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Approval Trends of Recombinant DNA (r-DNA) Therapeutics in India: A Five-Year Review

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Abstract

Introduction: Recombinant DNA (r-DNA) technology has revolutionized modern therapeutics, enabling the large-scale production of safe, effective, and targeted biologics. India has witnessed a growing adoption of r-DNA-based therapies in diverse disease areas over the past five years. This review systematically analyzes the approval trends of r-DNA therapeutics in India between 2020 and 2024, highlights regulatory frameworks, therapeutic areas, and discusses the associated market dynamics and challenges. Approval data were obtained from the Central Drugs Standard Control Organization (CDSCO) and supplemented with information from published literature, drug databases, and industry reports. Therapeutics were categorized based on indication, origin (indigenous/imported), and product type. A total of 111 r-DNA therapeutics was approved over the five-year period, with a significant surge in 2023. Oncology constituted the leading therapeutic area (38% of total approvals), followed by diabetes, hemophilia, and osteoporosis. The majority of approvals were monoclonal antibodies and recombinant proteins. Despite the progress, a substantial portion of the products remain imported, highlighting gaps in local manufacturing.

Conclusion: India is emerging as a significant player in r-DNA therapeutics. However, regulatory harmonization, indigenous development, cost containment, and infrastructure strengthening are essential to realize the full potential of r-DNA technology in improving public health outcomes.

Keywords: Biologics, Recombinant DNA, Approval Trends, CDSCO, US FDA, EMA, Biotechnology in India, Cancer, Haematological Disorder, Diabetes, Osteoporosis

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1. Introduction

Recombinant DNA (r-DNA) technology has fundamentally transformed modern molecular biology by enabling the isolation, modification, and expression of genes across a wide range of organisms. These techniques allow scientists to identify and sequence genes and their encoded proteins, track genetic traits across families and evolutionary transitions, and manipulate genetic material for therapeutic use. The production of therapeutic proteins such as insulin, erythropoietin, and growth hormone has been revolutionized by r-DNA technology, allowing for safe, consistent, and large-scale manufacturing of biologics that are structurally identical to endogenous human proteins. (1) These advancements reduce immunogenicity and eliminate the infection risks associated with non-human or cadaveric sources. (2)

In recent years, molecular therapies have expanded beyond recombinant proteins to include genetic and Ribonucleic Acid (RNA) based technologies that exploit previously untargeted regions of the genome. Although the human genome contains over 20,000 protein-coding genes, fewer than 700 unique proteins are currently targeted by approved therapeutics representing less than 3% of the genome's druggable potential. (3,4) This limited scope underscores the urgency for developing novel therapeutic platforms such as RNA-based drugs and gene-editing systems that can modulate intracellular and non-coding targets inaccessible to conventional therapeutics.

RNA therapeutics-including antisense oligonucleotides (ASOs), small interfering RNAs (siRNAs), aptamers, and Messenger ribonucleic acid (mRNA) based vaccines-have emerged as promising modalities in both research and clinical settings. These molecules are programmable, enabling precise gene silencing or upregulation with high specificity. While aptamers and antagomirs are widely used in preclinical studies, ASOs, siRNAs, and mRNA vaccines have achieved clinical success, particularly during the COVID-19 pandemic. (5,6) However, these approaches still face challenges such as off-target effects, endosomal entrapment, toxicity, and delivery limitations, especially in tissues beyond the liver. (7)

India's regulatory framework for r-DNA-based therapeutics is structured around a multi-agency approach involving:

- The Central Drugs Standard Control Organization (CDSCO), responsible for clinical trial oversight and drug approvals;
- The Department of Biotechnology (DBT) and the Review Committee on Genetic Manipulation (RCGM), which govern preclinical safety assessment for biologics derived from genetically modified organisms;
- The Genetic Engineering Appraisal Committee (GEAC), which provides environmental clearance where applicable. (8)

Two approval categories are recognized:

- Biologics derived using living modified organisms (LMOs), where the final product is not an LMO—typical of most protein-based r-DNA therapeutics.
- Therapeutics containing LMOs as the end product, such as engineered cell or gene therapies.

India's biotechnology journey began in 1982 with the formation of the National Biotechnology Board (NBTB), followed by the establishment of the DBT. This marked a significant institutional foundation for the country's biopharmaceutical ecosystem, which has since matured into one of the largest producers of biosimilars globally. (9) Despite this growth, the r-DNA and recombinant biologics industry faces challenges, particularly regarding affordability, regulatory consistency, skilled workforce availability, and the high cost of production relative to traditional pharmaceuticals. (10)

To ensure product quality, safety, and efficacy, India aligns its regulatory practices with international frameworks such as the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Q5C and Q6B guidelines and the World Health Organization (WHO) Guidelines on Evaluation of Similar Biotherapeutic Products. (Table 1) These standards provide robust criteria for product characterization, impurity profiling, and bioequivalence assessment for biosimilars and novel biologics.

Table 1. ICH Guidelines for Biotechnological Products (11)

Q3E	**Impurity Assessment and Control of Extractables and Leachable for Pharmaceuticals Biologicals**
Q5A-Q5E	Quality of Biotechnological Products
Q5A (R2)	Evaluate the Viral Safety of Biotechnology Products Derived from Human or Animal Cell Lines.
Q5(B)	Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products
Q5(C)	Stability Testing of Biotechnological/Biological Products
Q5(D)	Derivation and Characterization of Cell Substrates Used Production of Biotechnological/Biological Products
Q5(E)	Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process
Q6 (B)	Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products
Q11	Development and manufacture of drug substances (chemical entities and biotechnological/biological entities)
S6(R1)	Preclinical Stability Evaluation of Biotechnology-Derived Pharmaceuticals
M6	Virus and Gene Therapy Vector Shedding and Transmission

This review aims to evaluate the recent trends in the approval of r-DNA-based therapeutics in India between 2020 and 2024. It highlights major therapeutic domains, regulatory milestones, market dynamics, and gaps in local manufacturing capacity, offering insights into policy and innovation pathways that can strengthen India's leadership in biopharmaceuticals.

