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Review Article

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Comparative Study of Regulatory Requirement and Approval Process for Drugs in India, US and Europe

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Abstract

This review conducts a comparative analysis of drug approval for new and generic medicines across three jurisdictions: United States (US FDA), India (CDSCO), and the European Union (EMA) framed as a three-stage process (application, review, approval) and focusing on regulatory pathways, statutory timelines, documentation requirements, and application costs; it also compares review timelines and application costs across the three agencies. Primary data were gathered from official regulatory documents, guidelines, fee schedules, and the FDA, CDSCO (India), and EMA (current through mid-2025) agencies' websites. Secondary market data were procured from authoritative industry reports. Systematic search and cross verification of primary sources, taking into consideration the US Code of Federal Regulations (Titles 21 and 42), New Drugs and Clinical Trials Rules of India 2019, applicable rules, and Directives of the EU and procedural manuals of each agency. All jurisdictions, operationally, follow a three-stage approval process. The US FDA has high application costs, a 10-month standard review time, and many expedited pathways. India's CDSCO has low application costs, a prescribed 90-day review with a deemed-approval mechanism, and frequent waivers of local trials. The EMA's centralised procedure has an average lead time of 277 days and provides significant fee reductions to small companies and orphan drugs. All three use the eCTD for submissions, but the administrative details and form requirements differ.

Conclusion: Jurisdictional strategies are reflective of distinct priorities: the priority of the US for rigorous evaluation in high-value markets, the incentives of Europe for specialised therapies, and the priority of India on efficiency and cost-effectiveness are essential for drug development across the globe.

Keywords: drug approval; regulatory science; US FDA; CDSCO; European Medicines Agency; review timelines; marketing authorisation

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1. Introduction

The global pharmaceutical market is forecast to reach about $2.3 trillion by 2028, growing at roughly 5 to 8% annually. (1) The United States leads this market with about 53% of global sales, followed by Europe at 22.7%. (2) India, while representing about 3.7% of the global market, remains a vital centre for generic drug manufacturing and supply. (2) Regulatory approval of new medicines is a complex, resource-intensive process governed by strict legal and ethical standards to ensure safety, efficacy and quality, with varying global regulations making strategic planning essential for market entry. Across major jurisdictions such as the United States, the European Union and India, the approval process broadly follows three stages: submission of a comprehensive application, structured regulatory review and final market authorization. Substantive heterogeneity exists in pathways, data expectations, timelines and costs. Previous literature has examined approval processes in India (3,4), the United States (5,6) and Europe (7,8), as well as comparative analyses. (9,10) Despite its importance for market selection, detailed comparative information on regulatory requirements, timelines and costs remains limited, and this review summarizes regulatory processes across jurisdictions to support global drug development planning.

2. Methodology

This review is based on official regulatory documents and guidelines from India, the United States, and the European Union, with data cross-verified and contextualized using selected peer-reviewed literature. Global pharmaceutical market metrics were obtained from IQVIA (1) and EFPIA (2). Application costs were standardized in U.S. dollars using IRS exchange rates for the relevant periods. (11)

3. Three-Stage Drug Approval Process

The regulatory framework differs widely across the USA, India, and Europe. However, the drug approval across all three countries converges into a simple three-stage process, i.e. Drug Application, Drug Review and Drug Approval respectively.

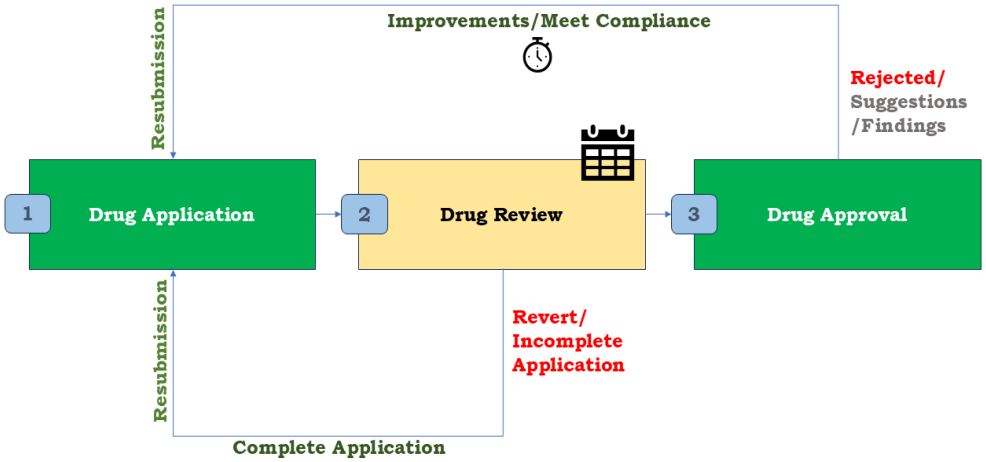


Figure 1. Three-stage process of drug approval across the USA, India, and Europe Jurisdictions

4. United States

The United States Food and Drug Administration (USFDA) has a detailed drug approval system. The Center for Drug Evaluation and Research handles drug application reviews, regulatory compliance, and approvals

4.1 Drug Application

a) Regulatory Framework:

For registration of the drug to market or sell in the USA, the manufacturer has to submit an application to the CDER for regulatory approval. The various drug approval pathways in federal regulations form the basis of these drug registration applications, as shown in Table 1.. **1**

Table 1. Drug approval pathways in the Federal Regulations (USFDA)

