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A Regulatory and Analytical Study on the Approval of Generic Drugs in India with a Survey of CDSCO Guillines Perceptions

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ABSTRACT: The goal of the study is to understand the process of approving generic drugs in India under the Drugs and Cosmetics Act of 1940 and the New Drugs and Clinical Trials (NDCT) Rules of 2019, managed by the Central Drugs Standard Control Organization (CDSCO). The research highlights key requirements for getting generic drug authorization, including quality standards, bioequivalence studies, Common Technical Document (CTD) dossier submission, relevant Clinical Trial (CT) forms, and post-approval obligations to ensure safety, effectiveness, and product consistency.

The research used a systematic review of official CDSCO guidelines, laws, regulatory notifications, and public approval data. Sofosbuvir, an antiviral drug for treating Hepatitis C, was chosen as an example to show how the approval process for generic drugs works in India, given its importance to public health and its patent situation. The analysis points out the classification, documentation needs, and bioequivalence expectations involved in approving generic drugs.

Additionally, a survey was conducted among professionals in the pharmaceutical industry and regulatory staff to evaluate the clarity, usability, and practical challenges of CDSCO guidelines. Survey results reveal interpretational and operational gaps that could impact regulatory compliance and approval times.

Overall, the study shows that India's regulatory system allows for the timely approval of high-quality generic medicines while keeping in line with international standards. It also identifies areas where clearer regulations and better processes could make the approval of generic drugs more efficient.

I. INTRODUCTION

The pharmaceutical industry plays a key role in improving global healthcare by providing access to safe, effective, and affordable medicines. Among the different types of pharmaceutical products, generic drugs are vital for making essential treatments available to a larger population. These medicines match their branded counterparts in dosage form, strength, route of administration, quality, performance characteristics, and intended use. They are sold once the patent for the original drug expires.

In India, the need for affordable medicines has increased significantly, making the production and approval of generic drugs an important part of the healthcare system. India has gained the name "PHARMACY OF THE WORLD" for supplying low-cost, high-quality generic medicines to both domestic and international markets. The Central Drugs Standard Control Organization (CDSCO), which operates under the Ministry of Health and Family Welfare, is responsible for ensuring that all drugs, including generics, meet quality, safety, and effectiveness standards according to the Drugs and Cosmetics Act of 1940 and related rules.

The approval of generic drugs in India follows a clear regulatory process that includes assessing bioequivalence, stability, and quality assurance data, along with compliance with good manufacturing practices (GMP). This process ensures that generic medicines meet the same therapeutic standards as innovator drugs, maintaining patient trust and clinical effectiveness.

One notable example of successful implementation of India's generic drug policy is Sofosbuvir, a direct-acting antiviral used to treat chronic Hepatitis C virus (HCV) infection. The

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introduction of its generic versions has significantly lowered treatment costs, improved patient access, and shown India's ability to meet both domestic and international regulatory standard.

This study aims to understand the existing regulatory framework, approval process, and analytical evaluation methods involved in the authorization of generic drugs.

SCOPE OF STUDY

→ The scope of the study focuses on understanding and analyzing the regulatory framework involved in the approval of generic drugs in India.
→ Studying analytical testing requirements for generic drugs.
→ Evaluating the case of Sofosbuvir as an example of successful generic approval and market authorization.
→ (The study does not include clinical trial data collection, laboratory testing, or primary research; instead, it is based on secondary data analysis, review of guidelines, and regulatory documentation.

GENERIC DRUGS

Generic drugs are pharmaceutical products intended to be interchangeable with innovator or reference drugs after patent expiration. They contain the same active pharmaceutical ingredient (API), strength, dosage form, route of administration, and therapeutic use as the original product, although they may differ in appearance or excipients.

Unlike innovator drugs, generic drugs do not require extensive clinical trials; instead, they must demonstrate bioequivalence to ensure similar safety and efficacy. Regulatory authorities enforce strict quality standards, Good Manufacturing Practices (GMP), and bioequivalence requirements before approval.

In countries like India, generic drugs play a crucial role in improving access to affordable healthcare and supporting public health systems. Their approval is regulated by the Central Drugs Standard Control Organization (CDSCO) under the Drugs and Cosmetics Act, 1940 and the New Drugs and Clinical Trials Rules, 2019. Despite a simplified development process, the regulatory pathway remains structured and requires strict compliance for successful market entry.

REGULATORY FRAMEWORK

The regulatory framework of generic drugs in India consists of laws, authorities, and procedures established by the government to ensure medicines are **s**afe, effective, and of goodquality. It aims to balance public health protection with affordable access to medicines. India follows a dual regulatory system, where the central government sets laws and standards, and state governments handle implementation**,** licensing, inspection, and enforcement.

DRUGS AND COSMETICS

- The Drugs and Cosmetics Act (1940) and its 1945 Rules form the primary legal framework for the pharmaceutical industry in India. Its main purpose is to ensure that all drugs and cosmetics are safe, effective, and meet high-quality standards.
- Schedule M: Good Manufacturing Practice.
- Schedule Y: Requirements for Clinical Trails and New Drugs.
- Schedule D: Exemptions for Certain Categories of Drugs.
- Schedule C and C1: Biological and Special Products.
- Schedule H, H1and X: Prescription Drug Control.