2. Methodology

This study employed a structured and systematic approach to gather, analyse, and interpret approval trends for r-DNA based therapeutics in India from January 2020 to March 2025. The primary data source was the CDSCO database—India's apex regulatory body under the Ministry of Health and Family Welfare—which provides publicly accessible information on approved drugs, biologics, and biosimilars.

The search strategy focused exclusively on biopharmaceuticals classified under "r-DNA technology", including both original biologics and biosimilars. Approval documents, product registration details, and regulatory circulars were meticulously reviewed to confirm the r-DNA-based nature of the therapeutic products and their respective approval timelines.

To ensure comprehensive data collection and contextual depth, additional information was retrieved from:

- Peer-reviewed scientific journals indexed in PubMed, Scopus, and Web of Science,
- Global biomedical databases such as Drug Bank, the WHO Drug Information System, and the Biotechnology Industry Research Assistance Council (BIRAC) archives,
- Annual reports and product pipelines of Indian pharmaceutical companies,
- Regulatory filings, investor presentations, and press releases published by biopharmaceutical firms.

Each approved r-DNA therapeutic was categorized using a four-dimensional classification:

- Therapeutic area – based on the International Classification of Diseases (ICD-11) and further aligned with regulatory terminology (e.g.,

oncology, endocrinology, haematology, immunology).
- Molecular class – such as monoclonal antibodies (mAbs), fusion proteins, recombinant enzymes, cytokines, and recombinant hormones.
- Manufacturing origin – classified as indigenous (developed and manufactured in India) or imported (manufactured overseas and marketed in India).
- Approval chronology – year-wise approval trend from 2020 to 2025.

Data analysis included both quantitative and qualitative methods. Descriptive statistics were used to summarize the number and type of approved products across different categories. Graphical representations, including bar graphs and pie charts were generated to visually depict the growth trajectory and therapeutic focus of the biotherapeutic landscape.

To explore policy-level implications and market dynamics, secondary sources such as regulatory policy briefs, expert committee reports, and industry white papers were critically analysed.

This multi-source, multi-dimensional methodological framework ensured robustness, reproducibility, and a comprehensive understanding of r-DNA therapeutics approval trends in India.

3. Market Status and Potential of Biotherapeutics in India

India's biotherapeutics sector has emerged as a critical growth engine within its pharmaceutical landscape, underpinned by cost-competitive manufacturing, scientific expertise, and a rapidly expanding domestic and global demand for biosimilars and other biologics. The market includes a broad spectrum of r-DNA-based products such as monoclonal antibodies, hormones, cytokines, vaccines, diagnostics, and animal biologicals. (12-14) India's biosimilars market has demonstrated exponential growth, driven by cost-effective manufacturing, regulatory reforms, and increasing demand for biologic therapies. While precise scientific literature on market valuation remains limited, industry analyses provide critical insights. The biosimilars market was valued at $349 million in 2022 and is projected to grow at a CAGR of 25.2% to reach $2.1 billion by 2030. (15) India's broader biologics market, which includes biosimilars, reached $12.3 billion in 2024 and is expected to grow at an 8% CAGR to $24.6 billion by 2033. (16) India's increasing biosimilars production capacity, coupled with supportive regulatory frameworks and rising healthcare demand, positions it to capture a substantial share of the global market. (13,14,17) Historically, India's introduction of over 50 biosimilar and biotherapeutic products at up to 85% lower prices than originator biologics has dramatically improved patient access and affordability. In FY 2009–2010, leading biologics such as Erythropoietin and Interferon generated $22 million each in sales, while Granulocyte Colony-Stimulating Factor (G-CSF) and Streptokinase contributed $11 million and $15 million respectively—early indicators of market acceptance. (18,19) However, despite these gains, the penetration of biotherapeutics in India has been hindered by low health insurance coverage, limiting the affordability and reach of high-cost biologic therapies. This challenge is gradually being offset by a rising middle class, increasing health awareness, and a growing prevalence of chronic and lifestyle-related diseases, which are creating a robust demand for biologic treatment options. (20-22)

The Government of India has played an enabling role through targeted policies such as the ongoing "National Biotechnology Development Strategy 2020–2025." These frameworks promote innovation, encourage investment in biopharmaceutical R&D, support infrastructure development, and aim to streamline regulatory pathways for biologics and biosimilars. (23)

India's export capability remains another major strength, supplying more than 50% of the global demand for vaccines and around 40% of the generic drugs consumed in the U.S. However, entry into highly regulated developed markets continues to be constrained by the complexity and cost of clinical trials, stringent regulatory requirements, and intellectual property challenges. To navigate these barriers, Indian biopharmaceutical companies increasingly pursue strategic alliances, licensing agreements, and co-development partnerships with multinational firms. These collaborations allow for risk-sharing, technology access, and accelerated market entry into regions such as North America, Europe, and Latin America. (24)

4. Approval Process for r-DNA Therapeutics in India

The regulatory approval pathway for r-DNA-based therapeutics in India involves a complex, multi-agency process designed to ensure the safety, efficacy, and quality of these biologics before they reach patients. This pathway begins with preclinical development, which requires prior authorization from either the State Licensing Authority (SLA) or the CDSCO, depending on the nature of the study. Developers must submit specific forms—Form C3 to seek permission for conducting preclinical studies involving genetically modified materials, and Form C5 to present study protocols and reports for approval from the RCGM, operating under the DBT (Table 2). (25) Institutional Biosafety Committee (IBSC) clearance is also mandatory prior to any genetic manipulation. Following successful preclinical evaluation, sponsors must obtain approval from CDSCO to initiate clinical trials, which requires submission of an Investigational New Drug (IND) dossier containing preclinical data, chemistry and manufacturing information, clinical protocols, ethics committee approvals, and registration with the Clinical Trials Registry of India (CTRI).

