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Generic Drug Registration Requirements in Row Countries

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Abstract

The regulatory requirements of several countries of the world vary from each other. Therefore, it's challenging for the companies to develop one drug submitted by the countries for approval. The regulatory strategy for product development is crucial to be established before developmental work to avoid significant surprises after applying. The crucial role of the regulatory authorities is to ensure the quality, safety, and efficacy of all medicines in circulation in their country. One of the primary challenges for regulatory authorities is to make sure that the pharmaceutical products are developed as per the regulatory requirement of that country. Product registration within the rest of the world could also be challenging because the regions thereunder aren't harmonized. This region comprises mainly Asia Pacific, Latin America, Eastern Europe, Africa, and Gulf countries.

Keywords: Generic, Global, Regulatory, Registration, Row Countries

INTRODUCTION

GENERIC DRUG MARKET

A generic drug is a pharmaceutical product that is usually defined as interchangeable with an innovator product manufactured and marketed after the expiry date of the patent or other exclusive rights. [1]

Generic drugs are marketed under an approved name or non-proprietary other than a proprietary or brand name. They're less expensive than brand-name drugs. Due to their low price, generic drugs are often the sole medicines that the poorest can access. https://www.who.int/medicines/areas/access/NPrices_Glossary.pdf

The global generic drugs market reached a worth of US$ 386 Billion in 2020. The global market for generic drugs should grow from $411.6 billion in 2020 to $650.3 billion by 2025, a compound annual growth rate (CAGR) of 9.6% for 2020-2025. https://www.h.cobccresearcm/market-research/pharmaceuticals/generic-drugs-markets-report.html

The significant factors contributing to the growth of the generic drugs market include the increasing prevalence of chronic diseases, diabetes & cardiovascular diseases, growth in the geriatric population, increasing high demand for generic medicines, healthcare expenditure, and a large number of patent expired branded drugs. However, stringent governmental regulations and adverse effects associated with drugs are expected to restrain the market development. The rising demand for newer versions of generic drugs, different clinical trials, and large numbers of licensing & partnering strategies to launch new products by key vendors contributes to significant demand for generic drugs.

https://www.alliedmarketresearch.com/generic-drugs-market

ROW COUNTRIES:

This region comprises mainly the countries from the Asia Pacific, Latin America, Eastern Europe, Africa, and Gulf Countries While countries from the Asia Pacific and Gulf have almost harmonized their regulatory environment through The Association of Southeast Asian Nations (ASEAN) and Gulf Co-operation Council (G.C.C.) organizations, the remainder of the regions are yet to return up with the harmonized regulations in their respective regions. a positive regulatory environment in these countries has also allowed easy entry of foreign companies.

In the ASEAN regions, the applicant can suit the standard requirements set within the ASEAN Common Technical Dossier (ACTD) to urge approval within the member countries (Indonesia, Malaysia, Philippines, Singapore, Thailand, Brunei, Myanmar, Cambodia, Laos, and Vietnam). Almost identical documents are often used for national approval within the non-member countries of the Asia Pacific region with simple amendments.

https://www.fda.gov.ph/wp-content/uploads/2021/03/ASEAN-Common-Technical-Dossier-ACTD-December-2016-from-ASEAN-Secretariat.pdf

DRUG FILING REQUIREMENTS IN SOUTH AFRICA: http://www.santr.gov.za/

South Africa's pharmaceutical market is one of the main attractive markets in Africa. Most of the local drug manufacturers and distribution are within the hands of major international Pharmaceutical Firms. GBI Research valued South Africa in the pharmaceutical market at $ 7 Billion in 2018 and expects it to achieve $14 billion in 2023 at a Compound Annual Growth Rate (CAGR) of 6.8%

http://www.pharmabiz.com/NewsDetails.aspx?aid=85525&sid=21

South African Development Community (SADC) was established in 2002 as a part of the Pharmaceutical Programmer under the SADC Secretariat's Directorate of Social and Human Development and Special Programmer (SHDSP). Currently, SADC features a membership of 15 Member States, namely: Angola, Botswana, Democratic Republic of Congo (D.R.C.), Lesotho Madagascar,

