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Product Approval Pathways in South Asia: Insights from India, Pakistan, and Nepal

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ABSTRACT

A regulatory process, by which an applicant gets authorization to launch a drug in the market, is known as drug approval process. Submission of INDA, conducting clinical trials, application to marketing authorization of drug and post-marketing studies are the key steps in the drug approval process. The current landscape of regulatory affairs highlights that different countries have distinct regulatory requirements for the approval of Marketing Authorization Applications (MAAs) for drug products. Each country has a designated regulatory body tasked with implementing laws, issuing guidelines, and overseeing the marketing and distribution of pharmaceutical products. In this study we compare the regulatory bodies, drug approval process of India, Nepal and Pakistan. India's regulatory system, led by the CDSCO, demonstrates a mature and structured approach, whereas Nepal and Pakistan must prioritize regulatory reform, enhance technical expertise, and foster collaboration with global health agencies to ensure the safety, efficacy, and quality of pharmaceutical products.

Keywords: CDSCO, DRAP, DDA.

INTRODUCTION

Drug product: A drug product is dosage form that contains one or more active and/or inactive ingredients

Pharmaceutical Finished Drug Products: Finished drug Product is defined as the medicinal product that has undergone all stages of production, including packaging in its final container

New drugs: New drug is medication or therapy that has not been used in the country.

Generic drugs: Generic drugs are identical to innovator drugs in terms of dosage form, route of administration, quality, performance, and intended use.

Biological products: Biological products are a diverse category of products and are generally large, complex molecules. Biological products include a wide range of products such as vaccines, blood and blood components, allergenic, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins

New drug discovery

Drug development involves rigorous testing and regulatory approval to ensure the new medication is safe and effective for human use. It is a difficult, time-consuming, and expensive process—less than 1% of molecules that enter testing ultimately receive regulatory approval. In the past, many drugs were discovered by identifying the active substances in traditional remedies. Today, diseases are controlled at the molecular and physiological levels. The average cost for research and development for each efficacious drug is likely to be $900 million to $2 billion. For every 5,000-10,000 compounds that enter the investigation and development pipeline, ultimately only one attains approval. These statistics

challenge imagination, but a brief understanding of the R&D process can explain why so many compounds don‘t make it and why it takes such a large, lengthy effort to get one medicine to patients.

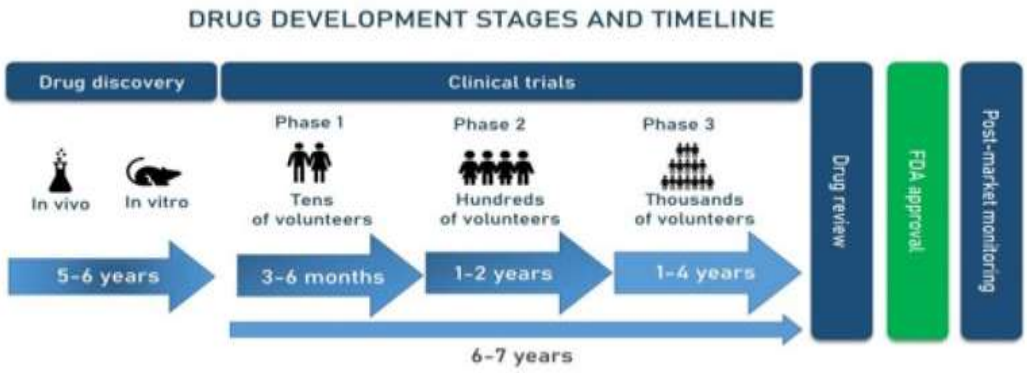


Figure No 1: Drug development pipeline

The new drug discovery process includes pre-clinical research on microorganisms and animals, filing for regulatory status, for an investigational new drug to initiate clinical trials on humans. Once we have completed preclinical and clinical studies. If results are positives then sponsor can apply new drug applications to regulatory body. Once it is applied, initially reviewed and inspected by regulatory authority and if everything found to be acceptable then product will approved. Even after the approval drug product post marketing studies has to be conducted. The process of drug discovery and development is very long and needs 10-12 years which includes the close interaction of large number of scientific disciplines. Most biotechnology and pharmaceutical companies employ teams to mentor the process of various stages of drug development and making the drug candidate into therapeutic products.[1] Regulatory affairs is a profession developed from the desire of governments to protect public health by controlling the safety and efficacy of products in areas including pharmaceuticals, veterinary medicines, medical devices, pesticides, agrochemicals, cosmetics and complementary medicines, and by the companies responsible for the discovery ,testing, manufacture and marketing of these products wanting to ensure that they supply products that are safe and make a worthwhile contribution to public health and welfare. Regulatory affairs play a crucial role in the pharmaceutical industry and are involved in all stages of drug development and also after drug approval and marketing.

