Good Clinical Practice (GCP) Key Topics

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Office of Good Clinical Practice

FDA's Clinical Investigator Course
Cosponsored by

FDA's CDER, Office of Medical Policy
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U.S. Department of Health and Human Services
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Topics

- Investigator responsibilities
- Clinical Investigator financial disclosure
- Expanded access to and charging for investigational drugs and devices
- Resources

Investigator responsibilities

- Both 21 CFR Part 312 and 812 hold the clinical investigator (CI) responsible for the conduct of the study at the study site
- Lack of appropriate study oversight by the CI is a commonly cited noncompliance in bioresearch monitoring (BIMO) inspections

Investigator responsibilities

- FDA final guidance document issued October 2009
- Guidance covers:
  - Appropriate delegation of study tasks
  - Appropriate training of study staff
  - Supervision of staff, including contracted personnel
  - Subject protections, including necessary medical care

Investigator responsibilities

- Appropriate delegation of study tasks
  - Any individual to whom a task is delegated must be qualified by education, training, and experience (and state licensure where relevant)
  - Individuals delegated must meet any protocol specified requirements
  - Listing of tasks and individuals delegated should be maintained

Investigator responsibilities

- Appropriate training of study staff
  - Familiarity with protocol and specific tasks
  - Knowledge of applicable regulations and HSP and GCP principles
  - Individuals competent or trained to cover tasks assigned
  - Updates and additional training provided as needed

Investigator responsibilities

- Supervision of staff, including contracted personnel
  - The level of supervision should be appropriate to the staff, the nature of the trial, and the subject population
  - A supervisory plan should include routine meetings with study staff and procedures for determining appropriate completion of delegated tasks
  - Oversight extends to SMO staff, CI-contracted providers (radiologists, labs), and medical device engineers

Investigator responsibilities

- Subject protections, including necessary medical care
  - Reasonable medical care for study-related medical problems
  - Provision of access to appropriate medical care when specialized care is required
  - Adherence to the study protocol

Clinical investigator financial disclosure

- 21 CFR Part 54 – final regulation issued 1998
- Investigators and sub-investigators (those who play a significant role in the conduct of the study) are required to supply information (+ spouse and dependent children)
- Requires reporting to the study sponsor prior to participation in the study and updates yearly, as needed, until one year after study completion

Clinical investigator financial disclosure

- Requires applicant of a marketing application/permit to
  - Certify that there are no financial arrangements with each investigator

    or
  - Disclose specific financial arrangements with study investigators and what was done to minimize bias

Clinical investigator financial disclosure

Disclosable arrangements

1. Compensation where the value could be affected by the study outcome (e.g., royalties)
2. Significant Payments of Other Sorts (SPOOS) – i.e., not including the payments for conducting the study – to either the investigator or the institution (e.g., grants, equipment, retainers for on-going consultation, honoraria)

Clinical investigator financial disclosure

Disclosable arrangments (cont.)

3. Proprietary interest in the product, such as a patent, trademark, copyright, or licensing agreement
4. Equity interest in a publicly traded company whose value >$50,000

   or

   Equity interest such as ownership interest or stock options whose value cannot be readily determined through reference to public prices

Clinical investigator financial disclosure

- OIG inspection in 2009
- Recommended
  - Greater accountability of CIs, sponsors, and FDA
  - Additional guidance/training for FDA review staff
  - Follow-up during CI and sponsor inspections

Clinical investigator financial disclosure

- Final guidance issued February 26, 2013
- Specifically, the guidance describes:
  - Disclosure requirements
  - Responsibilities of various parties
  - Further explanation of terms used in regulations
  - How FDA will review financial disclosure information
- Describes FDA's policy to publicly post FDA's reviews summarizing financial disclosure information related to an approved marketing application

Expanded access

- Long history of providing access outside of study participation
  - Emergency use
  - Treatment INDs/IDEs
- FDAMA (1997) provides for access to experimental therapies for individuals and small groups of patients with serious or immediately life-threatening diseases

Expanded access – investigational drugs

- August 13, 2009 – final expanded access regulation issued
- Strives to balance competing issues
  - Access to unproven therapies for patients with serious or life-threatening diseases/conditions who have no satisfactory alternative
  - Potential to impede development and marketing of life-saving therapies
  - Minimizing risk to individuals

Expanded access – investigational drugs

- Regulation recognizes
  - primary goal is treatment
  - evidentiary standard necessary to support use varies by size of population:
    - Individual patients, including emergency use
    - Intermediate-size patient populations
    - Treatment IND or treatment protocol

Expanded access – investigational drugs

- Draft guidance issued May 9, 2013
  - provides information on implementation of FDA's regulations on expanded access to investigational drugs for treatment use under an IND
  - addresses most frequently asked questions

Charging for investigational drugs

- Removal of 312.7(d) + renaming 312.7 "Promotion of investigational drugs"
- Addition of 312.8 – "Charging for investigational drugs under an IND"
- Changes/addition issued August 13, 2009, with expanded access regulations

Charging for investigational drugs

- Draft guidance issued May 9, 2013
  - provides information on implementation of 21 CFR 312.8
  - addresses most frequently asked questions

Charging for investigational drugs

Purpose of changes/additions:

- Provide clarity about circumstances under which charging in a clinical trial is permitted
  - Evidence drug has potential clinical benefit and a clinical trial is essential to demonstrating safety and effectiveness
  - Cost extraordinary due to manufacturing complexity, scarcity of a natural resource, large quantity needed, or some combination of the above

Charging for investigational drugs

Purpose of changes/additions (cont):