Table 2. The following application forms can be used to submit requests to regulatory agencies

Phase	Regulatory Agency Involved	Form for Application	Form for Approval
Manufacturing Licence for Inspection, Testing, and Assessment	State FDA or CDSCO	Form 30	Form 29
Permission for preclinical research	RCGM	Form C3	Form C4

Preclinical study report submission	RCGM	Form C5	Form C6
Clinical Trial	CDSCO	Form 44	Approval letter
Permission for Manufacturing and Marketing	CDSCO	Form 44	Form 45/46 (Finished product)
Form 46A (Bulk product)	-	-	-
Production Permit	State FDA/ CDSCO	Form 27 D	Form 28 D
License for Import and Registration	CDSCO	Form 40/ Form 8	Form 41/Form 10

5. The Approval Trend of r-DNA Therapeutics in India

Over the previous five years, there has been a notable growth in the approval of r-DNA therapies (2020–2025). These medicines are being used to treat a wide range of ailments, such as blood clotting disorders, diabetes, and migraine. (26) This suggests that r-DNA therapies have a greater chance to enhance medical outcomes in India. Upon closer inspection, the vast majority of authorized medications fall under the class of monoclonal antibodies. This illustrates the field's efficacy and expanding capabilities. It's crucial to remember that a sizable percentage of these r-DNA treatments are still imported. This restricts accessibility for certain patients because of possible increased expenses and logistical difficulties. All things considered, the data points to a promising future for r-DNA therapies in India. Continued research funding, smoother regulations, and affordability efforts can unlock r-DNA technology's potential to revolutionize Indian healthcare. The r-DNA is approved for different indications of use and is most of approved for different types of Cancer diseases.

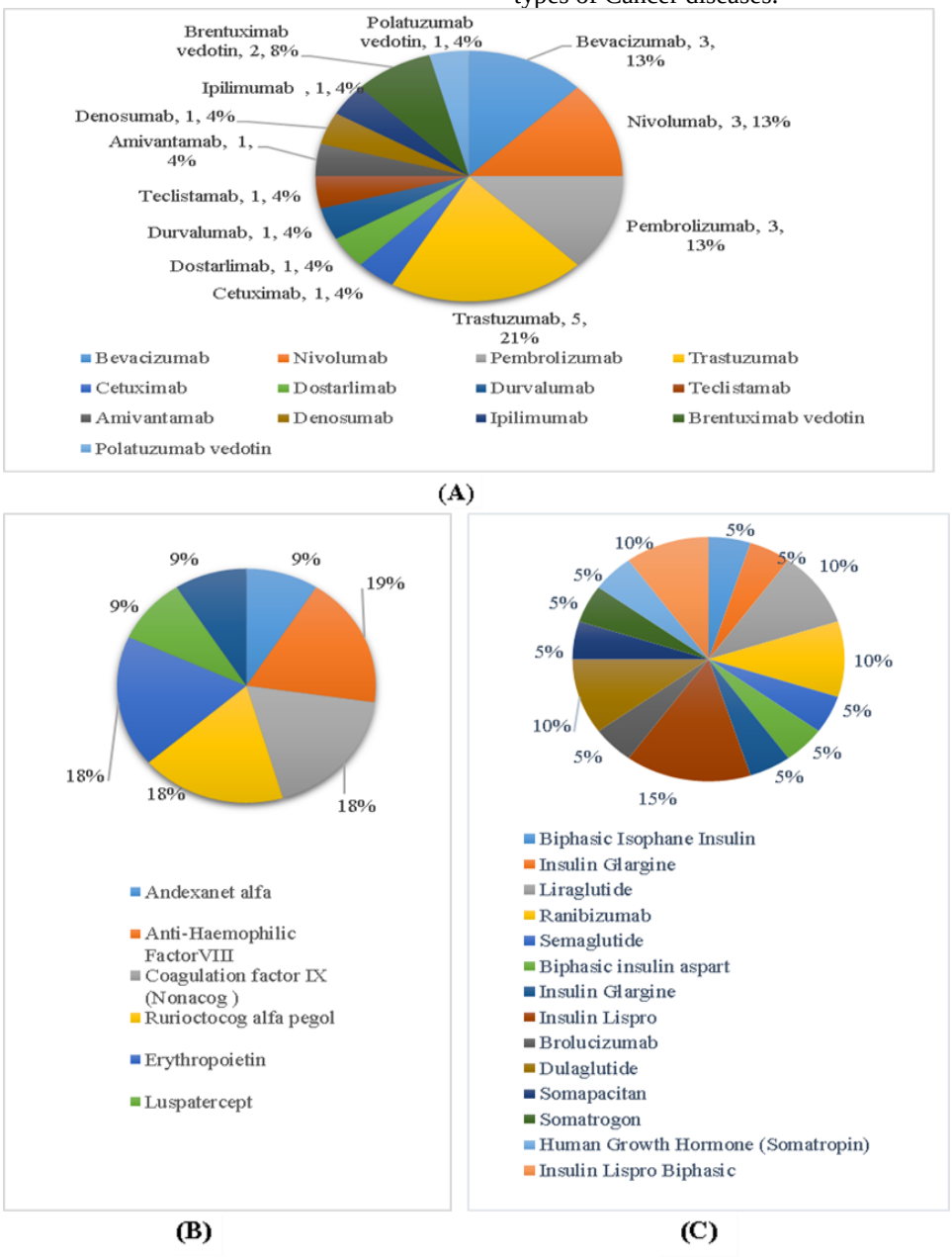

Figure 1. Representation of approved r-DNA therapeutics in India, categorized by indication: (A) cancer, (B) haematological disorders, and (C) endocrine disorders

Figure 1 illustrates the total number of r-DNA based therapeutics approved in India for the treatment of (A) cancer, (B) haematological disorders, and (C) endocrine disorders.