Pathway	Type	Purpose	Data Requirements
505(b)(1) (12)	NDA	For **new drugs** never been approved before	Full clinical and preclinical data from scratch
505(b)(2) (12)	Modified NDA	For **modified versions** of approved drugs	Mix of original data + published/FDA data
505(j) (12)	ANDA	For **generic drugs** identical to approved ones	Proof of bioequivalence, no new trials

b). Application Types

- ***Investigational New Drug Application (IND):***

Federal regulations require an approved marketing application before interstate transport of new drugs. To ship investigational drugs to clinical sites, sponsors obtain an IND, which also authorises clinical trials and human use. (13-15) INDs are governed by 21 CFR Part 312, (16) Part 314, (17) Parts 50, 56, (18,19) Part 54, (20) and 42 U.S.C. § 282(j).(21) Two IND types exist: Commercial (for marketing approval) and Investigator (physician-led research, non-commercial). (15) Submission requires Forms 1571 (primary), 1572, 3674, investigator statements, compliance certification, and Forms 3454/3455 for marketing. (22)

Table **3** covers the attachments required to be submitted with the IND application.

Table 2. USFDA forms required for commercial and investigator-initiated IND application, their purpose, and applicability

Form Number	Form Name	Commercial IND	Investigator IND
FDA 1571	Investigational New Drug Application	Required	Required
FDA 1572	Statement of Investigator	Required (for each investigator)	Required
FDA 3674	Certification of Compliance	Required	Usually Not Required (Depends on study)
FDA 3454	Certification - Financial Interests and Arrangements	Required (for marketing applications)	Not Required
FDA 3455	Disclosure - Financial Interests and Arrangements	Required (when applicable)	Not Required

Table 3. Required attachments along with the IND application forms (23-32)

Form Number	Key Attachments
FDA 1571	Cover letter; Clinical protocol; CMC information; Pharmacology and toxicology; Investigator's brochure; Environmental assessment
FDA 1572	Curriculum vitae or qualifications; IRB documentation; Protocol outline or complete protocol
FDA 3674	ClinicalTrials.gov registration numbers; Compliance documents
FDA 3454	Form 3455 if required; Due diligence documents
FDA 3455	Financial arrangements; Compensation agreements; Bias minimization plan

- **New Drug Application (NDA):**

The NDA is the primary application for registering new pharmaceuticals for marketing in the USA. Sponsors submit an NDA to demonstrate safety and efficacy through nonclinical and clinical data, drug information, and manufacturing details for FDA review. (17) The regulatory framework includes 21 CFR Part 314 (NDAs), (17) Parts 210–211 (GMP), (33,34) Part 201 (labelling), (35) Part 202 (prescription advertising), (36) Part 54 (financial disclosure), (20) and Section 505 of the FD&C Act. The primary submission form is Form 356h, (37) accompanied by Forms 3674, 3397, 3454, and 3455. (25–27,38) USFDA requires applicants to pay the fees under the Prescription Drug User Fee Act (PDUFA). (Table 6.)

Table 4. USFDA forms required for New Drug Application (NDA), their purpose, and applicability

Form No.	Form Name	Purpose	Status
FDA 356h (37)	NDA Application	Main application and applicant certification	Required
FDA 3674 (25)	Certification of Compliance	ClinicalTrials.gov registration	Required
FDA 3397 (38)	PDUFA Fee Cover Sheet	User fee processing	Required (unless exempt)
FDA 3454 (26)	Financial Interests Certification	Investigator financial disclosure	Required
FDA 3455 (27)	Financial Interests Disclosure	Detailed financial arrangements	Required (if applicable)

Table 5. Required attachments along with the NDA application forms

Form No.	Key Attachments
FDA 356h	Cover letter; Table of contents; Summary; CMC information; Nonclinical pharmacology/toxicology; Human pharmacokinetics/bioavailability; Clinical data; Statistical reports; Case report tabulations/forms; Safety update; Methods validation; Drug samples (if requested); Proposed labeling; Patent info/certification; Establishment description; Debarment/field copy certifications; Environmental assessment
FDA 3674	ClinicalTrials.gov registration numbers; Supporting compliance documents
FDA 3397	Application fee payment
FDA 3454	Form 3455 (if required); Due diligence documents
FDA 3455	Financial arrangement documents; Compensation agreements; Bias minimization plan

Table 6. New Drug Application (NDA) fees for FY 2026 (39)

Fee Type	Amount (FY 2026)	Type of Application
Full Application Fee	$4,682,003	For applications requiring clinical data
Half Application Fee	$2,341,002	For applications not requiring clinical data
Annual Program Fee	$442,213	For approved products
Orphan Drug Exemptions	Available	For designated orphan drug products
Small Business Waivers	Available under conditions	Qualifying small businesses may get fee waivers

- **Abbreviated New Drug Application (ANDA):**

An ANDA is the regulatory submission for generic drugs, demonstrating bioequivalence to the Reference Listed Drug without new clinical or preclinical data. (12,13) Governed by 21 CFR Part 314, Section 505(j) FD&C Act (39), 21 CFR Part 320, Part 54, and 42 U.S.C. § 282(j), (17,20,21,40,41) it uses Forms 356h and 3794. Petitioned ANDAs require an FDA suitability petition, (42) 505(b)(2) NDAs partly rely on prior data, (12) and authorised generics are marketed by the innovator under the original NDA. (43)

Table 7. USFDA forms required for Abbreviated New Drug Application (ANDA), their purpose, and applicability

