# 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

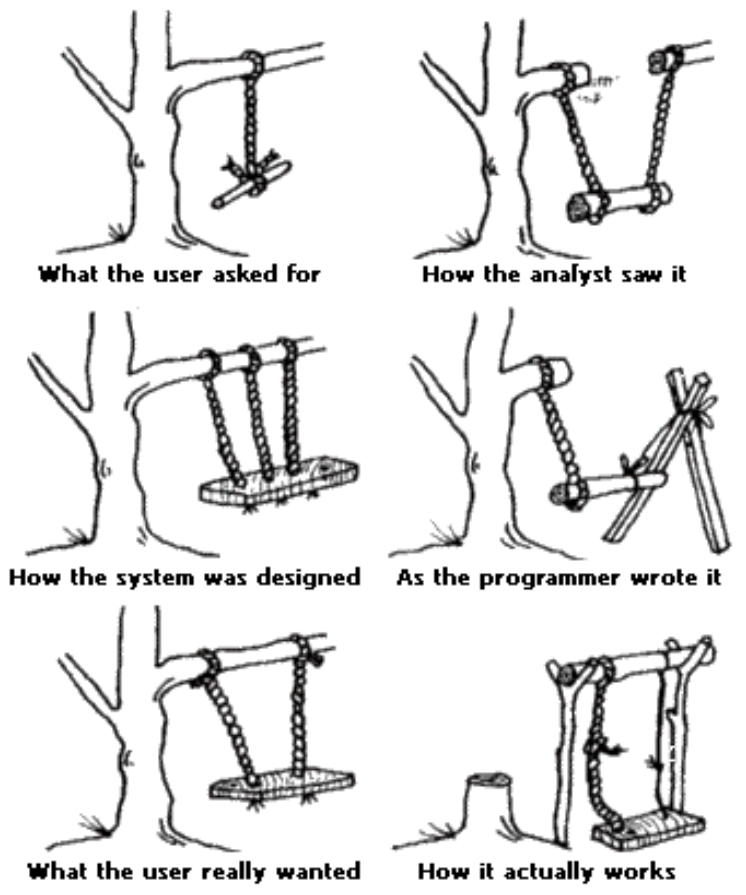
# Outline

- Components of a new application
- Form1571and 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)

**New IND Application. PDF**

**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

# Application content (example)

## 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

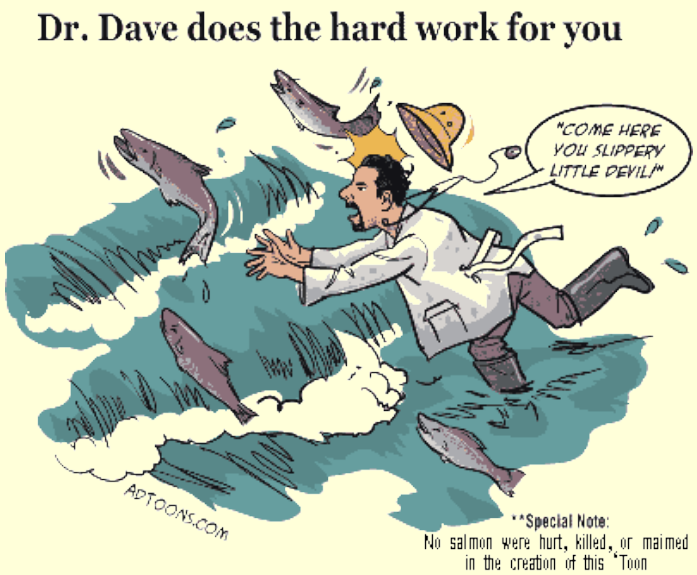
- FDA Forms Distribution Page for CDER

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

Edition: March 26, 2009


Should I write a new application for an IND or write an application for an IND exemption for use in adolescents?

# New IND Application: Fish Oil to reduce fatty liver in obese adolescents




- New condition: NAFLD
- Population: new=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

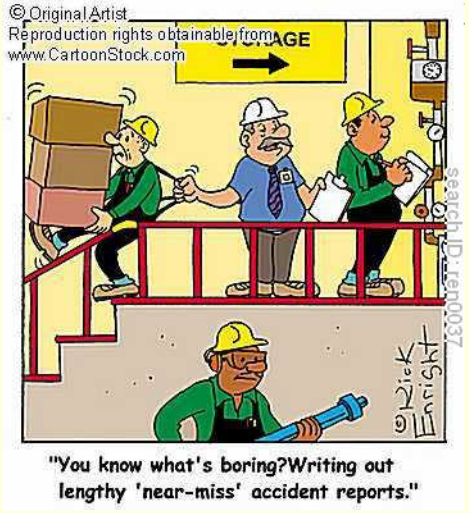

- New condition:T2DM risk
- Population: used before in newborn up to adulthood
- Dosage: 0.2-0.4g/kg (FDA approved in adults with short gut syndrome - SGS)
- Potential risks: low at this dosage
- Commercial distribution/labeling:
  - SGS in adults
  - current INDs for other studies
  - not well controlled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

Adverse Events.doc


Mum, what does the FDA do?
Hmmm . . . .
FDA FILES AMICUS for PFIZER

# 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 prior to submitting a new application