Preclinical Data Package for IND Submission

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Investigational New Drug (IND) Exemption

- "New Drug", "New Biological"
- IND: What and why?
- Elements of the IND data package
- How does FDA review an IND ?
- Special types of INDs
- IND Information Resources





"New Drug" and "Biological"

- New Drug Product: "articles <u>intended</u> for use in the diagnosis, cure, mitigation, treatment, or prevention of disease..<u>and</u> (B) articles (other than food) <u>intended</u> to affect the structure or any function of the body of man or other animals" [FD&C Act, sec. 201(g)(1)].
 - Synthetic or extracted small molecules (exceptions, vitamins, etc)

Biological product:

- virus, therapeutic serum, toxin, antitoxin, or analogous product available to prevent, treat or cure diseases or injuries in man (eg Blood etc)
- Therapeutic proteins
- Diagnostic devices, including immunologically-based, allergenic
- Gene therapy
- Human tissues, cellular products
- Vaccines, Xenotransplantation products





Other FDA-regulated products

- Animal drugs and biologicals
- Cosmetics
 - "articles <u>intended</u> to be <u>rubbed</u>, <u>poured</u>, <u>sprinkled</u>, <u>or sprayed on</u>, <u>introduced</u> into, or otherwise applied to the human body...for cleansing, beautifying, promoting attractiveness, or altering the appearance" [FD&C Act, sec. 201(i)].
- Medical Devices
- Dietary Supplements
- Nutritional
- Food Additive
- Foods





What is an IND?

- IND = exemption to requirement for NDA approval
 - Permits transport of experimental drug across state lines
 - Legal permit to expose humans to experimental drug
- IND categories
 - Commercial, Investigator
 - Paper, Electronic, Hybrid
- Special types of IND's
 - Exploratory
 - Emergency Use
 - Treatment





Why is an IND required and How did it come about?

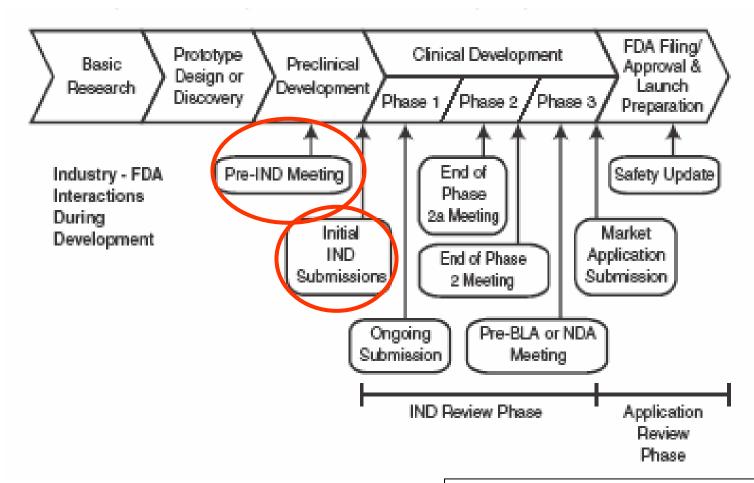
- IND is required to protect human subjects
- Some history*
 - First IND regulations ('40's) required assertion of sponsor use only
 - IND Formalized in 1962, motivated by thalidomide tragedy
 - Informed consent
 - Patient tracking
 - Documentation
 - 1983-87 IND "Rewrite" streamlined and clarified IND's
 - "clinical hold" established
 - Treatment IND
 - European regulatory authorities slow to follow

* R Crout, P Hutt, R Temple, personal communication





When to submit an IND and how does it fit in?



