Tip #1: As the Sponsor-Investigator and IDE holder, when do I need to submit an IDE Supplement to the FDA?

- **Changes** in the Investigational Plan should be approved by the FDA and, when appropriate, IRB, prior to implementing any change to a previously accepted Investigational Plan. The following types of protocol changes would require an approved IDE Supplement because they are likely to have a significant impact on the scientific soundness of the trial design and/or validity of the data resulting from the trial:
  
  - Change in indication,
  - change in type or nature of study control,
  - change in primary endpoint,
  - change in method of statistical evaluation, and
  - early termination of the study (except for reasons related to patient safety).

- In addition, FDA believes that expanding the study by *increasing either the number of investigational sites* or the *number of study subjects* participating in a clinical investigation affects the rights, safety, and welfare of the subjects. Therefore, the study may not be expanded without submission and approval of an IDE supplement.

Tip #2: Some exceptions from prior IRB and FDA approval are allowed:

- **a. Emergency use.** If PI deviates from the investigational plan to protect the life or physical well-being of a subject in an emergency, the emergency use of an IDE device must be reported to the IRB within 5-working days of its use.

- **b. Certain changes to the device.** Advanced IRB notification is not required if the changes do not constitute a significant change in design or basic operation and are made in response to information gathered during the course of an investigation. Examples include: creditable data generated under the device control procedures, preclinical/animal testing, peer reviewed published literature, and clinical information gathered during a clinical trial or marketing.

  For a developmental or manufacturing change to a device, the “Notice of IDE Change” must include:

  - a summary of the relevant information gathered during the course of the investigation upon which the change was based;
  - a description of the change to the device or manufacturing process (i.e., cross-referenced to the appropriate sections of the original device description or manufacturing process); and
  - if design controls were used to assess the change, a statement that no new risks were identified by appropriate risk analysis and that the verification and validation testing, as appropriate, demonstrated that the design outputs met the design input requirements. If another method of assessment was used, the Notice shall include a summary of the information, which served as the creditable information supporting the change.

- **c. Certain clinical protocol changes** that do not affect (i) the validity of the data or information resulting from the completion of the approved protocol, or the relationship of the likely patient risk to benefit ratio relied upon to approve the protocol; (ii) the scientific soundness of the investigational plan; or (iii) the rights, safety, or welfare of human subjects involved in the investigation. For a clinical protocol change, the “Notice of IDE Change” must include:

  - a description of the change (cross-referenced to the appropriate sections of the original protocol);
  - an assessment supporting the conclusion that the change does not have a significant impact on the study design or planned statistical analysis; and
  - a summary of the information that served as the creditable information supporting the sponsor-investigator’s
determination that the change does not affect the rights, safety, or welfare of the subjects.

4. Changes that will be submitted in the annual report. A sponsor may make minor changes to an Investigational Plan without prior FDA approval; provided that the respective changes are reported in the annual progress report for the IDE (see Progress Reports). These minor changes to the purpose of the study, risk analysis, monitoring procedures, labeling, informed consent materials, and IRB information may not affect (i) the validity of the data or information resulting from the completion of the approved protocol, or the relationship of the likely patient risk to benefit ratio relied upon to approve the protocol; (ii) the scientific soundness of the investigational plan; or (iii) the rights, safety, or welfare of human subjects involved in the investigation. However, such changes will require prospective IRB approval.

Tip #3: What do I need to submit?

- A summary of the relevant information gathered during the course of the investigation upon which the change was based;
- A description of the change to the device or manufacturing process (cross-referenced to the appropriate sections of the original device description or manufacturing process), and
- Documentation of the credible information to support the change.

- A notice for a protocol change should include: 1) a description of the change (cross referenced to the appropriate sections of the original protocol); 2) an assessment supporting the conclusion that the change does not have a significant impact on the study design or planned statistical analysis; and 3) a summary of the information that served as the credible information supporting the sponsor’s determination that the change does not affect the rights, safety or welfare of the subjects.

- According to the IDE Modification regulation (§ 812.35(a)(3)(iii)(B)), credible information to support changes to the clinical protocol is defined as the sponsor’s documentation supporting the conclusion that a change does not have a significant impact on the study design or planned statistical analysis, and that the change does not affect the rights, safety, or welfare of the subjects. Documentation may include information such as peer reviewed published literature, the recommendations of the clinical investigator(s), and/or the data generated during the clinical trial or marketing. As previously stated, FDA would also consider IRB approval or concurrence of the DSMB to serve as credible information to support the protocol change.

Tip #4: How do I prepare the package for shipment to the FDA?

The IDE supplement should be identified with the IDE number on the cover sheet and submitted in triplicate. The outside wrapper of the submission should identify the contents as "IDE Supplement."

- Use one of these fonts: Times New Roman or Courier (11 point)
- Print area for all pages should fit on 8.5 by 11 inches paper
- Allow margin of 1.5 “ 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.
- 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)
- When the materials can be securely held together with a standard office staple, then there is no need to place the report in any type of binder.
- If the report is 15 pages or less, stapling is sufficient. If the report is longer than 15 pages or it cannot be securely held together with a staple, then it will need to be bound by another means.
- When using a binder, indicate on the binder front that the submission is for a IDE Supplement.
- If applicable, provide a table of contents
- Use sequential page numbers
- For pages in landscape orientation, allow ¾ “at the top to allow more information to be displayed legibly on the page.
- Use single sided copies
- Keep the copy of the shipping form/airbill for your files
**Tip #5: How many copies of the IDE Supplement are submitted to the FDA?**
- Submit these materials in triplicate to the FDA (1 original and 2 copies)
  - Make an additional 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),
  - Scan a copy of the entire package including shipping form/air bill to the Clinical Research Support Center

**Tip #6: Where do I send the Reports?**
- Check your IDE approval letter for details and instructions.
- Unless otherwise noted, all Reports are mailed to:

  Food and Drug Administration  
  Center for Devices and Radiological Health  
  Document Mail Center - WO66-G609  
  10903 New Hampshire Avenue  
  Silver Spring, Maryland 20993-0002

**Tip #6: For more information, go**
  - or call the Clinical Research Support Center at (303) 724-1111