FDA – IND Application Process and Maintenance

1. IND Application
   a. IND Application Components
      i. Cover Memo from sponsor-investigator outlining contents of submission
      ii. Study Protocol
      iii. FDA Form 1571 – IND Application
      iv. FDA Form 1572 – Statement of Investigator
      v. FDA Form 3674 – Certification of Compliance
      vi. CV for all investigators participating in the research
      vii. Medical License for all investigators participating in the research
      viii. Laboratory normal values for the lab in use for the research
      ix. CAP and CLIA certificates for the lab in use for the research
      x. Letter permitting an IND cross-file from the pharmaceutical company providing IP. If a pharmaceutical company holds the original IND, marketed drug product must be identified in the cross-file letter by trade name, dosage form, strength, and lot number.
      xi. Optional: A request to add key personnel to an IND may be included in the cover letter with the initial IND application.
   b. IND Application Process
      i. Compile the components of the IND Application (listed above)
      ii. Items with original signatures (1571, 1572, 3674 Forms) should be scanned as PDF files
      iii. Refer to FDA website for submission addresses.
   c. IND Application Submission
      i. FDA will send an acknowledgement via email and in a letter with the following information: Date of IND receipt; IND number; contact name, phone at FDA for questions; address and instructions for future submissions of the IND
      ii. FDA has up to 30 days in which to respond to the sponsor-investigator regarding the IND if there are clinical, regulatory, or other concerns

2. FDA Administrative Actions
   a. Response from FDA: Comments or Requests for Modifications
      i. FDA communications to the sponsor-investigator within the 30-day window following FDA receipt of the IND must be answered promptly
      ii. Updated materials submitted to the FDA in response to a request for changes/information should be submitted in the same manner as the original IND.
      iii. Include a 1571 Form with the response to the FDA, numbering each submission serially in box 10
   b. Response from FDA: Approval of IND
      i. Research may commence 30 days following of receipt of the IND if the FDA has not made any request for additional information or changes to the IND Application as submitted
      ii. FDA Approval of the IND will be sent electronically and in a letter to the sponsor-investigator
   c. Response from FDA: IND Exemption
      i. An IND may be exempt from FDA oversight if it meets the following 5 criteria:
         1. The study is not intended to support FDA approval of a new indication or a significant change in the product labeling
2. The study is not intended to support a significant change in the advertising for the product
3. The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product
4. The study is conducted in compliance with the IRB and informed consent regulations set forth in 21 CFR parts 56 and 50.
5. The study is conducted in compliance with § 312.7 (promotion and charging for investigational drugs)

ii. The FDA will notify the sponsor-investigator if the study meets the criteria for exemption status and therefore does not require oversight by the FDA

3. IND Maintenance
   a. Protocol Amendments
      i. Amendments to the protocol must be submitted to the FDA with a summary of changes, a Word version of the protocol with changes highlighted or tracked, and a clean version of the protocol
      ii. Include a 1571 Form with the submission to the FDA, numbering the submission serially in box 10
   b. Informational Amendments
      i. Changes in essential information (i.e., toxicology, chemistry, technical information, etc.) should be submitted to the FDA as the information becomes available, but not more frequently than every 30 days
      ii. Include a 1571 Form with the submission to the FDA, numbering the submission serially in box 10
   c. Annual Reports
      i. FDA requires an annual report within 60 days of anniversary of the IND approval.
      ii. Annual reports should contain the following information:
         1. Title of Study
         2. Purpose of Study
         3. Patient Population
         4. Statement of Study Status (open, closed, etc.)
         5. Table with Enrollment Information: Number of subjects screened, enrolled, completed, withdrawn; demographic information for all subjects
         6. Interim Results (if any)
         7. IND Summary Information: SAE summary; subject deaths (with relation to study drug); subject withdrawal reason
         8. Scientific Information Updates: New information related to drug action, dose response, information from outside studies, etc.
         9. Preclinical Studies (if any): Include any preclinical information for the study in the past year
         10. Manufacturing Changes (if any)
         11. Description of Investigational Plan for Upcoming Year
         12. Summary of Protocol Changes in Previous Year
      iii. Include a Cover Memo
iv. Include a 1571 Form with the submission, numbering the submission serially in box 10
d. Safety Information / Serious Adverse Event Reporting / Unanticipated Problems Involving Risks to Subjects or Others (UPIRTSOs)
i. For FDA regulated research, safety information including SAEs and UPIRTSOs must be reported to the FDA per the guidelines and in accordance with the study protocol
ii. For deaths or life-threatening SAEs, notification of the FDA must be made no later than 7 calendar days within the sponsor-investigator becoming aware of the event
iii. SAE reports can be submitted electronically, via fax, or via mail using the FDA Medwatch Form 3500
iv. Include a 1571 Form with the submission, numbering the submission serially in box 10
e. Correspondence: Addition of Research Staff as Approved Personnel on IND
i. Anyone other than the sponsor-investigator who wishes to communicate to the FDA regarding the IND must be added as key personnel
ii. A request to add key personnel is made by the sponsor-investigator
iii. Submit letter of request to FDA
iv. Include a 1571 Form with the submission, numbering the submission serially in box 10
f. Other Correspondence
i. Changes in sub-investigators, key personnel, or other changes to the 1572 Form
ii. Study suspension due to changes in funding, drug availability, etc.
iii. Any other correspondence related to the research that impacts its conduct
iv. Include a 1571 Form with the submission, numbering the submission serially in box 10

4. IND Withdrawal
a. At any time a sponsor may withdraw an effective IND
b. If an IND is withdrawn, the FDA must be notified and all activities pertaining to the study should be suspended
c. If an IND is withdrawn due to safety reasons, the sponsor-investigator must notify the FDA, all participating investigators and the IRB

5. IND Termination
a. FDA may terminate a study for a variety of reasons including safety concerns; methods, facilities, or controls for manufacture are concerning; major deviation in conduct of the study from the protocol; failure to report SAEs in a timely fashion; failure to submit an annual report; IND is inactive for 5 years or more; failure to honor a clinical hold initiated by the FDA; study presents an immediate and substantial danger to research subjects

6. IRB Requirements for Sponsor-Investigators with INDs
a. The IRB must be notified of IND status of a protocol
b. A copy of the FDA Approval or Exemption letter should be included with the IRB Initial Application

References:
21CFR Part 50 Protection of Human Subjects
21CFR Part 56 Institutional Review Boards
Instructions for Completing IND Forms 1571, 1572, and 3674
21CFR Part 312 Investigational New Drug Application