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Comparative overview of Registration and Approval process for Generic Drugs in BRICS Countries

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Abstract

BRICS are economically incorporated the developing markets of Brazil, Russia, India, China, and South Africa. In, the Pharmaceutical market rapidly increasing growth in the administration framework of Medication and Administrative Medication Law. The main objective of this study is to compare the Registration and Approval process in different Countries for Generic Drugs. The Registration process in India and China are different. Even, though Brazil, Russia, and South Africa also follow CTD format in Module I for Requirement of registration. All countries include the highest world pharmaceutical economy in the world to create a significant opportunity for pharmaceutical companies by direct foreign investment and showing growth. They have the largest entity on the global stage of the world. The main goal of this study is to the comparison of generic medication of drug registration process in BRICS countries, in, that Russia and Brazil have different approval processes so that the newer technologies we have found in the countries. India, South Africa, and China have CTD format requirements so, that this Module-1 is very different. More rising largest globally emerging BRICS markets are having significant or beneficially Opportunities. According to different guidelines, we are opinion to and that regulation is carrying out. In, Brazil is having good, human service and current medication it is economically good for the developing market in global prospect. ICH prefers that the anniversary of preparing a dossier for Safety, Quality, and Security of API and Product Specification. So, that in this review we have discussed the above Registration and Approval Process BRICS countries.

Keywords: Regulatory Requirement, BRICS, Generic Products, CTD, GMP, CDSCO, DCGI, API, CFDA, SFDA, ICH

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1. Introduction

Generic drug: Any medicinal product having a dossier that is containing reviewing and assessing by the regulatory authority of the particular country. A Generic drug is that drug, which is compare to **Reference Listed Drug (RLD)**, a product containing performance, quality and dosage form. It also contains some active moieties that are no longer protected by patent. It is the biological equal to the brand or new drug.

The regulatory authority for drug product approval allows the holder to sell a product in the market all the generic drugs meeting the standard of safety, quality, and efficacy for marketing authorization in countries.

Drug Registration

Drug registration is mainly important for health protection. All the medicines are not normal "Commodities" essential medicines according to WHO, All the medicines are having own social value. In, addition to quality, safety, and efficacy requirements these are arguments for regulation in an industry more generally and controlling supplies. BRICS has a developing market that is a new advanced and economical trend. (1)

Generic Product: Drug Registration

It is similar to the new chemical moieties newer dossier contains information about all the chemistry of the product. Any assumption an innovator product exists and innovator has shown clinically effective and safety of a drug. All the data for a generic drug product is designed and establish in clinically interchangeable with an innovator in terms of safety, quality and efficacy. (2)

A regulatory new drug approval process by any person or sponsor to get authorization for launching a drug in markets. Currently, different countries have different regulatory requirements for the approval of a generic drug. The Marketing Authorization Application is a single regulatory approach that is applicable to various countries is difficult to task. The necessity of MAA for approval of various stages to conduct clinical trials for **post-marketing safety studies (PASS)**. After completion of clinical studies of the drug, submit an application to a competent authority of a country for drug approval. After all, are comes to the competent authorities for checking and reviewing the application and approve only areas like safety and effectiveness of the drugs. After, approval of a new drug, the government of the country monitors the safety of a drug by some side effects, and when it is use in a larger population.

NDA is an application submitted to the individual regulatory authority for authorization market a new drug that is an innovator product. To bring this permission form sponsor to submit the preclinical and clinical test data for analyzing the drug information and description of trials. (3)

Role of Regulatory Affairs in BRICS Country

The role of BRICS countries to rising protagonists in worldwide improvement collaboration to all together countries and quickly changing. BRICS have expanded monetary just as specialized help and built up unmistakable available resources of financial cooperation, through south participation with **Low-Income Countries (LIC)**. BRICS are create political impact, changing the customary in westers givers. (4)

2. Brazil

Regulatory Authority: Agencia Nacional de Vigilancia Sanitaria (National Health Surveillance Agency; ANVISA)

More than 80% of the Brazilian population has access to basic medicines covered by the national health insurance scheme (Sistema Unico de Saude). Legislation pertaining to the control of therapeutic products, foods, and cosmetics is the Law on Marketing of Medicinal Products, Pharmaceutical Ingredients, and Medical Devices, No 6,360 (1976). ANVISA, established in 1999, has based its regulatory system on that of the US FDA. It is responsible for the regulation of food, medicines, medical devices, cosmetics, tobacco, and health services.

ANVISA is an ICH member.156 Companies must be registered with *ANVISA* before they can access the electronic submission portal. Drug registration is valid for five years. Brazil requires documentation to be translated into Portuguese and submitted in CTD format.

The approval letter and a CPP from a major market are required for final approval for imported products. The agency reviews the dossier and sends queries to the sponsor, which has 30 days to submit its response. The Board of Health grants the final approval.157 Total New Chemical Entity approval time is approximately 400 days.158 local clinical testing is required.159 Priority applications may be processed in 180 days.160 The Brazilian government determines medicine prices based on the CMED (Medication Market Regulation Chamber), which defines prices and their annual adjustment.

Registration of Drugs in Brazil

Brazil is a largest country in South America. It has a second biggest pharmaceutical market in the rising world. A new administrative organization has a body and structure of this part where creators plan and share their opinion for registration procedure and it is not easy to the significance of this office. (5)

Types of Drug Product Registration

a) **Medicinal product:** used in humans, their active ingredients, and other inputs.

b) **Pharmaceutical raw material:** drug raw material should be used in medicines.

c) **Health product:** used in chemotherapy equipment, intended for laboratory and diagnosis an image.

