinic/Campbell Foundation including investigator-initiated, multi-center, and industry-sponsored studies.

Personnel responsible: Principal Investigator (PI), Co-PI(s) and, when delegated by the investigator, Sub-investigator(s), and Clinical Research Coordinator(s) [CRC(s)].

3. **BACKGROUND**

There is a checkered history in the ethical treatment of subjects in research studies. Three events have had a significant impact on the federal regulations for the protection of human research volunteers. In chronological order, they are the 1946 Nuremberg Doctors Trial, the 1960s Thalidomide Tragedy, and the 1972 Tuskegee Syphilis Study Expose. Despite an increased awareness and surveillance of research studies, tragedies have been documented as recently as 1999 (Penn State) with the death of Jesse Gelsinger, a subject receiving a gene transfer, and in 2001 (Johns Hopkins University) with the death of Ellen Roche, a healthy volunteer.

Campbell Clinic and the Campbell Foundation consider human subject protection to be the cornerstone upon which all clinical investigations are built. Compliance with human subject protection is essential because it protects the clinical subjects and maintains public trust in research. Our patients’ perception of research, its benefits and its risks, are shaped by the way research is conducted.

In accordance with:
- Declaration of Helsinki
- The Belmont Report
- 21 CFR 50 – Protection of Human Subjects
- 21 CFR 56 – Institutional Review Boards
- 45 CFR 46 Subparts A, B, C, and D – Protection of Human Subjects

4. **PROCEDURE**

4.1 Each key study personnel (KSP) member will complete and maintain current ethics training (Group 3 - Investigators and all Study Personnel) through the Collaborative Institutional
Training Initiative (CITI) program as a minimum standard. In addition, there may additional training requirements from either the sponsor and/or the Institutional Review Board (IRB) specific to the clinical investigation.

4.2 An electronic certificate of completion will be maintained on the individual KSP’s CITI profile.

4.3 The PI will delegate responsibilities of study procedures of the clinical investigation(s) to KSP based upon:

4.3.1 Education
4.3.2 Training
4.3.3 Study protocol needs
4.3.4 Sponsor requirements (if applicable)

Approval Date: May 30, 2017
1. **PURPOSE**

To outline activities and procedures for obtaining and documenting informed consent of clinical investigations conducted at Campbell Clinic in affiliation with the Campbell Foundation.

2. **SCOPE**

Applies to all personnel involved in the implementation and coordination of clinical investigations at Campbell Clinic/Campbell Foundation.

Personnel responsible: Principal Investigator (PI), Co-Pl(s) and, when delegated by the investigator, Sub-investigator(s), Clinical Research Coordinator(s) [CRC(s)], and other key study personnel (KSP) approved by the reviewing Institutional Review Board (IRB).

3. **BACKGROUND**

Informed consent is a process that provides the prospective subject or the subject’s legally authorized representative (LAR) with information pertaining to the clinical investigation and sufficient opportunity to consider whether or not to participate, thus minimizing the possibility of coercion or undue influence [21 CFR 50.20].

IRB approval of the consent process is a component of every clinical investigation and is reflected in the study protocol/design (see SOP 101 – Study Protocol/Design and SOP 103 – Obtaining and Maintaining IRB Approval). The request for consent to the IRB may be in the form of a written consent form (long form or short form), an alteration of written consent, or a waiver of a written consent form (see Sections 4 and 5 of this SOP).

In accordance with:
- 21 CFR 50.20- General Requirements for Informed Consent
- 21 CFR 50.23- Exception from General Requirements
- 21 CFR 50.25- Elements of Informed Consent
- 21 CFR 50.27- Documentation of Informed Consent
- 45 CFR 46.116- General Requirements for Informed Consent (when applicable)
- 45 CFR 46.117- Documentation of Informed Consent (when applicable)
- 45 CFR 46.408- Requirements for Permission by Parents or Guardians and for Assent by Children (when applicable)
- 45 CFR 164 – Security and Privacy
- U.S. Department of Health and Human Services (HHS) and Food and Drug Administration (FDA) – Informed Consent Information Sheet – Guidance for IRBs, Clinical Investigators, and Sponsors (July 2014)
- ICH GCP Consolidated Guidelines E6- part 4.8, Informed Consent of Trial Subjects
- The Declaration of Helsinki
4. **PROCEDURE**

**Note:** The determination of which version of the consent form to use when documenting the informed consent process depends upon the IRB of record. See SOP 103- Obtaining and Maintaining IRB Approval. It is the responsibility of the PI and Key Study Personnel (KSP) to utilize the correct version of the approved IRB stamped consent form.

4.1 The PI is responsible for assuring the subject’s informed consent for the clinical investigation. If permitted by the IRB(s) of record and the sponsor (when applicable), the PI may delegate the duty of obtaining informed consent to appropriate KSP. The PI is responsible for assuring that any such designated KSP is knowledgeable about the specific clinical investigation and the process of informed consent.

4.2 The decision of a short versus long consent form is dependent upon the determination by the IRB of record.

4.3 The PI is responsible for assuring that the content of the consent form is in compliance with Good Clinical Practice (GCP) regulations and IRB(s) requirements. The PI may delegate the development and processing of the consent form to appropriate clinical research personnel.

4.4 The PI is responsible for ensuring that the consent form submitted to the IRB(s) of record includes the elements of consent in compliance with 21 CFR 50.25.

4.5 The PI is responsible for assuring that the written consent form and any other written information to be provided to subjects is revised whenever important new information becomes available that may be relevant to the subject’s willingness to participate. The PI may delegate to appropriate clinical research personnel the development and processing of the revised consent form or any other written information to be provided to subjects. Any such revisions should receive approval by the IRB(s) prior to use.

4.6 Only IRB approved, stamped consent forms will be used, whether paper or electronic versions, to document informed consent.

4.7 Informed consent will be obtained per approval by IRB(s) of record for each research subject prior to initiation of procedures for the clinical investigation. The consent form must be completed according to study protocol, sponsor (if applicable), IRB(s), and GCP requirements. If each page of the consent form has a line for the patient’s initials, then each page must be initialed by the patient.

4.8 Upon identification of a potential study subject, the PI or designee(s) will be responsible for determining who is legally authorized to give consent. If the subject is less than 18
years of age or is physically or mentally unable to provide consent, the LAR may be approached to give consent. Careful attention should be given to reviewing the subject’s medical history to alert KSP to any potential impairment to the informed consent process.

4.9 If the subject or the subject’s LAR is unable to read or is blind, then the approved IRB of record stamped consent form must be read in its entirety in the presence of an impartial witness. This should be documented directly onto the consent form and signed by the witness accordingly directly onto the consent form [ICH GCP 4.8.9, 21 CFR 50.25 and 21 CFR 50.27 (b)(2)].

4.10 If the subject or the subject’s LAR is unable to speak or understand English, then the consent form must be translated by an approved medical translator and submitted to the IRB(s) for approval. This approved IRB of record stamped informed consent form and its review must be conducted in conjunction with an approved translator and the KSP. This translator will document directly onto the consent form as a witness of the informed consent process.

A translator must be secured for ongoing communication throughout the clinical investigation.

4.11 If a subject is deaf, a sign language interpreter should be contacted for review of the consent form with the study KSP as part of the informed consent process. The translator will document directly onto the consent form as a witness of the informed consent process.

A sign language translator must be secured for ongoing communication throughout the research study.

4.12 The PI or designee(s) will fully inform the subject or the subject’s LAR of all pertinent aspects of the clinical investigation including the written information as approved by the IRB(s). The consent process includes:

4.12.1 Giving the subject adequate information concerning the clinical investigation in language that is as non-technical as possible.

4.12.2 Providing ample time and opportunity for the subject or the subject’s LAR to inquire about the details of the clinical investigation and to decide whether or not to participate in the investigation as well as to consider other available options, if any.

