CHAPTER

1 Introduction to Research and Bio-statistics in Pharmaceuticals

Research in pharmaceuticals starts from study of etiology of a disease to the study of post marketing surveillance of a drug product in the market. When a disease is identified as an outbreak or for an existing disease, a study at the molecular level of the causative organism of the disease is conducted. In this process, the entire life cycle of the organism is established with the molecular mechanism of its growth. Such study is expected to identify all possible targets to inhibit the growth of the organism. Such targets usually include inhibition of cell wall synthesis, inhibition of enzymes that are responsible for growth of the organism etc. As a lead, scientists initiate research for possible natural herbs or new chemical entities (synthetic or molecular modeling) that can inhibit the growth of the organism. A promising natural herb is phyto-chemically/pharmacognically studied for the active constituents from different parts of the plant by collecting in various seasons, if necessary. Several times a naturally available chemical constituent, that is promising, further acts as a lead for chemical synthesis or on pure chemical synthesis basis, further new molecules are synthesized to minimize side effects and maximize beneficial effects that are established through pharmacological studies on animals. A promising molecule is established through animal studies (pre-clinical) for their pharmacological activity, safety, toxicity and proceeds further for human studies (clinical) as an investigational new drug. Once the investigational drug is through, the new chemical entity has transformed to new drug after scrutiny and approval by drug regulatory at each stage. It is necessary to understand that pre-clinical and clinical studies in most of the times overlap. During clinical studies (phases I to IV), pharmacodynamic and pharmacokinetic studies, route of administration, dosage form, strength, possible combinations are established. Contrary to innovator's drug, generic manufacturer establishes bio-equivalence studies for identical drug product or establish entire pharmacodynamic and pharmacokinetic data for a similar drug product. After the drug regulators review of the drug products for their safety, efficacy and reliability, the drug product is approved for release into the market with simultaneous monitoring of drug products for their therapeutic efficacy during long term by monitoring as pharmacovigilance or post-marketing studies.

Statistics are a compilation of a data and is generated through experimental or available retrospectively (data that is already available, but compiled for analysis). Statistics are derived from a huge population, but such compilations may not be

feasible and data is collected from a sample size of a population which itself is derived from statistical calculations. Statistics play a critical role right from individual growth to the economic growth of a country. In pharmaceuticals, bio-statistics are more prominent and have to be interpreted carefully so as to ensure that there is biological significance rather than mathematical significance/insignificance.

In pharmaceuticals, at every stage statistics apply. Any research study is aimed with a statistical planning and the end results are statistically concluded. In research, a problem is identified and is solved through experiments, validated through statistics for drawing final conclusions.

Several questions lead to research activity. For an initiator, the different questions that arise are what disease condition requires new treatments? What is the causative micro-organism or conditions for the disease? What are the molecular mechanisms for growth of the disease causative organism? What are the possible targets for inhibiting the growth of the micro-organism? What are the existing natural herbs, new chemical entities that have required inhibitory activity? How to identify past research conducted for a problem? How to identify the literature as review or research articles? How to compile the findings? How to draw conclusions from the findings for continuing research? How to isolate active ingredients from natural herbs? How to synthesize new chemical entities? How to design new chemical entities through molecular modeling? How to select animals and conduct pre-clinical studies? How to plan for clinical studies? What are the national/international guidelines for clinical studies? How to estimate a population of a disease in a country? How to draw a sample size from a population? What statistical methods to be used to draw conclusions for the studies? What dosage form, route of administration, strength to be planned? What kind of analytical techniques have to be established for biological fluids, for formulations? How to develop a similar, identical drug product? How to establish bio-equivalence studies for the generic drug product? How to file an IND, NDA, ANDA application for drug approval so as to market within a country?

Forth coming chapters are expected to empower the reader to acquire the various kinds of mental approaches to be followed to finally execute research activity, conduct some statistical calculations to achieve final conclusions.