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Maintaining your Investigational Device Exemption (IDE) with the FDA: Keys for Success

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Agenda

- How an investigator should prepare and submit and annual report/renewal to the FDA
- Required elements to be included in the annual report/renewal to the FDA
- Required elements that need to be included for an IDE protocol amendment to the FDA
- How to properly respond to an FDA protocol inquiry
- Understanding the FDA Guidance documents and how to successfully navigate

Learning Objectives

- How to determine when a IDE protocol amendment is necessary and the required elements that need to be included for the FDA
- Understanding the FDA Guidance documents and how to successfully navigate for information extraction
- Properly updating the investigator agreement and financial disclosure forms during an IDE change
- Review and understand the FDA Med Watch Form

Purpose of an IDE

“ To encourage discovery and development of useful medical devices for human use, to the extent consistent with the protection of the public health and safety and with ethical standards while maintaining optimum freedom for scientific”

Section 520 (g) of the Food, Drug, and Cosmetic Act

Upon Approval of an IDE…..
Never Forget

The approval of an IDE application is just the **BEGINNING**

An investigator must never forget that an IDE application is a "living" project that must be constantly monitored, updated, and nurtured from approval to closure to maintain compliance

Foundation of 21 CFR 812 Reporting Requirements

Annual Progress Reports

The Submission of an IDE Progress Report (Annual Report) to the FDA

At regular intervals and at least yearly, the IDE sponsor must provide a progress report to the FDA and all reviewing IRB's.

If the FDA requires a progress report more frequent than on an annual basis, the IDE approval letter will indicate the review cycle.

The Submission of an IDE Progress Report (Annual Report) to the FDA

- An investigator must always remember that the progress report date is based on the approval date, which will be stamped on the top of the IDE approval letter (as follows):

IDE Number: X160041

Indications for Use:

Dated: January 1, 2012

Received: January 10, 2012

CMS Reimbursement Category: B4

Annual Report Due: One Year From the **Stamped Date** of this Letter

Format for IDE Progress Report

1. Basic Elements

    1. IDE Number
    2. Device name and indication for use
    3. Sponsor's name, address, phone number, and fax
    4. Contact Person
        1. *Reliable research personnel working with investigator, contracted CRA, sponsor's secretary*

Format for IDE Progress Report

1. Study Progress

   a. Brief Summary of study progress in relation to investigational plan
   b. Number of investigators/investigational sites
      1. Include a list of current investigators
   c. Number of Subjects Enrolled
   d. Number of devices shipped
   e. Disposition of all devices shipped
   f. Brief summary of results
   g. Summary of anticipated and unanticipated adverse effects
   h. Description of any deviations from the investigational plan by investigators (Since last progress report)

Format for IDE Progress Report

2. Risk Analysis
   a) Summary of any new adverse information (since last progress report that could affect the risk analysis
      1. Pre-clinical Data
      2. Animal studies
      3. Foreign data
      4. Clinical Studies
   b) Reprints of any articles published from data collected from this study

3. Other Changes
   a) Summary of changes in manufacturing or quality control
   b) Summary of any changes in the investigational plan

Format for IDE Progress Report

4. Marketing Application and Future Plans
   a. Progress toward product approval (include date if possible) of PMA or 510K submission
   b. Future plans to submit another IDE application for device
   c. Future plans to submit another IDE application for a modification of the device

Submission Timeframe: Can an IDE Fall into Expiration??

Unlike an IRB approval, and IDE Application cannot fall into Expiration if the report is not submitted and reviewed before the annual renewal date

However, to maintain compliance, an IDE sponsor is REQUIRED to submit at least an annual progress report.

- Gold Standard: Begin the annual progress report 60 days prior to its due date
- Submit in triplicate form to the agency

Maintaining the IDE Between Annual Renewal

IDE Supplements

Maintaining the IDE Between Annual Renewal

Understanding What Should be Submitted in a Supplement

Understanding when to submit a “supplemental application” is vital for an investigator

Several differences have been identified by the agency to help investigators understand when the correct time to submit a supplemental application

Maintaining the IDE Between Annual Renewal

Understanding What Should be Submitted in a Supplement

Developmental Changes: Must not present a significant change in operation or design

Do NOT have to be submitted to the agency in a supplemental application

- Manufacturing changes
- Marketing changes
- Device design changes

Maintaining the IDE Between Annual Renewal

Understanding What Should be Submitted in a Supplement

Changes to the Clinical Protocol: Items associated must be reported to the FDA in the form of a supplemental application BEFORE implementing the change

- Scientific soundness of the investigational plan
- Rights, safety, or welfare of the subject
- Addition of investigational sites**

The changes listed above should be sent to the FDA and listed as "Notice of IDE Change"

Information Gathered and Report or Amendment has been Submitted

What Happens When the FDA has a Question?????