Requirement for Registration of Drug *(6)*

1. Proof of Registration fees payment
2. Manufacturing site certificate of API
3. Technical information of API
4. Pharmacodynamic and pharmacokinetic data
5. Quality Control of all raw material

Brazil is the largest Latin American generic market. Generics account for 30% of Brazilian pharmaceutical sales and enjoy a 25% market share in terms of revenue. ANVISA, the National Health Surveillance Agency, is the Brazilian regulatory body governing medical products. Brazilian regulations require the generic drug to be at least 35% less expensive than the originator product.

Generic medicines were effectively introduced in Brazil with the publication of Law No 9.787 in 1999, resulting from the Ministry of Health's objective to significantly reduce the costs of pharmacological therapy, stimulate commercial competition, and facilitate the population's access to drug treatment. In the same year, resolution No 391/1999 regarding the technical requirements for the registration of generics in Brazil was published.

The registration of generics will require pharmaceutical equivalence and bioequivalence studies to prove that the product is stable and therapeutically equivalent to the reference drug.
Resolution RDC No 73/2016 provides for post-registration changes and cancellation of drugs registration.

Registration Procedure for Generic Drug in Brazil

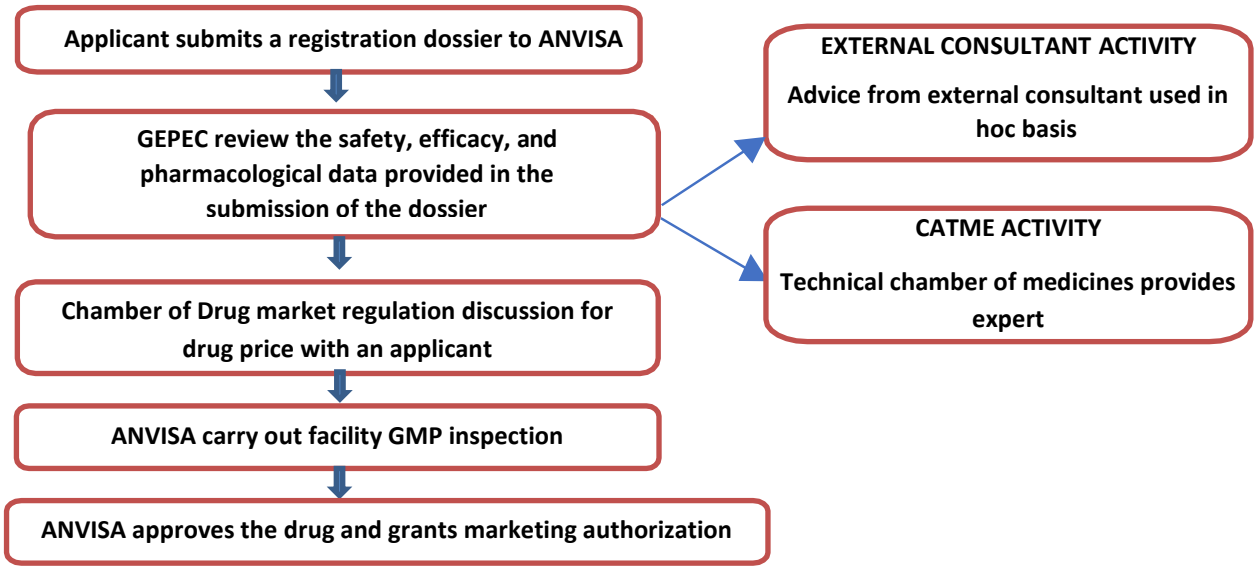

Figure 1. Flow chart for drug registration process in Brazil (7)

