LITERATURE REVIEW

1. Jaime R. Hornecker (2009) summarized the availability and utilization of generic alternatives to brand-name drugs and its significant effect on cost savings for health care consumers. The author states that in 2008, generic drugs accounted for more than 63% of total prescriptions filled in the United States. The author reviewed the overall cost of generics vs brand. The author believes that the direct cost savings are a significant advantage for generic drug products, studies have also shown improvements in indirect costs such as therapy adherence and compliance.

2. Gandhi Saurabh, et al (2011) studied pharmaceutical solid polymorphism in ANDA as per regulatory perspective. The author states that many pharmaceutical compounds exist in different crystalline forms and thus exhibit polymorphism. Polymorphism may affect Chemical and Physical Stability, Apparent Solubility, Dissolution, Bioavailability and Bioequivalence and Manufacturability of drug product, which require special attention during product development as it affects the quality, safety and efficacy of drug product.

3. Costas H. Kefalas, et al (2011) discussed the similarities to and differences from brand name drugs. The author describes that the generic drugs are essentially the same as brand-name drugs, with regard to intended indication/use, active ingredients, dosage form and strength, route of administration, safety, quality, performance, purity, and stability.

4. Swetha Handoo, et al (2012) studied the regulatory requirements of various countries of the world and concluded that they vary from each other. Therefore, it is challenging for the companies to develop a single drug which can be simultaneously submitted in all the countries for approval. The author described the importance of the regulatory authorities that one of the primary challenges for regulatory authority is to ensure that the pharmaceutical products are developed as per the regulatory requirement of that country. The author state that the USA is the major market for the pharmaceutical industry.

5. Mulaje SS, et al (2013) reviewed the procedures for drug approval in different countries. The author describes that the developing a new drug requires great amount of research work
in chemistry, manufacturing, controls, preclinical science and clinical trials. Similarly, the author describes the regulators that the drug reviewers in regulatory agencies around the world bear the responsibility of evaluating whether the research data support the safety, effectiveness and quality control of a new drug product to serve the public health. Every country has its own regulatory authority, which is responsible to enforce the rules and regulations and issue the guidelines to regulate the marketing of the drugs.

6. **Stephen Barlas (2014)** discussed the importance of generics slowing the growth of health care costs. The FDA has approved more than 8,000 generic equivalents to brand-name drugs; as a result, generics represent more than 85% of all U.S. prescriptions and have saved U.S. consumers and the health care system $1.5 trillion in the past decade alone, according to the GPhA. The author reviewed the objectives of GDUFA and expectations to give the industry a clearer idea of what the FDA expects in an ANDA in various areas.

7. **Jaspreet Kaur, et al (2014)** studied presented drug approval strategies for pharmaceutical industry. The author states that in Pharmaceutical Industry, The author focused on the US FDA drug approval strategies. These strategies playing core job in the pharmaceutical industry. These strategies having all the guidelines which are indispensable part of the IND, NDA and ANDA drug approval applications.

8. **B. Venkateshwarlu, et al (2014)** discussed the importance of the availability of generic medication in the ASEAN region and associated regulatory requirements of various countries. The author compares the requirements of various countries and challenges when they differ from each other specifically for the companies to develop a single drug which can be simultaneously submitted in various countries for approval.

9. **Suryakanta Swain, et al (2014)** studied pharma regulations for generic drug products in India and US and presented with case studies and future prospectives. The author states that among the developing nations of the world, India has already carved out a special niche for itself in many business verticals of the pharmaceutical industry and is currently being recognized as the ‘pharmacy of the world’ for the generic drug products.
10. M. Vaseem Akram, et al (2014) studied the various regulatory requirements of drug master files by FDA, EU, Canada and presented the comparison. The author describes the various aspects of DMF covering manufacturing process, confidential document used to provide detailed information about facilities, processes or articles used in the manufacturing process, packaging and storing of one or more human drug. The author reviewed various requirements and provides information on regulatory requirements of Drug Master Files by Food and Drug Administration (USA), European Medicines Agency (Europe) and Health Canada (Canada) and their comparison.

11. Useni Reddy Mallu, et al, (2015) studied the requirements of addition of an alternate API supplier in generic drug product. The author presents various activities involved in the qualification of an alternate API supplier in generic drug product. The article describes the supplier selection, quality requirements, change management such as process, notification as applicable to be the generic drug products meant for US and EU market. The article also discussed about the change classification associated guidance such as supac, variation filing, prior approval supplement.