5.1 Cancer disorders

Cancer treatment remains highly complex due to the significant overlap between the metabolic pathways of healthy and malignant cells. Achieving selectivity—targeting only cancer cells while sparing normal ones—continues to be the central challenge in therapeutic development. (27) In the past five years, a total of 13 cancer therapeutics have been approved. Among them, Bevacizumab, Pembrolizumab, Nivolumab, and Trastuzumab are the most frequently approved drugs. Bevacizumab, a vascular endothelial growth factor (VEGF) inhibitor, was approved in 2023 for hepatocellular carcinoma and metastatic colon carcinoma, and in 2024 for metastatic colorectal, breast, cervical, and hepatocellular cancers. It remains the most extensively approved anti-cancer drug to date. Nivolumab and Pembrolizumab, both PD-1 (programmed cell death protein 1) inhibitors, are used to treat a broad spectrum of malignancies, including lung, colorectal, melanoma, cervical, and renal cancers. Other recently approved drugs include Cetuximab (2023), Dostarlimab, Durvalumab, Teclistamab, Amivantamab, and Ipilimumab, all of which have been introduced for a wide range of cancer indications. (28, 29)

5.2 Haematological Disorders

Hemophilia A is a rare X-linked recessive disorder affecting approximately 1 in 10,000 males, caused by a deficiency in clotting factor VIII. Total six drugs have been approved for hematological disorders. Among them, Nonacog and Rurioctocog alfa pegol are anti-hemophilic factor VIII products, with Rurioctocog alfa pegol receiving approval in 2020 and again in 2023 by different manufacturers. Andexanet alfa, a recombinant factor Xa, was approved in 2024 and is used to reverse anticoagulation. Erythropoietin, approved in 2021 and 2023, and Darbepoetin alfa are widely used erythropoiesis-stimulating agents, with Darbepoetin alfa offering extended dosing intervals due to its longer half-life. Luspatercept is approved for the treatment of myelodysplastic syndromes and β-thalassemia. Crizanlizumab, an IgG2 monoclonal antibody, has been approved for the treatment of sickle cell disease. Myelodysplastic syndromes are rare hematologic malignancies caused by clonal stem cell abnormalities, involving disruptions in genetic processes such as transcription and cytokine signaling. (30-33)

5.3 Endocrine Disorders

Figure 1(C) presents 14 therapeutics approved for the treatment of endocrine disorders. Among them, Liraglutide and Insulin Lispro Ultra Rapid are peptide-based drugs widely used in diabetes management. Biphasic Isophane Insulin and Insulin Glargine are long-acting insulin formulations, categorized as recombinant protein-based hormones. Liraglutide and Semaglutide are glucagon-like peptide-1 (GLP-1) receptor agonists, belonging to the class of therapeutic peptides. Ranibizumab is a monoclonal antibody fragment (IgG1 kappa isotype) designed as a targeted biologic therapy. (34) Dulaglutide is also a GLP-1 receptor agonist and falls under the category of therapeutic peptides. Additionally, Somatrogon and Recombinant Human Growth Hormone (Somatropin) are hormone-based biologics approved in 2022 and 2020, respectively, and are classified as recombinant protein therapeutics. (35)

5.4 Neurological Disorders

A total of four drugs have been approved for neurological disorders (Figure 2 A). Erenumab, approved in 2024, works by inhibiting the calcitonin gene-related peptide (CGRP) receptor to prevent migraines. Galcanezumab, approved in 2023, targets the CGRP molecule itself using a monoclonal antibody, offering effective migraine management. (36) Tenecteplase, a modified form of recombinant human tissue plasminogen activator, is used for the treatment of acute stroke. Multiple sclerosis (MS) is an inflammatory and autoimmune disease of the central nervous system. (37) Natalizumab was the first monoclonal antibody approved for the treatment of relapsing-remitting multiple sclerosis (RRMS). Despite its clinical efficacy, its use is limited due to the risk of progressive multifocal leukoencephalopathy. (38-40) Ocrelizumab, which targets CD20-expressing B cells, was FDA-approved in 2017 and later in 2023 for treating severe adult MS. It depletes B cells through complement-dependent cytotoxicity, antibody-dependent cellular phagocytosis, and apoptosis, while sparing plasma cells to preserve innate, adaptive, and humoral immunity. (41)

5.5 Musculoskeletal Disorders

Tumor necrosis factor-alpha (TNF-α) is a key pro-inflammatory cytokine involved in the pathophysiology of rheumatoid arthritis (RA). A total of eight drugs have been approved for musculoskeletal disorders, including arthritis and spondyloarthropathies. In 2023, two drugs were approved for arthritis, while additional approvals occurred in 2021 and 2024. Guselkumab, approved in 2024, treats active psoriatic arthritis by selectively inhibiting interleukin-23. Adalimumab and Golimumab are TNF-α inhibitors used in rheumatoid arthritis. Infliximab is approved for multiple inflammatory conditions, including Crohn's disease, ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis. (42)
Ankylosing spondylitis (AS) is a common form of spondyloarthropathy, with significant progress made in its treatment over the past decade. Adalimumab, an anti-TNF-α antibody, is approved for severe active AS in patients who do not respond adequately to conventional therapies. (43)

5.6 Gastrointestinal Disorders

In the European Union, Fabry disease is treated with two approved alpha-galactosidase A formulation, based on human DNA, since 2001. Both are given as infusions every two weeks, with slight differences in production methods and glycosylation patterns. Adverse effects, mainly allergic reactions, may occur in the first three months, and treatment is lifelong. (44) Five drugs have been approved for gastrointestinal disorders. Ulcerative colitis (UC) causes inflammation of the colon and rectum, peaking in

onset between 30-40 years old. Biologics are more immunogenic than small molecular drugs and help control inflammation. (45) Crohn's disease (CD), a Th1 cell-mediated disease, commonly affects the colon. CD symptoms can be subtle, with major causes of death including lung disorders and cancers. (46-48) Agalsidase alfa and Vedolizumab treat Fabry disease, UC, and CD, with Vedolizumab approved for both UC and CD. Ustekinumab, approved in 2022, is also used for CD. (49)