Malawi, Mauritius, Mozambique, Namibia, Seychelles, South Africa, Swaziland, United Republic Of Tanzania, Zambia, and Zimbabwe. The foremost objective was to harmonize pharmaceutical trade and regulation. Though some activities are ongoing to date, each country follows its regulations.
https://www.mea.gov.in/Portal/ForeignRelation/southern-african-development-community-cooperation-april-2012.pdf

FEES:

1. Generic products (pharmaceutical, analytical and bioavailability evaluated) Rs 25000 per application.
2. Strengths and dosage form other than those referred above: Rs 8500
3. Screening fee on receipt of an application: Rs 1500
4. Generic products with clinical data: Rs 40 000
5. Inspections
   (a) Local manufacturing sites: Rs 600 per hour.
   (b)International manufacturing sites: Rs 3600 per hour.
6. New Chemical Entities – Rs 45000 per application

Drug registration specific requirements for South Africa:

- Quantity of samples: lowest pack size of minimum 100 units with minimum one-year validity
- CoPP authenticated by South African authority is not needed
- The notary is not needed
- Separate dossiers for different strengths
- Three pilot batches stability data (ACC-40^{0}C/75%RH, LT-25^{0}C/60%RH but 30^{0}C/75%RH is also acceptable)
- Stability studies must include microbial test
- Working standard sample is to be sent
- Process validation protocol is compulsory
- The label of the product should possess the schedule of the medicine
- The Patient Information Leaflet (PIL) should be in English and one other official language (Portuguese, Arabic etc.)
- IR spectra compulsory for the container closure system
- All the units must be in SI units
- The frequency of in-process quality control should be included
- Stringent limits for dissolution, stability release
- GMP certification is valid for 2 years, and it is not product-specific

MEDICINES CONTROL COUNCIL

The drug regulatory authority of South Africa is that the Medicines Control Council under the Ministry of Health. The registration of medicine was governed by the provisions and requirements of the Medicines and Related Substances Control Act No. 101 of 1965 to manage all aspects of the Manufacturing, marketing, and sale of medicines for human, veterinary use, biological products, and medical devices. South Africa is additionally modernizing its regulatory structure to hurry up drug approvals. to this end, the government established the South African Health Products regulatory agency (SAHPRA) to exchange the Medicines Control Council (MCC). http://www.mccza.com/

The new body will have an honest range of responsibilities, including helping to urge obviate the backlog of drug applications and speed up the registration process from five years at present to a minimum of one year. South Africa has taken positive steps to strengthen macroeconomic growth, including pushing for the country's official designation as a BRICS (Brazil, Russia, India, China, and South Africa) nation.

DRUGS REGISTRATION PROCEDURE [2,3]

REGISTRATION OF DRUGS:

The Proposed Holder of the Certificate of Registration (Phcr) is Eligible to launch the product within the market. The application submitted should be signed by the pharmacist authorized to talk with the council [4]. This pharmacist should be within the full-time employ of the company. The general format for the dossier is CTD. The approval process for both a replacement drug and a generic is that equivalent. The applicant must provide evidence that the product features a comparable therapeutic effect of the originator's product for generic medicines.
http://old.sfda.gov.sa/En/Drug/Topics/Regulations+-+Guidelines.html

This can be done by performing comparative clinical trials or providing proof of bioequivalence, or in some cases, by laboratory testing. In June 2010, the Medicines Control Council (MCC) announced implementing the South African Common Technical Document (ZA CTD) format from June 1, 2011, which replaced the MRF1. The new strategy to implement the eCTD format for dossier submission is ongoing, and it's mandatory from June 1, 2014.
http://www.rrfa.co.za/wpcontent/uploads/2012/11/CTD-implementation-road-map-Feb16-v6.pdf

DRUG FILING REQUIREMENTS IN NIGERIA

The local pharmaceutical Manufacturing industry is currently able to meet 25 percent of local demand. Nigerian manufacturers produce liquid preparations, tablets, capsules, ointments, lotions, creams, and ophthalmic preparations. The local pharmaceutical industries can meet domestic demand for some classes of medicines. The remaining 75% of the market is increasingly dominated by imports from Asian companies. Business Monitor International (B.M.I.) analyzed that Nigeria will earn $9.61billion from the pharmaceutical industry by 2025. Growth in the pharmaceutical market is expected to be driven by the increasing availability of low-cost generic drugs.
https://pharmexcil.com/docs/DRProcedures/NIGERIA/Aregprocedure_nigeria.pdf