Ministry of Health and Family Welfare (MoHFW)

Isthe main organization in charge of creating health policies and managing the drug and Cosmetics act. It supervises all regulatory bodies related to drug regulations. The main functions of (MoHFW) are policy formulation, legislative amendments, international regulatory cooperation, and oversight of CDSCO.

Central drug standard control organization (CDSCO)

CDSCO is the national regulatory authority of India for drugs, medical devices, cosmetics and clinical trials. It operates under (DGHS) directorate general of health service, ministry of health and family welfare, government of India headquartered in new Delhi, its work in co-ordination with state licensing authorities (SLAs) to regulate drug quality, safety and efficacy throughout the country.

Organization of CDSCO:

a) Central level

- Headed by DCGI.
- Located at CDSCO headquarters in New Delhi.
- It works under the directorate general of health services (DGHS).

b)Zonal offices:

- CDSCO has zonal offices in major cities to control drugs quality and imports.

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C) Sub zonal offices:

- Assist zonal offices in inspections and enforcement.

D) Port offices:

- Located at airports and sea-ports to regulate the generic drugs and cosmetics.

Drugs controller general of India (DCGI)

The Drugs Controller General of India (DCGI) is the national authority responsible for regulating drugs and medical devices in India. It functions under the Central Drugs Standard Control Organization (CDSCO) and operates under the Drugs and Cosmetics Act, 1940 and Rules, 1945.The DCGI is the final approving authority for generic drugs at the central level, and its decisions apply across all states and union territories. Its main responsibilities include approval of new and generic drugs, permission for bioequivalence studies and clinical trials, evaluation of safety, efficacy and quality, regulation of imported drugs, and ensuring compliance with regulatory standards.

Subject Expert Committee

SECsconsist of domain experts who evaluate applications related to new drugs, bioequivalence, and clinical trial proposals. They assess scientific data from bioequivalence studies and make recommendations to the DCGI for approval or rejection.

New Drugs and Clinical Trials Rules, 2019 The NDCT Rules, 2019 provide a framework for drug regulation in India, covering licensing, ethics, BA/BE studies, and clinical trials.

They include 13 chapters, 107 rules, and 8 schedules, and introduce a transparent, time-bound approach for generic drug approval.

Updated clinical trials forms according to NDCT rules 2019

FORM NO:	APPLICABILITY
CT-01	Application for registration or renewal of ethics committee relating to clinical trial or BA/BE study or biomedical health research.
CT-02	Grant for registration of ethics committee relating to clinical trial or BA/BE studies.
CT-16	Application for the grant of license to import new drug or investigational new drug for the purpose of clinical trial or BA/BE study or for examination test or analysis.
CT-17	License to import new drug or investigational new drug for the purpose of clinical trial or BA/BE study or for examination test or analysis.
CT-05	Application for the grant of permission to conduct BA/BE study
CT-07	Permission to conduct BA/BE study
CT-08	Application for grant of BA/BE study Centre
CT-09-	Grant of registration of BA/BE study Centre
CT-10	Application for permission to manufacture new drug for BA/BE study
CT-11	Permission to manufacture new drug for BA/BE study
CT-21	Application for market authorization
CT-23	Issuance of MAA

APPLICATION FEES FOR LICENCE

Types ofapplication	2019 fees structure (INR)	Old fees structure (INR)
1)Bioavailability bioequivalence	2,00,000	25,000 (drugs approval within 1 year) 15,000 (drugs between 1-4 years).
2)Registration for BA/BEstudies.	5,00,000	No fees.
3)Reconsideration of a) Clinical trials application. b)BA/BE study application. c)BA/BE study center application.	50,000 50,000 1,00,000	No fees No fees No fees

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II)STATE LICENCING AUTHORITY:

The state licensing authority (SLA), headed by state drug controller is responsibility for the issuing manufacturing and sales licenses for the new drugs, generic drugs.

Functions of state licensing authority:

a) granting of license:

s. No:	SERVICE NAME	APPLICATION FORM NAME	LICENSE FORM NAME
1.	Application for the grant of license of manufacture for sale are for distribution of drugs specified in schedule x and not specified in schedule C and C1.	FORM-24F	FORM-25F
2.	Application for grant of license to manufacture for sale or for distribution of drugs specified in schedules C and C1 excluding those specified in part XB and schedule X.	FORM-27	FORM-28
3.	Application for grant of license to manufacture for sale or for distribution of drugs others then those specified in schedules C, C1and X.	FORM-24	FORM-25
4.	Application for grant of a loan license to manufacture for sale or distribution of drugs specified in schedules C,C1 and X.	FORM-27B	FORM-28B
5.	Application for grant of a loan license to manufacture for sale or for distribution of drugs other than those specified in schedule C,C1 and X.	FORM-24B	FORM-25A
6.	Application grant for the loan license to manufacture for sale or for distribution of drugs specified in schedule C and C1 excluding those specified in part XB and schedule X	FORM-27A	FORM-28AA
7.	Application for grant of license to repack for sale or distribution of drugs, being drugs others hen those specified in schedules C and C1 excluding those specified in schedule X	FORM-24B	FORM-28B

Ethics committees (ECs)

Ethics Committees play an independent role in the regulation of generic drugs involving bioequivalence or clinical studies.