4.12.3 Responding to subject’s questions about the clinical investigation and answering to the satisfaction of the subject or the subject’s LAR.

4.12.4 Ensuring that the subject has comprehended this information.
4.12.5 Obtaining the subject’s voluntary consent.

4.12.6 Providing a copy of the signed consent form to the subject or subject’s LAR.

4.13 Informed consent will be documented by using the current written consent form as approved and stamped by the IRB of record. The written consent should be signed and personally dated by the subject or subject’s LAR, and by the person who conducted the informed consent discussion (if applicable) [ICH GCP 4.8.8]. The PI will sign the consent form (if applicable) stating that this subject has been fully informed of all aspects of the study per policy from the IRB of record.

4.14 If the consent form includes the signature of the person conducting the informed consent discussion and/or PI, a Consent Process Check-Off List document will be completed. (See Appendix 3) This document will be filed with the signed consent forms for all clinical investigations that the IRB(s) require the aforementioned signatures.

4.15 The completion of a Consent Process Check-Off List document is not required or maintained for short form informed consent forms.

4.16 The PI or designee(s) will file the original signed consent form (short or long form) with the subject’s source documents/regulatory records. Another copy may be filed in the subject’s Campbell Clinic electronic medical record and if applicable, in the hospital medical record.

4.17 Consent for a child should follow the guidelines set up by the IRB of record. Assent from a child does not constitute legal consent. The IRB of record will dictate final decisions regarding assent and its documentation. The minor subject’s LAR must give consent. The consent form should include documentation of the assent of the child as applicable.

4.17.1 It is assumed that children between 0-7 years of age are not capable of giving assent and that the child’s LAR will represent their consent to participate.

4.17.2 Children between 8-14 years of age may be able to understand the information presented to them and their assent should be attempted through a verbal agreement. This assent should be documented with the child’s signature in the appropriate assent section on the consent form.

4.17.3 Children 15-17 years of age should be able to give assent. The assent of this age group should include a written signature of the child on the consent form with the child’s LAR.

4.18 The PI and all site personnel are responsible for continuing the informed consent process throughout the subject’s participation in the study. The subject or the subject’s LAR should
be informed in a timely manner of any new information that becomes available relevant to
the subject’s willingness to continue participation in the clinical investigation. The
communication of the information should be documented in the clinical investigation
regulatory files [ICH GCP 4.8.2].

4.19 If the written consent form is revised during the course of a subject’s participation in the
clinical investigation, then the subject or the subject’s LAR shall be re-consented by the PI
or designee(s) per the direction of the IRB of record. The PI or designee(s) will file the
newly obtained original signed consent form with the subject’s source document or
regulatory files. A copy of the consent form will be provided to the person signing the
form at the time of consent.

Documentation of a subject by re-consent will comply with sections 4.14 and/or 4.15.

5.0 PROCESS OF INFORMED CONSENT

5.1 The process of informed consent is one of the most important parts of planning a research
study or clinical investigation. It is important that human subjects exercise their right of
free will in making the decision to participate. It is equally important that subjects be
given correct information, comprehend what is being said, and have time to make their
own decision about participation in the clinical investigation.

5.2 During the consent process, the following will occur:

5.2.1 The process of informed consent will take place in an area conducive to discussion
of study design and procedures for the clinical investigation.

5.2.2 The subject will be asked to read the IRB of record approved stamped consent form
in its entirety.

5.2.2 KSP conducting the consent process will review the consent form page by page.
The subject will be encouraged to ask questions during the process.

5.2.3 The PI or designee(s) will be available to discuss risks and benefits of the trial. The
subject will again be encouraged to ask questions. Only after the subject expresses
understanding of the risks and benefits of the trial and his/her time commitments
will the subject be asked to sign the Informed Consent Form.

5.2.4 Prospective subjects may elect not to sign the consent form at the initial time of the
informed consent discussion. It is their option to take the consent form home and
discuss it with family and friends. However, prospective subjects may not
participate in any study procedures until a consent form has been signed.
5.2.5 Subjects must be informed that it is their right to withdraw from the study at any time.

5.2.6 The subject or subject’s LAR will receive a copy of the signed consent form.

5.2.7 If a subject is ineligible for study participation following informed consent, the investigator must discuss with the subject treatment alternatives.

5.3 The IRB of record can choose to alter the written consent form in compliance with 45 CFR 46.116(d) or waive the written consent form in compliance with 45 CFR 46.116 (d)(2)(3), 45 CFR 46.117(c)(2) and 21 CFR 50.109(c)(1). This determination may apply to studies where the research presents no more than minimal risk of harm to subject and involves no procedures for which written consent is normally required outside of the research context such as data abstraction of existing medical records.

5.3.1 If an alteration of consent is approved, documentation of the informed consent process will comply with IRB(s) requirement(s). This applies to short form consent, survey administration, phone contact, registry survey consent… A subject log will be maintained to document subjects included in the clinical investigation.

5.3.2 The alteration of consent will include a mechanism for study staff to answer questions from the subject about the study.

5.3.3 If a waiver of consent is granted by the IRB(s), a subject log will be maintained to document subjects included in the clinical investigation (i.e. retrospective review of records).

5.3.4 Documentation of alteration and waiver of consent will be reported per requirement of the IRB(s).

5.4 A copy of the signed consent form or a notation citing this document may be recorded in the subject’s Campbell Clinic electronic medical record.

5.5 Secure storage of paper signed consent forms is maintained in the locked research area at the appropriate Campbell Clinic facility. Electronic consent forms will be stored in encrypted, secure data storage files per Campbell Clinic Information Technology security measures.

5.6 Copies of signed consent forms are stored for six (6) years following IRB closure as described in section 5.5.

Approval Date: May 30, 2017
1. **PURPOSE**

The safety and well-being of human subjects is of paramount concern to the Campbell Clinic research team. This standard operating procedure (SOP) applies to all clinical investigations conducted at Campbell Clinic in affiliation with the Campbell Foundation.

These steps are essential to fulfill the regulatory and clinical requirements to ensure adherence to study procedures for the evaluation of a subject’s response to the clinical investigational question(s). Through close monitoring and careful assessment of the subject, investigational outcomes, and adverse events [AE(s)] can be identified early and appropriate treatment initiated (when appropriate). By following these procedures, close attention is paid to the subject’s well-being and to the integrity of the data for the clinical investigation.

2. **SCOPE**

This SOP applies to the activities involved in managing subjects in clinical investigations conducted at Campbell Clinic/Campbell Foundation. These clinical investigations include investigator initiated, multi-center, and industry sponsored studies.

Personnel responsible: Principal Investigator (PI), Co-PI(s), Sub-investigators, Clinical Research Coordinator(s) [CRC(s)], and designated site personnel (if information collected is standard of care).

3. **BACKGROUND**

In accordance with:
- 21 CFR 11 – Electronic Records; Electronic Signatures
- 21 CFR 50.20 – General requirements for informed consent
- 21 CFR 50.25 – Elements of Informed Consent
- 21 CFR 56.109 – IRB review of research
- 21 CFR 812.100 – General Responsibilities of Investigators
- 21 CFR 812.110 – Specific Responsibilities of Investigators
- 45 CFR 46.116 – General Requirements for Informed Consent
- ICH GCP Consolidated Guidelines E6 – Part 4 Investigator
- ICH GCP Consolidated Guidelines E6 – Part 8 Essential Documents for the Conduct of a Clinical Trial

4. **PROCEDURE**

4.1 Subjects will be recruited from patients who are seeing a Campbell Clinic physician or are referred by a Campbell Clinic physician. The informed consent process will occur as follows in compliance with SOP 105 – Obtaining and Documenting Informed Consent.
4.1.1 Subjects will be approached about study participation in the clinical investigation in a manner that will not violate their right to privacy.