SCOPE OF REGULATORY AFFAIRS

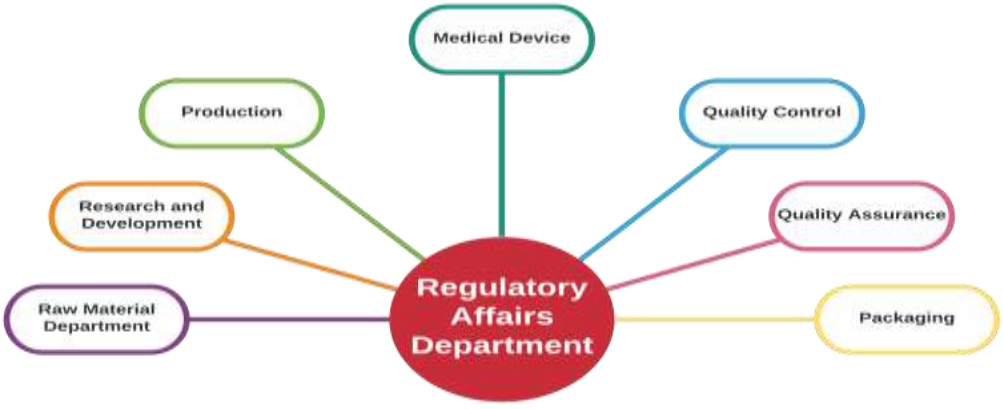


Figure 2: Scope of regulatory affairs

NEED OF REGULATORY AFFAIRS IN PHARMACEUTICAL ORGANISATION

Pharmaceutical industry is the most regulated industry of all the industries. These regulations are put in order to develop the most efficient and safe pharmaceutical products. It takes more than 8 to 15 years to develop a new drug product and costs more than $800million. Thus the regulatory affairs provide guidance into this development, through agency wisdom collected in guidance, previous experience, market precedence, etc. and hence helps to reduce number of development failures.

Currently, Indian pharmaceutical industry is depending on export market, across the world and this market is expanding every day. Each country is having respective guidelines and regulations. To cope up with their regulations and timely delivery, pharmaceutical industry needsRA experts in huge number.[1, 2]

HISTORICAL OVERVIEW OF REGULATIONS IN INDIA

India's drug regulatory framework has evolved significantly over the decades to ensure the safety, efficacy and quality of pharmaceutical products.

Pre-Independence period (British Era (1860-1947)

The initial regulation of drugs in India began under British rule. The first major regulation was the Poison Act of 1919, which focused on controlling the sale of certain poisonous substances.

Drugs and Cosmetics act, 1940

This was the first comprehensive law to regulate the import, manufacture, distribution and sale of drugs and cosmetics in India. The act also established the Central Drugs Standard Control Organization (CDSCO)

Post- Independence period

1950's – 1960's: The Pharmacy Act, 1948: Regulated the profession of pharmacy in India. It aimed to ensure the availability of qualified pharmacist in drug stores.

The 1955 amendment to the D&C Act brought more stringent regulations regarding the manufacture and sale of drugs.

Patent Act, 1970: Abolished product patents in pharmaceuticals and allowed only process patents, enabling the growth of a strong generic drug industry in INDIA.

1980's – 1990's: Drug Policy of 1986: Emphasized the self – reliance in the production of bulk drugs and formulations and also encouraged the growth of indigenous pharmaceutical industry.

Schedule M (1987): Introduced to establish Good Manufacturing Practices (GMP) standards for the pharmaceutical industry, ensuring that product are consistently produced and controlled according to the quality standards.

2000's:2005 Amendments to Patent Act: India became compliant with the Trade – Related Aspects of intellectual property Rights (TRIPS) agreement.

Good Clinical Practice (GCP) Guidelines, 2001: These were introduced to standardize the conduct of clinical trials in India, ensuring the protection of trial participants and the integrity of data.[3]

REGULATORY FRAMEWORK IN PAKISTAN

Pakistan is a lower-middle income country situated in the west of the Indian Subcontinent, with the sixth largest population in the world, exceeding 207 million. The country has annual pharmaceutical sales of 3.1 billion US dollars. In Pakistan, two major issues have gained both national and international attention. The first incidence was the case of contaminated cardiovascular drugs in December 2011 which caused death of more than 230 lives (The Fake Drug Crisis). November 2012, another major

incident of medicine quality failure has resulted in the deaths of hundreds after the consumption of contaminated cough syrup. Alarmingly, in the earlier case involving a cardiovascular drug, Pakistan's quality control laboratories failed to detect the presence of the harmful substance pyrimethamine, and similarly, in the recent case, they were unable to promptly identify dangerously high levels of the toxic compound levomethorphan in substandard dextromethorphan syrup. These two incidences revels that, in Pakistan inadequacy of the pharmaceutical drug regulatory system and led to the establishment of the autonomous Drug Regulatory Authority of Pakistan (DRAP) and also became a main force for improving the regulatory structures of the country both at state and federal levels.[4-5]

DRUG REGULATION IN NEPAL[6]

Pharmaceutical production in Nepal began in 1972. Currently, there are 63 pharmaceutical manufacturing companies producing allopathic medicines. The pharmaceutical industry in Nepal plays an invaluable role in the country's economic growth, generating around Rs 26 billion annually. The Department of Drug Administration (DDA) serves as the national regulatory body, overseeing all pharmaceutical and biological drug products. With increasing demand and local innovation, the industry continues to expand, contributing significantly to healthcare accessibility and employment.