NATIONAL AGENCY FOR FOOD AND DRUG ADMINISTRATION AND CONTROL (NAFDAC)
http://www.nafdac.gov.ng/
The drug regulatory authority of Nigeria is the National Agency for Food and Drug Administration and Control (NAFDAC) under the Federal Ministry of Health, is responsible for regulating and controlling the manufacture, importation, exportation, advertisement, distribution, sale, and use of food, drugs, cosmetics, medical devices, chemicals, and pre-packaged water.

PROCEDURE:
There are different steps each imported product must pass to get a license number.

STEP 1:
The applicant has got to register the name at the Ministry of Commerce in Nigeria. This brand name is the applicant's choice, and the sole criteria are it shouldn't infringe other brand names within the market. Then the applicant must undergo the Registration Division, NAFDAC, a written application, stating the manufacturer's name, generic name (brand name), strength, indications, and acquire the prescribed application form, which must be crammed adequately with all information required. This form, labeled "FORM D- R.E.G./001," shall be obtained on payment of N500.00 per product. A separate form shall be submitted for every drug product (means a separate drug formulation). However, the application for registration of 1 dosage form with different strengths could also be made on an equivalent form. [5]

STEP 2:
The necessary documents described by NAFDAC to register each product must be found satisfactory before any other process can be carried out. If the documents comply with the NAFDAC requirements, a permit to import samples of products is equipped for the applicant. The applicant must import specified samples to be used for vetting and laboratory analysis (National Chemical Laboratory).

STEP 3:
At this stage, samples of products presented are vetted, which incorporates checking the labels, leaflets, drugs information. There are minimum requirements for product labeling like name of the drugs name, name and address of the manufacturer, production and expiry date, batch no, and so on.
Documents to be submitted during the vetting are:
1. Copies of import permit and receipt of payment.
2. Dossier consistent with NAFDAC format for drugs.
3. Samples for every product.
4. Letter of invitation for inspection.
5. Compressive Certificate of study.

STEP 4:
After the vetting is completed, the applicant is required to bring some samples for lab analysis. Submit specified quantities of sample products alongside copies of the receipt for the processing fee and application letter for the submission of samples. Then product(s) go to the lab for analysis to make sure compliance with standard specifications.

STEP 5
At this stage, decisions are taken whether the product qualifies to tend NAFDAC registration number or not. If the product meets all the wants, a registration number is issued. Once the merchandise is given a registration number, the applicant has to collect the notification number, pay the required amount for the license certificate, and present the receipt to urge the notification. Now the applicant is qualified to import the product certificate lasts for 5 years. http://pharmabiz.com/Services/ExportImport/Countries/Nigeria.aspx

FEE:
- The registration form per drug product is five hundred nairas (N500:00).
- Registration form for other regulated products is two hundred and fifty nairas only (N250:00)
- Change of source for drugs to different manufacturer POM- N 250,000:00 + 5% VAT,OTC- N 1, 000,000:00 + 5% VAT
- Change of source for drugs to same name manufacturer POM- N150, 000:00 + 5% VAT,OTC- N 250,000:00 + 5% VAT
- Processing fee per regulated product for all additional sites belonging to same name corporation is one hundred and fifty thousand nairas only plus 5% VAT(N=150,000:00 + 5% VAT)

Note:
- Failure to respond promptly within 30 workdays to queries or inquiries raised by NAFDAC on the application will automatically lead to suspension of further processing of the application.
- The registration time line after submission of vetting samples is a hundred (100) workdays.

DRUG FILING REQUIREMENTS IN SRI LANKA
Sri Lanka is an emerging dharma market, and the market size is estimated to be around $400 million. The pharmaceutical industry is dependent upon imports. There is no essential drug production in the country.