4.1.2 Questions regarding study participation will be answered in a private area by key study personnel (KSP).

4.1.3 A description of the clinical investigation will incorporate the elements of consent in either a written informed consent form, consent letter, or consent script (21 CFR 50.25 and 45 CFR 46.116).

4.2 After informed consent is obtained, the PI and/or the designated study personnel will (appropriate activities per individual study protocol):

   4.2.1 Document the subject’s medical history through record review and interview

   4.2.2 Perform a complete and/or directed physical examination

   4.2.3 Establish the subject’s baseline signs and symptoms

   4.2.4 Review with the subject the use of the current medication

   4.2.5 Inform the subject about the required study procedures and visits

   4.2.6 Collect specimens as directed by the protocol

   4.2.7 Order tests/procedures as directed by the protocol

   4.2.8 Provide PI contact information to the subject

   4.2.9 Randomize subject (if applicable) via:

      4.2.9.1 Computer generated code in a sealed envelope

      4.2.9.2 Study assignment from remote data capture system

   4.2.10 Maintain blinding assignment per study protocol/design

   4.2.11 Administer study intervention or test article (if applicable)

   4.2.12 Schedule follow-up visits as directed by the protocol

4.3 The CRC or designated study personnel will review with the subject the use of any study aids, such as a diary.
4.4 EACH AND EVERY STUDY VISIT FOR INDUSTRY SPONSORED STUDIES:

4.4.1 Separate tabs in the source binder for study visits, medications, and AE(s) [device and non-device related per PI assessment] will be maintained and reviewed prior to the patient visit. Each tab will be updated following completion of the study visit.

4.4.2 Any unresolved AE(s) is/are to be assessed for resolution, change in severity, or need for follow-up intervention at each office visit. Documentation of the AE status is required with follow-up reporting to the sponsor or Institutional Review Board (IRB) of record as indicated by the IRB of record’s requirements. See SOP 103 – Obtaining and Maintaining IRB Approval and SOP 111 – Routine Adverse Experience Reporting.

4.4.3 The PI and/or CRC(s) will assess the subject for any concurrent illness and document any new AE(s) appropriately at all contacts. The CRC(s) will review the office visit note for any additional symptoms or possible AE(s) to be included.

4.4.4 AE information in the source document should include: date of onset, any related signs and symptoms, severity of the adverse experience, laboratory tests performed and results (if applicable), treatment(s), outcome, and date of resolution (if applicable).

4.4.5 The PI and/or CRC(s) will review concomitant medications (per protocol) with the patient at each visit. Medication start and stop dates and the reason for medication must be documented.

4.4.6 All AE(s) and medications must be updated and documented in the source document and corresponding case report form (CRF) per protocol following each visit as indicated.

4.4.7 The PI and/or the CRC(s) will assess the subject’s compliance with the test article per protocol at all follow-up visits.

4.4.8 The PI and/or the CRC(s) will complete all paper and electronic CRFs per study protocol.

4.5 The PI or designee(s) will document any concurrent illness and/or endpoints into the study records/CRF(s) or Campbell Clinic Electronic Medical Record (EMR) per study protocol.

4.6 The PI may confer with the subject’s primary care provider or specialist, as appropriate, per study protocol or per individual subject request.

4.7 Study data will be stored either in a paper format and/or electronic versions as dictated by approved study protocol and accessible only to authorized KSP.
4.7.1 All paper records will be stored in the locked research office at Campbell Clinic.

4.7.2 All electronic records will be stored in an encrypted file on password protected computers or designated study data platform per protocol.

4.7.3 If all data collected is standard of care at Campbell Clinic, a Registry of data may be an appropriate IRB to submit for approval.

4.8 Secure storage of paper subject management CRFs and/or study data records are maintained in the locked research area at the appropriate Campbell Clinic facility. Electronic CRF(s)/study data will be stored in encrypted secure platforms designated by sponsor protocol or Campbell Clinic Information Technology security measures.

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1. **PURPOSE**

To establish the requirements for completing and maintaining Case Report Form(s) [CRF(s)] of clinical investigations conducted at Campbell Clinic in affiliation with the Campbell Foundation. This standard operating policy (SOP) applies to all clinical investigations at Campbell Clinic/Campbell Foundation including investigator initiated, multi-center, and industry sponsored studies.

2. **SCOPE**

Applies to all personnel involved in the implementation and coordination of clinical investigations at Campbell Clinic/Campbell Foundation.

Personnel responsible: Principal Investigator (PI), Co-PI(s) and, when delegated by the investigator, Sub-investigator(s), Clinical Research Coordinator(s) [CRC(s)], and other designated Campbell Clinic personnel (if information collected is standard of care).

3. **BACKGROUND**

CRFs are data collection tools utilized to standardized clinical data from investigational studies. CRFs are utilized for data analysis and remote data capture (RDC) systems for sponsored and multi-center studies. CRFs are typically designed and supplied by the study sponsor (multi-center studies or industry sponsor). The storage and submission process of completed CRFs is dictated by the study protocol (includes investigator initiated, multi-center and industry sponsored). These CRFs may be in either a paper or electronic version.

The CRF or information from the Campbell Clinic electronic medical record may serve as the source document. The source document is defined as the original record in which data collected for a clinical investigation is first recorded. The ICH-GCP guidelines define source documents as “original documents, data, and records”. (ICH-GCP Consolidated Guidelines part 1.52)

In accordance with:
- 21 CFR 11 – Electronic Records; Electronic Signatures
- 21 CFR 812.140 – Investigator Record Keeping and Record Retention for Device Trials
- 45 CFR 164 – Security and Privacy
- ICH GCP Consolidated Guidelines E6 – part 1 Glossary
- ICH GCP Consolidated Guidelines E6 – part 4.9 Records and Reports
- ICH GCP Consolidated Guidelines E6 – part 8 Essential Documents for the Conduct of a Clinical Trial
4. **PROCEDURE**

4.1 The CRF(s) may be designed by either the:

4.1.1 Campbell Clinic/Campbell Foundation PI or designee for investigator initiated studies

4.1.2 Lead PI site or designee for multi-center studies

4.1.3 Sponsor or designee for industry sponsored studies

4.2 The PI is responsible for the accuracy, completeness, legibility and timeliness of the data reported in the CRFs and in all required reports. The PI may delegate CRF completion and maintenance to appropriate Key Study Personnel (KSP).

4.3 The lead CRC will provide the sponsor (multi-center and industry) representative(s), if applicable, with the correct shipping or email address for all clinical materials specified in the study protocol that are to be sent or transmitted to Campbell Clinic.

4.4 The lead CRC will perform an initial inventory upon receipt of the CRFs and related study materials, for applicable studies. All supplies will be stored in a secured, limited access area.

4.5 The lead CRC will contact the designated sponsor (multi-center and industry, when applicable) representative in the event of shipment discrepancies, problems, or if there is need for additional CRFs or other supplies.

4.6 The CRC(s) and other KSP will complete CRFs in a timely manner for each subject enrolled in a research study. Data reported on the CRFs should be consistent with the source document(s). Any discrepancy in the source document and CRF should be explained in a note to file or on the CRF.

4.7 The CRC(s) and other KSP shall make entries on CRFs according to protocol guidelines. In the event that written guidelines are not provided to the research personnel, the PI should request specific instructions from the sponsor or lead PI site representative.

4.8 Corrections to the CRFs may be made as authorized by the PI. Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an audit trail should be maintained); this applies to written and electronic changes or corrections. Records should be retained regarding changes and any corrections made to clinical data.