Their main function is to protect the rights, safety, and well-being of participants.

As per NDCT Rules, 2019, ECs must be registered with CDSCO, and prior approval is required before starting any bioequivalence or clinical study.

DRUG PRICE CONTROL ORDER (DPCO)

The DPCO is a government order issued under the Essential Commodities Act ,1955. Its purpose is to make sure essential medicines are available at low prices. Generic drugs listed in the National List of Essential Medicine (NLEM) are regulated by the DPCO. Key provisions relevant to generic drugs are Setting ceiling prices for scheduled formulations, Required compliance by manufacturers and marketers, Regulation of trade margins, Monitoring of overcharging and price increases.

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NATIONAL PHARMACEUTICAL PRICING AUTHORITY(NPPA)

The National Pharmaceutical Pricing Authority (NPPA) is an independent regulatory body functioning under the Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, Government of India.

PHARMACOVIGILANCE AND POST-MARKETING AUTHORITY

Pharmacovigilance is an important part of the regulatory framework. It enforces Adverse Drug Reaction (ADR) reporting, Risk management systems, Periodic Safety Update Reports (PSURs), and Market recall procedures. The Pharmacovigilance Programmed of India (PvPI) manages safety monitoring across the country.

REGULATORY REQUIREMENTS

ELIGIBILITY CRITERIA FOR GENERIC DRUG APPROVAL

Generic drug approval is granted by the Central Drugs Standard Control Organization (CDSCO) based on pharmaceutical equivalence and bioequivalence without full clinical trials. The drug must match the reference product and meet key criteria such as prior approval, patent clearance, valid manufacturing license under the Drugs and Cosmetics Act, 1940, and compliance with Schedule M (GMP) standards.

i. The drug substance and dosage form must already have approval in India or another country.
ii. Patent and exclusivity issues must be sorted out.
iii. The manufacturer must have a valid manufacturing license.
iv. The manufacturing facility must meet scheduled M (GMP) standards.

DOSSIER SUBMISSION REQUIREMENTS

CTD modules: document checklist for CDSCO submission:

CTD MODULES	CONTENT
MODULE-I	Administrative and legal details. Includes: Form 44, cover letter, GMP certificates, proposed labeling, import license copy (if applicable).
MODULE-II	High-level summaries. Covers pharma overview, non-clinical data, and clinical trial summaries. Helps reviewers scan the full application quickly.
MODULE-III	Quality and manufacturing data. Includes API details, excipient specs, batch records, formulation process, and long-term stability studies.
MODULE-IV	Preclinical data. Includes animal studies, pharmacology, toxicology, PK/PD profiles, and supporting literature.
MODULE-V	Clinical trial data (Phases I-IV). Includes study protocols, raw data, analysis, adverse events, and investigator brochures.

The Common Technical Document (CTD) Triangle

BIOEQUAVELENCESTUDYREQUIREMENTS

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BIO AVAILABILITY

Refers to the rate and extent at which amount of drug that get absorbed from the administered dosage form into the systemic circulation and becomes available at the site of action.

BIO EQUIVALENCE

BE of a drug product is achieved when there is no significant difference in rate and extent of absorption from that of reference product.

- Both In vivo and In vitro methods are used depending on the product type.
- The ministry of health estimates that about 5% of drugs in India are counterfeit and roughly 0.3% are labelled as spurious.

NECESSITY AND REQUIREMENTS OF BIOEQUIVALENCE STUDIES AND THEIR TYPES

A) In vivo Studies

It is especially important to document the bioequivalence of a specific dosage form in vivo, whether through a bioequivalence study, a comparative clinical pharmacodynamic study, or a comparative clinical trial. these include:

a) The following are the criteria for immediate release oral formulation that act systematically:

- Assured therapeutic response indicated for serious condition.
- therapeutic window which is narrow / safety margin; steep dose- response curve.
- Nonlinear PK, >70% first-pass metabolism, variable-affected pharmacokinetics, incomplete absorption, or absorption window.
- Low solubility, meta-stable modifications, and weak permeability are examples of unfavourable physicochemical properties.
- In case of high proportion of inactive substance to active substance.

B) Non-oral and non-parenteral drug formulations with the goal of acting via absorbed by systemic circulation (such as transdermal patches).

c) Systemic absorption is the mechanism by which sustained or modified release dosage forms work.

d) Fixed dose combination products work through systemic absorption.

e) pharmaceutical products that are not in the form of a solution and are intended for non-systemic use and absorption. In these situations, the concept of bioequivalence is inapplicable, and equivalence must be. demonstrated through comparative clinical or pharmacodynamics studies to access unintended partial absorption, drug concentration measurements are required.

Documentation of bioequivalence is also required to establish a link between, Formulations for early and late clinical trials, pharmaceutical formulations used in clinical trials, Clinical trial formulations and drug products that will be marketed and Other appropriate comparisons.

B) In vitro studies:

These are the condition where in vitro testing of dissolution is used to evaluate equivalence:

a. All the following criteria will support the data submitted by applicant for his drug:

- In 250ml at 37°C the oral dose may absorb by 90% of an aqueous media with a pH range of 1-7.5., as measured in comparison to an intravenous reference dose.
- Dissolution speed, as demonstrated by more than 80% dissolution within 15 miles
- The composition in terms of quality the strengths are principally the same;
- The ratio of active ingredients to inactive substance is roughly the same across strengths, or the ratio of inactive substance is similar in the instance of minor strengths.