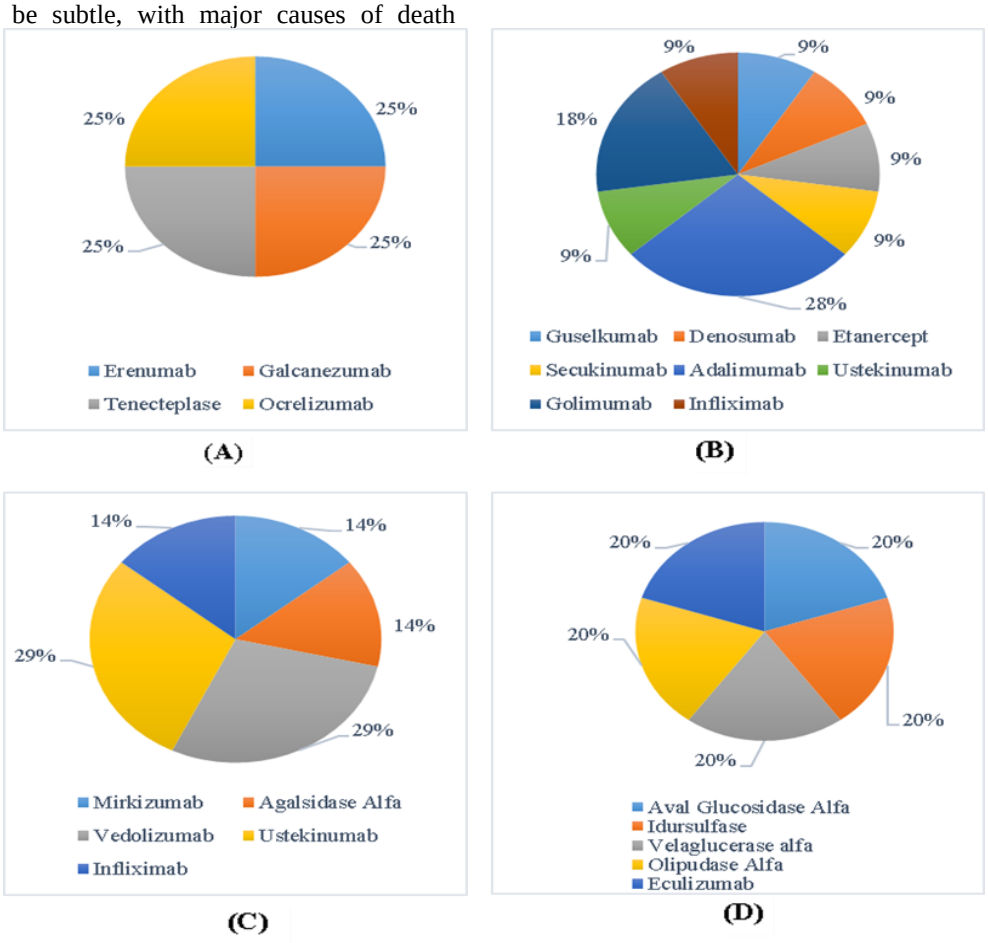

Figure 2. Representation of approved r-DNA therapeutics in India, categorized by indication: (A)Neurological Disorders, (B)Musculoskeletal Disorders, (C)Gastrointestinal Disorders, (D)Genetic Disorders

5.7 Genetic Disorders

Five drugs have been approved for genetic disorders. Pompe disease is treated with alglucosidase alfa, a recombinant enzyme approved since 2006. It is particularly effective for infantile-onset Pompe disease (IOPD) and is administered every two weeks. The introduction of Avalglucosidase alfa marks further advancements in treatment. (50-52) Hunter syndrome (MPS II) is treated with idursulfase, approved in 2023, though its effectiveness is limited in severe cases due to the blood-brain barrier. Gene therapy is showing promise. (53-55) Gaucher disease (GD) varies from asymptomatic to fatal forms. Velaglucerase alfa, a recombinant enzyme, is used to treat type 1 GD. (56,57) Acid sphingomyelinase deficiency (ASMD) is treated with Olipudase alfa, approved for non-CNS symptoms, with ongoing treatment expected to improve long-term outcomes. (58)

5.8 Bone Disorders

Figure 3 illustrates the total number of r-DNA based therapeutics approved in India for the treatment of (A)Bone Disorders, (B)Ophthalmic Disorders, (C) Reproductive Health Disorders, (D) Annual approval trends of r-DNA) therapeutics in India over the last five years.

A progressive skeletal disease that also increases the likelihood of fracture and reduced bone mass, (59) Osteoporosis is caused by disturbances in this physiological process that result in a decrease in bone mass. Unfortunately, current osteoporosis treatments have several side effects, including inadequacies and concerns about long-term safety. (60) The treatments combine bone-strengthening drugs targeting osteoclasts with anabolic steroids or bone minerals. Denosumab has been approved twice for the indication of osteoporosis at high risk of fracture generally in postmenopausal women. The Romosozumab and Teriparatide were approved once. (61)

5.9 Ophthalmic Disorders

Age-related macular degeneration, or AMD, is a major contributor to irreversible blindness in the industrialized world. The management and treatment of neovascular AMD (nAMD) have been completely transformed by anti-VEGF therapy. High drug costs, frequent clinic visits, and lifelong injections for some, strain both patients and healthcare systems. The application of genetic therapy techniques for the continuous delivery of several antiangiogenic proteins may be able to overcome these challenges. (62) There are two primary types of AMD: wet and dry. Neovascular AMD is driven by abnormal new

blood vessels growing from the choroid, the layer supplying the retina with nutrients and oxygen. If the condition is persistent, it can cause fibrosis and atrophy in addition to acute vision loss from leaking.