Form No.	Form Name	Status
FDA 356h (37)	ANDA Application	Required
FDA 3794 (44)	Generic Drug User Fee Cover Sheet	Required (unless exempt)
FDA 3674 (25)	Certification of Compliance	Required
FDA 3454	Financial Interests Certification	Required
FDA 3455 (27)	Financial Interests Disclosure	Required (if applicable)

Table 8. Required attachments along with the Abbreviated New Drug Application (ANDA)

Form Number	Key Attachments
FDA 356h	Cover letter; Administrative documents; Patent and exclusivity documents; Drug Master File references; Draft labeling; Quality and clinical summaries; Drug substance and drug product information
FDA 3794	User fee cover sheet; Payment confirmation; Facility and active pharmaceutical ingredient details
FDA 3674	ClinicalTrials.gov registration numbers; Supporting compliance documents
FDA 3454	Form 3455 if required; Due diligence documents
FDA 3455	Financial arrangement documents; Compensation agreements; Bias minimization plan

b) Submission Format:

The submission format for drug registration in the USA is primarily the eCTD format. (45) INDs must be submitted in triplicate; commercial INDs require eCTD, while research INDs may be electronic or paper. (46) Since May 5, 2017, all NDA and ANDA submissions use eCTD via the ESG (≤10 GB, versions 3.2.2 or 4.0), with larger files by special arrangement. Paper submissions are not accepted; all forms must be electronically completed and signed.(47–49)

4.2 Drug Review



Figure 2. Review Timeline (Months) for IND, NDA & ANDA Application (Standard & Priority) in USA

a) Investigational New Drug (IND)

After submission, the FDA has 30 days to review the original IND. (50) It becomes effective after 30 days unless placed on Clinical Hold, and trials cannot begin earlier unless FDA provides prior notification. (51) Deficiencies are issued in a Complete Response Letter, (52) while approvals are confirmed by an approval letter. In emergencies, an Emergency Use IND authorises experimental drug use when standard submission is not feasible. (53)

b) New Drug Application (NDA)

The FDA has 60 days to decide whether to file the NDA for review. (54) The standard review timeline is 10 months, reduced to 6 months for priority reviews. (55) The process includes thorough committee review, facility inspections, and report compilation, after which a senior FDA official makes the decision. (56) Any deficiencies or suggestions are communicated through a Complete Response Letter. (52)

c) Abbreviated New Drug Application (ANDA)

The ANDA review begins with the Division of Filing Review (DFR), which determines within 60 days whether the application is complete; incomplete applications receive a Refuse to Review (RTR) notice. (57) The standard review timeline is 10 months, (58) with shorter priority reviews for first generics, shortages, or public health emergencies. (59) Deficiencies result in a Complete Response Letter (CRL), and the applicant has one year to address issues before resubmission. (52)

4.3 Drug Approval

The basis for approval for a drug by the FDA is solely based on the risk-benefit ratio. (60)

a) Standard Approval Types (61)

Standard approval is granted when safety, efficacy, quality, and labeling requirements are met, with a 10-month review for NDAs, BLAs, and ANDAs. Tentative approval applies when criteria are met but marketing is blocked by patents or exclusivity. Expedited approvals such as Fast Track, Breakthrough Therapy, Priority Review, and Accelerated Approval enable faster review. (61,62) Fast Track approval facilitates the development and expedited review of drugs for serious conditions with unmet medical needs; the designation must be requested by the sponsor, and the FDA responds within 60 days. (63) Breakthrough Therapy designation applies when preliminary evidence shows substantial improvement over existing treatments, granting all Fast Track features plus intensive FDA guidance and organizational support. (64) Priority Review shortens the standard 10-month review to 6 months for applications offering significant improvements in safety or efficacy, with the FDA deciding within 60 days of receipt. (55) Accelerated Approval allows earlier approval of drugs for serious or life-threatening conditions based on surrogate endpoints, with the FDA able to withdraw approval if confirmatory studies fail to demonstrate clinical benefit. (65)

b) Specialized Approval Types:

Orphan Drug designation applies to drugs for rare diseases affecting fewer than 200,000 people in the U.S., offering benefits such as tax credits, user fee exemptions, and up to seven years of market exclusivity post-approval. (66) Emergency Use Authorization (EUA) allows unapproved drugs to be used during public health emergencies when no adequate alternatives exist and benefits outweigh risks; EUAs are temporary and issued under separate legal authority. (53,67)

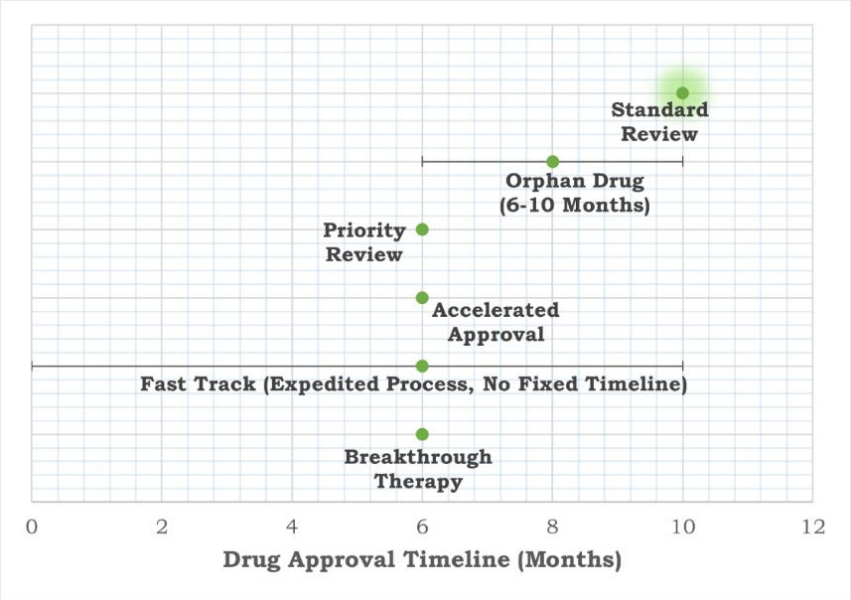


Figure 3. United States FDA's PDUFA goal targets for approval through expedited approval pathways

