Investigational Use Drugs

Definition:

Investigational use drugs are those compounds or mixtures which have not been released by the Federal Food and Drug Administration or by the legal authority of the respective country for general use.

Or

Investigational use drugs are defined as those, which are being considered for, but not yet received, approval by the Federal Food and Drug Administration/ legal authority of the respective country for human use.

Principles Involved in the Use of Investigational Drugs in Hospitals

Hospitals and related health care institutions, the primary centers for clinical studies on investigational drugs, must ensure the policies and procedures for the safe use of these drugs are established and followed.

Basic Principles

Procedures in the use of investigational drugs should be built around these basic principles:

1. An institution that is setting for investigational drug studies must assure that such studies contain adequate safeguards for itself, its staff, the scientific integrity of the study and, especially the patient.

   In doing so, the institution must have written policies and procedures for the approval, management and control of investigational drug studies.

2. All investigational drug studies must meet accepted ethical, legal and scientific standards and be conducted by appropriately qualified investigators.

3. All patients who participate in investigational drug studies must freely consent, in writing, to treat with the drugs. This consent must be obtained from the patient or his legally authorized representative before treatment is begun, and the patient has been fully informed about the study objectives and the risks and benefits associated with the study drug Guidelines for Institutions

4. The principal investigator is responsible for the proper maintenance of the case report forms and all other records required in the study by the drug sponsor, institution or Food and Drug Administration.

5. The institution's drug control system must proper packaging and labeling, ensure sufficient supply, storage condition, dose preparation and administration, should well informed to the nursing staff about the drug, inventory and control systems regarding investigational drugs

Guidelines for Institutions

The following recommendations serve as a guide to develop investigational drug procedures

1. As required by federal regulation, institutions in which clinical research is conducted, must have an Institutional Review Committee, often titled as a "Committee on Human Investigation" or Clinical research Committee". This committee must evaluate each proposed clinical research study in terms of its compliance with recognized ethical, legal and scientific standards.

2. Investigational drugs must be used only under the supervision of the principal investigator or authorized co-investigators, all of whom must be members of the institution's professional staff.

3. The principle investigator is responsible for obtaining the written, informed consent of the patient to participate in the study. The informed consent process must conform to current federal and state regulations.

Items must be addressed by the investigator

- a) A fair representation of the nature of the study, the expected benefits, and the risks or discomfort involved. Any compensation or treatment that will be furnished in the event of injury should be described. (Example: Rofecoxib-Vioxx, 2005)

- b) A balanced description of the alternative treatment available (Including their respective risks and benefits)

- c) A general description of the study procedures and the expected length of therapy with the drug.

- d) A statement to the effect that : (1) the patient may withdraw form the study at any time without penalty; and (2) the principal investigator may remove the patient from the study if circumstances warrant.

- e) The name of the drug(s), name and signature of the patient and name and signature of the principal or co-investigator

- f) A statement of who will have access to any study records that contain the patient's name.

4. The principal investigator is responsible for the proper maintenance of the case report forms and all other records required in the study by the drug sponsor, institution or Food and Drug Administration.

5. The institution's drug control system must contain the following elements regarding investigational drugs:

a) Drug must be properly packed in accordance with all applicable standards and regulations

b) Drugs must be labeled properly so as to ensure their safe use by the nursing staff and patient.

c) There must a mechanism to ensure that sufficient supplies of the drugs are always available in the institution for the duration of the studies.

d) Nurses should be informed about the drug's pharmacology (side effects), storage requirements, methods of dose preparation, and administration, precautions to be taken, authorized prescribers etc

e) Records of the amounts of drug received from the sponsor and its disposition must be maintained.

f) The institution's records on investigational drug studies should be designed so that various statistical reports may be generated conveniently and expeditiously.

Guidelines for Pharmacist

The pharmacist is responsible to the institution and the principal investigator for seeing that procedures for the control of investigational drug as developed and implemented. Suggestions to accomplish this are as follows:

1. A copy of the approved research protocol should be kept in the pharmacy.
2. Using the protocol and additional information supplied by the principal investigator, the pharmacy should prepare an investigational drug data sheet, which concisely summarizes for the medical, nursing and pharmacy staffs information pertinent to use of the drug. This form should contain (a) drug designation and common synonym, (b) dosage form and strength, (c) usual dosage range including route of administration, (d) indication, (e) expected therapeutic effect, (f) toxicities and their treatment etc.

3. Investigational drug supplies must be kept in the pharmacy. The pharmacy should maintain an investigational drug inventory record.

4. The dispensing of investigational drugs should be integrated with the rest of the drug distribution system with respect of packaging, labeling, profile maintenance, delivery and so forth.

5. Patient education and monitoring of therapy are two clinical functions which are particularly important and applicable to investigational drugs. These functions should be provided in a coordinated fashion by the pharmacy and nursing staff and authorized investigator(s).

6. At the conclusion of the study, the pharmacy should return all unused drugs to the principal investigator or sponsor.

7. The pharmacy should prepare for the institution's administrator an annual or semiannual statistical summary of investigational drug use.

8. Drug costs and other expenses associated with investigational drug studies should be properly allocated and reimbursed.

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Classification of Drugs

The statement of Principles Involved in the Use of Investigational Use Drugs in Hospitals espouses four distinct purposes:

1. To establish a drug classification.

2. To centralize pertinent information concerning drugs available for research use.

3. To define the availability of such drugs to staff members

4. To establish a single stocking and dispensing unit within the hospital.

One simple classification, which can be adapted to any hospital research program, is to categorize -

Class A: should contain all investigational use drugs that are in a preliminary experimental stage. The use of drug in this category is usually restricted to the principal investigator.

Class B: should consist of investigational use drugs which have passed through the preliminary research stage. Usually, drugs in this category are supplied to the department of pharmacy by the principal investigator and are dispensed only upon his written prescription.