Ranibizumab is approved in the years 2020 and 2023 inhibiting the vascular endothelial growth factor a (VEGF-a). Faricimab and Brolucizumab are approved once. (63)

5.10 Metabolic Disorders

Obesity is becoming more common and is becoming a serious health concern for both adults and children and teenagers. (64) Obesity-related diseases have been linked to the accumulation of DNA damage in those who suffer from the condition. (65) Because obesity-related DNA damage favors cancer cell migration it can accelerate the spread of the disease. Insulin glargine and Lixisenatide in combination are used to treat obesity with insufficiently controlled type 2 diabetes mellitus. which was approved in the year 2023. Semaglutide which is a glucagon-like peptide 1 receptor agonist used to treat obesity. (66)

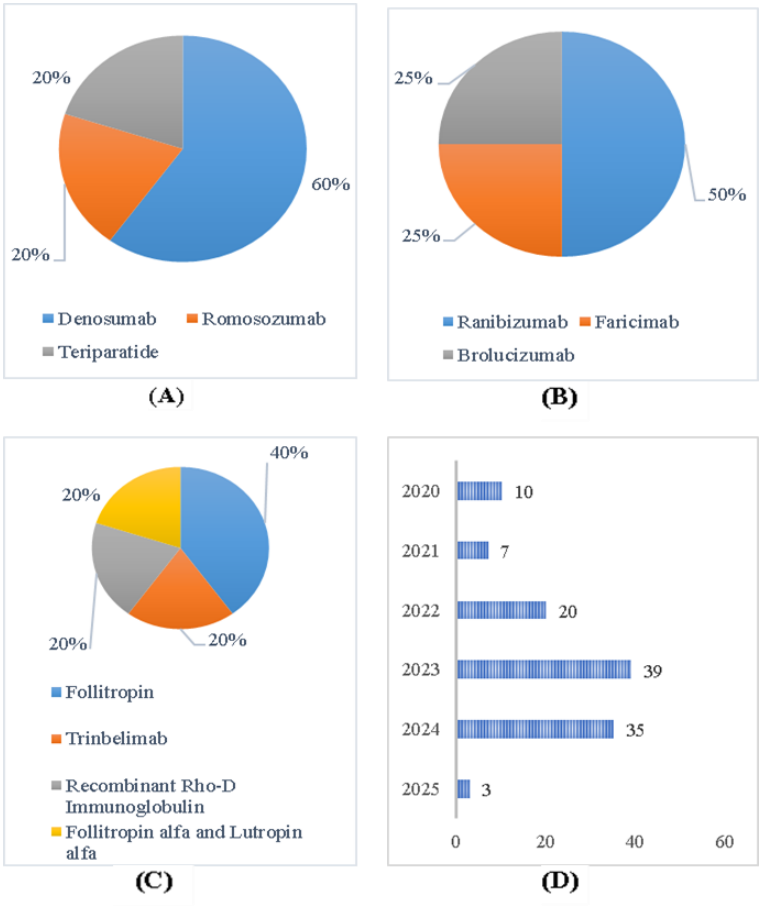

Figure 3. Representation of approved r-DNA therapeutics in India over the last five years, categorized by indication: (A)Bone Disorders, (B)Ophthalmic Disorders, (C) Reproductive Health Disorders, (D) Annual approval trends.

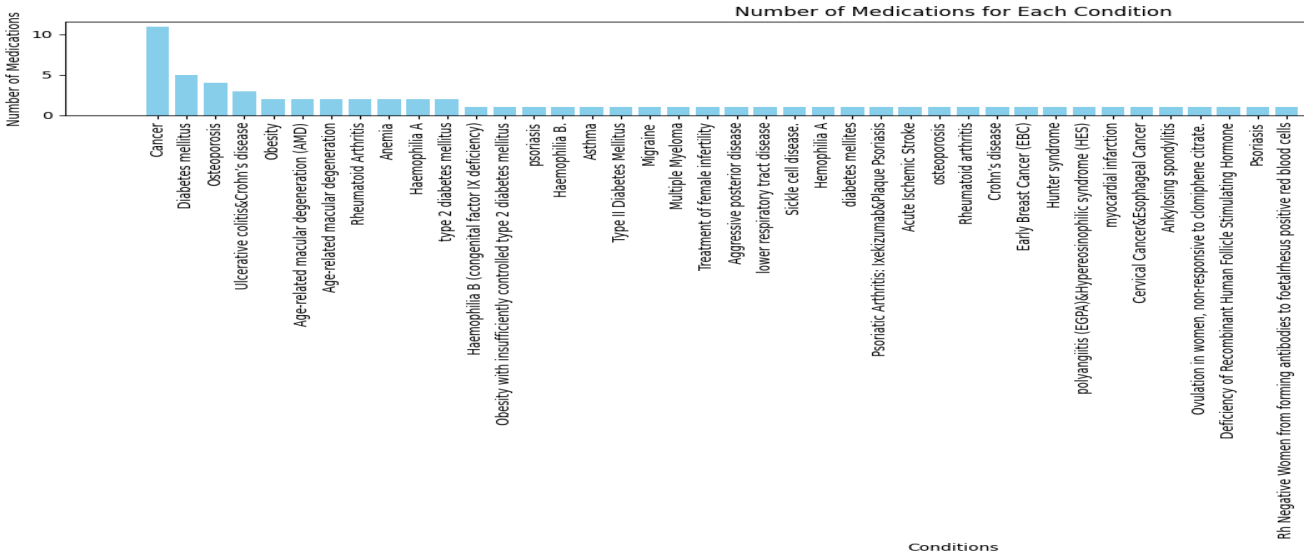

Figure 4. Total number of r-DNA therapeutics approved for the different indications in the last five years in India