COSMETICS, DEVICES AND DRUGS REGULATORY AUTHORITY (CDDRA)
CDDRA is the drug regulatory authority of Sri Lanka under the Ministry of Health framed to regulate and control the manufacture, import, sale, storage and distribution, recall of Cosmetics, Devices, and Drugs (including nutraceuticals and borderline devices) efficiently and effectively to ensure rational use. The Cosmetics, Devices & Drugs (C.D.D.) Act No. 27 of 1980 is the legislative framework that provides the legal authority to regulate CDD in Srilanka.

https://pharmexcil.com/uploads/countryreports/Sri_Lanka.pdf

REGISTRATION OF DRUGS:

There are no stringent regulations for getting market authorization in Sri Lanka. The dossier requirements are given to the manufacturer in a guidance document via an authorized local agent. The approval process for both a new drug and a generic is the same. In the case of generics, the bioequivalence study data is not required to be submitted. Only permission to import the drug to Sri Lanka is needed. The import is based on the necessity of the medicine in the country, which the State Pharmaceuticals Council decides by preparing Essential Medicines List and then informs to CDDRA. http://nmra.gov.lk/

INFORMATION REQUIRED FOR REGISTRATION OF A DRUG

Submitted as a word document and will contain all requirements as laid out in Form A- Schedule IV.

1. Name of the applicant
2. Address
3. Status of applicant
   - Manufacturer
   - Importer

If the applicant is an Importer, the name and address of the manufacturer must tend.

1. Name of the drug
2. Name (if any)
3. Official or approved name indicating the regulatory body that has given the name(whether B.P., U.S.P., etc.)
4. Composition
5. All ingredients, active and inactive, should be listed by their official or approved names and will include their exact quantities as per unit dose or, if it's not practical, as a percentage of the entire formulation.
6. Main pharmacological class and ATC-class (if known) to which the drug belongs.
7. A certificate from the Health authorities of the country during which it's produced, confirming that the drug is in use there and therefore the period of use and, if not, the reason for not marketing it within the country of origin (Free Sale Certificate, Certificate consistent with the WHO Certification Scheme on Pharmaceutical Products occupation International Commerce- the recommended format should be used.)
8. Published reports on controlled clinical trials-establishing the therapeutic efficacy of the drug. (Uncontrolled studies would be accepted as long as controlled clinical trials aren't necessary to prove efficacy). Within the case of combination drugs, the evidence must be provided to justify the inclusion of all the active constituents within the formulation.
9. Summary of toxicity tests for teratogenicity indicating the security of the drug
10. Datasheet giving the subsequent

A. Pharmacology

- Pharmacological actions
- Mechanism of action (if known)
- Relevant pharmacokinetic data

B. Clinical information

- Indications
- Contraindications
- Precautions [6]

The Processing fees at present are:

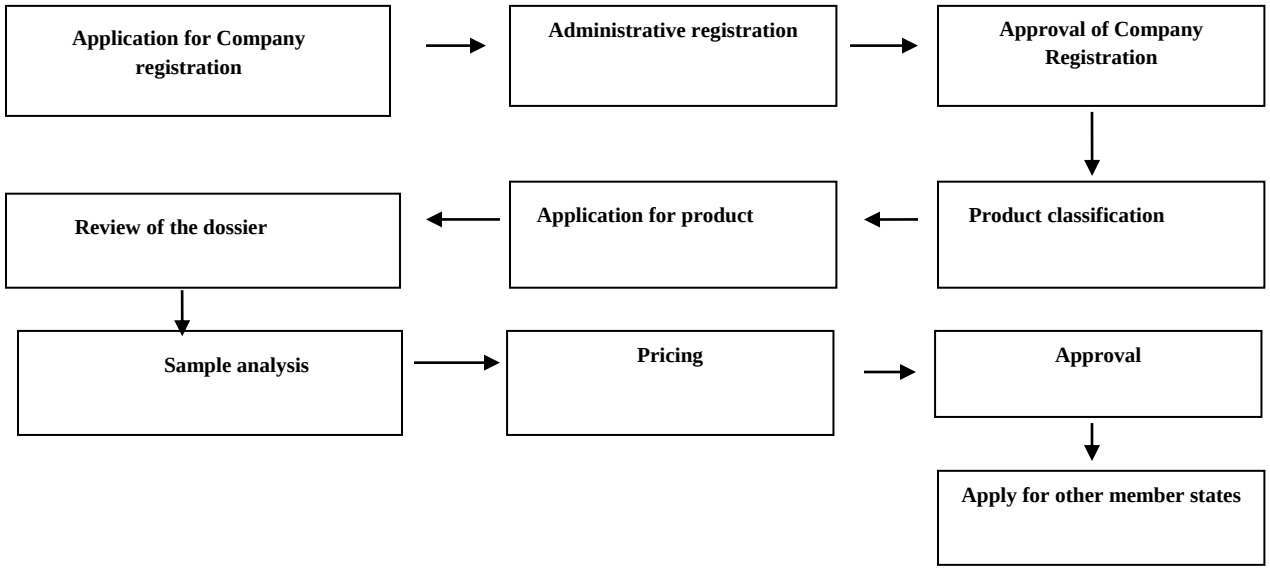
- New Chemical Entities for Sri Lanka (NCE) - Rs. 50,000/= + VAT
- New Dosage form application for Sri Lanka (NDF) - Rs.25,000 /= + VAT
- New fixed dose combination products (NFDCs) - Rs.50,000 /= + VAT
- New product of existing drugs - Rs.10,000 /= + VAT
- Re-registration application - Rs.10,000 /= + VAT