Class C: is limited to drugs approved by the USP, NF or passed by the Federal FDA for commercial distribution. Drugs in this category may be used within the hospital or its clinics if the physician complies with some specific procedures.

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 operation-

1. **General** - An FDA-approved drug which as recommended as essential for good patient care with a well established usage, once accepted, may be prescribed by all members of the attending and house staff.
2. **Conditional** – Certain drugs may be approved for a conditional period of trial. A drug approved by the FDA for general use, but which the Committee wishes to evaluate for given period before final consideration, may be prescribed by all members of the attending and house staff.
3. **Investigational** – Drugs which are not approved by the FDA for use other than under controlled clinical settings must be approved by the Research Advisory Committee. A protocol of any study involving drugs must be submitted to the pharmacy.

Control of Investigational Use Drugs

All investigational drugs should be registered with the Pharmacy and Therapeutics Committee. This may be accomplished by a letter from the principal investigator, which provides the following information:

1. New drug number
2. Generic name
3. Manufacturer
4. Chemical Name
5. Proprietary name
6. General Chemistry
07. Pharmacology
08. Toxicology
09. Dose Range
10. Method of Administration
11. Antidote
12. Therapeutic use.

Many pharmacists have developed various forms which may be used to disseminate the above information on an investigational use drug to the various staff doctors and nurses. These forms are usually titled:

- Physician's Data Sheet on Investigational Drugs
- Nurse's Data Sheet on Investigational Drugs
- Pharmacist's Data Sheet on Investigational Drug

Physician's Data Sheet

1. Name of the Investigational Drugs:
2. Manufacturer or other source:
3. Strength and Form of Investigational Drug:
4. Amount Received:

   Date Received:

   Control or Batch #
5. Pharmacologic and Therapeutic Properties, Dosage, Precautions:
6. Arrangements which have made for its administration

Sig. Investigator

Nurse's Data Sheet

1. Name of the Investigational Drugs:
2. Manufacturer or other source:
3. Strength and Form of Investigational Drug:
4. Pharmacologic and Therapeutic Properties, Dosage, Precautions to be observed:
5. Arrangements which have made for its administration

Chief Pharmacist

Pharmacist's Data Sheet

Investigational Drug:--------- Manufacture:------

Chief Investigator: ----------

Date	Physician	Patient	Rx.#	Amount	Ward
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Identification of Investigational Use Drugs

Whenever Class A or class B drugs are dispensed from the pharmacy, they should be labeled in such a manner as to differentiate them from routine prescription drugs. In some hospitals, investigational use drug labels are printed in red ink on white paper stock.

In addition to commonly required information are :

(I) Patient's name (II) Data (III) Prescription number

(IV) Doctor's name and (V) directions for use a space for the research drug number is provided.

This double set of number provides a two-way control relative to the identity of the product dispensed. 22

Authorization for Treatment with Drug Under Clinical Investigation

The Law Department of the American Medical Association states that drugs under clinical investigation should be administered only where:

1. The informed consent of the patient or his/her authorized representative has been obtained,

2. The physician is convinced of the reasonable accuracy of his diagnosis and, if necessary, has confirmed it by adequate consultation and

3. Existing methods of treatment have proven unsatisfactory.

The physician is advised to confine his clinical investigations of new drugs to those furnished by the reputable sources who have supplied him with comprehensive written information concerning:

1. Animal experimentation
2. Previous clinical investigations, if any
3. Recommended dosages
4. Contraindication
5. Possible side effects to be watched for, and
6. The safety and possible usefulness of the drug from existing data.

Authorization Form

I authorize **Dr. X** ……, the attending doctor /physician to treat **Patient Name**, with the drug presently identify as **YYYY** for the following condition: **Describe symptoms of disease.** It has been explain to me that the safety and usefulness of the drug in the treatment.

I voluntarily consent to treat with the drug and release the attending doctor/physician for liability from any results that may occurs.

Witness---- Signature-----

(Patient or Authorized representative of the patient)

Consent Form

Patient's Name: Date:-

Project title:

Description of Product to be undertaken:

I have fully explained to the patient…**Name of the Patient**….the nature and purpose of the producer described above and such risks as are involved in its performance.

Physician's Sign.

I have fully informed or the risk and possible consequences involved in the performance of the product described above, have been advised that unforeseen results may occur and nevertheless hereby authorized Dr. X

Witness---- **Patient Sig./Authorized representative**

Moreover, the hospital pharmacist is urged to consult the hospital's legal counsel for the law applicable to the area in which the hospital is located.

Role of the Pharmacist in the Clinical Evaluation of a Drug

Once the pharmacologist has demonstrated a new compound to be effective and safe in animal test, clinical trials are invariably commenced. These trials usually proceed in two steps-**preliminary** and **extended.**

During the preliminary stage, the principal investigator cautiously administers the drug to a limited number of selected patients and closely follows the results. After having gained experience and confidence in its use, the investigator is generally ready to conduct an extended comprehensive evaluation of its efficacy.

During this stage, the pharmacist can play an important role by assisting in the development of the protocol and the control of a double blind test/study—having the experimental drug and placebo prepared exactly the same dosage form and presentation. Neither the patient nor the doctor informed as to whether the placebo and the potent article.

Clinical Investigation

The kind and extent of the investigational drug test are crucial to producing the substantial scientific evidence of safety and effectiveness needed to approve the drug for marketing. This evidence is obtained in three phases:

- **Phase-I**: to determine toxicities, metabolism, absorption, elimination.
- **Phase-II**: Initial trial on limited patients for treatment (specific disease)
- **Phase-III**: involve extensive clinical Trial, information obtained from above
- **Phase – IV:** Post marketing surveillance

Thank You