5.11 Respiratory related disorders

Palivizumab is a humanized mouse immunoglobulin (IgG1 k) monoclonal antibody made by recombinant DNA technology. The antibody exhibits both neutralizing and fusion inhibitory activity. It targeted a conserved epitope site II of the respiratory syncytial virus (RSV) prefusion and post-fusion protein. The Palivizumab was approved in 2023. The Nirsevimab approved for the Respiratory Syncytial Virus disease in 2024. (67)

The major pathologic hallmarks of asthma are airway remodeling and inflammation. Which causes bronchial hyperresponsiveness and fluctuating airflow limitation. Asthma is a very widespread chronic respiratory disease. (68) Benralizumab exhibits two distinct modes of action. This humanized afucosylated IgG1/k monoclonal antibody attaches to Interleukin (IL)-5Rα via its fab fragments. Which hinders the formation of the ternary molecular complex that consists of IL-5, IL-5Rα, and the βc subunits of the IL-5 receptor. Consequently, IL-5 is unable to affect target cells (eosinophils, basophils, ILC2). Benralizumab was approved in 2020 for the indication of severe asthma with an eosinophilic phenotype. (69)

5.12 Dermatological Disorders

Psoriasis is a skin condition that is characterized by red, scaly plaques that are elevated and persistent. Chronic interactions between invading, activated immune cells and hyperproliferative keratinocytes lead to psoriasis. Psoriasis is caused by a malfunction in the mechanism that limits keratinocyte proliferation. (70) Spesolimab is an Interleukin-36 (IL-36) receptor antagonist used to treat pustular psoriasis. Ustekinumab is indicated for use in moderate to severe plaque psoriasis. Ixekizumab is used to treat psoriatic arthritis and plaque psoriasis. (71)

5.13 Reproductive health disorders

Failure to conceive a clinical pregnancy after 12 months or more of consistent, unprotected sexual activity is known as infertility. The reproductive hormonal profile, ovulation rates, time to pregnancy (TTP), pregnancy rates, and normal embryo development. All are some of the ultimate endpoints that can be used to assess fertility results, which are a crucial factor

Female infertility is cured by the recombinant human follicle-stimulating hormone (Follitropin). Which was approved in 2020,2021and in 2022 for the same indication but differs in the manufacturing company. The Recombinant Rho-D Immunoglobulin is used to treat conditions like, Rh Negative Women. In these forming antibodies to fetal rhesus-positive red blood cells. Which may pass into the maternal blood during childbirth which can lead to abortion or certain other sensitizing events. (72)

5.14 Cardiovascular Disorders

Familial hypercholesterolemia is a prevalent hereditary condition. Patients with familial hypercholesterolemia (FH) are challenging to treat with current lipid-lowering medications. Because they often fail to produce the desired lipid target levels, especially when treating homozygous FH patients. Genetic therapy is most effective in hypercholesterolemia. Evolocumab is used to treat hypercholesterolemia. It is used in combination with other lipid-lowering therapies by inhibiting the proprotein convertase subtilisin kexin receptor. (73) There is a total of five years of r-DNA approval data given in 2025 till March, which shows that in the year 2024, a total of 35 therapeutics were approved. In the year 2023, the highest r-DNA approval was 39. In the years 2022, 2021, and 2020, r-DNA approval was 20, 7, and 10. As shown in Figure 4, r-DNA therapeutics were mostly approved for the cancer and endocrine disorders in the last five years in India. After that r-DNA was frequently approved for the diabetes mellitus and osteoporosis.

6. Market Dynamics of r-DNA Therapeutics in India

The market dynamics of r-DNA therapeutics in India are driven by regulatory oversight under the Drugs and Cosmetics Act, 1940, with CDSCO approval mandatory for clinical use. Research, biosafety, and environmental clearances are managed by DBT bodies like IBSC, RCGM, and GEAC, while most biologics, except a few like recombinant insulin under DPCO, 1995, remain outside price control. Indian r-DNA products are priced three to seven times lower than those in high-income countries, influencing accessibility and affordability.

6.1 Technological Advancements in r-DNA Applications

r-DNA platforms have significantly advanced since their inception in the 1970s. Modern recombinant techniques now enable precise genome manipulation—either through gene insertion, knockdown, or silencing—using engineered vectors. These tools have revolutionized gene therapy, therapeutic protein production, and vaccine development. Clinically, viral vectors such as lentiviruses and adeno-associated viruses are widely employed for their high transduction efficiency; however, their immunogenicity and insertional mutagenesis risks are driving increased interest in non-viral delivery systems, such as plasmid-based “naked DNA” vectors, which offer improved safety profiles and scalable manufacturing. Innovations in vector design and expression systems, including bacterial hosts like *E. coli* and Polymerase Chain Reaction (PCR)-amplified low-copy vectors, continue to expand the scope of recombinant therapeutics. (74)

6.2 Molecular Stability of RNA-Based Therapeutics

RNA-based therapeutics, integral to r-DNA platforms, are inherently susceptible to chemical and physical degradation. Factors such as RNA length, the integrity of the 5′ cap and 3′ poly(A) tail, solution pH, ionic strength, and the presence of nucleases and divalent cations critically affect RNA stability. Studies have shown a negative correlation between mRNA length and thermodynamic stability, with pH and buffer composition also altering melting temperatures and molecular integrity, thereby influencing shelf life and bioavailability. (75)

6.3 Regulatory Landscape and Market Affordability

In India, recombinant products are regulated as novel drugs under the Drugs and Cosmetics Act, 1940, necessitating evaluation and approval from the CDSCO for clinical use, whether produced domestically or imported. Research and biosafety aspects are overseen by

the DBT through the IBSC and RCGM, while commercial and environmental approvals fall under the GEAC. Although some r-DNA-derived products like recombinant insulin are included under the Drug Price Control Order (DPCO), 1995, most biologics currently evade price regulation, creating variability in market accessibility. Nevertheless, India offers r-DNA therapeutics at significantly lower costs—often three to seven times less than in high-income countries, making it a critical hub for affordable biologics in low- and middle-income settings. (76)

