1 PURPOSE

This procedure describes the process for developing, reviewing, approving, and distributing Investigator Brochures, Investigational Plans, or similar documents that are intended to inform participating Investigators about the investigational product(s) they will be using in an FDA-regulated human subject research study. The Investigator Brochure typically is an extensive summary of all that is known about the research compound to date with regards to pre-clinical and clinical data.

2 GENERAL INSTRUCTIONS AND RESPONSIBILITIES

The Investigator or qualified designee is responsible for:

a) Preparing the initial draft of the document, then forwarding the draft to all designated individuals for review and approval, and then distributing the final approved Investigator Brochure or comparable document(s) to all relevant personnel (Reference SOP 102, Document Development and Change Control).

b) Forwarding the final, internally approved Investigator Brochure or comparable documents to the FDA (as part of the applicable regulatory submission) and other applicable regulatory authorities, for their review and approval as required.

c) Submitting the Investigator Brochure or comparable document(s) to the IRB, and other internal regulatory authorities as applicable.

d) Distributing the most current, approved Investigator Brochure or Investigational Plan to all applicable personnel including the Regulatory Coordinator, Pharmacist, Sub-Investigators and key study personnel.

3 SPECIFIC PROCEDURES

3.1 Investigator Brochure (Drug/Biologic Studies)
a) The Investigator or designee should create the Investigator Brochure before the clinical protocol is written, as the information in the Investigator Brochure will contribute substantially to the development of the protocol.

b) Follow SOP 102 for developing, reviewing and approving the Investigator Brochure, which is a controlled document.

c) The Investigator Brochure must address the following:
   i. Brief description of the drug/biologic substance and the formulation, including the structural formula, if known.
   ii. Summary of the pharmacological, toxicological, and/or biological effects of the drug/biologic in animals and, to the extent known, in humans.
   iii. Summary of the pharmacokinetics and biological disposition of the drug/biologic in animals, and if known, in humans.
   iv. Summary of information relating to safety and effectiveness in humans obtained from prior clinical studies; reprints of published articles on such studies appended when appropriate and available.
   v. Description of possible risks and side effects (all known or expected adverse events) to be anticipated on the basis of prior experience with the drug/biologic under investigation or with related drugs/biologics, and of precautions or special monitoring to be done as part of the investigational use of the drug/biologic.

d) Each participating Investigator should receive a copy of the Investigator Brochure prior to beginning the clinical study (i.e. during the qualification and/or initiation site visit(s)) for distribution to key study personnel (e.g. Pharmacist or other designee dispensing drug).

e) The Investigator will include the original Investigator Brochure (if applicable) as part of the IND submission, as well as submissions to any other applicable institutional and regulatory authorities.

f) The Investigator will update the Investigator Brochure regularly and as frequently as necessary to keep it current, as the study proceeds through the clinical phases of testing (Phases 1, 2, 3, and 4) or as new information becomes available.

g) The Investigator will submit the updated Investigator Brochure as an amendment to the IND (at the time of updating) and in the IND Annual Report to include all the changes that occurred during the prior year (Reference SOP 201).

h) If any adverse event occurs that is not listed in the Investigator Brochure, it must be treated as an unexpected adverse event and reported accordingly (Reference SOPs 202, Required Reports for FDA, and 605 Adverse Event Recognition and Reporting).

i) In addition to the Investigator Brochure, the Investigator should use all other available information/tools for keeping relevant personnel informed about the investigational drug, e.g. published reprints or articles and letters to editors, adverse event reports, etc.

