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Review on Non-Clinical Studies

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Review Article

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ABSTRACT

Non-Clinical testing is done throughout all phases of the drug development in order to survey the safety profile, pharmacokinetic and toxicokinetic (PK/TK) characteristics of therapeutic substances. If the Non-Clinical and Pre-clinical studies improvement is performed well, it can enhance the chances of success in the clinical development phases. Techniques for the Non-Clinical advancement of products follow general regulatory guidelines, but are also designed on a case-by-case premise as per the specific medication.

INTRODUCTION

Pre-clinical trials and clinical trials are the techniques carried out by researchers to examine drugs and medical devices of their safety and efficacy. Pre-clinical trial is a laboratory test of a new drug or a new device that is typically done on animal subjects to check, if the expected treatment practically works and if it is safe to test on humans [1-26].

Steps Involved in the Pre-Clinical Trial Process

1. Get an idea for drug target.
2. Bioassay has to be developed. A Bioassay is a live system that can be used to measure the drug effect. It might be a culture of cells or organs or an animal.
3. Assay method carried out on particular drug and screening the results safely.
4. Effective doses and toxic doses should be established.
5. Application is made to the Food and Drug Administration (FDA) as an Investigational New Drug (IND) [25-46].

Reasons behind the Non-Clinical Studies in Animals before Administrated to Man

1. To check the pharmacological effects are same in man as in animal.
2. Toxic effects in species will predict adverse effects in man.
3. Giving high doses in animals improve predictability to man.
4. Risk assessment can be made by differentiation of toxic doses in test species with predicted therapeutic dose in man [47-62].

According to Good Laboratory Practices and Non Clinical Studies explain about

1. Safety Pharmacology
2. Pharmacokinetics
3. Pharmacodynamics

4. General Toxicology
5. Local Tolerance
6. Genotoxicity
7. Carcinogenicity
8. Reproductive Toxicology

Safety Pharmacology

Safety pharmacology study uses the basic principles of pharmacology in a regulatory-driven process to find out the risk/benefit assessment. Safety pharmacology mainly plays an important role in pharmacodynamic/pharmacokinetic relationship of a drug's adverse effects [63-79]. These methods are used for the detection of an adverse effect liability, projection of the information into safety margin computation and finally clinical safety monitoring. Safety pharmacology is the discipline that looks to anticipate, whether a therapeutic substance (in the most sense of the word) if administered to human (or animal) populations is liable to be discovered dangerous and its professional mandate is to prevent such an occurrence.

Safety Pharmacology provides early information to clinicians regarding risk assessment in terms of product viability. A Therapeutic window for acute dosing in man and a set of anticipated side-effects for the clinicians involved in Phase I design. Safety pharmacology study embraces the principles of physiology, pharmacology and toxicology.

Pharmacokinetics

Pharmacokinetic evaluation in Non-Clinical studies should be comprehensive enough to ensure that compounds do not fail in the clinic.

Pharmacodynamics

Pre-clinical pharmacodynamics and safety studies are important to improve drug development outcomes and to predict human responses for that particular drug. These studies are helpful to predict the safety and efficacy of the drug [80-87].

General Toxicology

Pharmaceutical and biopharmaceutical companies use Pre-clinical toxicology studies to evaluate the safety of new medication applicants. The pressure to finish these studies accurately, quickly, furthermore, financially, while holding fast to FDA and universal regulatory requirement is more prominent than ever [85-93]. With the developing diversity of products in development, assessing the safety of a compound has turned out to be progressively.

Local Tolerance

The estimation of local tolerance must be conducted in laboratory studies prior to human exposure to drug substance or product. The main purpose of these studies is to discover about the medical products i.e., both active substance and placebo are tolerated at sites in the body, which may interact with the drug as a result of its administration in clinical use. The testing procedure ought to be such that any mechanical effects of administration or purely physico chemical activities of the drug can be distinguished from toxicological or pharmacodynamic studies [94].

Tests Involved in Local Tolerance Study are

1. Tolerance testing at the site of administration
2. Systemic toxicity testing

Genotoxicity

Genotoxicity is the assessment of the harmful impacts of chemical or physical agents on the hereditary material and related genetic processes of living cells. Genotoxicity provides the nature of chemical substances that damage to collapse the genetic information within a cell which leads to mutations and then causes cancer [95,96]. Genotoxin is a chemical substance that can cause DNA/RNA or chromosomal damage and finally malignant transformation i.e., cancer.

Genotoxicity screening tests carried out on molecular level, gene level and chromosomal level.

Carcinogenicity

As per the regulatory approval process, all the new drugs should be tested for their carcinogenic potential. The safety testing for the carcinogenetic potential of a pharmaceutical substance is the two years rodent bioassay in rats and mice. Carcinogenic agents may include Chemical (mutagenic compounds), physical (radiation, asbestos) and biological (oncogenic viruses like human T-leukemia virus) [97].

Carcinogenicity studies should be performed for all medications that are required to be clinically utilized for over six months and in addition medications [98,99].

Reproductive Toxicology

Reproductive toxicology study explains with the effects of chemicals on reproductive and neuroendocrine systems.

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