Regulatory Filing Process

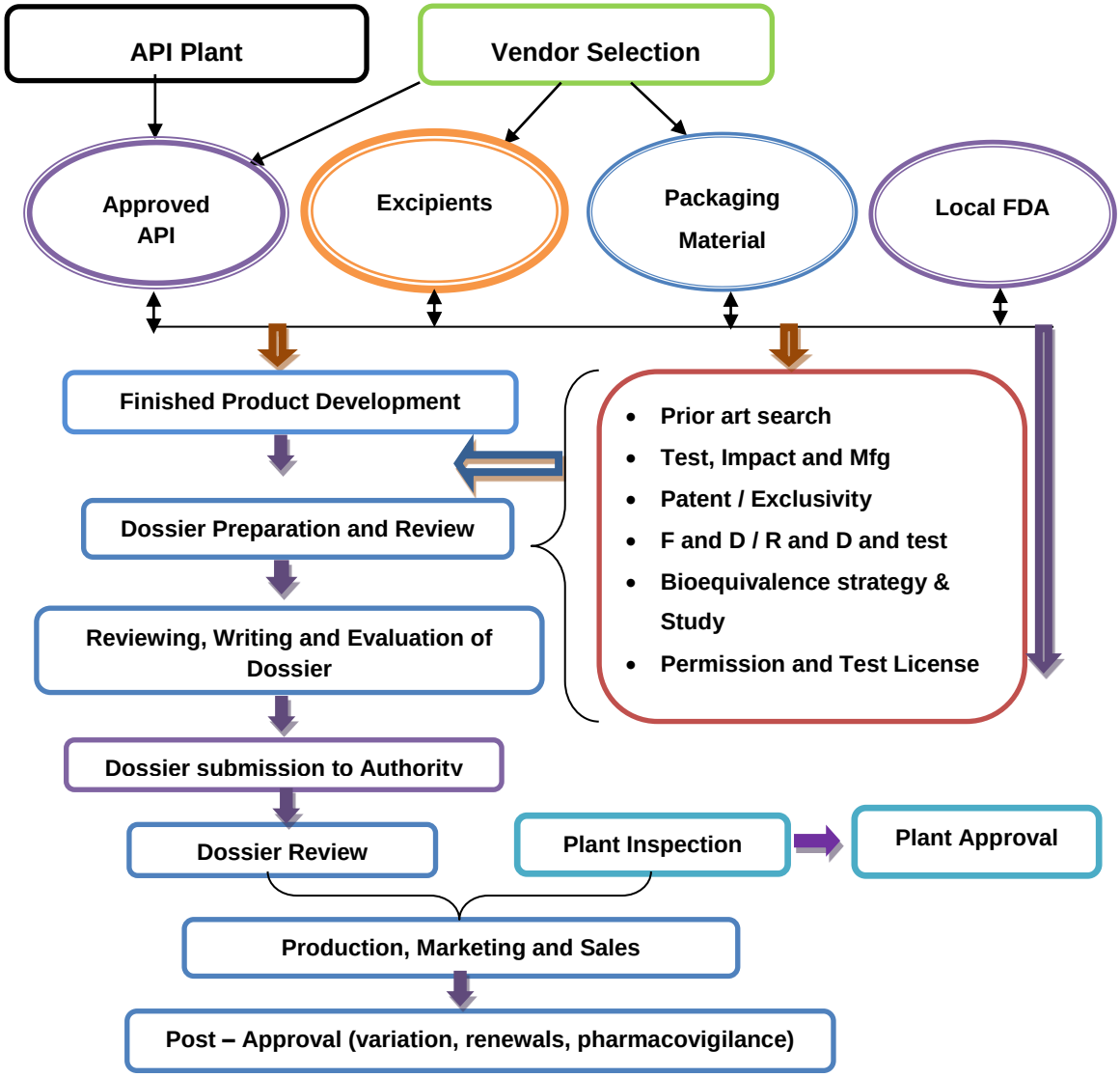

Figure 2. Regulatory Filing Process- Brazil (8)

3. Russia

Regulatory Authority

- State Regulatory Authority Federal Service on Supervision of Public Health Service and Social Department. It is also call **Roszdravnadzor.**
- National Centre of Nutrition
- National Center of Pharmaceutical Products Expertise **(FGU)**

Roszdravnadzor takes a choice to involve in the item and issues the registration certificate. The Russian government has human services issues for fitness of **ministry of healthcare and service development** and **federal service on healthcare and social development** supervision. The ministry of health has characterized for state's approach and issue regulatory medicinal services to identify with creation, quality, and dispersion in pharmaceuticals. The federal health service plays important role in control and supervisory function in this procedure.

Registration Procedure for Generic Drug in Russia

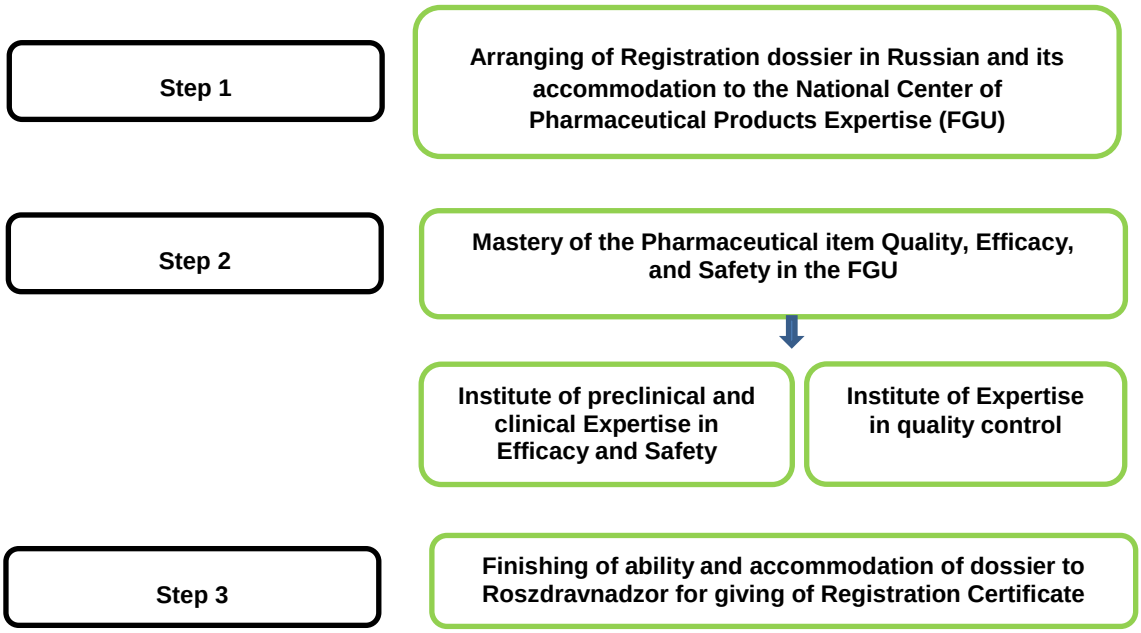

Figure 3. Flow chart for the drug registration process in Russia (9)