3.2 Investigational Plan (Device Studies)

   a) While the clinical protocol is being developed, the Investigator should also be developing the Investigational Plan.
b) The general procedure for developing, reviewing, and approving controlled documents in SOP 102 Document Development and Change Control should be followed for the documents that constitute the Investigational Plan.

c) The Investigational Plan should include:

i) Purpose: the name and intended use of the device and the objectives and duration of the investigation.

ii) Protocol: a written protocol clearly describing the methodology to be used, and an analysis of the protocol demonstrating that the investigation is scientifically sound.

iii) Risk analysis: a description and analysis of all increased risks to which subjects will be exposed by the investigation; the manner in which these risks will be minimized; a justification for the investigation; and a description of the study population, including the number, age, sex, and condition.

iv) Description of the device: a description of each important component, ingredient, property, and principle of operation of the device and of each anticipated change in the device during the course of the investigation.

v) Monitoring procedures: the Investigator’s written procedures for monitoring the investigation and the name and address of any Monitor.

vi) Labeling: copies of all labeling for the device.

vii) Consent materials: copies of all forms and informational materials to be provided to subjects to obtain informed consent.

viii) IRB information: a list of the names, locations, and chairpersons of all IRB’s that have been or will be asked to review the investigation, a certification of any action taken by any of those IRB’s with respect to the investigation.

ix) Additional records and reports: a description of records and reports that will be maintained on the investigation in addition to those prescribed in 32 CFR 812 Subpart G (Records and Reports).

d) The Investigator or other designated Author should reference SOP 201 Attachment G, IDE Submission Checklist, for additional guidance on the format for the Investigational Plan.

e) In some cases, a detailed clinical protocol may include additional applicable elements of the Investigational Plan, or even all its elements. Any remaining elements not covered in the protocol must be provided in a separate document.

f) The Investigator will include the Investigational Plan as part of the FDA IDE and IRB submissions, as well as submissions to other applicable regulatory authorities.

g) The Investigator will update the Investigational Plan as the study proceeds through the clinical phases of testing, or as new information becomes available.

h) The Investigator will update the FDA and IRB on changes in the Investigational Plan through appropriate submissions (IDE Supplement, other written notification).

i) The Investigator will update the ICF when deemed necessary as new information regarding the investigational device becomes available.
3.3 Report of Prior Investigations (Device Studies)

a) While the Investigational Plan (including the clinical protocol) is being developed, the Investigator or designee should also be developing the Report of Prior Investigations.

b) The general procedure for developing, reviewing, and approving controlled documents in SOP 102, Document Development and Change Control, should be followed for developing, reviewing, and approving the documents that constitute the Report of Prior Investigations.

c) The Report of Prior Investigations includes reports of all prior clinical, animal, and laboratory testing of the investigational device and must be comprehensive and adequate to justify the proposed investigation.

d) The Report of Prior Investigations also includes:
   i. A bibliography of all publications, whether adverse or supportive, that are relevant to an evaluation of the safety or effectiveness of the device, copies of all published and unpublished adverse information, and, if requested by an IRB or FDA, copies of other significant publications.
   ii. A summary of all other unpublished information (whether adverse or supportive) in the possession of, or reasonably obtainable by, the Investigator that is relevant to an evaluation of the safety or effectiveness of the investigational device.

e) The Investigator or other designated Author should reference IDE Submission Checklist for additional guidance on organizing the Report of Prior Investigations (See SOP 201 Attachment G).

f) The Investigator will include the Report of Prior Investigations as part of the IRB and FDA IDE submissions, as well as submissions to other applicable regulatory authorities.

4 REFERENCES TO OTHER APPLICABLE SOPS

- 102 Document Development and Change Control
- 201 Contacts and Submissions for FDA
- 202 Required Reports to FDA
- 605 Adverse Event Recognition and Reporting

5 ATTACHMENTS

- None

6 APPLICABLE REGULATIONS AND GUIDELINES

- IND Content and Format (21 CFR 312.23)
- Informing Investigators (21 CFR 312.55)
- Investigational Plan (21 CFR 812.25)
- Report of Prior Investigations (21 CFR 812.27)
Investigator Standard Operating Procedures

- Informing Investigators (21 CFR 812.45)
- The Principles of ICH (ICH E6, Section 2.4)
- Information on Investigational Product(s) (ICH E6, Section 5.12)
- Safety Information (ICH E6, Section 5.16)
- Investigator’s Brochure (ICH E6, Section 7.0)
- Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (ICH E2A, March 1995)