

Investigational Use of Drugs



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Introduction

Developing a chemical from the status of an interesting or unique pharmacological entity to that of a useful therapeutic tool involves the efforts of many individuals.

Description Of Investigational Drug Use

- Safe
- Effective
- Need
- Potential benefits
- Side effects
- Treatment options
- Etc

Principal Involved In Investigational Drugs

Research or Investigational Drugs are those compounds or mixtures which have not been released by the Food And Drug Administration for general distribution and use.

Classification of Investigational Drugs

- ① **Class A:-** Drugs that are in Preliminary experimental stage.
- ② **Class B:-** Drugs which have passed through the preliminary research stage.
- ③ **Class C:-** Drugs approved or passed by the FDA for commercial distribution.
- ④ **Class D:-** Drugs are preparations which have been accepted for use in the hospital and are listed in the hospital formulary.

Another Simple classification which can be adapted to any hospital pharmacy operations:

- ① General
- ② Conditional
- ③ Investigational

INVESTIGATIONAL USE DRUGS

○ Research Drug

- Pharmaceutical entity that is not permitted for its general distribution and use by the health authorities
- Drug may be **considered** for human use but not **approved** for human use
- Preclinical animal models evaluation
- Safety and efficacy has **established** in animals but not **evaluated** in human
- Research drug or Experimental Drug

INVESTIGATIONAL USE DRUGS

- Research Drug can be
 - Well known drug (old drug) with new formulation
 - Formulation w.r.t Excipients, Coating solvent, Vehicles
 - Stability
 - shelf life
 - cost effectiveness
 - Allergic Properties
- Old drugs and new Combinations
 - subject to safety and efficacy evaluation
- Old Drug and new dosage forms
 - Also require evaluation

INVESTIGATIONAL USE DRUGS

- **Special Labeling**

- Caution: New Drug-Limited to Investigational use only
- Or Caution: Research Drug

- **Approval for marketing**

- Require adequate proof of its effectiveness

- **Future aspects**

INVESTIGATIONAL USE DRUGS

- ◉ **Review and Approval**
 - Clinical research on human is risky and uncomfortable
- ◉ **Committee on Human Use in Research**
 - Safety and benefits of clinical investigation overweight the risk in priori review
 - Approved clinical projects

INVESTIGATIONAL USE DRUGS

◉ Informed Patient Consent

- Informed patient consent is **willing acceptance** by a patient to be subjected in research after having a complete information on the aim, protocol and procedures of research.
- Legal capacity to give consent
- free power of choice to withdraw
- Hospital must have policies to protect human subject

INVESTIGATIONAL USE DRUGS

- Either written or verbal
 - Nature and purpose of the study and expected benefits
 - All inconveniences, risks discomfort and hazards reasonably expected
 - Alternative treatments available with respect risk
 - General description of the **study procedures** and expected length of therapy

INVESTIGATIONAL USE DRUGS

- A statement that
 - Patient may withdraw from the study at any time without penalty
 - The investigator may remove patient from the study if the circumstances warrant
- Any compensation or treatment that will be furnished in the event of injury
- The name of the person to be person to be contacted for answer to question about the study
- A statement of whom will have to access to any study records that contain the patient's name

INVESTIGATIONAL USE DRUGS

- Exception for patient consent
 - Communication barrier
 - Patient is in coma
 - Pt's representative can not be approachable
 - To be in best interest of pt
- Consent must be in writing in Phase I and Phase II
- Phase III obligation of investigator
 - It is responsibility of investigator to obtain verbal consent
 - Record that fact(s) in the medical record of the person receiving the drug
 - Physical and mental status should be considered while obtaining data

INVESTIGATIONAL USE DRUGS

- ◉ Intimation to the drug authorities
 - Evaluation of drug in human beings have legal and ethical issues
- ◉ Duty of investigator to notify drug authorities before initiating a research involving human
- ◉ Application submission
- ◉ Authority scientists
 - Physician, pharmacologist, chemist, biometrician, microbiologist (if req)
- ◉ This review ensures that the pt are not exposed to unwarranted risks

INVESTIGATIONAL USE DRUGS

- ◉ The NID (new investigational drug) only for in-vivo studies
 - Are exempted for prior notification or intimation to authorities
 - Are labeled as:
 - Caution- “Contains a new drug for investigational use only in laboratory research animals. Not for use in human
 - Or Caution- “A new drug for tests in vitro. Not for use in human”
- ◉ But if
 - Research drug influences or change diagnosis and treatment then notify authorities
 - Antibiotics ... new strain sensitivity and/or resistance

INVESTIGATIONAL USE DRUGS

- The intimation or notification must have following information:
 - Complete composition of drug, its source, and manufacturing data, to show that appropriate standards exist to ensure its safety.
 - Result of preclinical investigations, particularly on drug's safety, rather than its efficacy
 - Data demonstrate..... No hazard on Humans
- Required information are
 - Pharmacological profile
 - Acute toxixcology in serveral species of animals
 - The route of administration used
 - Very short term studies from 2 wks to 3 months to evaluate toxicity

INVESTIGATIONAL USE DRUGS

- ◉ A detailed outline of the planned investigation
- ◉ Information regarding training and experience of the investigator
- ◉ An agreement from the sponsor to notify the drug authority and all investigators if any adverse effects arise during either animal or human test
- ◉ The investigator's agreement to obtain consent of the person on whom the drug is to be tested before the test is made
- ◉ Agreement to submit annual progress report and commitments regarding disposal of drugs when studies are discontinued