5. India

5.1 Drug Registration:

The New Drug and Clinical Trial Rules (NDCTR) 2019 govern drug registration in India, with the DCGI acting as the Central Licensing Authority (CLA). (68) Updated as the NDCTR (Amendment) Rules 2024 (G.S.R. 581(E), notified 19 Sept 2024; effective 1 Apr 2025), they cover clinical trials, BA/BE studies, and import, export, and licensing of new drugs and investigational products. The Eighth Schedule lists 27 application forms (CT-1 to CT-27). (69)

Table 9. Required Forms for the Drug Registration in India (69)

Form No.	Title
CT-04	Application for permission to conduct clinical trial of a new or investigational drug
CT-10	Application for permission to manufacture new or investigational drug for clinical trial or BA/BE study
CT-18	Application for permission to import new drug for sale or distribution
CT-19	Permission to import new API for sale or distribution
CT-20	Permission to import new drug formulations for sale or distribution
CT-21	Application for permission to manufacture new drug formulation for sale or distribution
CT-22	Permission to manufacture new API for sale or distribution
CT-23	Permission to manufacture new drug formulations for sale or distribution

a) Application Types:

The CDSCO classifies drug registration into four categories: Investigational New Drug, (70) New Drug, (71) Subsequent New Drug, (72) and Fixed Dose Combination (73):

- **Investigational New Drug (IND):**

According to NDCT Rules 2019, an Investigational New Drug (IND) is a new chemical or biological entity or substance not approved for marketing in any country. (70) To conduct clinical trials on an IND, Form CT-04 must be submitted with Ethics Committee approval. (74) For manufacturing and import, Forms CT-10 (75) and CT-16 (76) are required. The Central Licence Authority (CLA) issues Form CT-06 for trial permission, (77) Form CT-11 for manufacturing, (78) and Form CT-17 for import of an IND. (79) An IND application must include the applicant's identity, product details, trial information, clinical trial protocols, Investigator's Brochure, CMC data, and Ethics Committee approval. (80)

Table 10. Required forms and mandatory enclosures for clinical trials in India

Form	Mandatory Enclosures
CT-04	Chemical/pharmaceutical data; Non-clinical and clinical summaries; Investigator's Brochure; Clinical trial protocol; Consent documents; CRFs; Ethics approval; Sponsor and investigator undertakings; Sample labeling; Fee receipt
CT-10	Cover letter; Manufacturing licence/GMP proof; CMC data; Master formula/batch record; Process validation; Analytical methods; CoAs; Stability data; Label/package specimen; Site Master File; Protocol/Ethics approval; Fee receipt
CT-11A	CT-10 reference; Declaration of initiation; Fee receipt
CT-16	Investigator's Brochure; Trial protocol; Ethics approval; Sponsor undertakings; Free Sale/GMP certificate; CoAs of imported batches; Label/package specimen

- **New Drug:**

A new drug in India is a chemical or biological substance not previously approved or widely used, or an approved drug with modified claims, a novel delivery system, or new formulation, including vaccines and r-DNA products. (71) Marketing or manufacturing requires Form CT-21, (81,82) while imports require Form CT-18. (83) Local clinical trial data is generally needed under the Second Schedule but may be waived if approved in specified countries with no major safety concerns and Phase IV studies conducted. (84) For clinical development, sponsors must submit Form CT-04 for trial permission, (74) and Form CT-10 for manufacturing clinical supplies in India. (75)

Table 11. Required forms for New Drug registration in India (85-89)

Stage	Purpose	Application Form	Grant Form
Import (API)	Import of new API for sale/distribution	CT-18	CT-19
Import (formulation)	Import of the pharmaceutical formulation of a new drug	CT-18	CT-20
Manufacture (formulation)	Manufacture of a new drug formulation for sale/distribution	CT-21	CT-23
Manufacture (API)	Manufacture of new API for sale/distribution	CT-21	CT-22

The key data required for the New Drug application in India are CMC, Non-clinical, and Clinical data. The exact data requirements and attachments with each form are detailed in Table 12.

Table 12. Key data and attachments required to be submitted with New Drug Application forms in India

Form	Mandatory enclosures
CT-18	CMC summary (identity, specs, methods, stability), non-clinical/toxicology summary, clinical safety/PK summaries, CoAs & QA/QC, draft PI/labels, GMP/Free-Sale, fee receipt
CT-19	Full API dossier (identity, phys-chem, specs, methods, impurities), batch CoAs, GMP/Free-Sale certs, shipping docs, fee receipt
CT-20	Finished product CMC (composition, methods, CoAs, release data), stability for closure, draft PI/labels, GMP/Free-Sale, shipping docs, fee receipt
CT-21	**Category A (full):** complete CMC, non-clinical toxicology, clinical CSRs, QA/QC records, risk management/PI, licences, fee receipt. **B–D:** abridged/targeted datasets per category (stability, CoAs, PI, phytodata etc.)
CT-22	API dossier (identity, properties, specs, method validation, impurities), process/validation/batch records, Site Master File, GMP certificate, fee receipt
CT-23	FPP CMC (master formula, processes, IPCs, validations, CoAs), stability for packaging, method validation, draft PI/labels, distribution plan, fee receipt
CT-24	Clinical justification (physician letters, patient summaries), manufacturer details & safety evidence, CoAs if available, legal undertakings (restricted use, compensation), fee receipt