12. P. Nagaraju, et al (2015) studied and compared registration requirements of generic drugs in ASEAN countries. The author concludes that although ACTD is harmonized for all 10 countries but still every country is differing in some of the local requirements such as Administrative, technical, clinical and non-clinical documents. This review article will give the easy understanding on the drug registration requirements for Asian region.

13. S.M. Shakeel, et al (2016) studied and compared the regulatory requirements for generic drugs dossier submission in US and Canada. The author concludes that although the CTD makes multinational filings easier, there are significant differences in the dossier submission requirements in these countries.

14. Brahmaiah Bonthagarala, (2016) studied regulatory requirements for generic drugs dossier submission in united states and Canada. The author presents the differences in registration requirements for generics in United States and Canada. Generic drugs in US they are approved under the Abbreviated New Drug Application. Bioavailability and Bioequivalence
study data is critical in the generic drug approval process. Generic manufacturers must file an Abbreviated New Drug Submission (ANDS), and the manufacturer is obligated to establish bioequivalence of their drug to the ‘Canadian Reference product’ (CRP).

15. Nithika Kaushal, et al (2016) studied the regulatory requirements for the conduct of bioequivalence studies in US, Europe, Canada, India, ASEAN and SADC countries and its impact on generic drug substitution. The author’s study highlights the relevant regulatory guidelines for the conduct of bioequivalence studies in US, Europe, Canada, India, South Africa and South East Asian Nations. A comparative study of the differences in study design and specifications have also been addressed.

16. Joseph Linsey et al, (2016) studied the comparison of the generic drug approval and registration process in the regulatory market of Europe, USA and Brazil. After analysing the various requirements for the generic drug approval in the above stated countries, the author concluded that the regulatory guidelines of Europe and Brazil was not well defined. But FDA gives very much well defined requirements.

17. B. RAMYA, et al (2017) studied the regulatory requirement for marketing of generic drugs in USA. The author states that it is challenging for the companies to develop a single drug which can be simultaneously submitted in various countries for approval. The role of regulatory authorities is to ensure the quality, safety, and efficacy of all medicines in circulation in their country.

18. S Sravika, et, al (2017) studied regulatory requirements for development and filing of generic drugs globally. One of the primary challenges for regulatory authority is to ensure that the pharmaceutical products are developed as per the regulatory requirement of that country. This process involves the assessment of critical parameters during product development.

19. Chennamsetti Srilakshmi (2017) discussed the details of a marketing authorization application (MAA) in all countries, the importance to know exactly the pharmaceutical legislations (regulations, directives and guidelines) and the regulatory requirements in each of the country in advance. The author presented the analyses especially concerning the
aspects required for marketing authorization and accepted dossier requirements for the registration of API in US and EU.

20. AnupRajan, et, al (2017) studied the need of regulatory affairs knowledge in pharmaceutical industry. The author stats that the Indian pharmaceutical sector is rising very rapidly and there is a need of regulatory affairs professionals to provide the current needs of industries for the global competition. Regulatory affairs professionals are the link between pharmaceutical industries and worldwide regulatory agencies. They are required to be well versed in the laws, regulations, and guidance of the regulatory agencies. There is a growing need to incorporate the current requirements of pharmaceutical industries. The author discussed the regulatory education and its need, learning resources, courses available, syllabus contents, and job opportunities in regulatory affairs.

21. Ana CerúliaMoraes do Carmo, et, al (2017) studied the reasons for registration application refusal of generic and similar pharmaceutical drug products by the Brazilian Health Regulatory Agency. The author’s study evaluated the main reasons for registration refusal of generic and similar pharmaceutical drug products in Brazil. The author’s study aimed to help future applicants to better organize the proposal Methods. The study results concluded that the drug product quality control, drug product stability study, deadline accomplishment, API quality control made by drug manufacturer, active pharmaceutical ingredient (API), and production report were the main reasons for marketing authorization application refusal of generic and similar pharmaceutical drug products in 2015.

22. Stephen Barlas (2017) presents that the generics account for 89% of the prescriptions written in the U.S. but only 27% of the total spent on drugs. Even with that market penetration, the opportunities for generics and biosimilars are still considerable. There are currently 182 brandname drugs that are off-patent with no generic competition. There are 546 drug categories in which the brand name has stopped selling product and there is only one generic competitor- a sole-source situation. Of course, part of the reason for lack of competition in brand-name-only or sole-source markets is that the potential markets are small, so the incentive to develop an entrant is small. In addition, brand-name companies are loath to provide samples to generics and biosimilars companies. However, where markets are
large, there can be enthusiastic competition. For example, last year the FDA had timely approvals of nine generic versions of Crestor (rosuvastatin calcium, AstraZeneca), a cholesterol drug with approximately $5 billion in annual sales. The author also summarized the details of GDUFA I and GDUFA II and its impact on the industry and generic drugs.