The product quality and performance features are ensured by in vitro dissolution testing carried out after the minor formulation or manufacturing changes have been approved.

GENERIC DRUG APPROVAL PROCEDURE IN INDIA

BE-NOC:

BE-NOC is a No Objection Certificate issued to allow bioequivalence studies in human subjects.

To conduct BE studies, companies must submit documents such as the study protocol, EC registration, BA/BE centre approval, required application forms, and other supporting details.

Applications for test licences for import or studies must include the BE protocol. For new drugs, a BE-NOC is required, while for old drugs, regulatory approval details in India must be provided.

BE-NOC APPLICATION

1. Applications for BE NOC for export of new molecule not approved in India but approved in other countries.
2. Application for BE NOC for export of new drugs approved in India within period of 1 year.
3. Application for BE NOC for export of new drug approved within period of >1 year and <4 years.
4. Application for BE NOC for export of a drug product in modified release form.

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5. Application for test license for BA/BE study of old drugs.

GOOD MANUFACTURING PRACTICE COMPLIANCE

A) Ensuring bioequivalence:Generic drugs must demonstrate bioequivalence to their brand- name counterparts, which requires precise manufacturing processes.

B) Maintaining quality: GMP practice ensure that products meet the same quality standards as the original drugs.

C)Regulatory approval: Compliance with GMP standards is mandatory for obtaining and maintaining regulatory approvals from agencies like the FDA, EMA, AND WHO.

D)MARKET COMPETITIVENESS: High quality products enhance brand reputation and competitiveness in the generic drug market.

Key good manufacturing process requires for generic drug manufactures.

1. Process validation.
2. Quality control and assurance.
3. Documentation and traceability.
4. Facility and equipment maintenance.
5. Training and competency development.

STABILITY STUDY REQUIREMENTS

BE-NOC is a certificate that allows companies to conduct bioequivalence studies in human subjects.

To obtain it, firms must submit the study protocol, EC registration, BA/BE centre approval, and required documents.

It is required for new drugs, while for old drugs, existing regulatory approval details must be provided.

Storage condition for stability testing

Study type	Temp:	Relative humidity	Minimum duration
Long term study	30℃ ± 2℃	75% ± 5% RH	12 months
Intermediate study	30℃ ± 2℃	65% ± 5% RH	6 months
Accelerated study	40℃ ± 2℃	75% ± 5% RH	6 months

LABELLING REQUIREMENTS

Labelling rules ensure medicines provide clear and accurate information for safe use.Primary labels include drug name, ingredients, strength, dosage form, and batch number, while secondary labels cover storage, expiry, warnings, and usage instructions.Proper labelling is mandatory, as errors can delay approval and require correction.

PACKINGING REGULATION

Packaging regulations ensure that pharmaceutical products are protected from contamination, damage, and environmental factors during storage and transport.

They require suitable materials, child-resistant features for certain products, and traceability elements like barcodes or serial numbers.

All packaging must follow GMP to maintain product quality, safety, and effectiveness.

Post approval regulatory requirements

a) Pharmacovigilance:

Marketing Authorization Holders must monitor and report adverse drug reactions (ADRs) to CDSCO as part of the Pharmacovigilance Programme of India (PvPI).

b) Post-Marketing Surveillance (Phase IV):

In some cases, additional safety or efficacy studies may be needed after approval.

c) Variation and Change Management:

Any changes in:

- Manufacturing site
- Formulation
- Labelling
- Packaging
- Shelf life

must be approved by the regulatory authority before implementation.

d) Periodic Safety Update Reports (PSUR)

PSURs must be submitted regularly for newly approved drugs to ensure ongoing safety monitoring.

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e) Renewal of Licence

Manufacturing and import licenses must be renewed according to set timelines. Failure to comply with post-approval requirements may lead to suspension, cancellation of licenses, or legal penalties.

APPROVAL PATHWAY OF GENERIC DRUGS IN INDIA

PRE-SUBMISSION REGULATORY ASSESMENT

1. **Permission for bioequivalence-**For most generic drugs, bioequivalence (BE) studies are required to prove similarity with the reference drug. The process includes submitting the BE study protocol to CDSCO through the SUGAM portal, applying in Form CT-04, followed by review and approval by DCGI, along with approval of the study site and investigator.BE studies can be conducted only after receiving permission from DCGI.

2. **EC approval-**Parallel to obtaining DCGI permission, the applicant must get approval from a CDSCO- registered EC. The EC is responsible for – reviewing this study protocol and assessing the risks benefits, Approving informed consent documents, overseeing subject safety and composition and reviewing serious adverse events (SAES). Approval from the EC is a mandatory requirement before starting the BE studies.

3. **Conduct of BE study-**The approved BE studies take place at CDSCO approved BE centres and following Good Clinical Practice (GCP). The main activities involve, subject recruitment and informed consent, administration of test and reference products, sample collection and bioanalysis and pharmacokinetic and statistical analysis. The study must show equivalence of Cmax and AUC parameters within the acceptance range of 80-125 percent.
4. **Preparation of regulatory dossier-** upon completing the BE study we prepare a regulatory dossier in CTD format. The accuracy and completeness of the dossier and essential for regulatory acceptance.