4.9 The PI will sign required signature pages, as needed, after data is reviewed documenting that the entries are complete and accurate.
4.10 The CRC(s) will submit CRFs as instructed by the sponsor (multi-center and industry). Changes must not be made to the investigator’s copy of CRFs once original CRFs have been submitted to the sponsor, unless specifically requested by the sponsor. If additions or corrections need to be made after CRF submission, the lead CRC shall notify the sponsor representative of the necessary modification(s). Changes to CRF(s) can be made according to sponsor policy (multi-center and industry studies) or study protocol/design.

4.11 For industry-sponsored studies, data clarifications may be requested by the sponsor after submission of the CRFs as part of the sponsor data management edit procedures and data analysis. The PI or designee(s) should process the data queries and clarifications in a timely manner. Copies of all sponsor requested data edits should be retained with the study files as part of the official audit trail at Campbell Clinic.

The PI is responsible for the accuracy of all data submitted to the sponsor.

4.12 A legible copy of all CRFs will be maintained at the investigative site or appropriate designated storage facility per protocol of the lead PI (investigator-initiated or multi-center) or industry sponsored contract. The long term maintenance of the investigator’s copies of the CRFs is the responsibility of the PI who conducted the study.

4.12.1 In the case of industry-sponsored studies, the PI will be required to retain all study documentation until notified in writing by the trial sponsor, according to contractual agreement, but for not less than a period of two years after the final action of the Food and Drug Administration (FDA) for the marketing application or two years after the marketing application had been officially discontinued by the sponsor [21 CFR 812.140(d)], unless otherwise specified by contract.

4.12.2 In the case of investigator-initiated studies, CRFs will be maintained for two years following IRB closure.

4.12.3 In the case of multi-center studies, CRFs will be maintained per the instruction of the lead PI site.

4.12.4 Signed informed consent forms will be maintained for 6 years following IRB closure per SOP 105- Obtaining and Documenting Informed Consent.

4.13 Appropriate physical and technical controls will be used to maintain confidentiality of CRFs and clinical investigation materials.

Approval Date: May 30, 2017
1. **PURPOSE**

   To describe the requirements for preparing and managing source documents of clinical investigations conducted at Campbell Clinic in affiliation with the Campbell Foundation.

2. **SCOPE**

   Applies to all site personnel involved in the implementation and coordination of clinical investigations at Campbell Clinic/Campbell Foundation. This applies to investigator initiated, multi-center, and industry sponsored clinical investigations.

   Personnel responsible: Principal Investigator (PI), Co-PI(s) and, when delegated by the investigator, Sub-investigator(s), Clinical Research Coordinator(s) [CRC(s)], and other designated site personnel (if information collected is standard of care).

3. **BACKGROUND**

   PIs are required to prepare and maintain adequate and accurate case histories designed to record all observations and other data pertinent of the clinical investigation on each subject. Source documents include all original records (e.g., progress notes, laboratory reports and radiology reports) from which case report form(s) [CRF(s)] or medical record abstraction are completed. These records may be in either a paper or electronic version.

   A source document is defined as the original record in which data collected for a clinical investigation is first recorded. The ICH-GCP guidelines define source documents as “original documents, data and records”. (ICH-GCP Consolidated Guidelines part 1.52)

   In accordance with:
   - 21 CFR 11 – Electronic Records; Electronic Signatures
   - 21 CFR 50.26 – Documentation of Informed Consent
   - 21 CFR 812.140 – Investigator Record Keeping and Record Retention for Device Trials
   - 45 CFR 164.501 – Security and Privacy ICH GCP Consolidated Guideline E6- part 4.9 Records and Reports
   - ICH GCP Consolidated Guidelines E6 – part 1 Glossary
   - ICH GCP Consolidated Guidelines E6 – part 8 Essential Documents for the Conduct of a Clinical Trial

4. **PROCEDURE**

4.1 The PI is responsible for documenting consent for subject participation in clinical investigations at Campbell Clinic/Campbell Foundation in the regulatory binder. The signed informed consent form may be placed in the Campbell Clinic electronic medical
record (EMR) per SOP 105 – Obtaining and Documenting Informed Consent.

4.2 The PI is responsible for ensuring source documentation is sufficient to support subject participation in an investigator initiated study, multi-center study or industry sponsored clinical trial and the CRF entries are verifiable. The PI may delegate the task of source documentation to appropriate Key Study Personnel (KSP).

4.3 The PI and/or designee(s) may develop study-specific source document templates to ensure thorough, prospective data collection. Multi-center or sponsor generated data collection tools may be used for source documentation if applicable.

4.4 The PI will review protocol requirements and data collection procedures with applicable clinical research personnel. The PI will work closely with KSP to ensure study protocol/design compliance and appropriate documentation of data.

4.5 The lead CRC will ensure that all study-related source documents are labeled with appropriate subject identification. All documentation pertaining to clinical assessments and medical evaluations should be signed and dated by the appropriate KSP.

4.6 Appropriate KSP are permitted to make late entries or addendums to medical records if appropriate, for the purpose of research documentation. Late entries must be signed and dated by the appropriate KSP without obscuring the original entry. Audit trails will be maintained in paper and/or electronic CRFs through a date reconstruction.

4.7 The lead CRC will ensure that personal identifying information on copies of source documents that are to be submitted to the sponsor in support of CRF entries will be blacked-out and replaced with the subject’s initials and study identification number, in order to protect subject confidentiality.

4.8 A note to file will be placed in the regulatory files as needed to document pertinent information in to clarify source date [CRF(s), medications, subjection interactions,…). All note to file documents will be dated and signed by the appropriate KSP.

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1. **PURPOSE**

To establish standard procedures to collect, store (as indicated), and ship specimens (as indicated) that are collected as part of clinical investigations conducted at Campbell Clinic in affiliation with the Campbell Foundation. These specimens may be biologic (i.e. blood, synovial fluid,...) or radiographic or clinical information abstracted from the electronic medical records (EMR) or collected from the clinical investigational subject. The information may be captured on case report form(s) [CRF(s)] and entered into remote data capture (RDC) systems per approved protocol.

The proper collection and processing of specimens obtained from a study subject is part of the data collected in a clinical investigation. For industry sponsored studies, the specimens provide important information about the drug or device’s action within the body and the subject’s biologic and/or clinical response. To ensure accurate data, specimens must be collected at specified time points, processed, possibly preserved, and then shipped appropriately according to the approved study protocol. Additionally, the collection of specimens must adhere to good laboratory practices and universal precautions when collecting, processing, and arranging for shipment of the specimens according to the approved study protocol. This standard operating procedure (SOP) describes the steps for fulfilling the regulatory and clinical requirements, as applicable, involved in specimen collection and handling.

2. **SCOPE**

Applies to all site personnel involved in the implementation and coordination of clinical investigations at Campbell Clinic/Campbell Foundation including investigator-initiated, multi-center, and industry-sponsored studies.

Personnel responsible: Principal Investigator (PI), Co-PI(s) and, when delegated by the investigator, Sub-investigator(s), Clinical Research Coordinator(s) [CRC(s)] and other designated Campbell Clinic personnel (if information collected is standard of care).

3. **BACKGROUND**

In accordance with:
- Campbell Clinic Specimen and Biowaste Handling Policy and Procedure
- Title 21 CFR 312.62 – Investigator Record Keeping and Record Retention
- ICH Good Clinical Practice Consolidated Guidelines, Part 4 – Investigator

4. **PROCEDURE**

4.1 All research team members will be instructed to observe appropriate precautions based upon Occupational Safety and Health Administration (OSHA) guidelines as approved by and documented in the Campbell Clinic Specimen and Biowaste Handling Policy and Procedure Manual.
4.2 The PI or designee(s) will collect the appropriate specimen(s) identified in the study protocol. In the subject’s medical record and/or on the CRF, the date and time of collection will be noted as well as any relevant information pertaining to the subject’s status at the time of the procedure.