- **Subsequent New Drug:**

A subsequent new drug is an approved product proposed with new or modified claims, such as a new indication, dose, route, strength, or dosage form. (72) Permission to manufacture or market requires Form CT-21 with a case-specific data package. Chemical or pharmaceutical data may be omitted if the same formulation is already approved, but additional non-clinical or clinical data are needed if the change affects the risk–benefit profile. (90,91)

- ***Fixed Dose Combination (FDC):***

NDCTR classifies fixed-dose combinations (FDCs) into four groups (73):1) FDCs with one or more new ingredients are treated as new drugs and require full data. 2) FDCs combining approved ingredients for the first time need chemical, stability, and interaction data and may require clinical trials if novel claims exist. 3) Marketed FDCs with ratio or claim changes require supporting rationale. 4) Long-used combinations generally need only stability and interaction justification.

Table 13. Required forms for the Fixed Dose combination registration in India

Stage	Purpose	Application Form	Grant Form
Import (FDC Formulation)	To import a Fixed Dose Combination for sale or distribution in India	CT-18	CT-20
Manufacture (FDC Formulation)	To manufacture a Fixed Dose Combination for sale or distribution in India	CT-21	CT-23
Clinical Trial (FDC)	To conduct a clinical trial for an unapproved FDC (New Drug)	CT-04	-

The Sixth Schedule of the NDCT Rules 2019 outlines the fees for various drug registration applications in India. India has clear, structured fee requirements for each stage and permission (

Table **14**), which increases economic efficiency in drug approval. The standard New Drug Registration application fee in India is 500000 Indian Rupees.

Table 14. Application fee for drug registration in India (91)

Form No.	Purpose / Submission Type	Fee (₹)
CT-04 (Phase I–IV)	Permission to conduct clinical trials	2,00,000–3,00,000
CT-18: New Molecule / FDC Group 1	Import of new drug or FDC treated as new	3,00,000
CT-18: Approved Elsewhere / FDC Group 2	Import of approved drug abroad or first-time combination	2,00,000
CT-18: Annual Renewal	Renewal of import license	50,000
CT-21: New Molecule / FDC Group 1	Manufacture of new drug or FDC treated as new	5,00,000
CT-21: Approved Elsewhere / FDC Group 2	Manufacture of approved drug abroad/first-time combination	2,00,000
CT-21: Annual Renewal	Renewal of manufacturing license	1,00,000

5.2 Drug Review:

In India, IND, New Drug, and Subsequent New Drug applications are regulated under the New Drugs and Clinical Trials Rules, 2019, with the CDSCO and DCGI as the Central Licensing Authority (CLA). (68) The CLA has 90 working days to review INDs, compared with 30 days for the US FDA, (92,15) with notification via Form CT-06A and legally valid deemed approval. (93) IND approval requires scientific validity, ethical conduct, and sufficient non-clinical safety data, (94,95) with benefit–risk assessed through toxicology, manufacturing, and protocol review. New drug applications follow the same 90-day timeline; import requires Form CT-18,(83) manufacture Form CT-21, (82) and applications are processed under Rules 75–76 (96,97) and 80–81 (98,99), yielding CT-19/CT-20 for import and CT-22/CT-23 for manufacture. Approval ensures safety, efficacy, and quality per trial data and Second Schedule CMC information, (100) with CLA and expert committees confirming benefits outweigh risks. Subsequent new drugs rely on existing data, with abbreviated Second Schedule requirements, (101) depending on changes such as new indication, dosage form, route, or strength, while the CLA ensures justified claims, maintained quality, and favorable benefit–risk. (99) Fixed-dose combinations follow the new drug pathway, requiring full NDA data for new drugs, (82,102) stability and clinical evidence for new combinations, scientific rationale for changes to marketed FDCs, and stability plus therapeutic advantage for long-used safe combinations. (103)

Table 15. Summary of Application forms, their purpose and review timeline for drug approval in India

Category	Purpose	Application Form(s)	Statutory Timeline for CLA Decision
Investigational New Drug (IND) (74)	Permission to Conduct a Clinical Trial	CT-04	90 working days
New Drug / Subsequent New Drug / FDC (82,83)	Permission to Manufacture for sale/ distribution	CT-21	90 working days
	Permission to Import for sale/distribution	CT-18	90 working days
Manufacture of Clinical Trial Supply (75)	Permission to Manufacture an IND/New Drug for clinical trials	CT-10	90 working days
Import of Clinical Trial Supply (76)	Licence to Import an IND/New Drug for clinical trials	CT-16	90 working days

5.3 Drug Approval:

In India, the standard drug approval mechanism is deemed approval, where applications are considered approved if the CLA does not respond within the stipulated timeframe. Expedited pathways complement this, including accelerated approval, local trial waivers, priority review, and orphan drug provisions. Deemed approval applies to clinical trial permission (90 working days, Rule 22), (92) ethics committee registration (45 days, Rule 8),(104) and manufacturing permission (90 days, Rule 53), with notification via forms such as CT-06A and legal validity ensured. Accelerated approval targets drugs for serious, life-threatening, or rare conditions, allowing reliance on surrogate endpoints if a meaningful therapeutic benefit is shown. (105-106) Local trial waivers shorten development for drugs approved abroad, provided there are no major adverse events, no population-specific safety differences, and a Phase IV commitment in India. (98,107) Expedited review prioritizes drugs with significant advantages, including those for serious diseases, unmet needs, or extraordinary circumstances such as disaster management. (108) Orphan drugs, treating conditions affecting fewer than 500,000 people in India, may qualify for these pathways. (62,109)

