Investigational New Drug Applications: two cases

April 15, 2009

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Objectives

• Describe several types of Investigational New Drug Applications and the process for working with the FDA for each

• Describe the process for determining whether your investigation may meet the criteria for IND exemption

• Provide examples of how communication with the FDA can be facilitated
Outline

• Components of a new application
• Form1571 and 1572
• Contrast two cases
  – New application for an IND
  – Application for an IND Exemption
• Communication with the FDA
• How to use FDA web site
• Conclusions
IND content requirements [21 CFR 312.23]
For sponsors and sponsor-investigators
Cover Sheet (& Form FDA 1571)

- Table of Contents
- Introductory Statement and General Investigational Plan
- Investigator’s Brochure
- Clinical Protocol
- Chemistry, Manufacturing and Control (CMC) Information
- Pharmacology and Toxicology Information
- Previous Human Experience
- Additional Information
Application content (example)

1. Cover letter (2-pager)
   - Brief background
   - Faculty strength and experience (PI & co-PIs)
   - Proposed treatment plan
   - Drug supply
   - Informed consent/assent & approval status
   - List of attachments
2. Attachments

• Cover sheet: Form FDA-1571
• Protocol (Summary, Specific Aims, Proposed plan, References, Study schedule)
• Investigator’s Brochure
• Support letter from drug company or organization providing product data
• Conditional approval from the Boston Medical Center IRB – pending IND status
• Updated Curriculum Vitae
Form 1571 and 1572

• FDA Forms Distribution Page for CDER

http://www.fda.gov/opacom/morechoices/fdaforms/cder.html

Edition: March 26, 2009
New IND Application: Fish Oil to reduce fatty liver in obese adolescents

- New condition: NAFLD in adolescents
- Dosage: 4g/d (FDA approved in adults with high triglycerides)
- Potential risks: bleeding (unclear)
- Commercial distribution/labeling:
  - high triglycerides in adults
  - current INDs for other studies
  - may support change in labeling

More than one item makes this application unsuited for an IND exemption
IND Exemption: glutamine to reduce HOMA-IR in obese adolescents

- **New condition:** T2DM risk
- **Population:** used before in newborn up to adulthood
- **Dosage:** 0.2-0.4g/kg (FDA approved in adults with short gut syndrome - SGS)
- **Potential risks:** low at this dosage
- **Commercial distribution/labeling:**
  - SGS in adults
  - current INDs for other studies
  - not well controlled and thus will not support change in labeling

All the items acceptable to submit this application for an IND exemption
Communication with the FDA

• Identify and know your FDA contact
  – Emails
  – Call

• Use 1571 for all your communications
IND Safety Reports

• Sponsor promptly reviews all information relevant to the safety of the drug received from any source

• Notification varies with the type of AEs
  – Unexpected, likely related SAEs (life-threatening/death)
    • 7-day (calendar) report
    • Notify FDA via phone or fax
  – Unexpected, likely related SAEs (not life threatening) & Information from non-IND studies, or finding in laboratory animals suggesting increased risk
    • 15-day (calendar) report
    • Notify FDA & all investigators in writing
  – All other information relevant to the safety of the drug
    • At annual report
IND & the role of the FDA

• The FDA assures the safety and rights of subjects regardless of the phase of a study

• The FDA does not approve INDs, but assigns an IND to a study

• The IND is “in effect” 30 d after submission of the application (except if there is a clinical hold)
How to get the information you need on FDA web site

• FDA Home page (e.g. is it a drug or else?)
  http://www.fda.gov/
• Approved drugs
  http://www.accessdata.fda.gov/scripts/cder/drugsatfda/
• Specific searches (e.g. FDA and omega 3)
  http://www.google.com/
• FDA regulations
  http://www.fda.gov/oc/gcp/regulations.html
• CDER contact information
  http://www.fda.gov/cder/office.htm
• CDER division information
  http://www.fda.gov/cder/biologics/default.htm
Conclusions

• Before you start a IND application, try to identify a PI who previously submitted an IND application

• Identify the division at the FDA that best fit your study outcomes

• Contacts with your project manager/officer will vary based on personal styles and rules of the product management division

• Evaluate the criteria for an exemption status with the IRB prior to submitting a new application