- Module 1: Administrative documents.
- Module 2: quality summaries.
- Module 3: complete CMC data for API and finished products.
- Module 4: nonclinical literature and waiver justification.
- Module 5: bioequivalence study.

5. **Submission of applicant to CDSCO-**The applicant submits the complete application through the CDSCO SUGAM portal. This submission includes appropriate application from CT -21, CT-23, or Form 44), CTD dossier, prescribed fees, supporting certificates and undertaking. Electronic submission ensures traceability and transparency in the review process.
6. **Technical and scientific review by CDSCO-**Following submission, CDSCO conducts a through technical review. The review activities involve the evaluation of quality (CMC) data, assessment of BE study results, verification of GMP compliance, identification of deficiencies or clarification. If deficiency letters are issued, the applicant must address them within the required timeline.
7. **Evaluation by subject expert committee (SEC)-**Applications needing the expert input are send to the SEC. their responsibility includes, evaluation of BE data, assessment of risk- benefits profile- recommendation for approval, rejection are additional data. SEC recommendations form the basis for DCGI's regulatory decision.
8. **Grant of marker authorization by DCGI-**Based on the CDSCO review and SEC recommendation, the DCGI either grants or rejects marketing authorization. Approval includes permission to Manufacture or import the generic drug, labelling and package insert, conditions for post approval compliance. This approval is valid across the country and is binding on all state licensing authorities.
9. **Grant of manufacture license by SLA-**After receiving the central approval, the manufacturer applies to the SLA state level requirements includes submission of DCGI approval letter, inspection of the manufacturing facility, verification of schedule M compliance, once everything is stationary, the SLA grants the manufacturing licence. This allows for commercial production.
10. **Market launch and distribution-**Once all licenses are obtained, the generic drugs can be introduced in the market. The requirements for this include compliance with labelling and packing regulations, adherence to price control regulation (DPCO) and distribution through authorized channel only should take place.
11. **Post marketing surveillance and pharmacovigilance-**Post approval, the

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manufacture must keep monitoring the safety of the generic drugs. Their action should involve, reporting ADR, submitting periodic safety update reports (PSURSs) managing risks, recalling the drug pharmacovigilance program of India (PVPI).

12. **Post approval changes and variations-**Any changes to the approval product or process must go through regulatory variations. The changes may include, manufacturing site or process exchange, formulation or packaging modification, labelling update, etc. depending on the type of change, you may need prior approval from CDSCO.
13. **Renewal, compliance and enforcement –** Manufacturing licence and approval need to be renewal and maintained for compliance. Regulatory authorities may conduct routine or for cause inspection, suspend /cancel license for noncompliance and they can take legal action under Drugs and Cosmetics Act.

GENERIC CLASSIFIED AS 'NEW DRUG' (WITH IN 4 YEARS OF 1ST

IF GENERIC IS NOT CLASSIFIED AS 'NEW DRUG' IN NDCTR 2019 (AFTER 4 YEARS FROM 1ST APPROVAL IN INDIA):

ILLUSTRATION OF GENERIC DRUG APPROVAL PROCESS (SOFOSBUVIR)

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I)PATENT HISTORY OF SOFOSBUVIR

Discovery of sofosbuvir (2007)

Sofosbuvir was discovered in 2007 by scientist Michael J. Sofia at the biotechnology company Pharmasset. The drug was developed as a direct-acting antiviral for treating Hepatitis C virus (HCV) infection. It works by blocking the NS5B RNA polymerase enzyme of the hepatitis C virus, which prevents the virus from replicating.

Acquisition of Pharmasset by Gilead (2011)

In 2011, Gilead Sciences purchased Pharmasset for about $11 billion. This purchase gave Gilead the rights to develop and sell Sofosbuvir worldwide. After the buyout, Gilead sped up the clinical development and approval process for the drug.

Regulatory Approval in the United States (2013)

In December 2013, the U.S. Food and Drug Administration approved the drug under the brand name Sovaldi for treating chronic hepatitis C infection. This approval was a major milestone in hepatitis C treatment. Sofosbuvir enabled shorter treatment times and better cure rates than earlier therapies.

Patent Application in India (2014)

Gilead Sciences filed an application for patenting Sofosbuvir in India with the Indian Patent Office in July 2014. If Gilead Sciences had been granted the patent for Sofosbuvir, it would have had exclusive rights over the sale of Sofosbuvir in India, which would have barred other pharmaceutical companies from manufacturing its generics.

Pre-Grant Opposition by Public Health Groups (2013-2014)

Several organizations opposed the patenting of Sofosbuvir through pre-grant opposition, including Natco Pharma, I-MAK, and the Delhi Network of Positive People.

They argued that Sofosbuvir did not meet patentability criteria under Section 3(d) of the Indian Patents Act, 1970.

Section 3(d) prevents evergreening by restricting patents for minor modifications of existing drugs.

Rejection of Patent by Indian Patent Office (January 2015)

The Indian Patent Office rejected the patent application of Gilead Sciences in January 2015. This rejection was based on Section 3(d) of the Indian Patent Act of 1970, which states that a new form of a known compound needs to show a significant enhancement in therapeutic efficacy to be considered for a patent. The patent office found that the changes in the Sofosbuvir compound did not show a significant enhancement in therapeutic efficacy over previous compounds.