6. Europe

The European drug approval system operates under a comprehensive legal framework anchored by Regulation (EC) No 726/2004 and Directive 2001/83/EC, which establishes the statutory basis for marketing authorisation procedures across the European Union. (110)

6.1 Regulatory Framework

The EU regulatory framework comprises three layers: the EMA as the central scientific evaluator, the European Commission (EC) as the legal authorising body, and National Competent Authorities (NCAs) for country-specific implementation. (110) Under Regulation (EC) No

726/2004, the EC issues legally binding authorisations based on EMA recommendations. EMA evaluates and supervises medicines, while NCAs regulate them locally, collectively ensuring quality, safety, and efficacy.

a) Committee for Medicinal Products for Human Use (CHMP)

Being the EU's leading scientific authority, CHMP comprises experts from all member states, as established under Article 5 of Regulation (EC) No 726/2004 (110-111) It assesses quality, safety, and efficacy data through a peer-review process, with a rapporteur and a co-rapporteur (111) ensuring independent evaluations by at least two states as per Article 62 of Regulation (EC) No 726/2004. (110)

b) Pharmacovigilance Risk Assessment Committee (PRAC)

The Pharmacovigilance Risk Assessment Committee (PRAC), established in 2012, (112-113) reviews risk management plans, post-authorisation safety studies, and pharmacovigilance data. Its recommendations directly inform CHMP opinions, ensuring continuous assessment of a medicine's risk-benefit balance throughout its lifecycle, a core principle of the EU pharmacovigilance framework. (114)

6.2 Drug Registration

a) Centralised Procedure:

The Centralised Procedure allows a single EU-wide marketing authorisation via the EMA. (110) CHMP evaluates scientifically, and the European Commission issues a binding authorisation valid across the EU, Iceland, Liechtenstein, and Norway. (115-117) Mandatory for new active substances, biotech, advanced-therapy, orphan, and certain veterinary drugs. (110) Sponsors bear costs; SMEs get 90% reduction, orphan drugs are exempt, and no fees apply for trials, renewals, or PRIME. (118–121)

Table 16. Required Forms and their applicability for Drug Registration in Europe (122-124)

Application Type	Form / Description	Purpose
Clinical Trial	Clinical Trial Application Form (Annexe 1, EU CTR 536/2014)	Authorisation for clinical trials across EU via CTIS
Initial MA	Human Marketing Authorisation eAF	Submission for initial approval of a new medicinal product (centralised)
Line Extension	Human Line Extension eAF	Add new strengths, forms, or indications to existing MA
Type IA Variation	Human Type IA Variation eAF	Minor administrative changes, no safety/efficacy impact
Type IB Variation	Human Type IB Variation eAF	Moderate changes, prior approval needed
Type II Variation	Human Type II Variation eAF	Major changes needing full scientific assessment
Renewal	Human Renewal eAF	Renew MA (typically every 5 years)
Transfer MA	Human Transfer eAF	Change holder of marketing authorisation

Table 17. Fees for drug registration in Europe

Application Type	Standard Fee (EUR)
INITIAL MARKETING AUTHORISATION (Human - Annexe I, Sec. 2)	
New Active Substance (NAS)	865,200
Known Active Substance	690,700
Fixed Combination	571,100
Biosimilar	732,400
Hybrid Application	780,900
Generic	177,900
Similar Biological	426,100
LINE EXTENSION / VARIATIONS (Human)	
Extension of MA (Level I)	168,500
Extension of MA (Level II)	196,800
Type II Variation (e.g., new indication)	163,200

b) Decentralised Procedure (DCP)

The Decentralised Procedure allows simultaneous marketing authorisation in multiple EU Member States for products not yet authorised in the EU, requiring submission of a full eCTD v3.2.2 dossier (Modules 1–5) via the Common European Submission Portal with one Reference Member State and multiple Concerned Member States, while administrative requirements in Module 1 differ due to national forms, fee proofs, local contacts and translation of product information into each CMS language, making the submission more complex than a single EMA application. (116–117)

c) National procedure (NP)

The National Procedure seeks marketing authorisation within a single Member State for products targeting a local population, ineligible medicines, or as a precursor to a Mutual Recognition Procedure (MRP). (116) It involves one national competent authority, a single fee, and submission of the full eCTD and product information in

the official language. Authorisation is territorially restricted, requiring separate processes for other markets. (116) Scientific and technical data (Modules 2–5) must meet EU standards, and Module 1 plus full Product Information (SmPC, PL, labelling) must comply with national templates, forms, and any additional local requirements. (122–123)

d) Mutual Recognition Procedure (MRP)

The Mutual Recognition Procedure extends an existing national marketing authorisation from a Reference Member State to Concerned Member States, which recognise the RMS approval rather than conduct a new assessment, requiring submission of the RMS-approved eCTD dossier, Assessment Report and approved product information (SmPC, PL and labelling), along with precise translations for each CMS and necessary administrative documents, while the process remains dependent on prior national authorisation in the RMS. (116,124)