4.3 The test tubes or other container(s) should be labeled with subject identifiers, date, time, and any other required information.

4.4 The specimen(s) will be processed according to the specifics defined in the protocol (for example, centrifuge speed, duration, temperature requirements,…). The specimen(s) will either be stored/shipped/transmitted as directed in the approved protocol.

4.5 The specimen(s) will be prepared and packaged according to the shipping instruction specified in the protocol and/or central laboratory procedure manual.

4.6 A laboratory requisition slip will need to accompany the specimen(s). Include one copy with the specimen(s) when shipped. Retain one copy and file with the other study-related subject records.

4.7 The transmission of radiographic and/or clinical data will occur per study protocol/design in the designated secure format (Medidata, remote data capture, de-identified images,…) and utilize a subject code in place of protected health information.

Approval Date: May 30, 2017
1. **PURPOSE**  
The establishment of a standard operating procedure (SOP) for the receipt and handling of an investigational product(s) as part of industry sponsored clinical investigations/trials conducted at Campbell Clinic in affiliation with the Campbell Foundation.

2. **SCOPE**  
Applies to all industry sponsored clinical investigations/trials conducted at Campbell Clinic/Campbell Foundation.

Personnel responsible: Principal Investigator (PI), Co-PI(s) and when delegated by the investigator, Sub-investigator(s), and Clinical Research Coordinator(s) [CRC(s)].

3. **BACKGROUND**  
An Investigational Product (IP) is a drug, device, or biologic being studied in a clinical trial. These clinical trials are conducted by an industry sponsor on products that are not yet approved by the Food and Drug Administration (FDA) for marketing or the sponsor is seeking approval for a new indication. It is imperative that the sponsor and Campbell Clinic/Campbell Foundation have systems in place to adequately meet the regulatory requirements for handling of the IP.

The clinical trials conducted at Campbell Clinic/Campbell Foundation involving IP will comply with regulations for Investigational Device Exemptions (IDE). These are devices that have not yet been approved by the FDA for marketing but meet the FDA definition of a significant risk device.

A sponsor can only ship IP to qualified investigators who are participating in the FDA regulated clinical trial [21 CFR 812.43(b)]. These investigators will permit the IP to be used only with subjects under his/her personal supervision and will not supply the device to anyone not authorized to receive it [21 CFR 812.110(c)].

In accordance with:
- 21 CFR 812 – Investigational Device Exemptions
- 45 CFR 46 Subparts A, B, C, and D – Protection of Human Subjects
- ICH GCP Consolidated Guidelines E6 – Part 4 Investigator
- ICH GCP Consolidated Guidelines E6 – Part 5 Sponsor
- ICH GCP Consolidated Guidelines E6 – Part 8 Essential Documents

4. **PROCEDURES**

4.1 The Campbell Clinic/Campbell Foundation PI is responsible for completing the following prior to scheduling the site initiation visit (SIV) with the clinical trial sponsor or designee.
4.1.1 Securing Institutional Review Board (IRB) approval per SOP 103- Obtaining and Maintaining IRB Approval

4.1.2 Securing Campbell Foundation Research Committee approval per SOP 100-Campbell Foundation Research Committee

4.1.3 Completing necessary contracts/agreements per SOP 102-Sponsored/Multi-Center Clinical Investigations

4.2 The SIV will be conducted on site at Campbell Clinic/Campbell Foundation with all approved study personnel. Documentation of the SIV will be recorded in the regulatory binder.

4.3 The PI is responsible for handling the IP per the sponsor’s approved study protocol/design. This includes ensuring adherence to study protocol for:

   4.3.1 Randomization
   4.3.2 Blinding
   4.3.3 Unblinding as indicated by protocol or for emergency
   4.3.4 Device accountability documentation (see section 4.5)
   4.3.5 Device storage (see section 4.6)

4.4 A shipping record will accompany the IP. The PI or designee will check for accuracy against the contents of the shipment. This invoice will be signed, dated, and filed in the regulatory binder. Alternately, the sponsor’s protocol may direct shipment of the IP for an individual subject with appropriate documentation for placement in the regulatory binder.

4.5 Device accountability will be maintained by the PI and/or designee in the regulatory binder per sponsor protocol. The sponsor will provide documents either for an individual subject or generate a device accountability log. This log will reflect:

   4.5.1 Receipt of IP: date, quantities, lot number, and expiration date (as applicable)
   4.5.2 Distribution of IP: subject number/identifier, date, quantities, lot number, and expiration date (as applicable)
   4.5.3 Destruction of IP: date, reason(s) for destruction, quantities, lot number and expiration date (as applicable)

4.6 The IP will be stored in a designated secure area as specified in the approved study protocol/design. The study sponsor is responsible for supplying equipment necessary (i.e.,
4.7 Transfer of the IP between sites will be conducted with oversight of the PI and include only authorized study personnel as documented on the delegation of authority log.

4.8 Destruction of the IP will be completed and documented at the direction of the sponsor or designee.

4.9 A final inventory of the IP will be completed with the sponsor or designee at the study close-out visit and documented in the IP accountability log.

Approval Date: May 30, 2017
1. **PURPOSE**

   To establish the standard operating procedures (SOP) for reporting unanticipated problems, including routine Adverse Events [AE(s)] and unanticipated adverse device effects [UADE(s)] (if applicable) that occur in conjunction with research procedures of clinical investigations conducted at the Campbell Clinic in affiliation with the Campbell Foundation.

   This SOP applies to all categories of clinical investigations (investigator initiated, multi-center, and industry sponsored clinical trials). It should be noted that investigator initiated and multi-center clinical investigations would rarely have reportable events.

2. **SCOPE**

   Applies to all site personnel involved in the implementation and coordination of clinical investigations conducted at the Campbell Clinic/Campbell Foundation.

   Personnel responsible: Principal Investigator (PI), Co-PI(s) and, when delegated by the investigator, Sub-investigator(s), Clinical Research Coordinator(s) [CRC(s)], and other designated site personnel (if information collected is standard of care).

3. **BACKGROUND**

   The Institutional Review Board (IRB) reporting requirements of unanticipated problems, including AE(s) and UADE(s) vary by the policies of the IRB of record. Each PI is responsible for knowing and adhering to these requirements.

   **Definitions:**
   - An *unanticipated problem* may be completely unrelated to the clinical investigation such as an accident, relocation of residence, loss/change in employment,…The PI will be responsible for determining the impact of these occurrences on the clinical investigation and actions that are required for follow-up.
   - An *adverse event* (AE) is any untoward medical occurrence in a patient or clinical investigation subjected administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment.
   - An *unanticipated adverse device effect* (UADE) means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigation plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.
In general, unanticipated problems, including AEs are considered reportable to the IRB when the research procedures involve occurrences that are:

1) Unexpected.
2) Related to or possibly related to research study activities.
3) Significant enough to suggest that the research may place subject or others at a greater risk of harm than was previously known or recognized.

For a clinical investigation involving a **test article** (a drug, biologic or device that is regulated by the Food and Drug Administration (FDA):
It is the responsibility of the PI to report routine AEs and/or UADEs to the sponsor, as required, and to the IRB of record as indicated per their respective policies. Routine AE/UADE reports include any undesirable change in or worsening from a subject’s baseline condition, regardless of causality or severity to the test article. Routine AE/UADE(s) also include reports of unwanted effects such as symptoms or physical findings. The PI is responsible for the monitoring and reporting of AE/UADE occurrence(s), causality (if known), severity, treatment or follow-up, and reporting to IRB (when indicated by IRB requirements) and to the sponsor (when applicable).