FDA Initiative: Innovation vs Stagnation -Challenge & Opportunity on the Critical Path to New Medical Products, March 2004





Elements of the IND data package*

Form 1571 (IND)

- Introductory Statement & General Investigational Plan
- Investigators Brochure
- Protocol(s)
- Pharmacology and Toxicology Information
- Previous Human Experience with the investigational Drug
- References

Form 1572 (Investigator)

CV

Guidance for Industry. Content and Format of Investigational New Drug Applications (INDs) for Phase 1 Studies of Drugs, Including Well- Characterized, Therapeutic, Biotechnology-derived Products. http://www.fda.gov/cder/guidance/phase1.pdf, AND http://www.fda.gov/cder/guidance/phase1.pdf, AND http://www.fda.gov/cder/regulatory/applications/ind https://www.fda.gov/cder/guidances/20for%20Investigational%20New%20Drugs





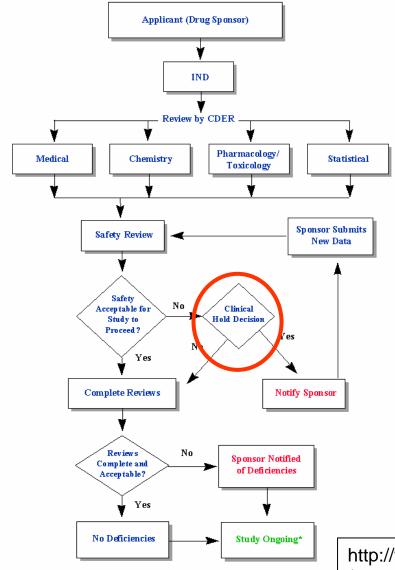
eCTD-formatted IND

- eCTD = electronic Common Technical Document (ICH)
 - ICH = International Committee on Harmonization of Technical Requirements for Drug Approval
 - □ ICH M4: Organization of the CTD
 - M4E: Efficacy
 - M4Q: Quality
 - M4S: Safety
- US IND can be mapped into eCDT
 - 2005 43 CTD-formatted IND's received by FDA





IND Review Process



http://www.fda.gov/cder/handbook/ind.htm



Contains Nonbinding Recommendations

Guidance for Industry, Investigators, and Reviewers

Exploratory IND Studies

Office of Training and Communication
Division of Drug Information, HFD-240
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857
(Tel) 301-827-4573
http://www.fda.gov/cder/guidance/index.htm

U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER)

> January 2006 Pharmacology/Toxicology





Emergency Investigational New Drug Application (EIND) Request for Information

Please fax the following information to the Division of Antiviral Products regarding your request for Emergency Use of the Investigational Product as soon as possible:

- 1) Patient's initials:
- 2) Patient's gender:
- 3) Patient's date of birth:
- 4) Patient's weight
- 5) Brief medical summary (to include diagnosis of underlying illness):

- 6) Diagnostic lab results for identifying viral infection that will be treated with the investigational product:
- Dosing regimen of the investigational agent (including loading and maintenance dosing):
- 8) The Name, Address, Phone and Fax numbers of the person sponsoring the EIND:



Treatment IND

- Treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments
- Granted only if the drug "may be effective" and does not have unreasonable risks
- Serves to expand the body of knowledge about the drug

Requirements:

- the drug is intended to treat a serious or immediately lifethreatening disease
- no satisfactory alternative treatment available
- drug is already under investigation, or trials have been completed
- trial sponsor is actively pursuing marketing approval.
- prospective IRB review and informed consent







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Electronic Submissions

- Introduction
- Pre-IND Consultation Program
- Guidance Documents for INDs
- CDER Investigational New Drug (IND) Renumbering
- Information for Clinical Investigators
 - Institutional Review Boards and Protection of Human Subjects in Clinical Trials
 - Federal Regulations for Clinical Investigators
- · Laws, Regulations, Policies and Procedures
 - · Code of Federal Regulations
 - Manual of Policies and Procedures (MaPPs)
- IND Forms and Instructions (FDA 1571 and FDA 1572)
- Emergency Use of an Investigational Drug or Biologic
- Drug Development and Review Definitions
- Frequently Asked Questions on Drug Development and Investigational New Drug Applications
- · Frequently Asked Questions on the Pre-Investigational New Drug (IND) Meeting
- Organization, Contact, and Meeting Information
- Related Topics





End of Presentation



