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Comparative Study of Regulatory Requirements of Drug Products in Emerging Market

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ABSTRACT

Registration of Pharmaceutical drug products in Emerging Markets is the most demanding task. Regulatory requirements are harmonized in regulated countries by Common technical document (CTD) filing, while there is a diversity of requirements in emerging markets. The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) has brought regulatory authorities and pharmaceutical industries of the US, Japan, and Europe together for various aspects of drug registration but there is no such harmonized guideline for emerging market except Association of Southeast Asian Nations (ASEAN) and Gulf Co-operation Council (GCC), ZAZIBONA where harmonization exist in clusters with their mutual concern. The optimization and harmonization requirements have become mandatory and can be examined by the incidence of the higher cost involved in the availability of drugs, quality requirement of premise and research and development, and regional registration requirements. Quality, Safety, and Efficacy data have significant importance in dossier registration. Pharmaceutical Industries have to comply with the regulatory requirement in the Emerging market for the betterment of public Health and safety. The review explains a brief about Emerging Markets Key Challenges, Regulatory barriers, Global Regulatory Plan, general filing procedure, documents required, and different regulatory requirements for the Registration of Pharmaceuticals in Emerging Markets with a tabular comparison. Keywords: Dossier Registration, Emerging Markets, GCC, ASEAN, Common technical document (CTD), WHO, Harmonization, WAEMU, ZAZIBONA, Drug Product.

1. INTRODUCTION

Drug Regulatory Affairs has evolved and growing and is the one which is least impacted during the Acquisition and Merger, and also during recession. Global harmonization standards have led to consistent approach in regulatory submissions.

The Systematic formulation development acts as a back bone for any dossier preparation in export registration. (1) The Registration requirement are Varies countries so it is difficult for any company to develop product for each region. Therefore; we need to consider Asia is expected to overtake. Europe in pharmaceutical market within the next decade and sales are driven by growth in key emerging markets. More than 85% population lives in the emerging market and so the real economic growth has come from these Korea, Saudi and Mexico. (1)

The growth is increasingly moving beyond the use of include early-stage research and technology aimed at specific medical need of patients in these regions. One way to launch new drugs in a timely manner in specific medical needs of patients in these regions. One

way to launch new drugs promptly in emerging markets is to include majority of patients from relevant countries in clinical development programs. This practice is routine for most pharmaceutical companies. These development programs attributed to longer life expectancy and lifestyle changes that are possible through rapid economic growth. (2)

Emerging markets are important and expanding globally and has raised the demand for general and lifesaving medicines. Regional cooperation is required to ensure that the scientific capacity is developed. Apart from this, regional manufacturing capacity is the most expected way to enable economic growth, specified quality standards should meets international export requirements. Legislative and political factors are the most critical one, countries need to have support to develop effective national legislation, as well as cooperating regionally which helps to access to essential medicines. (2) Pharmaceutical Companies and regulatory agencies are collaborating for improving drug development

process and approval ex: ICH guidelines for eCTD submission and QbD which contribute to better first time product quality shortening the review time required by regulatory agency and these guidelines are well accepted by regulated markets and some countries

of Emerging market like India and China uses the CTD format. (2)Pharmaceutical Market is divided into following groups (3):

1. Regulated Market: US, EU (Germany, France, Ireland, and Sweden etc.) UK, Japan, Canada, Australia, New Zealand, and South Africa.

2.Emerging market:

(a)Asia: (Sri-Lanka, India, Bangladesh, China, Pakistan, Bhutan, Nepal).

(b)ASEAN: 10 Countries group - Philippines, Vietnam Singapore, Malaysia, Thailand, Indonesia, Laos, Cambodia, Brunei Darussalam, and Myanmar.

(c)African countries: (Algeria, Zambia, Ethiopia, Ghana, Kenya, Malawi, Mozambique, Namibia, Nigeria, Sierra Leone, Tanzania, Zimbabwe etc.)