**Reporting AEs to IRBs in Clinical Trials of Devices Under the Investigational Device Exemption (IDE) Regulations**

per

U.S. Department of Health and Human Services (HHS) and FDA – Guidance for Clinical Investigators, Sponsors, and IRBs, Adverse Event Reporting to IRBs – Improving Human Subject Protection (January 2009), page 6:

UADEs must be reported by the PI to the sponsor and the reviewing IRB, as described below:

- For device studies, PIs are required to submit a report of a UADE to the sponsor and the IRB of record as soon as possible, but in no event later than 10 working days after the investigator first learns of the event [21 CFR 812.150(a)(1)].

- Sponsors must immediately conduct an evaluation of a UADE and must report the results of the evaluation to FDA, all reviewing IRBs, and participating investigators within 10 working days after the sponsor first receives notice of the effect [21 CFR 812.46(b), 812.150(b)(1)].

The IDE regulations require sponsors to submit reports to the reviewing IRBs for each site in a manner consistent with the recommendations made above for the reporting of unanticipated problems under the Investigational New Drug (IND) regulations.

In accordance with:
- 21 CFR 312.32 – Investigational New Drug Safety Reports
- 21 CFR 812.3 – Investigational Device Exemptions-Definitions
- 21 CFR 812.140 – Investigational Device Exemptions- Records
- 21 CFR 812.150 – Investigational Device Exemptions- Reports
4. **PROCEDURE**

4.1 The PI is responsible for ensuring and protecting the safety of all study subjects based upon his/her qualified medical experience and training.

4.2 The PI is responsible for reporting all AE(s) and unanticipated problems (as indicated per PI judgment) to the IRB of record and/or sponsors, as indicated per the study protocol/design and/or IRB policy. The PI or designee(s) will enter the information describing the occurrence(s) on the CRFs or create a Note to File (NTF) for the regulatory binder. The responsibility for diagnosis and evaluation of AE(s), however, remains with the PI.

4.3 Subjects should be questioned regarding changes in their current or previous health status during study visits by the PI and/or designee(s). This information will first be documented in the subject’s medical record and/or CRF [location(s) of documentation per study protocol/design] and will serve as the source document.

4.4 For clinical investigations involving a **test article**: AE/UADE information should be assessed by the PI and be documented per protocol by the PI or designee(s) in the source document and include:

   4.4.1 Date of onset
   4.4.2 Any related sign(s) and symptom(s)
   4.4.3 The severity of the adverse experience
   4.4.4 Laboratory or diagnostic tests performed and results (if applicable)
   4.4.5 Treatment(s) [if applicable]
   4.4.6 Outcome(s)
4.4.7 Relationship to test article (if applicable)

4.4.8 Date of resolution (if applicable)

4.4.9 Assessment and documentation of the relationship between the test article and the AE/UADE(s).

4.5 The PI and designee(s) should refer to the study protocol/design for AE/UADE definitions, severity scoring systems, reporting time frames, and other reporting requirements as specified by the sponsor and/or IRB of record.

4.6 The PI or designee(s) will forward local/internal AE/UADE reports to the sponsor as required by the protocol and report to the IRB of record as indicated. [21 CFR 812.46 (b) and 21 CFR 812.150 (a)(1)]

4.7 The PI or designee(s) will forward external AE/UADE reports from the sponsor to the IRB of record.

4.8 The PI in conjunction with designee(s) will follow AE/UADE(s) until they are tolerated, resolved, or etiology determined, and/or appropriate follow-up is arranged. Any changes in the subject associated with the AE/UADE will be reported to the sponsor and/or IRB of record (if applicable), as required by the study protocol/design for the clinical investigation.

4.9 The PI is responsible for securing appropriate medical treatment for any unanticipated problems, AE(s) or UADE(s) that result from participation in the clinical investigation. The PI should communicate with the subject’s primary care physician as appropriate and should obtain permission from the subject for this communication.

Preparation Date: January 2017
1. **PURPOSE**

To provide a standard operating procedure (SOP) for the accurate and timely reporting of Serious Adverse Event(s) [SAE(s)] that occur in conjunction with research procedures conducted at Campbell Clinic in affiliation with the Campbell Foundation. This SOP will rarely apply to and Campbell Clinic/Campbell Foundation clinical investigations except those involving a Food and Drug Administration (FDA) regulated clinical trial. The lead Principal Investigator (PI) is responsible for reporting SAE(s) to the Institutional Review Board (IRB) of record and to the industry sponsor as dictated by the requirements of each organization. This SOP may be superseded by the sponsor’s SOP except when they conflict with federal regulations or other points of law.

2. **SCOPE**

Applies to all personnel involved in the implementation and coordination of clinical investigations at Campbell Clinic/Campbell Foundation. Of note again, a SAE(s) would rarely be associated with investigator initiated or multi-center clinical investigations.

Personnel responsible: Principal Investigator (PI), Co-PI(s) and, when delegated by the investigator, Sub- investigator(s), Clinical Research Coordinator(s) [CRC(s)], and other designated site personnel (if information collected is standard of care).

3. **BACKGROUND**

SAEs are any Adverse Event(s) [AE(s)] temporally associated with the subject’s participation in research procedures that meets any of the following criteria regardless of causality or severity [21 CFR 312.32 (a)]:

(1) results in death;
(2) is life-threatening (places the subject at immediate risk of death from the event as it occurred);
(3) requires inpatient hospitalization or prolongation of existing hospitalization;
(4) results in a persistent or significant disability/incapacity;
(5) results in a congenital anomaly/birth defect; or
(6) any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject’s health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).
PIs are obligated to report all SAEs to both the sponsor and to the IRB of record immediately. Sponsors and IRBs may have specific requirements for reporting SAEs that must be followed by clinical research personnel.

In the case of devices, the sponsor must evaluate any unanticipated adverse device effect (UADE) immediately [21 CFR 812.46 (b)] and report the results to the FDA, IRBs, and participating investigators within 10 working days after the sponsor first receives notice of it [21 CFR 812.150(b)(1)]. If the sponsor determines that an UADE presents an unreasonable risk to study subjects, the sponsor will terminate part or all the investigation as soon as possible, but no later than 5 working days after the sponsor made the determination and no later than 15 working days after the sponsor first received notice of the effect [21 CFR 812.46(b)(2)]. Sponsors must receive FDA and IRB approval to resume a terminated study of a significant risk device [21 CFR 812.46(c)].

In accordance with:

- 21 CFR 312.32 (a) – IND Safety Reporting
- 21 CFR 812, Subpart C – Responsibilities of Sponsors
- 21 CFR 812, Subpart E – Responsibilities of Investigators
- 21 CFR 812, Subpart G – Records and Reports
- ICH GCP Consolidated Guidelines E6 – Part 4.11 Investigator Safety Reporting
- ICH GCP Consolidated Guidelines E6 – Part 4.3 Medical Care of Trial Subjects
- ICH GCP Consolidated Guidelines E6 – Part 8.3.17 and 8.3.18 Essential Documents

4. PROCEDURE

4.1. The PI is responsible for ensuring and protecting the safety of all study subjects based upon his/her qualified medical experience and training.

4.2. The PI is responsible for ensuring that adequate medical care is provided to a subject for any AE(s) of SAE(s). The PI should communicate with the subject’s primary care physician as appropriate and should obtain permission from the subject.

4.3. The PI is responsible for reporting all SAEs to the clinical trial sponsor immediately, except for those events that the protocol identifies as not requiring immediate reporting.

4.4. The PI is responsible for reporting SAEs to the study sponsor. However, he/she may delegate the data collection and communication of such events to appropriate clinical research personnel. The PI and/or designee(s) will:
4.4.1. Identify SAEs occurrence and obtain details for reporting

4.4.2. Report findings in the appropriate section of the Case Report Form(s) [CRF(s)]

4.4.3. Follow SAEs according to applicable regulations and report changes to sponsor, as required by protocol

4.4.4. Obtain additional source documents regarding SAE as needed (i.e. hospital records, lab results, diagnostic test results,…)

4.5. The PI is responsible for reporting SAEs to the IRB of record according to their requirements. He/she may delegate the data collection and communication of such events to the appropriate clinical research personnel.

