1 PURPOSE
This procedure outlines the process for conducting effective correspondence with the FDA, both oral and written, for conducting meetings with the agency, and for preparing certain formal submissions to the agency.

2 SPECIFIC PROCEDURES
2.1 Oral and Written Correspondence with the FDA
   a) The Investigator or designee should contact the FDA as early as possible to learn the name of the appropriate administrative reviewer (Consumer Safety Officer or CSO) to call with questions concerning correspondence and submissions.
   b) For unique situations (e.g. treatment use of an investigational drug/biologic/medical device, compassionate use of a drug/biologic, research involving humanitarian use of a device), or other situations in which the appropriate FDA review process is uncertain or evolving (combination investigational products, novel or controversial therapeutic products/procedures), the Investigator or designee must contact the OHR and inform of the pending submission before proceeding. The OHR should be consulted for advice and support.
   c) The date, time, parties, and discussion summary of all oral discussions with the FDA personnel should be documented in a follow-up email to all persons involved...
   d) If the FDA requests a written response in its correspondence, the Investigator must submit replies by the due date or obtain an extension in advance from the agency.
   e) The Investigator or designee must maintain a current and complete Regulatory Master File of FDA correspondence, including copies of all oral contact summaries, electronic mail, and written correspondence. The OHR must have access to all study files as necessary to ensure clinical research compliance.
2.2 Meetings with the FDA

a) The Investigator should refer to guidelines on setting up and conducting a meeting with the FDA (Attachment B, FDA Meeting Guidelines).

b) For meetings specified in the FDA regulations and guidance, the Investigator should ascertain additional, specific requirements by calling the CSO and asking for further instructions.

c) All meeting materials and related correspondence must be maintained in the appropriate section of the Regulatory Master File.

2.3 Investigational New Drug (IND) Development and Submission

a) The Investigator or designee should follow the guidance provided for preparing the content of a new IND and ensure that all required forms and documents are collected (Attachment C, IND Submission Checklist).

b) The Investigator or designee should obtain current versions of the FDA-required forms by following the instructions in SOP 201 Attachment D (Accessing FDA forms over the Internet).

c) Before submitting an IND application to the FDA, the Investigator or designee must provide the OHR with a full copy of the submission.

d) The Investigator or designee will maintain a copy of the completed IND and all related submission material in the appropriate section of the Regulatory Master File.

e) The Investigator may proceed with the clinical study after receiving the FDA's determination letter that either assigns an IND, or grants an exemption from filing the IND.

f) If the FDA requires any additional information prior to granting approval of the IND, the Investigator or designee should provide the additional information as soon as possible, within the specified timeframes.

g) The Investigator or designee should ensure that the Institutional Review Board (IRB) reviews and approves changes to the study as required by SOPs (See SOP 302, Clinical Protocol Amendments).

h) The Investigator or designee should file IND amendments as required by the FDA. The Investigator may not proceed with the change to the IND until it has been submitted to the FDA and approved by the IRB.

i) If significant safety issues arise during the conduct of a clinical study, the Investigator or designee must ensure carrying out the required reporting and notifications to the FDA, the IRB, other applicable internal parties, and other applicable Principal Investigators.

j) If any regulatory authority (e.g. the FDA or IRB) issues a clinical hold, the Investigator may not proceed with the study until all issues identified by the regulatory authority are resolved.

k) If the clinical hold is issued after the study has begun, the Investigator must cease enrolling new subjects to the study, and ascertain how to treat subjects currently enrolled (e.g. stop study medication, continue study medication, follow-up etc.).

l) If the clinical hold letter from the FDA specifies that the study may proceed after certain corrections are made without its prior approval, then the Investigator may proceed with the study after the required corrections have been addressed. If the terms of the clinical
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hold require notification from the FDA to proceed with the study, then the Investigator may not proceed with the study until all the terms of the clinical hold are satisfied and the notification from the FDA is received.

m) If the FDA orders termination of all or part of the IND, then the Investigator must stop the study and arrange for disposal or recall of unused investigational product (See SOP 505, Study Closeout Visit, SOP PH 75-01 Investigational Drug Policy).