The major regulations for pharmaceuticals in Nepal includes,

- Drugs Act 1978,
- Drugs Registration Rules1981 (DRR),
- Drug Investigation and Inspection Rules 1983,
- Codes on Good Manufacturing Practice 2016,
- Drug Standards Regulation 1986,
- Codes on Sales and Distribution of Drugs 2014,
- Drug Advisory Committee (DAC) Regulation 1980,
- National Drug Policy 1995

LEADING REGULATORY BODIES OF WORLD

Regulatory bodies provide strategic, tactical and operational direction and support for working within regulations to expedite the development and delivery of safe and effective healthcare products to individuals around the world. Every country has its own regulatory agency. Prominent regulatory agencies of the world are

Table No 1: Regulatory Authority[2]

Serial Number	Country	Authority
1.	USA	USFDA (Food and Drug Administration (FDA)
2.	UK	MHRA (Medicines and Healthcare Products Regulatory Agency)
3.	Australia	TGA (Therapeutic Goods Administration)
4.	India	CDSCO (Central Drug Standard Control Organization)

5.	Canada	Health Canada
6.	South Africa	SAHPRA (South African Health Products Regulatory Authority)
7.	Brazil	ANVISA (Agencia Nacional de Vigiloncia Sanitaria)
8.	European Union	EMA (European Medicines Agency)
9.	China	SFDA (State Food and Drug Administration)
10.	New Zealand	MEDSAFE (Medicines and Medical Devices Safety Authority)

India, with a population of 1.4 billion, holds the position of the most populous country in the world. As of this year, it ranks fifth in global GDP. The Indian pharmaceutical industry is among the largest worldwide, standing third in terms of volume and eleventh in terms of value. The pharmaceutical sector includes 3,000 companies and 10,500 manufacturing facilities, offering drug production at substantially lower costs. We are examining the regulatory frameworks and product approval processes across the eight member countries of the South Asian Association for Regional Cooperation (SAARC), a regional organization

- Afghanistan
- Bangladesh
- Bhutan
- India
- Maldives
- Nepal
- Pakistan
- Sri Lanka

Among South Asian nations, India has the most stringent rules and regulations for pharmaceutical drug production under GMP standards and is also on the path to becoming a full member of the ICH. Despite being neighboring countries, India, Pakistan, and Nepal each maintain distinct regulatory systems. Although the data submitted to their respective regulatory authorities regarding quality, safety, and efficacy is largely similar, differences exist in terms of timelines, fees, review processes, and marketing authorization requirements. The present study aims to compare the regulatory bodies and drug approval processes for pharmaceutical products in India, Pakistan, and Nepal.

MATERIALS AND METHODS

MATERIALS

The data and information for the study was collected and collated from the research papers, review articles and published journals and from the information available on the websites related to

1. Central Drugs Standard Control Organization
2. Drug Regulatory Authority Pakistan (Official website)
3. Department of Drug Administration (official website)
4. Researchgate.net

METHODOLOGY

A comparative study was conducted to examine the regulatory frameworks of the Central Drugs Standard Control Organization (CDSCO), the Drug Regulatory Authority of Pakistan (DRAP), and the Department of Drug Administration (DDA). This analysis aims to examine the similarities and differences in the organizational structures and new drug approval processes of CDSCO, DRAP, and DDA, while also identifying current challenges and potential areas for improvement. The study is based on data sourced from the official websites of these regulatory bodies, as well as from various peer-reviewed journal articles.

RESULTS AND DISCUSSION

THE CDSCO

The Central Drugs Standard Control Organization (CDSCO) is India's National Regulatory Authority (NRA) for Cosmetics, Pharmaceuticals and Medical Devices. It works under the Ministry of Health and Family Welfare, Government of India. It is responsible for implementing the guidelines and policies laid down by the Drugs and Cosmetics act 1940. DCGI (Directorate General of Health Services) is the key official of CDSCO and holds the authority for licensing of new drugs, approval of clinical trials, and biological products. CDSCO comprises of six zonal offices, four sub-zonal offices, 13 port offices and seven laboratories under its control.

Vision

To protect and promote public health in India.

Mission

To safeguard and enhance the public health by assuring safety, efficacy and quality of drugs, cosmetics and medical devices.

Function of CDSCO

1. Approval of new drugs and clinical trials.
2. Import Registration and Licensing
3. Licensing of Blood Banks, LVPs, Vaccines, r-DNA products and some Medical devices and Diagnostic agents.
4. Amendment to D&C Act and Rules.
5. Participation in WHO GMP certification schemes.
6. Banning of drugs and cosmetics.
7. Grant to test license, personal license, NOC's for export.
8. Testing of drugs by Central Labs.
9. Publication of Indian Pharmacopoeia.
10. Monitoring adverse drug reactions.
11. Guidance on Technical matters.[9]

5.2. THE DRAP

Drug Regulatory Authority of Pakistan (DRAP) is self-governing body under the federal government of Pakistan which works under the administrative supervision of the Ministry of National Health Services, Regulations and Coordination which responsible for providing effective coordination and enforcement of The Drugs Act, 1976 and to bring harmony in inter-provincial trade and commerce of therapeutic goods.

Vision and mission

1. To ensure access of safe, quality and efficacious medicine at affordable prices.
2. Earliest availability of new treatment opportunities for the people of Pakistan.
3. Working as a highly Professional & world class regulatory organization and best practices, through effective management, regulations and enforcement and to support national health system management through effective therapeutic goods management and strategies.

Responsibility

1. Marketing authorization of pharmaceuticals, medical devices and their post and export registration.
2. Marketing authorization of biological.
3. Marketing surveillance and control and import export control.
4. Licensing of the drugs manufacturing facilities.
5. Development and promotion of pharmacy services.
6. Costing and pricing of drugs and biological.
7. Conduct inspections.[10]

THE DDA

The Department of Drug Administration (DDA) is a regulatory agency in Nepal which works under Ministry of forest & soil conservation and then went under Ministry of Health and population.

Mission & Vision

1. To improve and manage the activities related to drug production, import, export, storage, supply, sales, distribution, quality assessment, regulatory control, rational use and information flow by establishing co-ordination among governmental, non-governmental and private organizations.
2. To achieve the aim and objectives of National drug Policy.