(d)Middle East countries: (Gulf Co-operation Council countries i.e. Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, UAE)

(e)Latin America (Mexico, Brazil, Panama, Peru, Guatemala, Argentina, Chile, Dominican Republic)

(f)CIS: (common wealth of independent states): There are nine member states of the Commonwealth of Independent States. These CIS states are Armenia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, and Uzbekistan)

2. Emerging Market overview Emerging market consists of mainly the countries from Asia pacific, Latin America, Africa and Gulf countries. These countries are differing in their

region and also in many other aspects as regulation of Pharmaceuticals, Using different Guidelines for registration, registration fees, Requirements to maintain registration, duration of registration Patent regulation and legislation for the drug. (1The optimization in requirements is mandatory and can be judged by the incidence of higher cost involved in availability of drugs, research and development facilities. For better treatment safety and efficacy for the drugs must be justified and rationalize for public security. The quality, safety and efficacy data has its own importance in the registration dossier. The

commercial significance of markets is increasing globally. (1) WHO is continued to play a major role in terms of scientific capacity development, through its prequalification project and other activities. Given that the quality of pharmaceuticals is such a major issue, the

WHO and other international organizations, such as developed country drug regulatory authorities, should be encouraged and supported to expand their current programmes which are supporting to developing countries.

GCC: Ministry of Health of GCC states (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia and UAE) are regulatory authorities for the regional pharma sector. They also regulate prices of pharmaceutical products and bring about harmonization of varying prices and the

regulatory process, the GCC implemented a centralized system, Gulf Central Committee for Drug Registration (GCC-DR) in May 1999, which currently runs parallel to the regulatory regimes in the region. (1) Fast-Track Registration and Reliance pathway: In July 2020, GHC published a circular indicating that a reliance model can be applied for products approved in at least 2 GCC countries. In this case, GHC centrally approves the product within 60 calendar days from submitting the scientific reports issued by the GCC countries.

LATAM:

The regulatory regime in LATAM countries can be divided into three categories i.e. Countries which have established regulations (Brazil, Mexico, and Venezuela) to demonstrate the efficacy, safety through clinical trials or Bioequivalence studies with the innovator‘s product in the drug approval process. The countries as Argentina, Chile, Columbia, Ecuador, and Paraguay also have the regulations for registration of new or generic drug but are less stringent from first category. The last category of countries (Guatemala, Barbados, Bolivia, Nicaragua and Peru) has imperfectly formed drug regulations for the approval of drugs.

As per our report, the size of the Latin America Generic drugs market has been calculated at USD 37.14 billion in 2022. It is expected to reach USD 50.67 billion by 2027, growing at a CAGR of 6.41% from 2022 to 2027. (4) The pharmaceutical industry plays a vital role in the growth of generic drugs. The primary drivers of the Latin American generic drugs market are patent expiration it helps initial developer produce lower-cost generic variants and introduce into the market. Generic drugs are of same quality there may some changes

in flavor, size, and color but it acts same as the branded drugs. Dosing, safety, strength, quality, how it operates, how it is taken, and how it should be utilized are all the same as the branded drugs. This market will increase tremendously during the forecast period. Among Latin America (LATAM) countries, some have established regulations (Brazil, Chile, Mexico and Venezuela) to demonstrate efficacy, safety through clinical trials and therapeutic equivalence studies with the proper drug approval systems, while others (Argentina, Columbia, Ecuador, Paraguay) have regulations to register a new drug or generic that are not as stringent as the first category. (4)Finally, other countries (Guatemala, Barbados, Bolivia, Nicaragua and Peru) have imperfectly formed regulations for drug approval.

ASEAN: Rest of the region countries insist on following ICH region for some data like stability, clinical trials though it follows majorly its own regulations e.g., the ASEAN countries require data as per ASEAN CTD which is same as ICH CTD for data requirements organized in Parts. The brief contents of CTD and major requirements for various regions are tabulated in Table 1.

Table 1 Structure of Common Technical Document (CTD)

ICH CTD	ASEAN CTD	Description	Remarks
Module 1 Regional and Administrative Information	Part I	Contains documents that are specific to each region. This module is not part of CTD. Basically consists of administrative documents like Application form, legal documents (GMP, Licenses etc.), labeling etc	Required for generics and New Drug
Module 2 Overall Summary	Part II	This module summarizes the Module 3, 4 and 5. It includes Quality Overall summary, Non Clinical Overview and	Required for generics and New Drug. For generics summary on Quality part & non-clinical and clinical: literature summary

		Summary and Clinical Overview and Summary. The summary provides reviewer the abstract of documents provided in the whole application.	and overview is required for some regions.
Module 3 Quality		The documents related to Chemistry, manufacturing and Control of both Drug Substance and Drug Product is included in this module.	Required for generics and New Drug
Module 4 Safety	Part III	Non Clinical Study Reports – Data on pharmacologic, pharmacokinetic, and toxicological evaluation of the pharmaceutical product is provided.	Not required for generics
Module 5 Efficacy	Part IV	Clinical Study Reports - A critical assessment of the clinical data and related reports is provided in this module.	Not required for generics except Bioequivalence study

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