### Tip Sheet
**PROTOCOL OR INFORMATION AMENDMENT TO AN IND**

#### Tip 1: Once the IND is active, what must be reported to the FDA?
- After the initial IND is submitted and is in effect, a sponsor-investigator must make changes to the IND as needed to ensure that the clinical investigations are conducted according to protocols included in the application.
- The FDA expects Sponsor-Investigators to submit amendments for new protocols or changes to existing protocols prior to their implementation.
- Sponsor-investigators also need to provide essential information on the IND that is not within the scope of any protocol amendment, IND safety report, or annual report. All these written communications to the FDA are called **amendments** to the IND.
- The FDA representative will review these amendments as they are received.
- When it is unclear whether a change to an existing protocol or a new protocol should be communicated as an amendment to an existing IND or under a new IND the sponsor-investigator should seek guidance from the relevant FDA review division.

#### Tip 2: When do I need to submit a Protocol Amendment to the IND?
- New protocol
- Change in protocol
  - Phase 1: Change significantly affecting subject safety
  - Phase 2/3: Changes significantly affecting safety, scope, scientific quality
- New investigator
  - A sponsor of an IND application is expected to submit a protocol amendment when a new investigator is added to carry out a previously submitted protocol. The amendment should include the investigator’s name, the qualifications to conduct the investigation, and any reference to the previously submitted protocol, if relevant. FDA should be notified within 30 days of the investigator being added.

#### Tip 3: When do I need to submit an Information Amendment to the IND?
- New information (e.g. clinical, clinical pharmacology, pharmacology/toxicology, chemistry, statistical reports)
- Discontinuation of study (within 5 days of decision)

#### Tip 4: Does the 30-day waiting period apply after I submitted to the FDA?
- In contrast to the initial IND submission, if the IND is not on clinical hold, the sponsor investigator may implement changes to the IND immediately after sending the amendment to the FDA, without waiting 30 days (though new protocols and protocol changes to ongoing trials still require prior approval by an IRB unless the change to the protocol is necessary to eliminate apparent immediate hazards to human subjects).
- Note that the FDA reserves the right to suspend an ongoing trial (by placing it on clinical hold) at any time they determine a suspension is warranted.

#### Tip 5: What do I need to submit?
- Cover letter
- FDA form 1571 (serial number must be sequential, increase serial # by 1 for each submission to the FDA
- Revised protocol (if applicable)
- FDA form 1572 (if applicable, e.g. changes to investigators, study sites)
- CVs (if applicable. e.g. new investigators)
- Description of new information or discontinuation of study
Tip #6: How do I prepare the package for shipment to the FDA?
- Protocol Amendments that are received by the FDA loose or inadequately bound may be returned to the Sponsor- Investigator for proper binding and resubmission. This can significantly delay the FDA review process.
- If the revised Protocol is 15 pages or less, stapling is sufficient. The coverletter, Form 1571, and optional documents can be clipped to the protocol with a large paper clip.
- If the revised Protocol is longer than 15 pages or it cannot be securely held together with a staple, then the entire amendment submission will need to be submitted in a 3-ring binder.
- When using a binder, indicate on the binder front that the submission is for a Protocol Amendment.
- Print area for all pages should fit on 8.5 by 11 inches paper.
- Allow margin of at least 1 “ on the left side of page (to avoid obscuring information when the pages are subsequently printed and bound) and 3/8 “ on the other sides.
- For pages in landscape orientation, allow ¾ “at the top to allow more information to be displayed legibly on the page.
- Header and footer information can appear within these margins as long as it is not within 3/8 “ of the edge (to avoid text is lost when pages are subsequently printed and bound)
- Use one of these fonts: Times New Roman or Courier (11 point)
- Use single sided copies
- Have a naive reader proofread your submission
- Keep the copy of the shipping form/airbill for your files

Tip #7: How to I label the outside of the three binders:
- Label the outside using Times New Roman or Courier (18 point), with the following information

  Name of sponsor: __________________________
  Name of product: __________________________
  IND number: __________________________
  IND AMENDMENT
  Date of submission: __________________________

Tip #8: How many copies need to be submitted?
- Triplicate to the FDA (1 original and 2 copies)
- Keep one copy for your own records, additional copies for other parties if needed (e.g. outside funding entity or company providing the investigational drug for the study)

Tip #9: Where do I send the Amendment?
- Check your IND Acknowledgement letter for details and instructions.
- Address it to the FDA Division that reviewed and approved your IND
- Typically all communication needs to be mailed to one of these addresses:

  For a Vaccine, Blood or Biologics Product (CBER):
  Food and Drug Administration
  Center for Biologics Evaluation and Research
  Division of <include name>
  HFM-99, Room 200N
  1401 Rockville Pike
  Rockville, MD 20852-1448

  For a Drug (CDER):
  Food and Drug Administration
  Center for Drug Evaluation and Research
  Division of <include name>
  Central Document Room
  5901-B Ammendale Road
  Beltsville, Md. 20705-1266
Tip #10: Will I receive confirmation from the FDA once they receive the IND amendment?

- It is important to identify in the amendment whether a reply from the FDA is expected. If the sponsor-investigator wants the FDA to comment on the submission, the amendment must include a request for an FDA reply (e.g., a specific request to review new information and respond by a certain proposed date), which can be included in a cover letter of an amendment. In addition to including this request in the amendment, the sponsor-investigator can also contact the review division directly (e.g. for an informal discussion or to request a teleconference).

Tip #11: For more information, go to:

- or call the Clinical Research Support Center at (303) 724-1111