Roles and responsibilities

1. Ensuring safety, quality and efficacy of medicines.
2. Promotion of Rational Use of Medicines and health technology products.
3. Ensuring access to medicines and health care technology products.
4. Enforce provisions of drug law for regulatory compliances.
5. Institutional development including HR.[11]

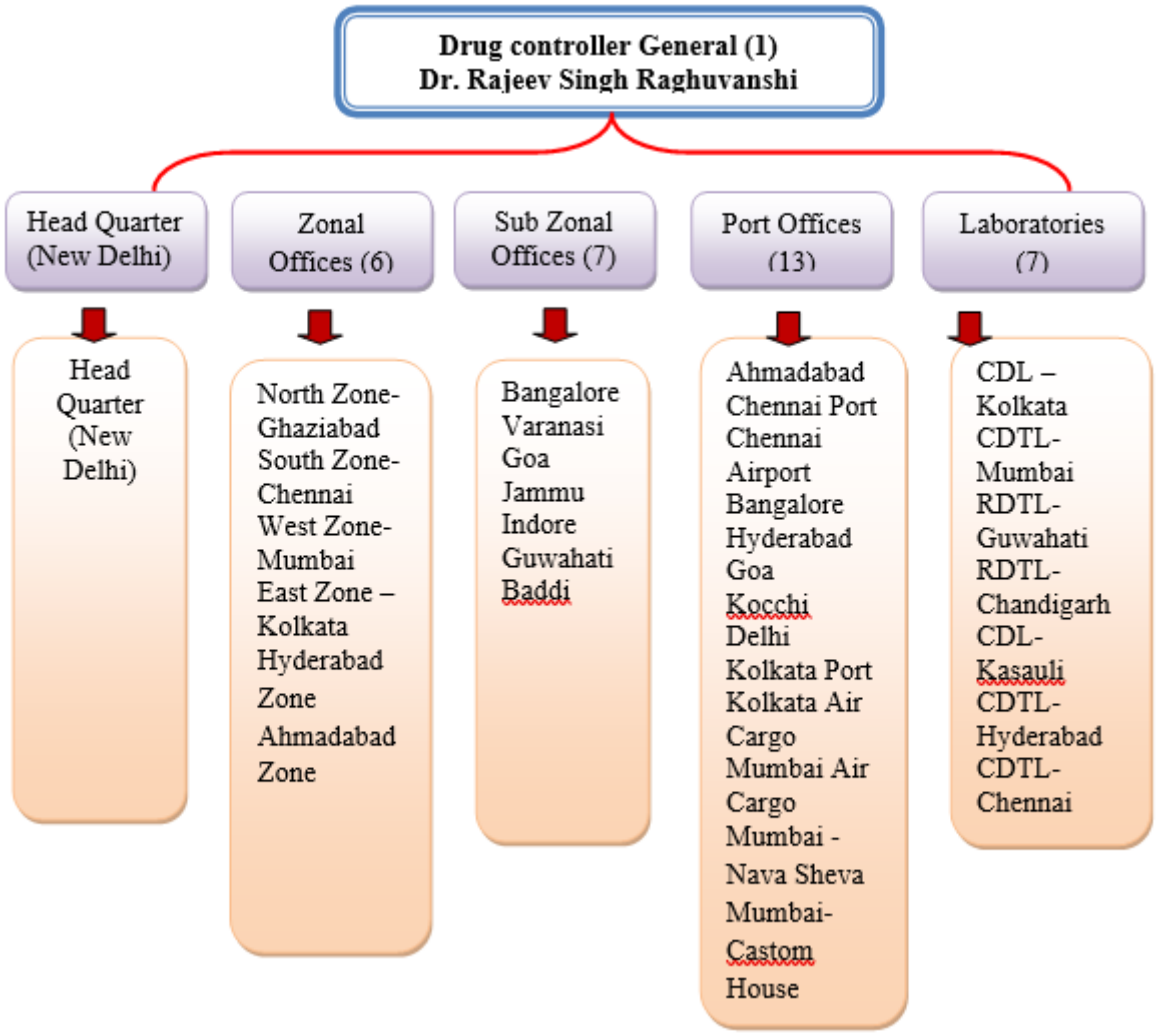


Figure No 3: Organization structure of CDSCO

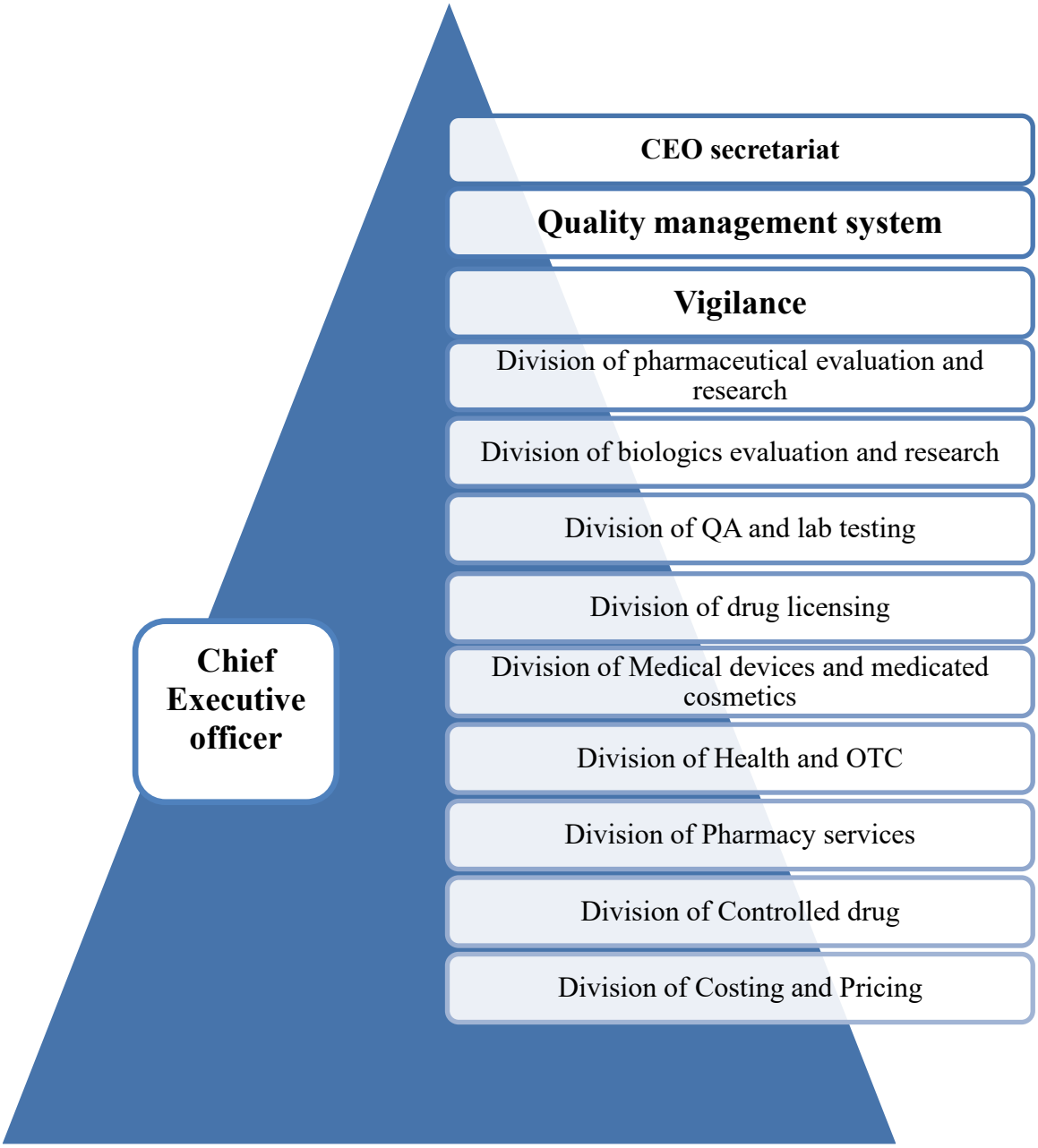


Figure No 4: Organization structure of DRAP (Pakistan Drug Regulatory Body)