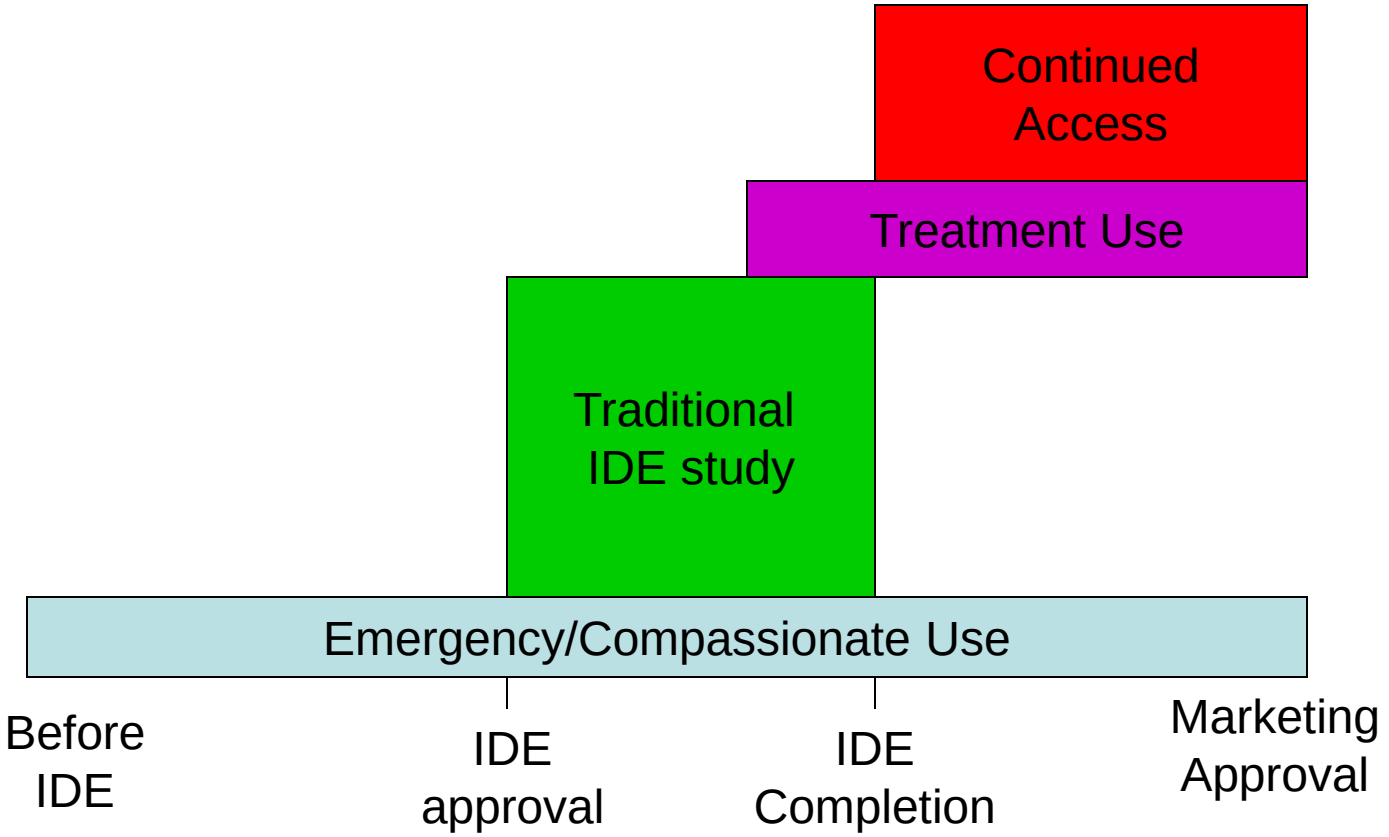
- Set criteria for charging for all types of access described in new expanded access regulations
  - In general, reasonable assurance charging will not interfere with development of the drug for marketing approval
  - For treatment INDs and protocols
    - Assurance to include evidence of sufficient trial enrollment and adequate progress towards marketing
    - Required to submit development milestones for the following year
    - Authorization limited to a specified number of patients and for a maximum of 1 year, though a request for reauthorization is possible

Charging for investigational drugs

Purpose of changes/additions (cont):

- Clarify what costs can be recovered
  - For a clinical trial – only the direct costs of making the investigational drug available (manufacturing and/or acquiring and shipping and handling, not research and development or labor)
  - For expanded access – cost of monitoring, complying with reporting requirements, and other administrative costs may be added to direct costs

Early/Expanded access* – investigational devices



*http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm

Charging for investigational devices

- 21 CFR 812.7(b) – prohibits a price larger than necessary to recover costs of manufacture, research, development, and handling
- 21 CFR 812.20(b)(8) – IDE application to include amount to be charged and an explanation of why sale does not constitute commercialization of the device
- 21 CFR 812.(c)(1)(x) – treatment IDE – if device to be sold, application must include price, which is to be based on manufacturing and handling costs only

Resources

- Guidance for Industry, Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects – final October 2009 – http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM187772.pdf
- Financial Disclosure by Clinical Investigators, Guidance for Industry – final February 2013 - http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM341008.pdf

Resources

- Expanded access to and charging for investigational drugs
- http://edocket.access.gpo.gov/2009/pdf/E9-19005.pdf
- http://edocket.access.gpo.gov/2009/pdf/E9-19004.pdf
- Include preambles explaining rationale and comments received to proposed rules

Resources

- Expanded Access to Investigational Drugs for Treatment Use – Qs & As – draft May 2013 - http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM351261.pdf
- Charging for Investigational Drugs Under an IND – Qs & As – draft May 2013 - http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM351264.pdf

HSP/GCP Resources

GCP website – http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm

alias – www.fda.gov/gcp

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