4.6. For reported deaths, the PI and designee(s) should supply the sponsor and IRB with any additional requested information (e.g., hospital records and autopsy reports).

4.7. The PI is responsible for immediately discontinuing a device trial upon receipt of notification from the sponsor in the event that the sponsor determines that an UADE presents an unreasonable risk to study subjects [21 CFR 812.46(2)].

4.8. The PI will complete Form FDA 3500A as directed by the study sponsor.

4.9. In order to resume a previously terminated study of a significant risk device, the PI may not resume a terminated investigation without IRB and FDA approval [21 CFR 812.46(c)]. The sponsor is responsible for obtaining FDA approval to resume the clinical trial and communicate in writing this authorization to all investigative sites and all IRBs of record.

Approval Date: May 30, 2017
1. **PURPOSE**

To establish a procedure for reporting research procedure deviation(s) occurring in the execution of clinical investigations at Campbell Clinic in affiliation with the Campbell Foundation.

2. **SCOPE**

Applies to all site personnel involved in the implementation and coordination of clinical investigations at Campbell Clinic/Campbell Foundation.

Personnel responsible: Principal Investigator (PI), Co-PI(s) and, when delegated by the investigator, Sub-investigator(s) and Clinical Research Coordinator(s) [CRC(s)].

3. **BACKGROUND**

The term “protocol deviation” is not defined by either the Health and Human Services (HHS) human subject regulations [45 CFR 46 Subpart A] or the Food and Drug Administration (FDA) human subject regulations [21 CFR 50].

A protocol deviation at Campbell Clinic/Campbell Foundation will be defined as a deviation from:

- study procedures specified in the study protocol/design (investigator initiated and multi-center clinical investigations).
- approved study protocol (multi-center or industry sponsored clinical investigations).

Federal regulations require that institutions promptly report changes in research activities to the Institutional Review Board (IRB). This procedure allows the IRB to determine whether the risk-benefit ratio for the study is adversely affected.

In accordance with:

- 45 CFR 46 Subpart A – Protection of Human Subjects – Basic HHS Policy for Protection of Human Research Subjects
- 21 CFR 812.150 (a)(4) – Reports
- ICH GCP Consolidated Guidelines E6 – Part 4.5 Compliance with Protocol

4. **PROCEDURE**

4.1 The PI is responsible for monitoring all study procedures and key study personnel (KSP) for compliance with study protocol/design. The PI and/or designee will complete the required reporting form(s) for the IRB of record within 5 business days for
a major protocol deviation or 10 business days for a minor protocol deviation. (The IRB of record may not require that minor protocol deviations be reported until the next annual renewal.) The PI will determine if a protocol deviation is a minor or major event.

- **Minor** protocol deviations are those events that have no substantive effect on the risk or benefit to the subject, will not affect the integrity of the study data, and is not the result of KSP misconduct.

- **Major** protocol deviations are those events that have resulted in harm or have posed a significant risk to the research subject, will affect the integrity of the study data, and are the result of KSP misconduct.

4.2 Study updates will be made as indicated by the PI based upon his/her evaluation of protocol deviation event(s) and will submit these amendments to the IRB of record for approval. Study updates may be implemented at the discretion of the PI if subject safety or welfare is at risk in conjunction with the occurrence.

4.3 For Investigational Device Exemption (IDE) studies the PI is responsible for reporting all:

- emergency protocol deviations from the approved study protocol to the study sponsor and the IRB of record no later than 5 days following the occurrence [21 CFR 812.150(a)(4)].

- protocol deviations from the approved study protocol/design per sponsor and IRB requirements.

Approval Date: May 30, 2017
1. **PURPOSE**

To ensure that all required study-related correspondence is securely maintained and available for long-term review for clinical investigations conducted at Campbell Clinic in affiliation with the Campbell Foundation.

2. **SCOPE**

Applies to all site personnel involved in the implementation and coordination of clinical investigation at Campbell Clinic/Campbell Foundation.

Personnel responsible: Principal Investigator (PI), Co-PI(s) and, when delegated by the investigator, Sub-investigator(s), Clinical Research Coordinator(s) [CRC(s)].

3. **BACKGROUND**

Correspondence pertinent to the conduct of the study, such as communication between the Campbell Clinic/Campbell Foundation site, sponsor (lead PI from multi-center study or industry sponsor), Food and Drug Administration (FDA), and/or the Institutional Review Board (IRB), must be maintained on file at Campbell Clinic as applicable to the individual clinical investigation.

The PI or designee(s) is/are required to prepare and maintain adequate records of all general correspondence to and from Campbell Clinic/Campbell Foundation. Appropriate physical and technical controls will be used to maintain secure storage of study correspondence. All records will be made available to the requesting monitor (Sponsor, IRB, or FDA) per written request from the respective reviewing body [21 CFR 812.145].

In accordance with:
- 21 CFR 11 – Electronic Records; Electronic Signatures
- 21 CFR 812.140 – Records
- 21 CFR 812.145 – Inspections
- 21 CFR 812.150 – Reports
- ICH GCP Consolidated Guidelines E6 – Part 4 Investigator
- ICH GCP Consolidated Guidelines E6 – Part 8 Essential Documents for the Conduct of a Clinical Trial

4. **PROCEDURE**

4.1 The PI will be responsible for all communications concerning the clinical investigations at Campbell Clinic/Campbell Foundation. He/she may delegate the duty of correspondence maintenance to the CRC(s) or appropriate clinical research site personnel as is acceptable to the sponsor and/or IRB.
Relevant communication/correspondence between the sponsor and/or IRB with CC/CF may include:

4.1.1 Notes of telephone calls pertinent to the conduct of the study

4.1.2 Newsletters and fax communications

4.1.3 Letter/e-mails to and from sponsor/Contract Research Organization (CRO) representative(s)

4.1.4 Letters to and from study subjects

4.1.5 Letters to and from colleagues regarding the study

4.1.6 Other pertinent general communications and meeting notes

4.2 The lead CRC will review the investigator regulatory files on a regular basis to ensure that all correspondence is filed in chronological order.

4.3 The lead CRC will review the correspondence in the regulatory binder on a quarterly basis with the PI, and more frequently if deemed appropriate.

4.4 The PI will request that the IRB and/or sponsor copy the lead CRC as appropriate on communications. This will enable the lead CRC to respond rapidly to requests and to assure that all official documents are filed in the investigator regulatory files.

4.5 The lead CRC will review the investigator regulatory files on a regular basis to ensure that outstanding correspondence issues are addressed and all required documents are current.

4.6 The lead CRC will review the investigator regulatory files on a regular basis to ensure that financial correspondence are maintained separately, as financial records are generally not considered part of the auditable regulatory files.

Approval Date: May 30, 2017
1. **PURPOSE**

To describe the activities for facilitating a sponsor, Institutional Review Board (IRB) and or Food and Drug Administration (FDA) initiated inspection of clinical investigation(s) at Campbell Clinic in affiliation with the Campbell Foundation.

The sponsor and IRB representative(s) will routinely monitor Campbell Clinic/Campbell Foundation as part of the standard operating procedure (SOP). An audit by the sponsor, IRB, or FDA is requested based upon site or sponsor actions that are cause for concerns (see discussion below).

2. **SCOPE**

Applies to all personnel involved in the implementation and coordination of clinical investigations at Campbell Clinic/Campbell Foundation.

Personnel responsible: Principal Investigator (PI), Co-PI(s) and, when delegated by the investigator, Sub-investigator(s), and Clinical Research Coordinator(s) [CRC(s)].