Appeal by Gilead in the Delhi High Court (2015)

Gilead Sciences, after being rejected, decided to appeal in the Delhi High Court, questioning the decision of the Indian Patent Office. The High Court directed the patent office to review the application, allowing Gilead to put forward additional arguments in support of their patent application.

Voluntary Licensing to Indian Generic Companies (2014-2015)

Gilead had entered into voluntary licensing agreements with various generic companies in India even before the final decision regarding patents. The generic companies were allowed to distribute and produce generic forms of Sofosbuvir in various developing countries. It was mandatory for the generic companies to pay a royalty of around 7% to Gilead.

Entry of Generic Sofosbuvir in India

When India rejected the patent and set up voluntary licensing deals, local drug companies jumped in and started making cheap generic Sofosbuvir. Suddenly, the price of hepatitis C treatment dropped— not just in India, but in a lot of other countries too. Just to give you an idea: In the US, a 12-week course was about $84,000. Indian generics slashed that price all the way down to around $100 for the whole treatment.

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II)APPROVAL PATHWAY OF GENERIC SOFOSBUVIR IN INDIA (NATCO PHARMA)

III)Price Reduction and Public Health Impact of Generic Sofosbuvir in India

- The introduction of generics of Sofosbuvir in India had a strong impact on public health in India. The original branded drug Sovaldi, developed by Gilead Sciences, was initially priced at about $84,000 for a 12-week treatment regimen when it was first introduced in the United States. The high price of this drug made it inaccessible to most patients, particularly in low- and middle-income countries.
- The price of Sofosbuvir decreased dramatically after the entry of generic companies in India, including Natco Pharma. The generic companies launched their products at a price of $300-$900 for a complete regimen, a decrease of more than 95 percent from the original price of the drug.
- The availability of cheap generic drugs like Sofosbuvir also helped in increasing access to hepatitis C treatment. People who could not afford the drugs earlier are now able to access the drugs with the help of government schemes, hospitals, and other public health programs. Also, India has become a key supplier of generic drugs like Sofosbuvir to many developing countries, thereby increasing access to life-saving drugs for hepatitis C infection.
- Thus, the lowering of prices because of the availability of generic drugs like Sofosbuvir reflects the contribution of India's pharmaceutical industry in promoting public health.

II. METHODOLOGY

1)Study design

The study examines the regulatory approval pathway of generic drugs in India, supported by survey- based analysis to understand practical regulatory perspectives.

2)Sources of data

Primary data: Prinary data were collected through a structured questionnaire administered via Google Form to pharmaceutical and regulatory professionals**.**

Secondary data: These are obtained from CDSCO guidelines and notification, Drugs and Cosmetics Act and Rules, published research articles and regulatory reports.

3)Study Population

The study population for this research was 50 pharmaceutical professionals working in Regulatory Affairs, Quality Assurance, Productionand other areas in the pharmaceutical industry of India. Out of the total sample size of

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respondents, 15 were from two pharmaceutical companies from which interaction was possible. The remaining 35 respondents were professionals from different pharmaceutical companies in India.

4)Sampling technique and sample size

The participants were chosen based on their accessibility, availability, and willingness to participate in the survey.

50 completed responses were deemed sufficient for the exploratory and descriptive research, which aimed at understanding the process for the approval of generic drugs in India.

5)Source of Respondents

The data collection for the study was conducted through respondents from different pharmaceutical companies through direct company visits and personal contacts. Avoids need for company authorization.

6)Research instrument

A self-designed questionnaire consisting of multiple-choice and Likert- scale questions was used to assess awareness, usability and practical challengers related to generic drug approval.

7)Inclusion criteria

- Official regulatory guidelines and documents from CDSCO/DCGI, ICH and WHO related to generic drug approved in India.
- Articles and regulatory reports which are published.
- Regulatory affairs professionals involved in generic drug development or approval.
- Survey respondents with pharmacy or life science background who provided informed consent.
- Complete and valid survey responds.

8)Data collection

A structured questionnaire was prepared and shared with participants using online platforms such as Google Forms. Data were collected from the employees using a structured questionnaire.

9)Data analysis

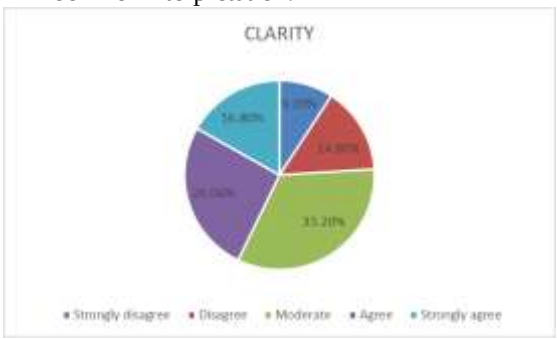
Data entered in Microsoft Excel and analysed.

III. RESULT AND DISCUSSION:

The study's findings reveal significant gaps in the clarity, usability and practical challenge despite well-established and successful operating generic drug approval process in India.