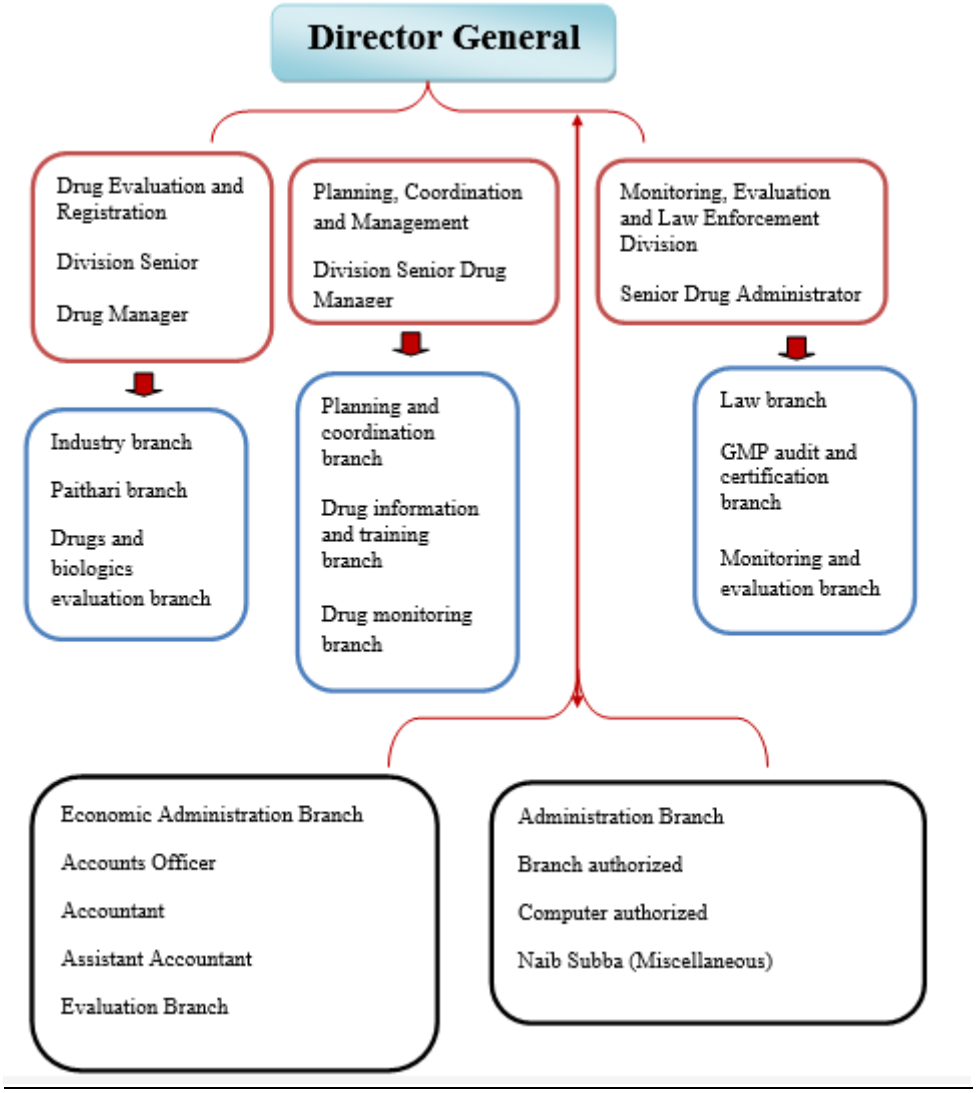


Figure No 5: Organization structure of DDA (Nepal Drug Regulatory Body)

PRODUCT APPROVAL PROCESS IN INDIA, PAKISTAN AND NEPAL

Categories of products approved are as follows:

- New drugs
- Biologics (Vaccines, Blood products, r-DNA products etc.)
- Generics
- Medical devices

DRUG APPROVAL PROCESS IN INDIA[3,9]

The Drugs and Cosmetics Act of 1940, along with the Rules of 1945, was enacted by the Indian Parliament to regulate the import, manufacture, distribution, and sale of drugs and cosmetics. In 1988, Schedule Y was introduced to the Rules, outlining guidelines and requirements for clinical trials. This schedule was further revised in 2005 to align with internationally accepted standards and practices. When a company in India intends to manufacture or import a new drug, it