CHAPTER 1

INTRODUCTION
INTRODUCTION

India is a signatory to WTO (World Trade Organization) and as such obligated to obey IPR (Intellectual Property Right). It is required to grant and protect product patent against application for the sale and marketing. Indian patent act had been already amended to meet the above objective from 2005 onwards.

A review of patent Literature would reveal that many new drug discoveries pertaining to therapeutic classes, viz psychotropics, anti-cancer, immunomodulators, memory enhancers, newer selective cardio vascular drugs and receptor specific agonists and antagonists belonging to various therapeutics classes are succeeded in getting patent-ceiling and are under different stages of investigation. On an average, span of 12 years is required for one out of many similar new molecule to pass through different batteries to test and finally the clinical trials before a drug is approved by the regulatory authorities viz. USFDA, EMEA and Drug Controller General (India), Govt. of India, for domestic marketing and then for export, registration.

Notwithstanding the fact that ICH guidelines (International Conference of Harmonisation) is a understanding to be followed strictly between three regions viz. North America/ Europe and Japan, there is a great emphasis on Good Clinical Practices (GCP) not only among the ICH member countries but also extending to non-member countries like India which can cater to the need of scientific and clinical data generation while participating in Global Trials. This is because there is an ever increasing disease burden in the Indian subcontinent and as such there is no dearth of patients and experienced clinical investigators throughout the length and breadth of country, once trained in GCP, would be very successful in establishing a discipline of science in clinical practice moreover the data if not generated as per GCP will not be entertain by the developed countries.

To sum up the various pre-clinical and clinical requirement, and quantitative and
qualitative difference that exist in registration of drugs and pharmaceutical need to be studied step by step in a critical manner which could assist the Indian Drug Industry and regulatory authorities of Central Government and prepare themselves for grant of approval of drug and pharmaceutical both for domestic market and export.

Keeping the above objective in mind, a topic of comparative new drug registration is selected that exist in developed nation U.S.A and India, that also include conduct of clinical trial of unapproved drug Butorphanol as per GCP guidelines and also bioequivalence studies of two drugs Valsartan and Deflazacort. The clinical trial and bioequivalence studies are conducted in India only and these investigations ultimately facilitates the sponsor company to finally get the marketing approval from Indian Regulatory Authorities. The bioequivalence studies are carried out as per the GCP guidelines and conducted in Drugs Controller General (India) approved bioequivalence center.

The comparative studies of New Drug Approval process between developed country U.S.A and India is carried out by extensive and exhaustive literature learning and survey. For the comparison, U.S.F.D.A is selected due to below mentioned reasons:

1. U.S.F.D.A provides most resourceful, detailed, structured rules and regulations to approved drugs
2. The third world developing countries like India always consider the U.S.F.D.A as most appropriate, reliable and perfect drug regulatory authority to be followed.
3. U.S.F.D.A has a strongest critical ability to audit most of the clinical investigations globally.
The comparative study is planned in such a manner that the results would give an insight of Indian New Drug Regulatory Process and the gaps in Indian regulations can be identified, which will be helpful to Indian Regulatory Authorities in finalizing various future policies.

All the clinical trial and bioequivalence studies planned would be conducted as per the Indian GCP guidelines, only after obtaining the regulatory approvals from Drug Controller General India. The Ethics Committee or Institutional Review Board (IRB) approvals are also taken before initiation of investigation. The clinical trial (CT) material and the reference standard are provided by the sponsor company. The bioequivalence studies are carried out at the Drug Controller General India approved center only, while clinical trials are planned in various hospitals. It is to be noted that all the clinical trials are conducted by the trained team including medical investigators i.e. doctors by qualification in various hospitals. The results and the data generated out of various proposed clinical investigations are also submitted to the Indian Regulatory Authorities enabling them to approve the new drug from manufacturing and marketing in India.

Clinical Investigation on Butorphanol had been selected due to following various reasons:

1. It was not approved and available in India, hence the proposed clinical trial give an opportunity to the Indian Company (sponsor) to carry out these bridge studies in order to obtained regulatory approval from Indian Drug Regulatory Authorities.
2. Butorphanol is available in atleast two dosage form i.e. injectable and nasal spray, hence gives the choice to clinician.
3. It is approved in U.S.A for both the dosage form recently. Injection is approved in 2000 and nasal spray is approved in 2005.
4. It is one of the most powerful opioid analgesic provide an option to the clinician against Pentazocin and Morphine injection.

Valsartan is nonpeptide, orally active and specific angiotensin II antagonist acting on the AT1 receptor subtype, approved by U.S.P.D.A and is still under patent obligation in
U.S.A., which means that no other company can take its generic approval in U.S.A. However, Valsartan is approved in India for many companies and patent act and rules does not become applicable in India due to the fact that the patent application for Valsartan had been filed pre-1995, due to which any Indian company can take the regulatory approval of this drug after conducting the Bioequivalence study requirements for such drugs had been laid down in schedule “Y” – The Indian Regulatory Authorities ask the applicant to conduct the bioequivalence study only in 12 human volunteers in a cross-over design in order to approve the drug to be manufactured and marketed in India.

Deflazacort is a prodrug of prednisolone, available in oral dosage form only, found to be effective and safe in various therapeutic applications. The selection of this drug is done due to the reason that first of all it is not approved by U.S.F.D.A, secondly only 2-3 companies in India got the manufacturing and marketing approval of the drug by Indian Regulatory Authorities. The bioequivalence study of Deflazacort is planned in such a manner that based on the results of bioequivalence studies the sponsor company got the regulatory approval of the drug. Deflazacort patent status is also pre-1995, means any Indian company can introduce the molecule in India after conducting the bioequivalence study.

To sum up the proposed comparative study of new drug approval process between India and U.S.A, along with a conduct of clinical trial and bioequivalence study would help in identifying the various gaps that exist in Indian Regulatory Laws and also provide an overview of Good Clinical Practices (GCP) compliance, while conducting the clinical research in India. The Butorphanol clinical study would also provide the efficacy and safety outcome parameters in Indian population and the data generated out of proposed clinical trials would help in getting the manufacturing and marketing approval from Indian Regulatory Authority. The bioequivalence studies conducted on two drugs i.e. Valsartan and Deflazacort would provide the data that would ultimately help in getting the manufacturing and marketing approval of these drugs from Indian Regulatory Authorities.