Approval process for Generic Drug in Russia

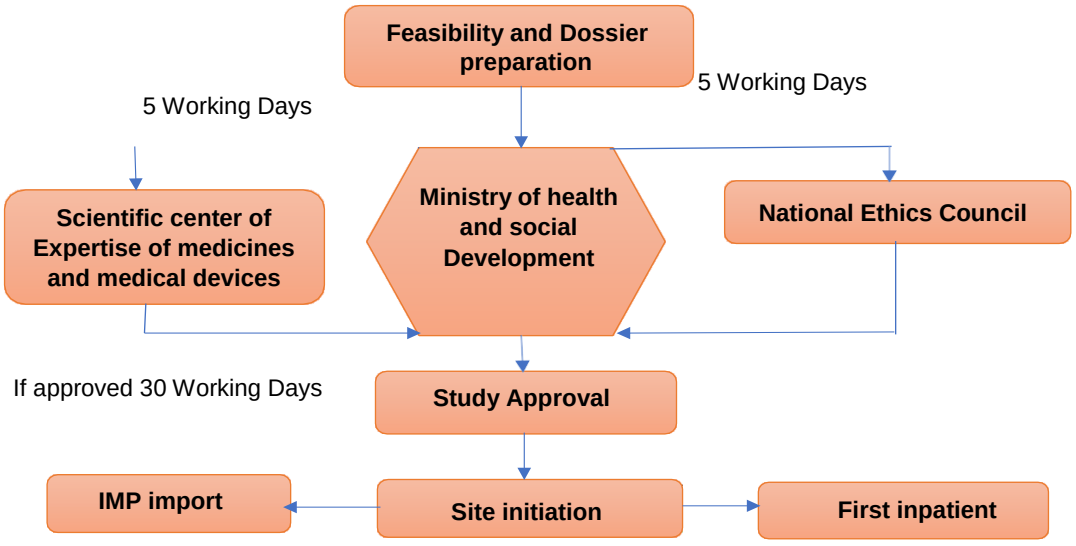

Figure 4. Flow chart for the drug Approval process in Russia (10)

Requirement for Registration of Drug

- Valid manufacturing license
- GMP certificate
- Power of Attorney
- Complete dossier of a drug in the Russian language
- Fees receipt of registration

Present this Information Must in the Russian Language *(11)*

- Trademark
- Data about Manufacture
- Country of Origin
- Composition
- Storage Condition Shelf life of drug

4. India

Regulatory Authority

Central Drugs Standard Control Organization **(CDSCO)**

The Pharmaceutical organization has a license for discharging new medicines in India. Significantly improved general approaches to remote ventures. To import a clinical device in India it is necessary required an import license. To prepare individual import helpful things in India also need to produce the registration certificate and import license. To get individual license needs for making an application for registration are allow within 60 days period. In this particular period, before the last date contraption has imported into the country. In India, import of clinical devices to take able underwriting authority is required. In this particular time, this application is expand to those devices, which are presently utilize and allow in the market.

Requirement for Registration of Drug *(12)*

Registration file represent all Documents and submit to CDSCO. It followed the ICH M4 CTD format. It contains five Modules.

- General information
- CTD summaries
- Quality Data
- Nonclinical Data
- Clinical Data

- If any company in India wants to manufacture or import a new drug, they need to apply to seek permission from the licensing authority (DCGI) by filing in Form 44 also submitting the data as given in Schedule Y of Drugs and Cosmetics Act 1940 and Rules 1945.To prove its efficacy and safety in Indian population they need to conduct clinical trials in accordance with the guidelines specified in Schedule Y and submit the report of such clinical trials in specified format.
- There's a provision in Rule-122A of Drug and Cosmetic Act 1940 and Rules 1945, that if the licensing authority finds out that if everything is in the interest of public health then he may allow the import of new drugs, based on the data of the trials done in other countries.
- Another provision is Rule-122A is that clinical trial may be allowed in any new drug case, which are approved and already being used for many years in other countries.
- Section 2.4(a) of Schedule Y of Drug and Cosmetic Act 1940 and Rules 1945 says for every drug which is discovered in India, will undergo all the phases of clinical trials.
- Section 2.4 (b) of Schedule Y of drug and cosmetic act 1940 and rules 1945 says for all the drugs which are undiscovered outside or in other countries except India, the applicant should submit all the documents or data from their or other countries or the other licensing authority may require the applicant to repeat all the studies or may provide a choice to proceed from phase 3 clinical trial.
- On overall, the exact requirements of the clinical trials keep on changing from case to case and also depend upon the satisfaction level of licensing authority about the safety and efficacy profile.
- All though the approval process of new drug in India is very complicated process, so it should meet necessary requirements related to NDA to FDA.

India's Central Drugs Standard Control Organization (CDSCO) issued a notice to all local State Drugs Controllers on 6 August 2014 (File No. QA/RI/NRA/ Compliance Report/63/14), setting uniform procedures on conducting GMP inspections of local pharmaceutical manufacturing facilities.

Local inspectors are to focus on the GMP requirements for establishing shelf life, validation studies and ensuring prompt recalls of noncompliant products when necessary. The inspection should last between two and five days (depending on the manufacturing site's size and complexity), and regulatory action is to be undertaken immediately in those cases where inspection observations uncover conditions that could compromise drug quality, safety, and efficacy.

CDSCO also states that the report of the inspection findings that prompted regulatory action should be finalized without delay at the end of the inspection.