must seek approval from the licensing authority (DCGI) by submitting an application through Form 44, along with data as outlined in

Schedule Y of the Drugs and Cosmetics Act, 1940, and the accompanying Rules of 1945. To demonstrate the drug's safety and efficacy within the Indian population, clinical trials must be conducted following the guidelines specified in Schedule Y, and the trial reports should be submitted in the prescribed format. Since most countries have adopted the Common Technical Document (CTD) format, the CDSCO has also decided to implement the CTD format for the technical requirements related to the registration of pharmaceutical products intended for human use.

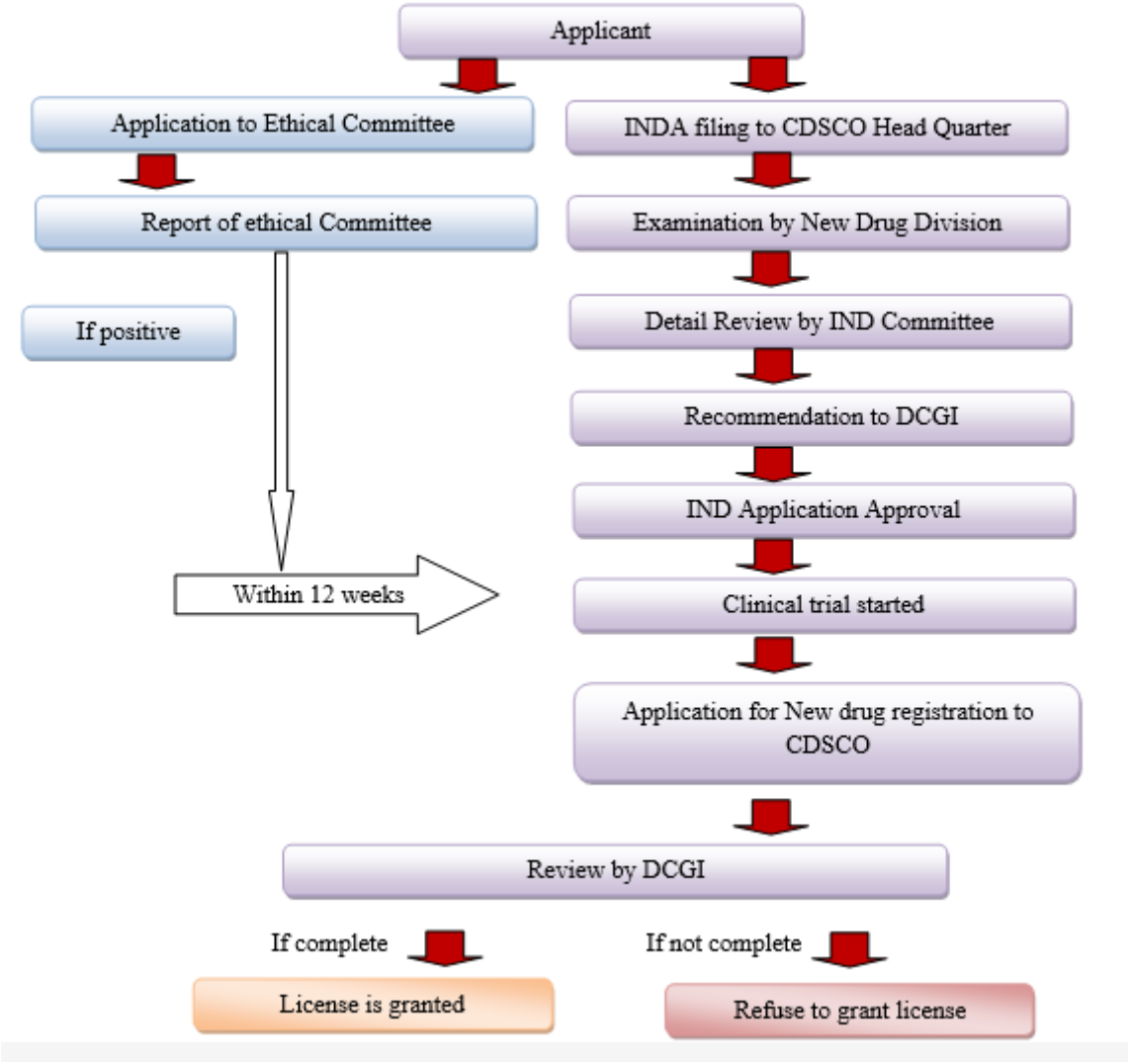


Figure No 6: New drug approval process in India

PRODUCT APPROVAL PROCESS IN PAKISTAN[4, 10]