Responding to FDA Inquiries

Investigators must be aware that it is not uncommon for the FDA to respond with questions/inquiries

Investigators must be prepared to systematically respond to each inquiry in an organized manner.

FDA gives no specific requirements or suggestions on how to respond

Responding to FDA Inquiries
An Organized Approach

1. Cover Letter
    1. *IDE Number*
    2. *Type of Supplement Response*
    3. *Submitted in Triplicate Form*
    4. *List of materials being submitted with the Response*
2. Point by Point Response
    1. *Header/Footer*
    2. *Rephrase FDA Question/Inquiry verbatim*
    3. *Response to inquiry*
3. Additional Items Requested by FDA

Responding to FDA Inquiries
An Organized Approach

- The FDA generally gives investigators a 45 day response window to provide additional information

Inquiries MUST be Taken Seriously

- If no attempt is made by an investigator to respond to an inquiry from the FDA, the agency will proceed with steps to withdraw the approval of an IDE.

Med Watch Reporting Form 3500

How to Complete the Process of Serious Adverse Event Submission to the FDA

Med Watch Reporting Form 3500

The Med Watch process is intended to report serious adverse events for human medical associated with the use of:

- FDA-regulated drugs,
- Biologics (including human cells, tissues, and cellular and tissue-based products)
- Medical devices (including in vitro diagnostics)

Med Watch forms can be submitted via fax, facsimile, or online. Be sure to keep a copy of the form for regulatory binder

Med Watch Reporting Form 3500

What NOT to Report to the Med Watch System:

- **Vaccines:** Report vaccine events to the Vaccine Adverse Event Reporting System (VAERS) online at https://secure.vaers.org/VaersDataEntryintro.htm.

- **Investigational (study) drugs:** Report investigational (study) drug adverse events as required in the study protocol to the FDA

Med Watch Reporting Form 3500 Reporting Differences

- **Form FDA 3500 - Voluntary Reporting**

For use by healthcare professionals, consumers, and patients.

- **Form FDA 3500A - Mandatory Reporting**

For use by IND reporters, manufacturers, distributors, importers

Med Watch Reporting Form 3500
Completing and Submitting the Form

- Complete all sections that apply to your report
- Provide as much information as possible regarding the patient
  - Age
  - Weight
  - Height
- Provide as much information as possible regarding the device
  - Device Serial numbers
  - Lot numbers
  - Model Numbers