Clarity:

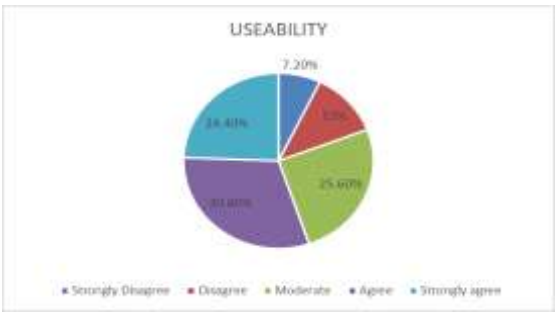
- The responses indicate that, majority of the participants gave the clarity of the CDSCO guidelines as moderate to positive.
- In particular 42.8% & 33.2% of respondents indicated agreement and moderate level of clarity respectively.
- However, a significant percentage of respondents 24% expressed disagreement indicating that sum aspects of the guidelines are un clear.
- This distribution shows that most people think the guidelines are clear, but there is still a lot of room for interpretation.



Usability:

- According to the responses, industry professionals generally view the CDSCO guidelines' usability favourably.
- Regarding the guidelines' usability, the majority of respondents (55.2%) agreed, while 25.6% gave it a moderate rating.
- Nonetheless, 19.2% of participants expressed disagreement, underscoring certain challenges in real-world implementation.

This distribution implies that even though the guidelines are generally regarded as useful, a significant percentage of respondents still find it difficult to apply them successfully in actual regulatory procedures. Partial ease of use is also reflected in the moderate responses, suggesting room for improvement.



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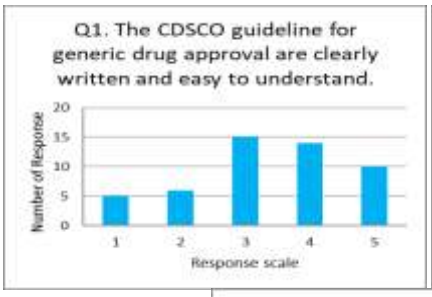
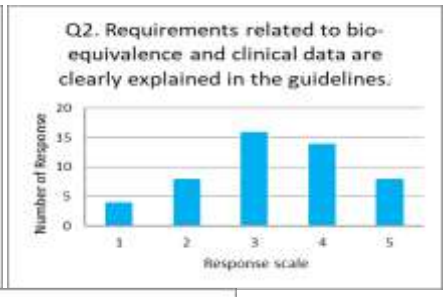
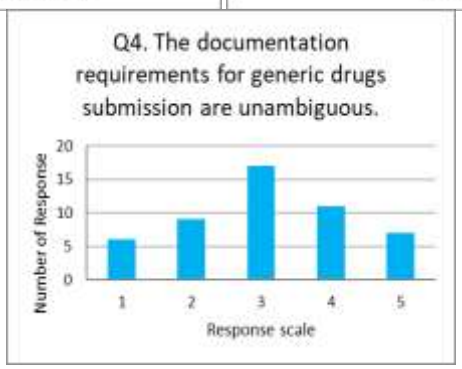
Practical challenges:

- According to the responses, a significant percentage of business professionals believe that putting CDSCO guidelines into practice will present practical difficulties.
- While 26% of respondents reported moderate difficulties, the majority of respondents (57.6%) indicated agreement. Merely 16.4% of respondents denied the existence of these difficulties.
- This distribution makes it abundantly evident that practical challenges are frequently encountered during the implementation process, even despite the structured regulatory framework. The moderate answers also show that there are difficulties to differing degrees at different stages of approval, highlighting the need for enhancements in operational ease and implementation efficiency.







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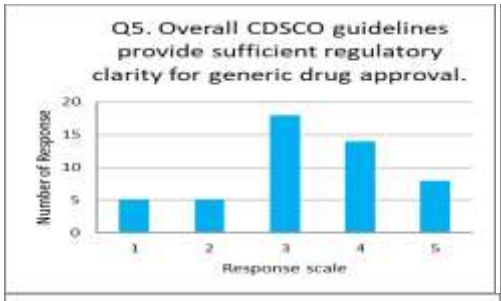