In Pakistan, the Drugs Act, 1976 governs the import, export, manufacture, storage, distribution, and sale of drugs. Under Section 7 of the Act, drugs are registered by the Registration Board, which serves as the competent authority for drug registration. An application for the registration of a drug shall be submitted in Form 5 (for locally manufactured drugs), Form 5-A (for imported drugs), Form 5-D (for new molecules), or Form E (for patented drugs), along with the prescribed fee in duplicate, addressed to the Secretary of the Registration Board. The applicant must also provide any additional information or materials requested by the Registration Board for proper evaluation of the drug. Prior to granting

registration, the Board may inspect the proposed manufacturing premises, either directly or through a sub-committee, a panel of inspectors, or experts appointed for this purpose. A detailed inspection report shall be submitted to the Registration Board by the designated inspecting body. If the Registration Board is satisfied with the information and documentation provided, it may proceed to register the drug. However, if it finds the safety, efficacy, quality, or economic value of the drug unsatisfactory, or if public interest so warrants, the Board may reject the application and shall communicate the reasons for rejection to the applicant in writing.

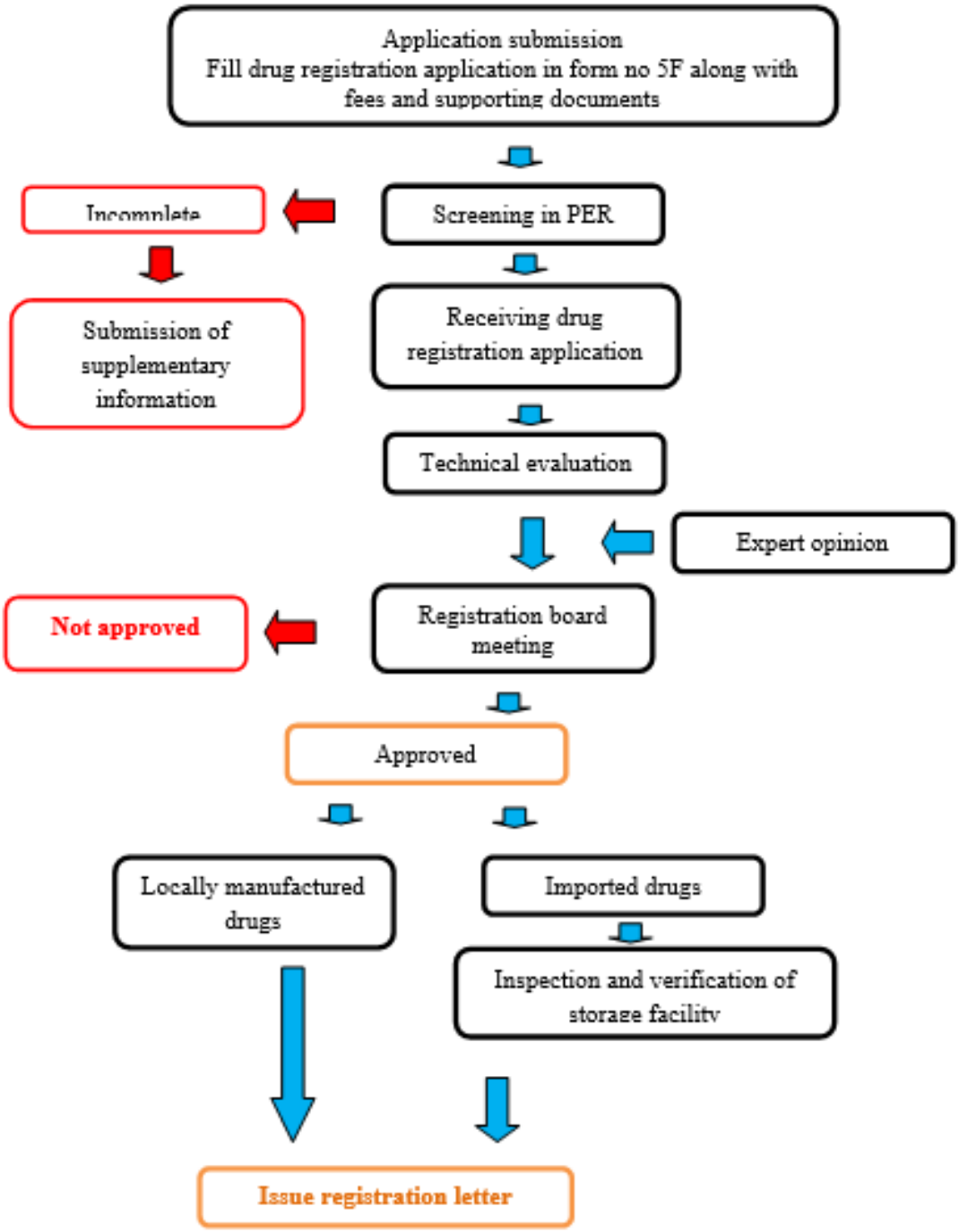
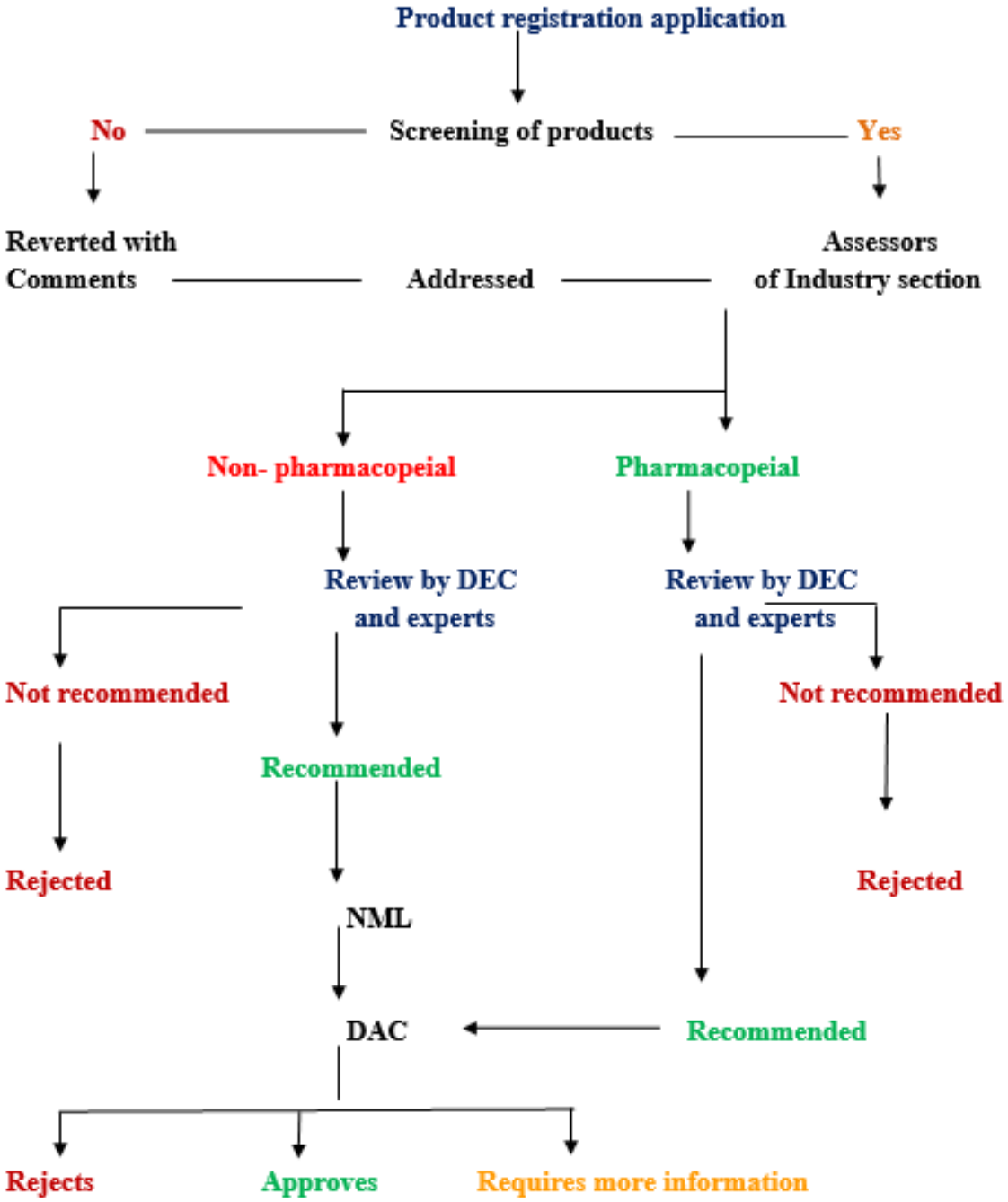


Figure No 7: New drug approval process in Pakistan

PRODUCT APPROVAL PROCESS IN NEPAL[11, 12]



DAC: Drug Advisory Committee, DEC: Drug Evaluation Committee,
NML: National Medicine Laboratory

Figure No 8: New Drug registration process in Nepal

CONCLUSION

In this study, we have compared the pharmaceutical regulatory bodies of India (CDSCO), Pakistan (DRAP) and Nepal (DDA) with their functions and drug approval process. Every regulatory body has its own distinct drug approval process and import and export regulations. The CDSCO has a comprehensive regulatory framework, characterized by stringent requirements for drug approval process and extensive

post-market surveillance, reflects a well-established system that prioritizes patient safety, quality and efficacy of the product. Its emphasis on rigorous scientific evaluation and continuous monitoring sets a high standard for pharmaceutical regulation, and it is in the verge of becoming an ICH member. Ultimately, this study underscores the urgent need for capacity building, infrastructure enhancement, adoption of international GMP standards, stringent quality control measures, and the implementation of the WHO prequalification system in both Pakistan and Nepal. Particular attention should be given to establishing distinct regulations for different categories of pharmaceutical products in Nepal. Regulatory authorities must take a leading role in harmonizing approval processes and guidelines to ensure the production of safe, effective medicines and to safeguard public health.

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