INVESTIGATIONAL USE DRUGS

- **An Abbreviated New Drug Application (ANDA)**
 - an application for an existing licensed medication or approved drug.
 - a. Identify of the compound
 - b. Justification for human use
 - c. Purpose of the use of drug and the statement of scientific training and experience of the investigator
 - d. Nature of the facilities available to the investigator
- **No control over prescription**
 - but encouraged to inform when they use a drug for purpose other than those approved

INVESTIGATIONAL USE DRUGS

- ◉ Termination of clinical investigation
 - The drug authority may direct sponsor to terminate investigation on drug after failure of one chance given to the sponsor for correction at any stage under following conditions
 - Evidence of significant hazard
 - Convincing evidence of drug ineffectiveness
 - Submission of false data
 - Omission of material information submitted to the drug authority
 - Unsatisfactory manufacturing practice

INVESTIGATIONAL USE DRUGS

- Non compliance of submitted and approved research plan
- Failure to submit progress reports at specific time
- Failure to report serious or potentially serious adverse reactions
- Failure to meet requirement for pt consent
- **Continuos monitoring**
 - The principal investigator should prepare a continuing Surveillance Report on quarterly basis and forward to Secretary of the committee on use of Human in Research

INVESTIGATIONAL USE DRUGS

○ Documentation

- The record should be kept and retained usually for two years
 - Reports
 - Data
 - Result
 - Inventory
 - Control

○ Documentation reqd for

- Drug amount received from sponsor
- Amount dispensed to patient
- Returned to sponsor

BASIC PRINCIPLES FOR INSTITUTIONAL CLINICAL RESEARCH:

- ◉ General Guidelines
- ◉ Guidelines for Research Drug Control System
- ◉ Guidelines for investigator
- ◉ Guidelines for pharmacist
- ◉ Guidelines for nurses


INVESTIGATIONAL USE DRUGS

○ General Guidelines

- Existence of **clear-cut written policies** and **procedures for the approval**, management and control of investigational drug studies in clinical research
- Assurance that all clinical studies contain adequate **safe guards** for the institution it self, staff of the institution, the scientific integrity of the study and specially for patients
- Assure that involved staff is fully **informed** about and complies with these policies and procedure

GENERAL GUIDELINES

- Patient consent
 - Written consent
 - Verbal consent
 - Proxy consent
- Supervised under competent personnel
 - qualified
- Availability of research facility
 - Research equipments
 - Other facilities



Before
initiation of
research

GENERAL GUIDELINES

- **Self-regulatory nature of research**
 - Research must be self regulated
 - Should be terminated on evidence
 - A significant hazards
 - Drug ineffectiveness
- **Study result should not be used for promotion**
 - Should not used for promotion
 - Data can be exchanged in scientific communication

GUIDELINES FOR RESEARCH DRUG CONTROL SYSTEM

- Existence for an effective control system
 - The institution's drug control system must be efficient to assure **surplus availability**, storage , proper packaging, labeling in accordance with standards
- Prescription from authorized practitioner
 - Authorized prescriber
- Record keeping
 - Record to maintain drug received from sponsor
 - Amount dispensed to patient
 - Returned to sponsor
- Receiving data at another facility
 - Different wards

GUIDELINES FOR INVESTIGATOR

◉ Competency of investigator

- Proper education , training, experience or potentials for such studies
- Phase-I .. Able to evaluate human toxicology
- Phase II .. The clinician should be familiar with the conditions and methods of their evaluation
- Phase III.. Large number of patient may be treated by different physicaians

GUIDELINES FOR INVESTIGATOR

- ⦿ **Authorization as co-investigator**
 - Principal investigator can authorized any hospital staff for co-investigator
- ⦿ **Patient consent**
 - Must obtain patient consent
- ⦿ **Record keeping**
 - Same as above
 - Record must be made available promptly to the drug sponsor and to the drug authorities
- ⦿ **Regular reporting to sponsor, drug authorities**
 - On process and adverse effects

GUIDELINES FOR PHARMACIST

1. Possession of an approved research copy
 - Must have copy of the institutional research committee-approved research protocol in pharmacy
2. Development of **investigational drug data sheet**
 - Drug designation and common synonyms
 - Dosage form and strength available
 - Usual dosage range, including dosage schedule, and route of administration
 - Indications
 - Expected therapeutic effect

GUIDELINES FOR PHARMACIST

- Expected and potential unwanted effects, symptom of toxicity, and their treatment
- Contraindications
- Storage requirement
- Instruction of dosage preparation and administration
- Instruction for disposition of unused doses
- Name and contact number of principal and co-investigator
- The drug data sheet is included with the study protocol submitted to IRC
- Copy should be distributed to the appropriate pharmacy staff to familiarize them and all patient care units where the drug will be used

GUIDELINES FOR PHARMACIST

- An integrated drug distribution system
 - Dispensing of IND should be integrated with Drug other system with respect to
 - Packaging
 - Labeling
 - Order review
 - Profile maintenance
 - Delivery
 - Label should be ???????????? Same or different
- There must be system to verify that IND is being dispensed to consented patient only upon the order of an authorized investigator

GUIDELINES FOR PHARMACIST

- Patient education and monitoring of therapy
 - The patient education and monitoring are clinical responsibilities of pharmacist
 - Should be performed in coordination with **authorized** nurses and investigator
- Return of unused drugs
 - at the conclusion of the study the pharmacist should return all the unused drugs to principal investigator or to sponsor

GUIDELINES FOR PHARMACIST

- Preparation of statistical summary
 - The **Pharmacy** Must prepare annual or semiannual statistical summary of investigational drugs use
 - Must include number of drugs studied
 - Number of drugs investigations are in progress
 - Listing of all studied during previous year
 - Cost allocation
 - The drug cost and other expenses should be properly allocated
 - Include record keeping, storage, drug administration and personel

THANK YOU