DRUG FILING REQUIREMENTS IN GCC: [7, 8]

The Gulf Cooperation Council (G.C.C.) is additionally referred to as The Cooperation Council for the Arab States of the Gulf. The member states of G.C.C. are Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, United Arab Emirates, and Yemen as members in Health Council).

G.C.C. Pharmaceutical Industry report (March 31, 2020) says that the G.C.C. pharmaceutical industry is predicted to experience sustainable growth in the medium to future. Increased domestic production, foreign investments, and generics consumption are likely to support the market's evolution. This market is overgrowing and is predicted to succeed in around 3 billion USD by 2020. According to the latest report given by IMARC Group, the G.C.C. generic drugs market size reached US$ 3.94 Billion in 2020. Saudi Arabia leads overall annual drug spending at more than $2.8bn, followed by the U.A.E. at $1.8bn, and Kuwait at $374m. Qatar, Oman, and Bahrain imitate at $227, 152, and 118m, respectively. Many analysts expect the Emirates' annual drugs spend market size to succeed at $9.7bn by 2025, with a per capita spend of on the brink of $500. The G.C.C generic drug market reached a value of US$ 3.94 Billion in 2020. https://www.giiresearch.com/report/imarc1006971-gcc-generic-drug-market-industry-trends-share-size.html

PROCEDURE FOR GCC-DR:



In 1999, a pharmaceutical harmonization initiative was launched by a committee called Gulf Central Committee for Drug Registration(GCC-DR), with the executive office being located in Riyadh, Saudi Arabia. https://ur.booksc.eu/book/39954826/1c1a3d

The main objective of the GCC-DR is to coordinate health policies and programs among the participating members via the exchange of information, knowledge, techniques, and expertise. It is responsible for the registration of pharmaceutical products, GMP inspection and compliance, approval of quality control laboratories, and review of technical and post-market surveillance reports.

The GCC-DR adopted the ICH guidelines as a primary source for developing its own. It follows a centralized procedure for drug registration with harmonized drug registration requirements and drug pricing for all the member states. After centralized approval of product, authentication and fee payment should be followed in each member state as per their local policies. By 2006, submission of application to the GCC-DR had become mandatory for most of the pharmaceutical classes. Most of the companies taking this routeing model their dossiers on the standing requirements of Saudi Arabia. Most companies reported that registration through the centralized system took longer than through the national procedure. The registration process of pharmaceutical products depends on two licenses: one for the company as a whole and the other specific to the product. In Saudi Arabia, Oman and Yemen, company registration must be approved before product registration, whereas in Kuwait, Qatar, UAE, company and product registration processes can be filed in parallel.

DRUG FILING REQUIREMENTS IN SAUDI ARABIA

Saudi Arabia is predicted to maintain its position because the largest pharmaceutical market within the Gulf, consistent with the G.C.C. Pharmaceutical Industry report. Saudi Arabia represents 65% or $7.1 billion of the pharmaceutical market within the member countries of the G.C.C.