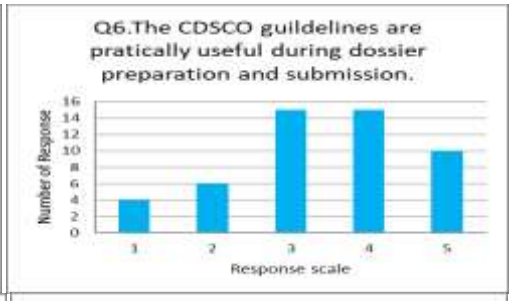

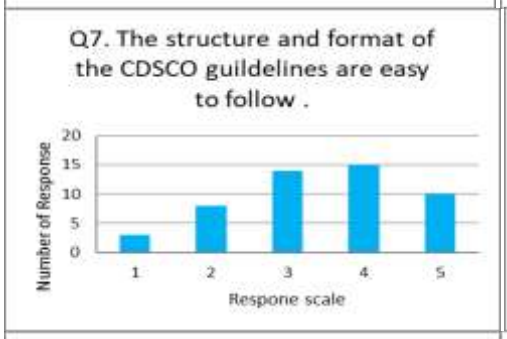

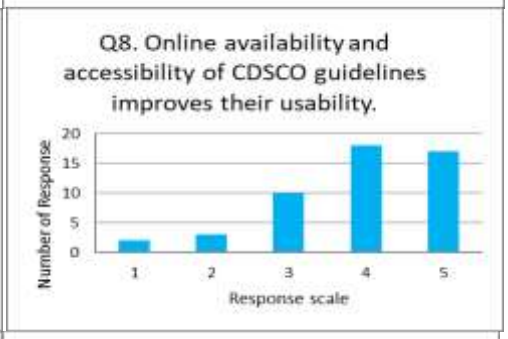

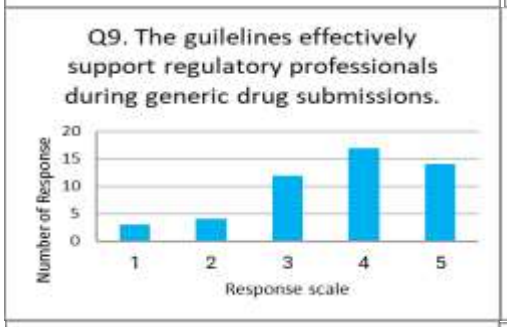

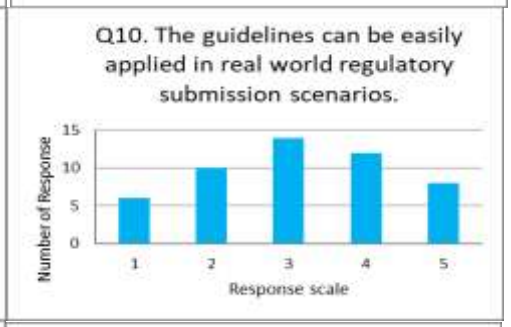

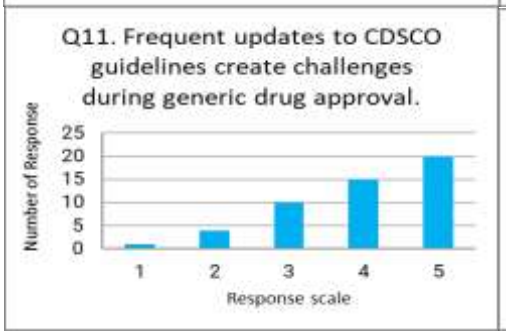

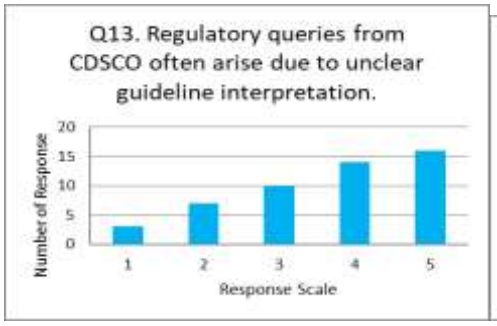

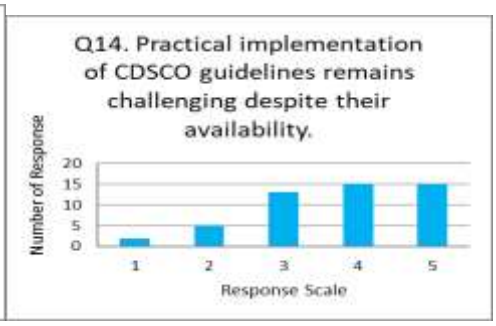

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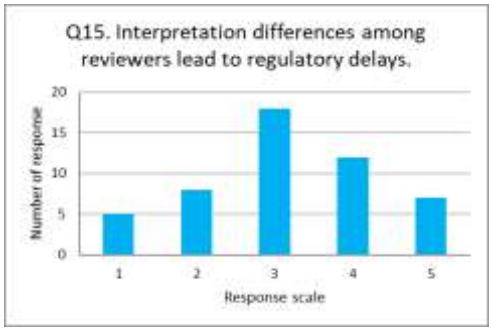

IV. CONCLUSION

The study concludes that the process of approval of generic drugs in India is well structured and regulated, which ensure the quality, safety and efficacy of the drugs. The case study of sofosbuvir also proves the success of the process of approval of generic drugs. However, despite the effective working of the approval process of generic drugs, the study identifies gaps in regulatory clarity, usability and practical challenges of the CDSCO guidelines, as stated by the industry professionals.

- Promote better understanding of guidelines among stakeholders' Periodic awareness or training initiatives can help industry professionals stay updated with regulatory expectations.
- Provide clearer interpretation of existing guidelines although CDSCO guidelines are available, additional clarification through detailed guidance documents or FAQs can help reduce ambiguity.
- Enhance transparency in the approval process better visibility of application status and reasons for delays can improve industry confidence and planning.

FUTURE RECOMMENDATIONS

Based on the study's conclusions, the following recommendations or proposed. The continuous growth will depend on:

- Improving clarity of regulatory guidelines, requirements can eliminate 2-3 week re submission delays, due to interpretation uncertainty.
- Enhancing the usability of regulatory systems, particularly digital platforms like SUGAM portal can improve efficiency in submission.
- Transparency and consistency in approval timelines through digital monitoring systems, can help the applicants to plan better on their regulatory submission and approval strategies.
- Strengthening pharmacovigilance mechanism to enhance post-marketing safety.
- Harmonization with ICH and WHO standards to support wider global acceptance of Indian generics.

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