Data Format

The Centralised Procedure requires eCTD v3.2.2 with EU Module 1 v3.1.1, (125,126) submitted via EMA e-Submission Gateway or Web Client (127) using eAF forms; digital signatures are not required, though some NCAs may request originals. (128) DCP/MRP submissions use the CESP, (129) but some countries require signed forms, national-language cover letters, or alternative methods (e.g., Bulgaria, (130) Greece, Slovakia. (131) National Procedures vary, with country-specific portals, paper submissions, and eCTD validation criteria. (132)

6.3 Drug Review:

European drug review uses a regulated "clock stop" system for rigorous assessment. (133) The 210-day review for Centralised, Decentralised, and Mutual Recognition procedures covers regulators' evaluation; clock stops let applicants respond without altering review of quality, safety, efficacy, or risk management. (134,135) Clock stop responsibility: EMA committees (Centralised), (133) RMS/CMSs (Decentralised/Mutual Recognition), (136,137) NCAs (National). Standard timelines: 210 active days plus finalisation; CMSs have 90 days to accept or object to RMS assessments.

Table 18. Review Timelines for Drug Application in Europe

Procedure	Evaluating Bodies	Decision Issued By	Total Drug Approval Time
Centralised	EMA CHMP, PRAC, CAT, EU-level expert groups	European Commission	277 days
Decentralised	RMS scientific experts, CMS reviewers, and CMDH arbitration	Individual NCAs (each CMS)	300 days
National	National scientific committees and expert sub-groups	Respective NCA	Around 210 days (Varies)
Mutual Recognition	RMS experts, CMS reviewers, and CMDH arbitration	Individual NCAs (each CMS)	90 days

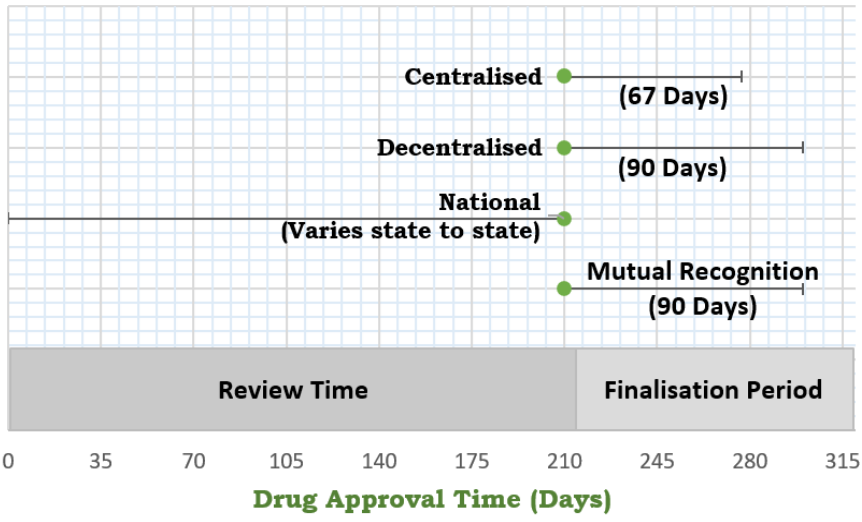


Figure 4. Drug approval Time in the Europe

6.4 Drug approval:

Standard Marketing Authorisation (MA) provides full, unrestricted approval based on complete data on pharmaceutical quality, non-clinical safety, and clinical efficacy, and is valid indefinitely subject to safety considerations. (110)

Conditional MA (CMA) allows early access for unmet medical needs despite incomplete data; under Articles 14a of Regulation (EC) No 726/2004 (110) and 507/2006, (138) CHMP may grant CMA if benefit–risk is positive, comprehensive data are likely post-approval, the product meets an unmet need, and immediate availability outweighs risks. Marketing Authorisation under

Exceptional Circumstances applies when comprehensive data cannot be obtained, such as very rare diseases, with annual re-evaluation and ongoing safety monitoring. (139) Accelerated Assessment is a procedural mechanism shortening review from 210 to 150 days for medicines of major public health interest or significant innovation. (139)

7. Comparison of drug approval in India, US and Europe

US, India and Europe regulations have adopted different systems for the drug approval. This causes the fundamental difference in the critical factors for drug approvals such as review speed, application cost.

7.1 Review Speed:

The comparison of drug approval timelines across Europe, India and the US is presented in the Figure 5. The complete analysis shows that the new drug applications have higher review periods than those of the abbreviated and investigational new drug applications. Europe has the slowest review process; the USFDA follows Europe, but shows a significant review time reduction in the priority conditions. The approval time for drug approval in India is significantly less than that of both the US FDA and the European Union. Figure 5 compares drug approval timelines across Europe, India, and the USA. New drug applications have longer review periods than abbreviated or investigational applications. Europe exhibits the slowest review process, followed by the US FDA, which shows reduced timelines for priority drugs. India's approval times are substantially shorter than both the US and EU.