According to Espicom, Saudi Arabia's pharmaceutical market "is expected to rise by a CAGR within the high single digits during 2017-2021." The drug company in Saudi Arabia with the most significant share of the pharmaceutical market in-country is G.S.K. However, most of the local production is predetermined for the export markets. Domestic production accounts for around 15 percent of the general supply of pharmaceuticals within the market. Around 15-20 pharmaceutical manufacturers are operating within the Kingdom, including indigenous companies and subsidiaries of multinational pharmaceutical giants. https://www.oatext.com/future-of-the-pharmaceutical-industry-in-the-gcc-countries.php

SAUDI FOOD AND DRUG AUTHORITY

The primary regulatory agency in Saudi Arabia is that the Ministry of Health. Therefore, the Saudi Food and Drug Authority was established in 2003 to be liable for developing and enforcing the regulatory system. The most purpose of the SFDA establishment is to manage, oversee, and control food, drug, medical devices and set mandatory standard specifications thereof, whether or not they are imported or locally manufactured. The control and testing activities are often conducted within the SFDA or other agencies ' laboratories. https://old.sfda.gov.sa/en/about

REGISTRATION OF DRUGS:

SFDA published draft guidelines on the official website guiding the procedure and requirements for filing generics. Pharmaceutical products are required by law to be registered before marketing. This applies to both locally manufactured and imported products. Foreign manufacturers must be represented by local agents. the entire dossiers are sent to the Department of registering human medicines.

- Drug Application
- Fill and export the application for module 1
- Pay the application fee.
- Submit the dossier.
- Receive and answer assessment inquiries
- RFI
- Receive the application review decision.
- Print the registration certificate.
- Manage the drug file life cycle.

https://pharmaknowl.com/sfda-drug-registration-requirements-approval-process

CONCLUSION

Medicine regulation may be a legislated function of any regulatory agency in a country. As such, the authority is accountable to the country's citizens regarding the supply, efficacy, quality, and safety of medicines. Across most regional pharmaceutical markets, generics are emerging as solid challenges to branded medications. Such robust expansions are attributed to the soaring demand for pharmaceutical products and energy to scale back the health care cost, at constant time, efforts by health plan providers to regulate spending on costly prescribed drugs, providing a lift to the drug industry.

REFERENCES:

1. Swetha Handoo, Vandana Arora, Deepak Khera.A comprehensive study on regulatory requirements for developing and filing generic drugs globally 2012 Jul-Sep; 2(3): 99–105. DOI: 10.4103/2230-973X.104392
2. B. Jayalakshmi, R. Seetharaman, R. Kamaraj. Registration and Regulatory Requirements of Generic Drugs Marketing Authorization in "BRICS" Countries. Research J. Pharm. and Tech. 2019; 12(3): 1403-1408. DOI: 10.5958/0974-360X.2019.00234.8
3. Senthil V, L. Srianitha R. Baviyapriyadharshini. Regulatory Requirements For Drug Products Registration In South Africa February 2018 International Journal of Drug Regulatory Affairs 3(4):1-8 DOI:10.22270/ijdra.v3i4.171
4. Adrea Keyter, Joey Gouws, Sam Salek, Stauart Walker. The Regulatory Review Process in South Africa: Challenges and Opportunities for a New Improved System Ther Innov Regul Sci 2018 Jul; 52(4): 449–458.Published online 2018 May30. DOI: 10.1177/2168479018776649
5. Nandini Warier, Priti Mehta. Comparative Study of Generic Drug Registration Requirements for Dossier Submission in African Region-Kenya, Ghana, Nigeria, and Botswana Volume 3 , Issue 2 , 2016. DOI : 10.2174/2213476X03666160605111335
6. D. Thambavita, P.Galappthy, R.L.Jayakody. Regulatory requirements for the registration of generic medicines and format of drug dossiers: procedures in Sri Lanka in comparison with selected regulatory authorities. Journal of pharmaceutical policy and practice 11, Article number: 14 (2018)
7. Jitendra Kumar Badjatya, Journal of Drug Delivery & Therapeutics.Overview of Drug Registration Requirements for Pharmaceuticals in Emerging Market2013, 3(2), 227-232 DOI https://doi.org/10.22270/jddt.v3i2.466
8. S. Pateriya et. Regulatory Aspects of Pharmaceuticals' Exports in Gulf Cooperation Council Countries J Young Pharm2011 Apr-Jun; 3(2): 155–162.DOI: 10.4103/0975-1483.80305