2.4 Investigational Device Exemption (IDE) Development and Submission

a) The Investigator should determine whether the investigational medical device is a Significant Risk (SR) or Non-Significant Risk (NSR) device (Attachment F, Medical Device Risk Determination Form).

b) The Investigator should check with the FDA website (www.fda.gov/cber) and the OHR to ascertain whether any device-specific written guidance for required submissions already exists.

c) For NSR devices, a regulatory submission to the FDA may still be required for marketing (See 510(k) notification). The Investigator should contact the FDA CSO to ascertain the best approach to acquiring FDA advice of such submissions, including protocol and clinical data requirements.

d) If the Investigator determines the investigational device is an SR device, the Investigator should contact the FDA to arrange for possible pre-IDE meetings or other FDA guidance (pre-IDE protocol review).

e) Once the investigational plan and clinical protocol are approved, the Investigator should follow the guidance (Attachment G, IDE Submission Checklist) for preparing the content of the IDE submission and for tracking that all the required information is collected for the submission.

f) The Investigator will provide a complete copy of the IDE submission to the OHR before proceeding with the submission to the FDA.

g) Once reviewed and approved, the Investigator or designee should mail the original IDE and two additional copies to the address provided in the checklist, using registered mail or an appropriate courier service.

h) The Investigator or designee will maintain a copy of the full IDE including all related submission material in the appropriate section of the Regulatory Master File.

i) The Investigator may proceed with the investigational medical device clinical study after receiving the IDE determination letter from the FDA, which assigns an IDE number or grants an exemption from filing an IDE.

j) If FDA requires additional information prior to granting approval for the IDE, the Investigator should provide that additional information as soon as possible, within the specified timeframes.

k) The Investigator should ascertain when additional information or changes to the study must be reported to the FDA in an IDE supplement by referring to additional guidance (Attachment H, IDE Supplement Checklist).

l) Once FDA approval has been received, the Investigator will ensure that the IRB reviews and approves changes to the study as required by its SOPs (See SOP 302, Clinical Protocol Amendments).
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m) The Investigator should file IDE supplements as required by the FDA, and may not proceed with the change to the IDE until it has been submitted to the FDA and approved by the FDA.

n) The Investigator must submit all required IDE reports (See SOP 202, Reporting Requirements for the FDA).

o) If significant safety issues arise during the conduct of a clinical study, the Investigator must ensure the carrying out of required reporting and notifications to the FDA, IRB, and other applicable investigators.

p) If the FDA disapproves an IDE, the Investigator may not proceed with the study until all the issues the FDA identifies are resolved and an approval is granted.

q) If the FDA withdraws an IDE after the study has begun, the Investigator must cease enrolling new subjects into the study, and must ascertain how to treat subjects currently enrolled (e.g. continue study treatment and follow-up, stop study treatments etc.).

r) If the disapproval letter from the FDA specifies that the study may proceed after certain corrections are made without its prior approval, the Investigator may proceed with the study after the corrections are put into place.

s) If the terms of the disapproval letter require an FDA notification to proceed with the study, then notification from the FDA is required to proceed with the study after the terms of the disapproval letter are satisfied.

t) If the FDA orders a termination of all or part of the IDE, then the Investigator must stop the study and arrange the disposal or recall of the unused investigational product (See SOP 505, Study Closeout Visit).

u) In certain cases, one copy of the application can be submitted electronically.

3 REFERENCES TO OTHER APPLICABLE SOPS

- 102 Document Development and Change Control
- 202 Reporting Requirements to FDA
- 301 Clinical Protocol Development, Implementation, and Compliance
- 302 Clinical Protocol Amendments
- 303 Developing Documents for Informing Investigators
- 503 Documentation and Records Retention
- 505 Study Closeout Visit
- PH 75-01 Investigational Drug Policy

4 ATTACHMENTS

A. FDA Meeting Guidelines
B. IND Submission Checklist
C. Accessing FDA Forms over the Internet
D. IND Amendment Checklist
E. Medical Device Risk Determination Form
5 APPLICABLE REGULATIONS AND GUIDELINES

- Exception from Informed Consent Requirements for Emergency Research (21 CFR 50.24)
- (IND) Applicability (21 CFR 312.2)
- Promotion and Charging for Investigational Drugs (21 CFR 312.7)
- (IND) Waivers (21 CFR 312.10)
- Investigational New Drug Application (21 CFR 312 Subpart B)
- Administrative (IND) Actions (21 CFR 312 Subpart C)
- Emergency Research Under 50.24 of This Chapter (21 CFR 312.54)
- Significant Risk Device Determination (21 CFR 812.66)
- Premarket Approval of a Medical Device (21 CFR 814.100-120, pertaining to Humanitarian Use Device Exemptions)
- Notification/Submission to Regulatory Authorities (ICH E6, Section 5.10)
- Content and Format of Investigational New Drugs (INDs) for Phase 1 Studies of Drugs, Including Well-Characterized Therapeutic, Biotechnology-derived Products (FDA, November 1995)