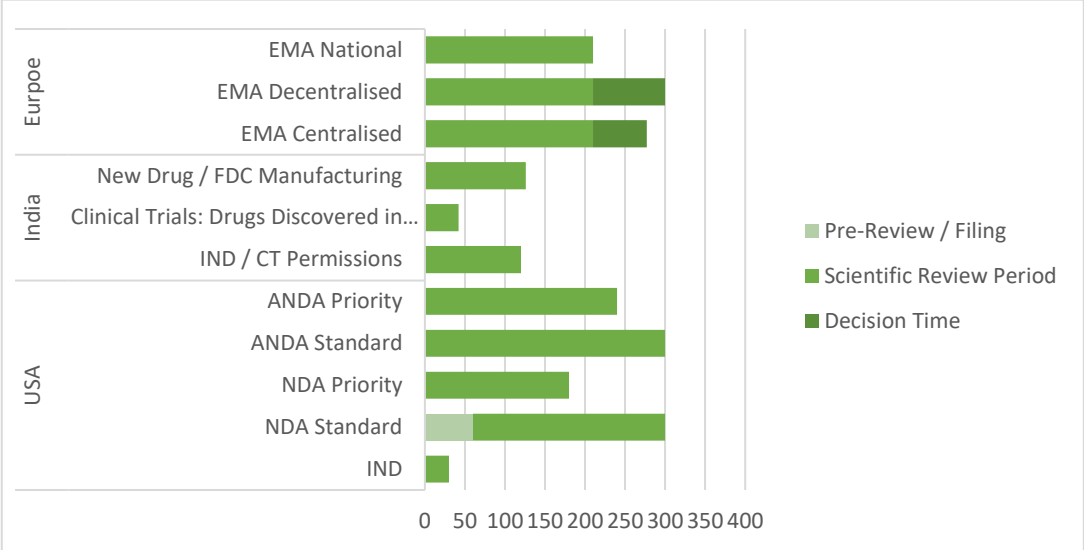


Figure 5. comparison of drug approval timelines across Europe, India and US

7.2 Application Cost:

Across the US, India, and the EU, new drug approval costs differ substantially. Regulatory filings were grouped into clinical trial authorisations, new drug applications (NDA in the U.S., New Drug Application in India, MAA in Europe), and generic applications (ANDA in the U.S. and equivalents). Fees were converted to USD using 2024 exchange rates (1 USD = INR 83.68; 1 EUR = 0.92 USD) for comparability. The U.S. has the highest fees: NDA ~$4.68 million (≈784× India, 5× Europe) and ANDA $358,247 (≈100× India, ~2× Europe). Europe offers structured relief for SMEs and orphan drugs, while India provides broad exemptions and the lowest generic entry costs. Despite high fees, the U.S. market remains the most lucrative (~53% global share), excluding lifecycle costs such as inspections, dossier preparation, compliance, and post-approval monitoring.

Table 19. Comparison of Regulatory Fee Waivers for Different Sponsor Categories Across the USA, India, and Europe

Category	Waiver Details	% Waiver		
		US	India	Europe
Orphan Drug	Application Fees	100	100	100
	Scientific Advice	100	100	100
	Marketing Authorization	100	100	100
SME	Scientific Advice	NA	NA	90
	Marketing Authorization	NA	NA	Fees Deferral
Micro Enterprises	All Fees	NA	NA	100
Academic/Government Institutions	Clinical Trials	Case by Case	100	100
	Application Fees	Case by Case	100	NA
Pediatric Development	Non-orphan pediatrics	NA	NA	100
Advanced Therapies	Scientific Advice	NA	NA	65
Special Situations	Public Health Emergency	Case by Case	Fast Track	100

	MSME Clinical Trials	NA	50	NA

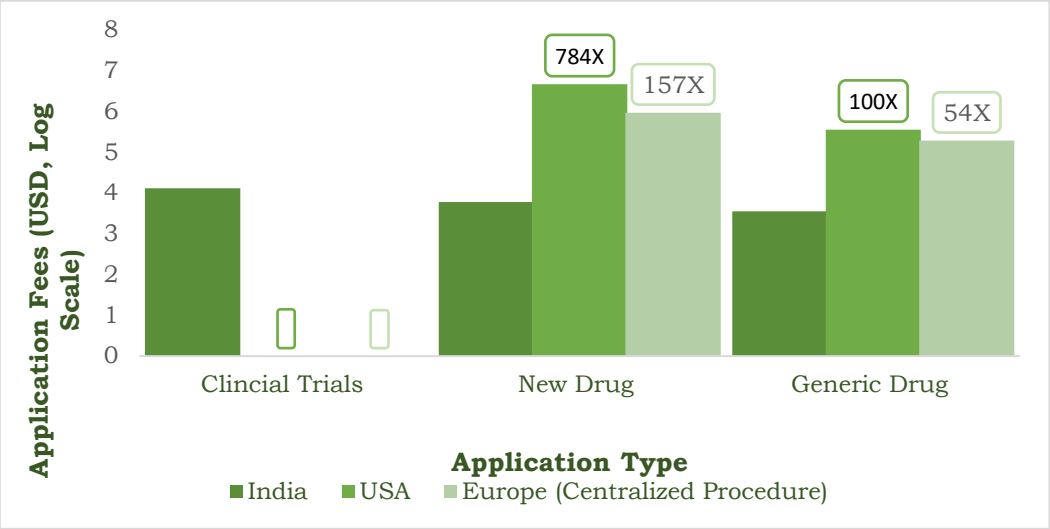


Figure 6. Application Cost Comparison for drug approval in India, US and Europe (Centralized Procedure)

8. Conclusion

This comparative analysis shows that while the U.S. Food and Drug Administration, European Medicines Agency, and Central Drugs Standard Control Organization follow a common three-stage approval framework, they differ significantly in cost, timelines, and regulatory incentives. The US adopts a high-cost, innovation-driven model suited to high-value therapies targeting a large market. The EU offers a structured, incentive-based system that strongly supports SMEs and orphan or specialised products. India provides the most cost-efficient and time-predictable pathway, favouring generics and cost-sensitive development. Overall, regulatory strategy must align with product profile and commercial goals, as jurisdictional choice directly shapes global market access and development efficiency

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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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