3. **BACKGROUND**

Sponsors and IRBs frequently inspect investigational sites to verify protocol compliance and adherence to the U.S. Code of Federal Regulations, during or after the completion of a clinical investigation. These routine inspections are usually scheduled at a mutually agreed upon date and time between the initiator (either the sponsor or the IRB) and Campbell Clinic/Campbell Foundation and are defined as a monitor visit.

Sponsors and IRBs will provide the Campbell Clinic/Campbell Foundation PI with a summary of finding from their monitor visit.

The FDA has the authority to audit an investigative site involved in a FDA regulated clinical trial by providing written notice (form 482 – Notice of Inspection) to the site or arriving unannounced for an inspection. An audit visit is usually triggered by an action as specified in the following section or may be generated by an audit of the sponsor. The Campbell Clinic/Campbell Foundation PI of the FDA regulated clinical trial will immediately notify the industry sponsor of any FDA inspection.

Site audits are likely to be conducted if:

1) There is high or low enrollment of study subject
2) Problems or concerns with the site have been reported by the monitor or other responsible personnel
3) The study is one of extreme importance
4) The investigator’s workload includes several studies with the same sponsor
5) The geographic location of the site coincides with other sites being audited

In accordance with:
- 21 CFR 312.62 – Investigator Record Keeping and Record Retention for Clinical Drug or Biological Trials
- 21 CFR 812.140 – Investigator Record Keeping and Record Retention for Device Trials
- 21 CFR 812.145 – Inspections
- ICH GCP Consolidated Guideline E6 – part 4.9 Records and Reports
- ICH GCP Consolidated Guidelines E6 – Part 5.15 Record Access

4. **PROCEDURE**

4.1 Upon the request of the sponsor, IRB, or FDA (if applicable), the PI and/or designee(s) should have readily available all requested clinical investigation or trial-related records.

4.2 Upon notification of an impending sponsor, IRB, or FDA monitor/audit visit, the study representative who first received notification will inform the PI of the request.

4.3 In the event of an FDA audit, the PI from the study is responsible for:

4.3.1 Notifying all Campbell Clinic/Campbell Foundation PIs involved in industry sponsored trials of the details for the FDA audit

4.3.2 Notifying all industry sponsors of clinical trials at Campbell Clinic/Campbell Foundation or the FDA audit

4.4 In preparation for the visit, the lead CRC will obtain all study-related records to include Case Report Form(s) [CRF(s)], source documents, and investigator regulatory files.

4.5 The lead CRC will organize all study-related files, arrange logistics, and prepare for the visit according to sponsor, IRB or FDA instructions.

4.6 The PI will designate a liaison to facilitate the visit. This designated liaison will communicate directly with the inspector prior to the visit, if possible, to make certain that all required records are obtained and necessary meetings are scheduled.

4.7 During the visit, the designated liaison will:

4.7.1 Greet the monitor/auditor(s) and verify identification/authorization

4.7.2 Provide requested records
4.7.3 Accompany monitor/auditor(s) during tours and interviews

4.7.4 Assist the monitor/auditor(s) as needed

4.7.5 Arrange for follow-up if required

4.7.6 Document monitor/auditor(s) date(s) and time(s) for inspection

4.8 The PI will meet with the monitor/auditor(s) as needed to discuss any questions or findings and develop an action plan to resolve findings as indicated.

Approval Date: May 30, 2017
<table>
<thead>
<tr>
<th>Clinical Investigation Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Literature Search Completed?</strong></td>
</tr>
<tr>
<td><strong>Full Title</strong></td>
</tr>
<tr>
<td><strong>Principal Investigator</strong> (must be Staff)</td>
</tr>
<tr>
<td><strong>Sub - Investigator (s)</strong> (all staff must have current CITI &amp; iMedRis)</td>
</tr>
<tr>
<td><strong>Resident section only</strong></td>
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</tbody>
</table>
| **List all active projects** (Title/Staff) | Example:  
  *Predictors of response to hyaluronic acid injections in the knee-FMA*  
  *Radiation Review in the Osteogenesis imperfecta Patient-JRS* |
| **Purpose** |  |
| **Hypothesis** |  |
| **Research Design** |  
  - Retrospective (ALL info in existence)  
  - Retrospective with Prospective  
  - Prospective |
| **Inclusion Criteria** |  |
| **Exclusion Criteria** |  |
| **Medical Records** (specify beginning & ending dates) |  |
| **Sites Involved** |  
  - Campbell Clinic Offices  
  - Campbell Clinic ASC  
  - Methodist  
  - LeBonheur  
  - ROH  
  - Baptist  
  - Other |
| **Risks to subjects** |  |
| **Benefits to subjects** |  |
| **Details of study procedure(s)** (medical record abstraction, KOOS, pivot shift, HgbA1c,...) |  |
| **Consent Process** (if unsure, consult with Research Coordinator) |  
  - Signed consent form (long vs. short)  
  - Alteration of consent  
  - Waived |
| **Outcome Measure(s)** |  
  - Primary: |
| **Statistical Details** (consult w Dr. Smith or BERD as needed) |  
  - Power analysis for Sample Size: |
| **Data Storage Details** (how will you store data? i.e. excel, CSV,...) |  |
| **Study Funding Needs/Itemized Budget** (patient stipends, statistical analysis, survey monkey fee,...) |  |
| **References** (list a minimum of 3) |  |
| **Publication Plan** |  |
Research Flow
Appendix 2

Research Question

See SOP 100 & 101

Complete FaceSheet
1. Complete literature review
2. Define study hypothesis & purpose
3. Identify Investigator(s)
4. Verify current CITI & IRB access for Investigators
5. Complete face sheet for CFRC
6. Identify sites(s) [office(s), hospital(s)]
7. Define study population (I/E, risk/benefit,...)
8. Create study protocol/design
9. Define study procedure(s)
10. Identify consent process
11. Determine outcome measures
12. Establish data management/storage
13. Schedule CFRC review & budget (if applicable)
14. Complete IRB application with CRC

Which Study Design?

RETOSSPECTIVE-All data in existence [SOP 106, 108, 111]

RETOSSPECTIVE + PROSSPECTIVE- All data in existence with collection of data not in existence (future) [SOP 105, 106, 107, 108, 111, 112, 113]

PROSSPECTIVE-Collection of data not in existence (future) [SOP 105, 106, 107, 108, 109, 111, 112, 113]

Is the study Funded?

YES

Complete review (as applicable):
NDA
Disclosures
Protocol/CRFs review
Site Feasibility
CTAs/Agreement(s)
Budget
SIV/Training
[SOP 102, 110, 114]

Is the study multi-center?

YES

- Implement Clinical Investigation after IRB approval and training (as applicable) completed [SOP 103, 104]
- IRB Renewal [SOP 103]
- Audit/monitor Visits [SOP 115]

NO
Appendix 3

______________________________

Patient name

________________________________________

Date

On the above date, I discussed the possibility of participation in the clinical research study with the above named subject.

☐ The study was explained in detail including, but not limited to the contents of the informed consent document (purpose of the study, visits and procedures involved, risks and benefits, alternative treatments, confidentiality, the right to withdraw from the study at any time without any consequence, treatments provided during the study period, arms of the study and randomization).

☐ The informed consent document was presented in the subject’s primary language.

☐ The subject was encouraged to ask questions. All questions were answered to the satisfaction of the subject. The PI was / was not available to answer any questions.

☐ The subject was given adequate time to read the informed consent and the opportunity to discuss it.

☐ The subject demonstrated understanding of the informed consent and would like to participate.

☐ The informed consent was signed and dated without alteration and a copy was given to the subject.

☐ There were no study procedures done prior to obtaining signed consent to participate in this study.

The informed consent was signed on ___________/______/______ at __________am/pm prior to any study-related procedures being performed.

Signature of person obtaining consent

Date