In November 2017, an amendment to the inspection process was issued (F. No: 7-5/2017/DCG(l)/ MISC(099), Directorate General of Health Services, Office of Drug Controller General (India)). This regulation addresses joint inspections by the CDSCO and state drugs inspectors.

Registration Procedure for Generic drug in India

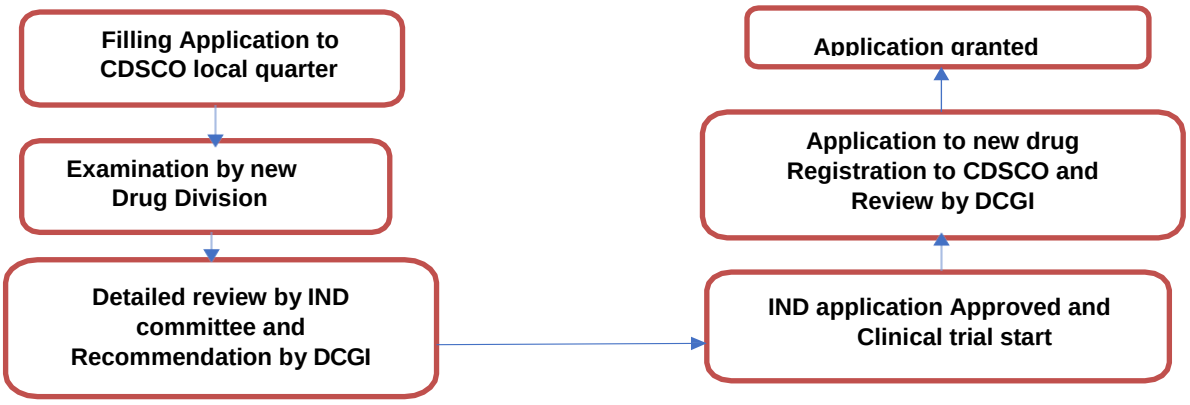

Figure 5. Flow chart for the drug Registration process in India (12)

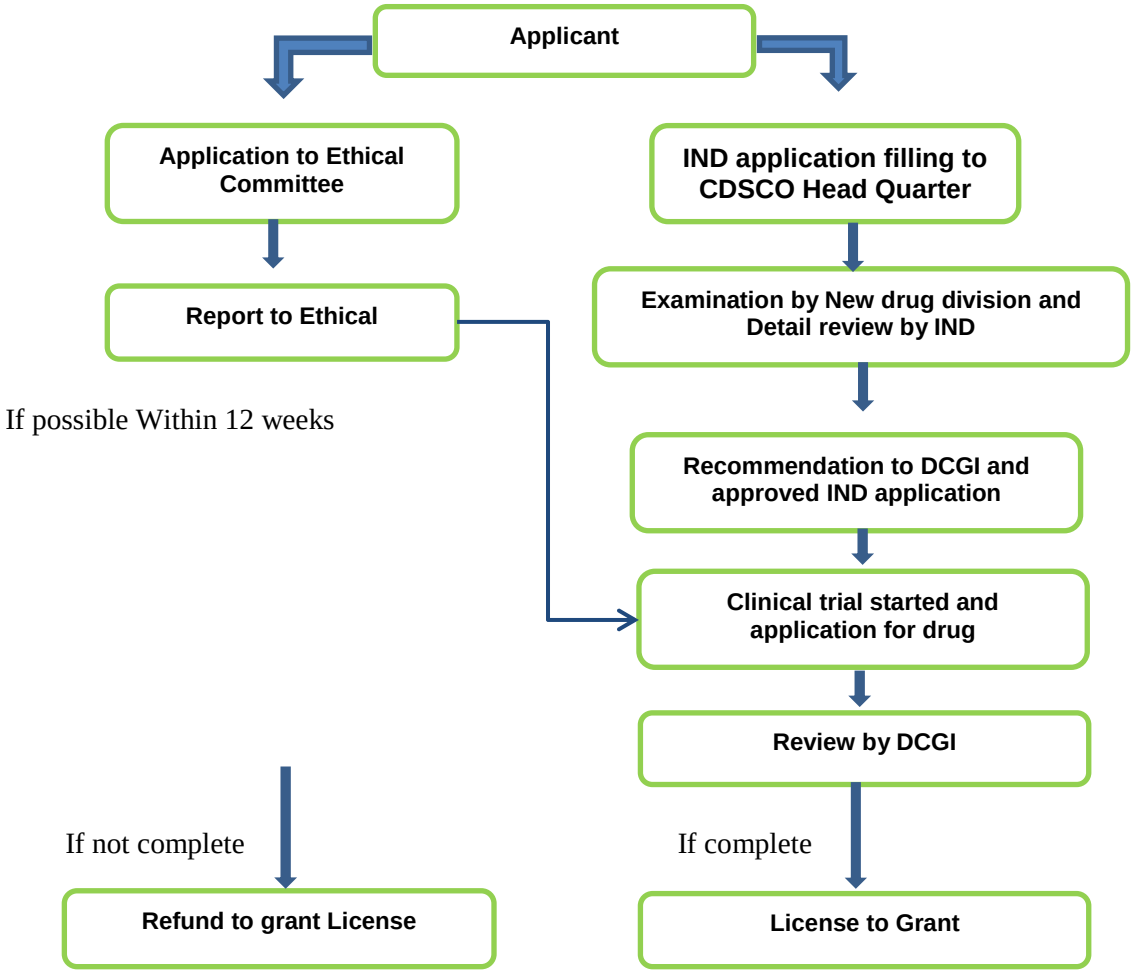

Figure 6. Flow chart for the drug Approval process in India (13,14)

5. China

Regulatory Authority:

- State Food and Drug Authority **(SFDA)**
- China Food and Drug Administration **(CFDA)**

To raising the ministerial level of agency regulatory body remark and rebuilt as the China Food and Drug Organization. The CFDA gathering supplanted an enormous for covering all controller with substance like FDA of US regulatory process for food and drug safety. CFDA is under the State Council of the people republic of China, which is comprehensive supervision in charge of the safety management of Food, Cosmetics, and Health Food and it is the complete authority of drug regulation in mainland China.