23. **Ernst R Berndt, et, al (2018)** studied the generic drug user fee amendments with an economic perspective. The author states that the vast majority of prescription drugs consumed by Americans are off patent (‘generic’), their regulation and supply is of wide interest. The author describes events leading up to the US Congress's 2012 passage of the Generic Drug User Fee Amendments (GDUFA I) as part of the Food and Drug Administration Safety and Innovation Act (FDASIA). The author explained how user fees required under GDUFA I erected barriers to entry and created scale and scope economies for incumbent manufacturers.

24. **P. Sindhuja, et, al (2018)** described that the generic drug registration is a very strenuous and complicated process in many countries. The author presents that the registration processes varies from country to country based on their regulations. The author discussed the US registration under the Abbreviated New Drug Application, whereas in China it is under the filing of provincial FDA. Understanding the differences in registration process will have a substantial impact on the success of its multicounty submissions strategy. Therefore, the author recommends an appropriate submission strategy in advance which could make a smooth review process without any significant delays or failures.

25. **Snehal Shah, et, al (2018)** studied the preliminary requirement for ANDA filing. The author states that the USFDA is very critical regulated agency for submission. The author presents that an abbreviated new drug application (ANDA) contains data which is submitted to FDA for the review and potential approval of a generic drug product. Once approved, an applicant may manufacture and market the generic drug product to provide a safe, effective, lower cost alternative to the brand-name drug it references.

26. **Naziya Rafi, et, al (2018)** studied the requirements and registration procedures for generic drugs in USA. The author describes the importance of generic drugs and the application
requirements for the same. The author states that the US has one of the most demanding regulatory authorities and registration of drug products will be a long process if not complied with the US Food and Drug Administration (USFDA) guidelines. The Documents or the application submitted to the FDA for the approval of a generic drug product is known as an Abbreviated New Drug Application or ANDA. It contains all the data for FDA review and approval.

27. D. Thambavita, et, al (2018) studied the regulatory requirements for the registration of generic medicine and format of drug dossiers procedures in Sri Lanka and compared with selected regulatory authorities. The author presents regulatory requirements for approval of generic medicines and the format of compiling drug dossiers and states that they vary among regulatory authorities. The variation is particularly wide between High-income countries (HIC) and lower and middle income countries (LMIC) with different regulatory frameworks. In this study, document requirements for approval of generic products, approval timelines, and consideration of bioequivalence and/or bio waiver data by Regulatory Authorities (RAs) of 10 selected jurisdictions.

28. Jawahar. N, et, al (2018) studied the generic drug application and their approval process in US, Europe and Japan. The author states that an Abbreviated New Drug Application (ANDA) contains data which when submitted to FDA's Centre for Drug Evaluation and Research (CDER), Office of Generic Drugs (OGD), provides for the review and ultimate approval of a generic drug product. Once approved, an applicant may manufacture and market the generic drug product to provide a safe, effective, low cost alternative to the American public. In other words, “It is an application which is filed with USFDA for generic drug approval of an existing licensed medication or approved drug.”

29. Alfredo García-Arieta, et, al (2019) studied the regulatory requirements for the acceptance of foreign products by participating regulators and organizations of the international generic regulators programme. The author states that the acceptance of foreign comparator products is the most limiting factor for the development and regulatory assessment of generic medicines marketed globally. The author concludes that there is currently no consensus amongst regulators on the acceptability of foreign comparator products.
30. Mainul Haque, (2019) assessed generic medicine and prescribing. The author states that the generic drugs are copies of brand-name drugs that have exactly the same dosage, intended use, effects, side effects, route of administration, risks, safety, and strength as the original drug. In other words, their pharmacological effects are exactly the same as those of their brand-name counterparts.

31. Puneet Dhamija, et, al (2019) presented comparison of branded and generic drugs. The author states that the branded versus generic medicines is a topic of debate and discussions among physicians, drug regulators, and policy makers across the world. Endocrinologists face a situation where chronic therapy is to be provided at a minimum financial burden to the patient with a minimum margin of error as far as control of disease process is concerned. The author presents various comparative aspects of generic and brand drugs such as quality assurance, economy, and approval process.

32. B. Jayalakshmi, et, al (2019) studied registration and regulatory requirement of generic drugs marketing authorization in BRICS countries. The author provides comparative study of generic drug registration in BRICS, and present the differences among the guidelines.