FDA Guidance Documents

How to Navigate the Documents to Retrieve Useful Information

FDA Guidance Documents
Using Their Content to the Advantage of the Sponsor

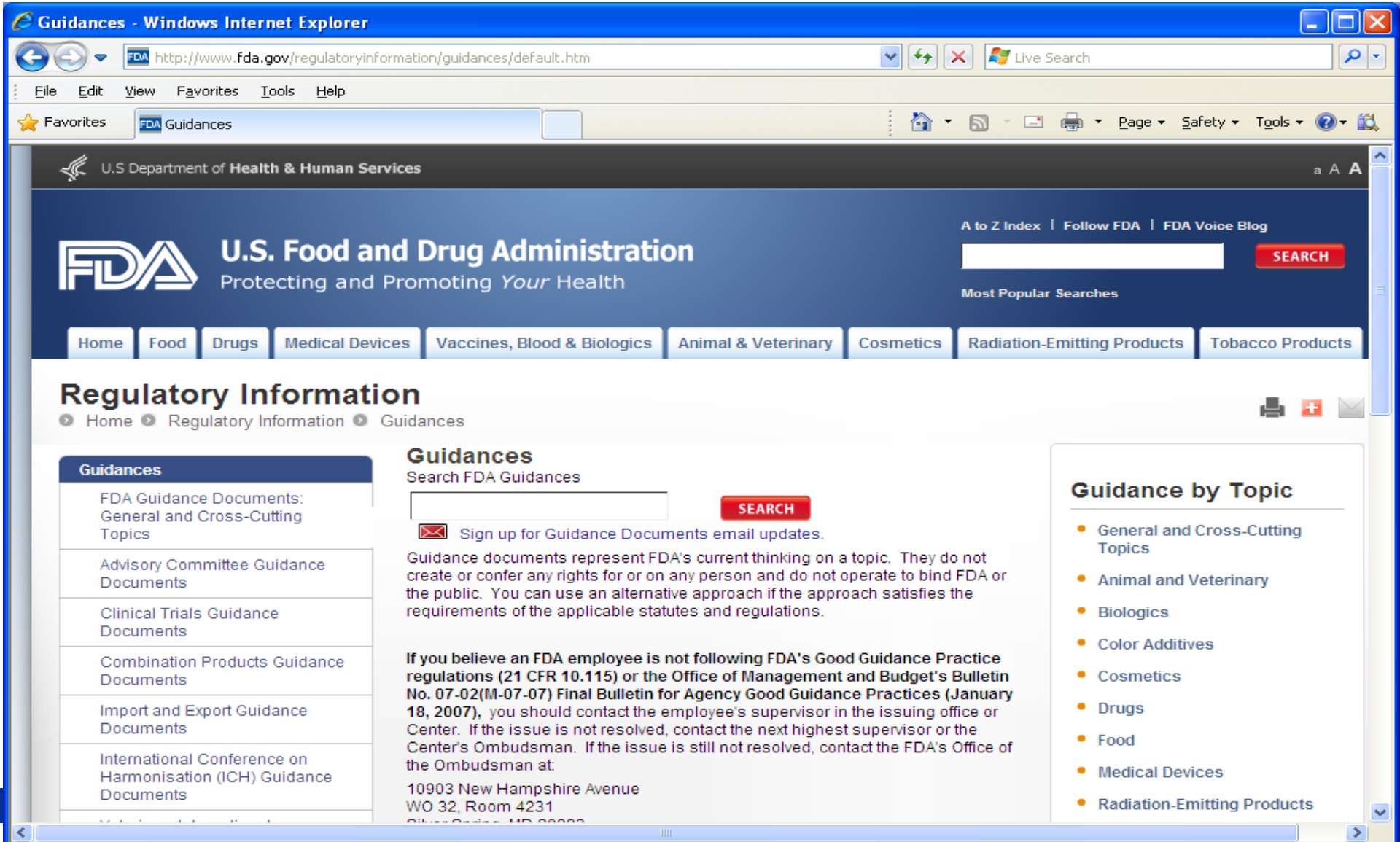
Good Guidance Practice (GCP) documents are prepared for industry and the public that relate to:

1) Processing, content, and evaluation of regulatory submissions
2) Design, production, manufacturing, and testing of products
3) Inspection and enforcement of polices and procedures

FDA Guidance Documents
Using Their Content to the Advantage of the Sponsor

Always Remember: Guidance Documents to NOT exist to bind the FDA to a particular thought or suggestion. They are merely tools to help the investigator/sponsor/research staff to better interpret particular sections of the Code of Federal Regulations

FDA Guidance Documents
Using Their Content to the Advantage of the Sponsor



IDE Guidance
Some of the Most Helpful

- Guidance on IDE Policies and Procedure
  - Issued on: January 20, 1998
- Financial Disclosure by Clinical Investigators
  - Issued on: March 20, 2001
- Considerations When Transferring Clinical Investigation Oversight to Another IRB
  - Issued on: June 2012
- IRB Review in Multicenter Research Study
  - Issued on: March 2006
- Design Considerations for Pivotal Clinical Investigations for Medical Devices
  - Issued on: August 15, 2011

Maintaining FDA and IRB Approvals

How to Ensure that Documents Submitted to Both Reviewing Bodies are Identical

Maintaining FDA and IRB Approvals
Tips and Helpful Hints

It is mandatory that both the FDA and IRB are provided and are reviewing the exact same version of research related documents.

Document Differences=Problem

- Obtaining FDA and IRB approval
  - In what order should the submissions be provided??

Thank you for Attending the Lecture

Questions….Comments