Approval Procedure for Generic Drug in China

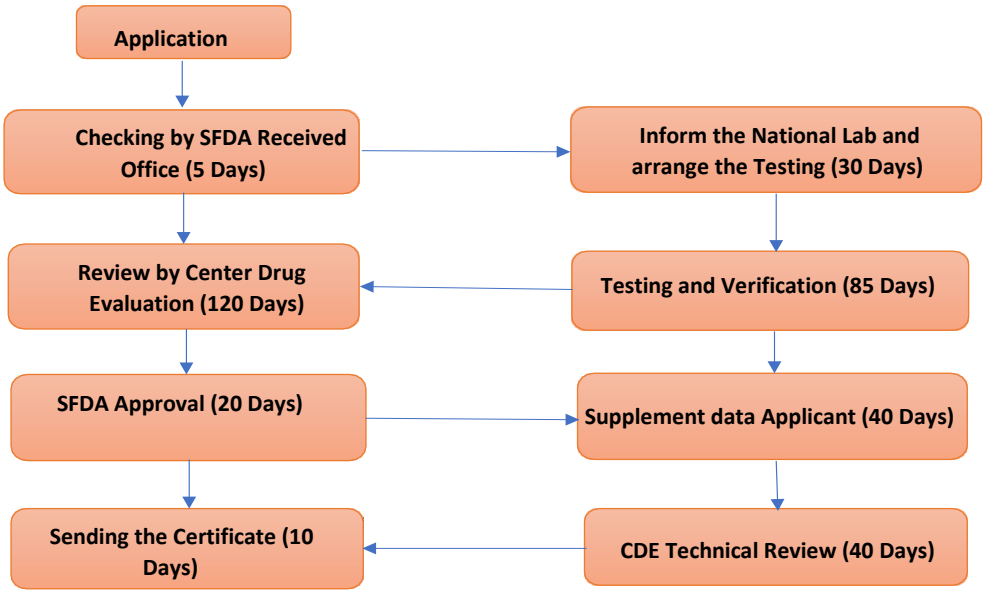

Figure 7. Flow chart for the drug Approval process in China (15)

