REGULATORY ISSUES: HOW TO APPLY FOR AN IND

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Outline

- What is the purpose of an IND?
- What types of INDs are there?
- When do you need one?
- How do you apply for one?
- How do you manage an active IND?

- IDEs are very similar with some minor differences
Purpose of an IND

- Exemption from the law requiring an approved marketing application for drugs to allow clinical testing
- Assess that the proposed clinical protocol is not unnecessarily risky
  - Evaluate preclinical data for safety
  - Evaluate investigators qualifications
  - Evaluate drug purity
Permissions needed for clinical trial

- The sponsor must apply for permission to study drugs in humans
  - From FDA for IND – traditional or exploratory
  - From an IRB for either
  - From various other entities at your institution
- “Sponsor”
  - Individual physician
  - Institution
  - Industry
Types of INDs

- Three types of traditional INDs
  - Sponsor-initiated
  - Emergency use
  - Treatment (Compassionate use and Expanded Access)

- Relatively new type of IND
  - Exploratory (‘phase 0’)


When do you need one?

Unapproved Product

- Required for a new drug or biological product to be used in a clinical trial

Approved Product

- Required to study a new aspect of an approved drug
  - Different indication
  - Different route of administration or dose
  - New drug combination
  - Different population
Off-label Use

- Approved products may be used by physicians outside of labeled indications for the practice of medicine
- No IND is needed
When is it not required?

Generally not required when all these criteria are met:

- No intent to support new use or labeling change
- No intent to support change in advertising
- No factor such as route of administration, dosage, or study population significantly increases risk
- Compliance with FDA informed consent and IRB review requirements
- No promotion or representation of product as safe or effective treatment for condition under study
IND needed?

- Study the therapeutic effect of a food supplement available OTC on the progress of type I diabetes
  - Yes! Therapeutic intent

- Study whether the use of fluoxetine (Prozac) enhances the effects of physical rehabilitation on motor function in stroke patients
  - No! (Surprise to us!) Meets all exemption criteria… (see previous slide)
Not sure?

- Read the guidance:
- Ask the IRB**
- Ask the FDA
So... you have to apply for an IND
Relax...we’re here to help!
How to apply for an IND

- Forms forms forms!
- Most important ones (will discuss in detail later):
  - 1571
  - 1572
  - 3674
  - 3454
- Clinical protocol should have been finalized
- Informed consent form should be available
Paperwork: in triplicate; fancy binders

Approved product

New product
Pre-IND meeting

- Formal way of communicating with the FDA about your plans
  - Request input on toxicity studies, protocol design, etc
- Not required
- Informal ways of communicating with the FDA are encouraged as well
  - Phone
  - Email
- **Benefit:** may move IND through the FDA more quickly
The application itself

- Pre-determined sections with certain types of information; sometimes information repeats

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IND application template

- We created a template to be used for UAB investigators
- Contains some ‘stock’ language
- Links to forms
- Instructions to forms
- Instructions what information goes where

- Let’s go through it!
What happens after submission?

- **Receipt of FDA Acknowledgment Letter**
  - Arrives 1-2 weeks after FDA receipt of IND submission
  - Assigns IND number, gives date of receipt, reminds sponsor-investigator of obligations under the IND
  - NOT an approval to begin

- **May not start until 30 days after IND receipt date**
  - Unless earlier notification indicates otherwise
  - Unless ‘hold’ placed on protocol
Possible FDA Actions

- Request additional information or place on clinical hold
  - Research cannot begin until all concerns are addressed in ways acceptable to FDA

- Conclude project is exempt
  - Research may be conducted without an IND

- Passive Activation
  - Allowing 30 days from filing to pass without comment
  - (confirm FDA non-objection is a good idea anyway)
Common reasons for hold

- Human subject exposure to an unreasonable and significant risk of illness or injury
- Incomplete information to assess the risk to subjects
- Deficient plan or protocol
- Misleading, erroneous, or materially incomplete investigator brochure
- Unqualified clinical investigators
After IND is active, how to manage?

- **Annual IND reports**
  - How is it going? Primarily safety issues!

- **Report (S)AEs**
  - Report to the FDA within 15 days of discovery of an event that is *serious, related and unexpected*.

- **Maintain required documents**
  - Updated documents
Critical: MONITORING

- Per subject monitoring
  - Independent monitor
- Safety and efficacy monitoring
  - Data and Safety Monitoring Board
Let us help!

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