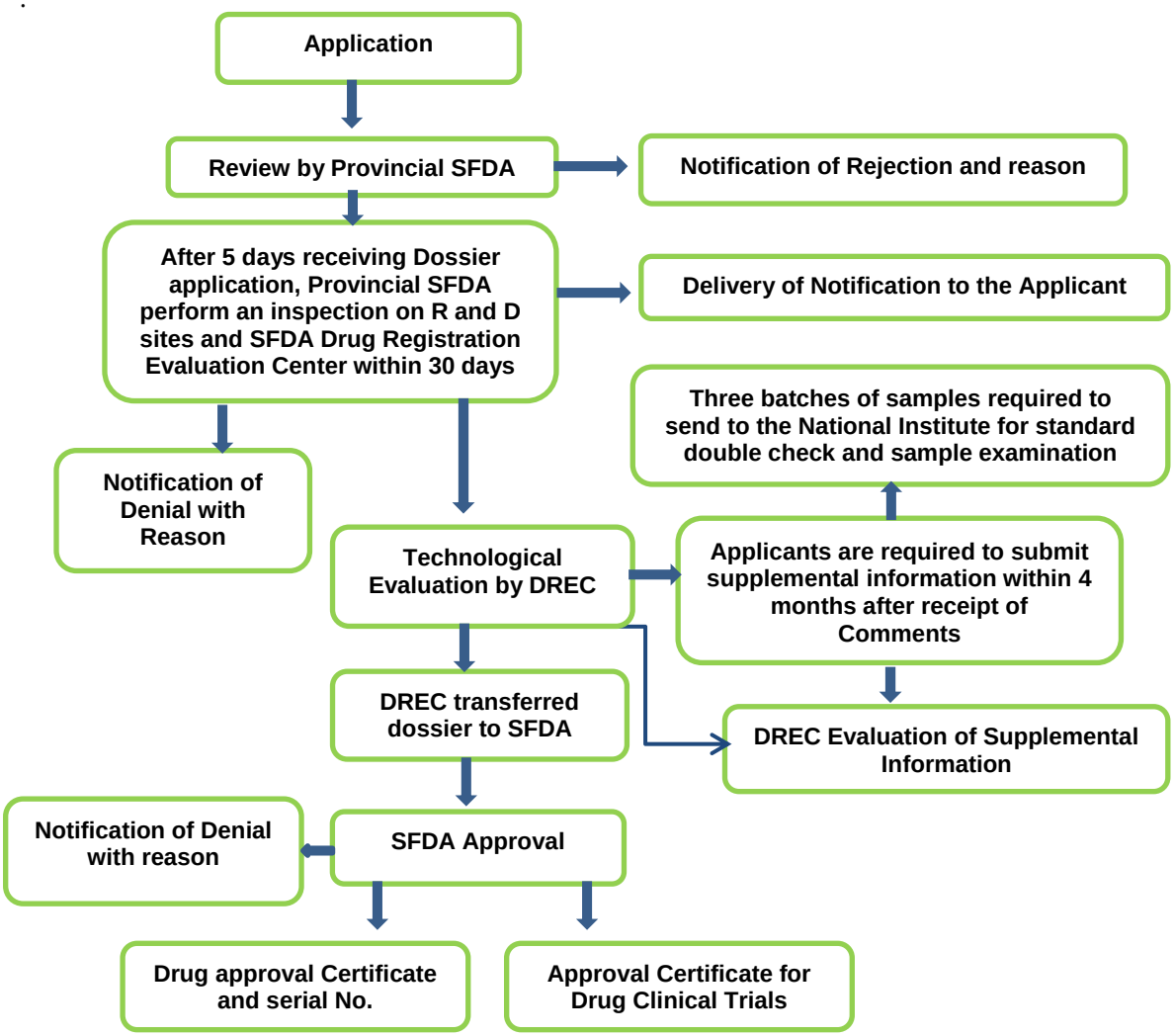

Figure 8. Flow chart for the drug Registration process in China

Requirement for Registration of Drug *(16)*

Registration file documents are submit to SFDA for registration and it allow ICH CTD format

Clinical study

In, Centre for drug evaluation will complete a survey of all test documentation that takes time 40 – 160 working days to completion and it is depending upon the product. When, the subject is on clinical trial or Bioequivalence to submit all survey Report CFDA for recommendation in China. If, CFDA are not consider in Clinical study is required in Examination lastly, the Application will enter in the final phase of registration

Requirement for Registration of Drug *(16)*

Registration file documents are required submit to SFDA for registration and it allow ICH CTD format.

- Administrative Information
- CTD summaries
- Quality Report
- Non-Clinical Report and Clinical Report

6. South Africa

Regulatory Authority

South Africa Health Products Authority ***(SAHPRA)***

It is responsible for the regulation of health products intended for human and animal use. Also licensing of manufacture, wholesalers, distributors of medicines, medical devices, radiation- emitting.

South Africa has developed medicines regulatory authority that is internationally recognized. The **Medicines Control Council (MCC)** is a statutory body that was establish in terms of medicines and related substance control act, 101 of 1965 to see regulation of medicines in South Africa. MCC is appointing by MOH and its main purpose is to protect and safeguard public health. MCC operates through an external expert who is members of committee structures. Experts are evaluating data submitted by any pharmaceutical industry for registration purposes. (17)

Requirement for the Registration procedure

- Administrative Information
- CTD Summaries
- Quality Data
- Non-clinical Data
- Clinical Data

Approval Procedure for Generic Drug in South Africa

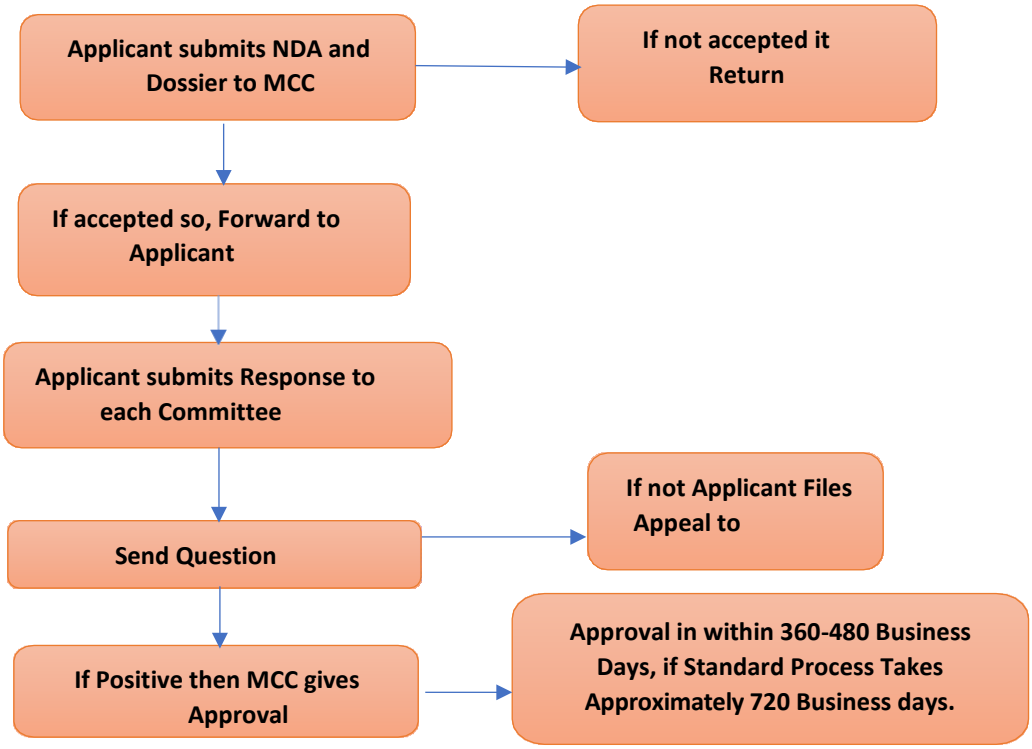

Figure 9. Flow chart for the drug Approval process in South Africa (18)

Registration procedure for Generic Drug in South Africa

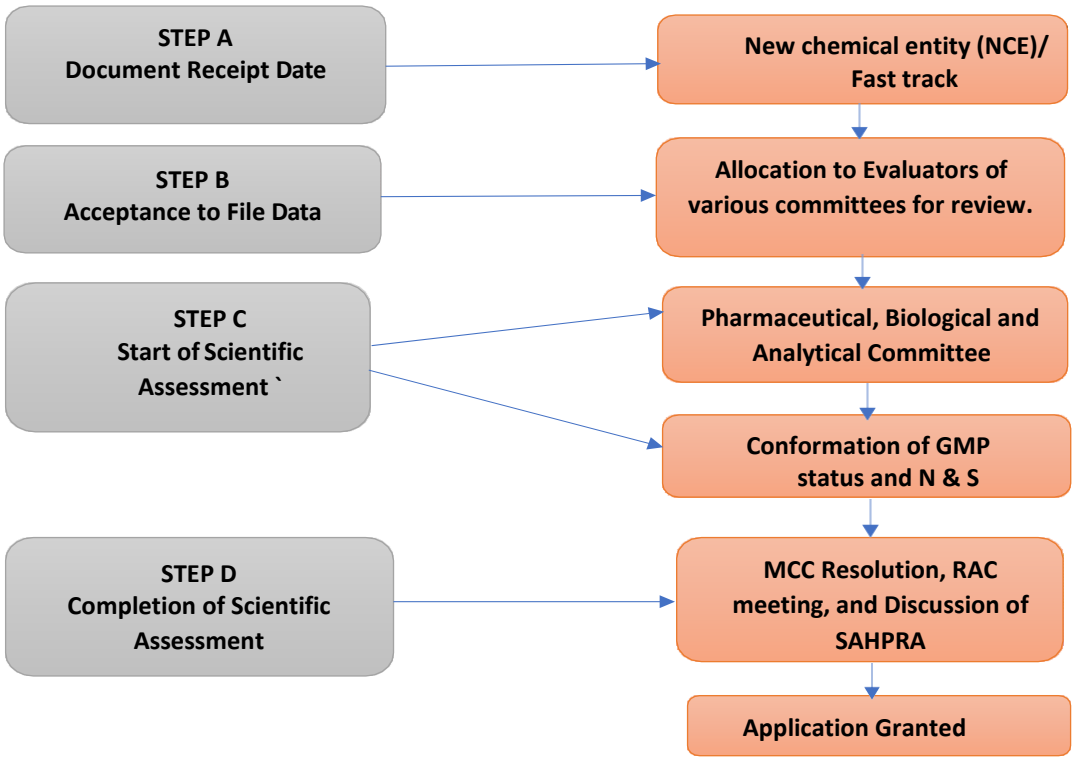

Figure 10. Flow chart for the Drug Registration process in South Africa (19)

Table 1. Difference Requirement for BRICS Countries (19)

Countries	Brazil	Russia	India	China	South Africa
Flag					
Drug Regulatory Authority (DRA)	ANVISA (Agencia Nacional de Vigilancia Sanitaria)	Roszdravnadz or (Federal Service on Healthcare and Social Development Supervision)	CDSCO (Central Drug Standard Control Organization)	SFDA (State Food and Drug Authority)	MCC (Medicines Control Council)
Drug Regulatory Law	Federal Law 6,360 of Sept. 23, 1976 and Amendments	Law on circulation of Medicines, 2010	Drug and Cosmetic Act, 1940 and Rules 1945	Drug Administration Law, 2001 and Regulation 2002.	The medicines and related substances control Act
Head of DRA	Director	Head	DCGI	Commissioner	Chairperson
Language	Portuguese	Russian	English	Chinese	English
Fees	2000 $	10000 $	1000 $	6600 $	3370 $
Validity	5 Years	5 Years	3 Years	5 Years	5 Years
Application Form	FP -1 and FP-2	Application for State registration of medicinal product (Form 11)	Form-44	Drug Registration application for review territory of the application in Form	6.01 MRFI
Timeline	6-8 Months	12-15 Months	6-12 Months	6-8 Months	8-12 Months

Administrative Content	Legal Aspects, Technical Aspects Quality Control Report on Raw material	Administrative Documents, Description of Pharmaceutical Properties	General Information, Common Technical Document Summaries	Administrative Information and Prescribing Information, CTD summaries	Administrative documents, CTD Summaries

7. Conclusion

The main purpose of this study was to compare Generic Drug Registration and Process to find out the difference, lacunae among the guidelines, Brazil, Russia, India, China, and South Africa are typically render "The BRICS Economies." In, above review article, it can be conduct that all clinical studies are report with related information regarding the Registration and Approval process of Generic drugs in these different Countries. It should provide necessary requirements also. Generally, drug approval process comprised mainly two steps, Application to conduct clinical trial and application to the regulatory authority for marketing authorization of drug. BRICS Countries are showing growth and directly increasing foreign investment by creating significant opportunities in pharmaceutical companies. It also describe Registration Cycle of generic drugs also provide Recommendation for application preparing a dossier for Registration of medicines for easy and fast track Marketing Authorization submission.

The registration of pharmaceutical medicines is a complex procedure that concludes the initial development phase for a new product. It takes variable amounts of time to traverse the requirements in different markets depending on the jurisdiction's legal evaluation requirements. However, there are common regulatory process aspects, such as a requirement for the sponsor to be a legal entity in the country, initial screening, evaluation, authority queries for sponsor clarification, advisory committee input, and the authority's final marketing approval decision.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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