6.4 Clinical Challenges in Genetic Data Interpretation

Despite advances in genomics, clinicians face challenges interpreting complex genetic data, particularly for multifactorial diseases such as cancer, where genotype-phenotype correlations are not always well-defined. Physicians often face difficulties selecting appropriate genetic tests due to limited actionable information, inconclusive results, and variability in test accuracy. These challenges underscore the need for improved bioinformatics tools, robust clinical-genomic databases, and physician training to bridge the gap between advanced genetic technologies and their effective translation into patient care. (77)

7. Identification of gaps and proposed strategy: Indian Perspective

The Indian national regulatory authority could benefit from creating product-specific criteria. Then evaluate the risk-benefit ratios of synthetic biological products due to the diversity of manufacturers. Furthermore, the bio-similar requires a distinct method of identification. The production of SBPs presents a variety of difficulties as well as significant potential. The development of skills, and government funding support with national and international universities. These are some of the challenges that must be overcome to become a contender in the similar biotherapeutics market.

There is still a need to bridge the skill gap between employee skill development and advancement. A review of the product's non-clinical toxicity evaluations is mandated under Schedule Y. In cases when bio-similarity is demonstrated through physical and biochemical descriptions. It is important to be clear about using species of animals that are suited for the specific SBPs. If necessary, these species can also take the place of non-clinical testing techniques. The National Research Agency (NRA) should collaborate with the Indian Council of Medical Research (ICMR) to activate the National Animal Resource Facility. Then promote the establishment of laboratories to conduct non-clinical toxicity studies in animals. The absence of facilities for doing so and the expected increase in the production of various biotherapeutics. (78)

The most important factor is evaluating SBPs. It is determining whether products' quality characteristics were very identical before and after manufacturing process modifications. Whether there was no negative effect on the drug product's safety or effectiveness including immunogenicity. Pharmacokinetic studies, pharmacodynamics studies, effectiveness studies, immunogenicity studies, and pharmacovigilance studies should come first in the study. Clinicians, hospitals, public health departments, and the general public are all involved in these investigations. (79)

8. r-DNA Approval Comparison: India, USA & Europe

Table 3 provides a concise comparison of the regulatory frameworks and approval processes for recombinant DNA (r-DNA) products across India, the USA, and the European Union. It highlights key differences in regulatory authorities, governing laws, submission requirements, and biosafety oversight, emphasizing the more layered biosafety review in India involving RCGM and GEAC. While all three regions mandate clinical trials, GMP compliance, and environmental risk assessments for GMO-based products, the timelines and complexity of approvals vary. The USA and EU have more streamlined, centralized procedures, whereas India involves multiple regulatory bodies, potentially extending the approval process. Despite procedural differences, all regions maintain rigorous standards to ensure the safety, efficacy, and quality of r-DNA products. (80)

Table 3. Comparison of approval process of r-DNA in India, USA & Europe

Parameters	India	USA	Europe
Regulatory Authority	CDSCO, rDNA-specific oversight by RCGM & GEAC	FDA (CBER & CDER handle r-DNA biologics and drugs)	EMA (European Medicines Agency) via CHMP
Governing Acts/Rules	Drugs and Cosmetics Act, 1940; Rules, 1945; Recombinant DNA Guidelines (DBT, 1990 & 1999, 2016)	FD&C Act, PHS Act, BPCIA (for biologics)	Directive 2001/83/EC; Regulation (EC) No 726/2004
Biosafety Oversight Bodies	• RCGM (DBT): Preclinical stage • GEAC (MoEFCC): Environmental clearance	FDA & NIH Recombinant DNA Advisory Committee (RAC)	EMA does not have specific r-DNA biosafety oversight; countries manage GMO risks
Application Submission	Form 44 (for biologics), with CTD format Clearance from RCGM, GEAC before clinical trials	• IND- BLA (for biologics); • NDA (for r-DNA derived drugs)	Centralized Procedure (via EMA); uses Common Technical Document (CTD) format
Clinical Trial Requirement	Phase I–III trials mandatory unless exempted Requires prior clearance from RCGM/GEAC	Full clinical development program (Phases I–III)	Similar to USA; comparative data required

GMP Compliance	Required; Schedule M guidelines	Required; FDA's 21 CFR Part 210/211/600	Required; EU-GMP guidelines apply
Time to Approval	2–3 years depending on complexity	1.5–3 years (post IND clearance)	1.5–2.5 years post submission
Environmental Risk Assessment	Mandatory if GMOs are involved	Mandatory if GMO based	Mandatory under Directive 2001/18/EC for GMOs
Post-Marketing Surveillance	PVPI (Pharmacovigilance Programme of India)	REMS (Risk Evaluation and Mitigation Strategy), MedWatch system	EU Pharmacovigilance system; EudraVigilance
r-DNA Product Examples	Insulin (Biocon), Erythropoietin (Wockhardt)	Humulin, Neupogen	Omnitrope, Genotropin

9. Conclusion

Over the past five years, India has experienced a notable rise in the approval of recombinant DNA (r-DNA) therapeutics, highlighting the rapid evolution of its biotechnology sector. Regulatory processes involving agencies such as CDSCO, IBSC, RCGM, and GEAC have ensured rigorous oversight from preclinical development through to marketing authorization. Approval trends show clear momentum: in 2025 (till March), approvals continued steadily, while in 2024, a total of 35 therapeutics were approved, and in 2023, the highest number of approvals at 39 was recorded. In earlier years, 20 approvals were noted in 2022, 7 in 2021, and 10 in 2020, illustrating a sharp upward trend that reflects both regulatory maturity and growing innovation within the sector.

Therapeutic areas dominated by r-DNA approvals predominantly include cancer, with a wide array of monoclonal antibodies and targeted therapies such as Bevacizumab, Nivolumab, Pembrolizumab, and Trastuzumab gaining clearances for multiple cancer types. The emphasis on oncology reflects the critical need for advanced treatment options capable of addressing tumor heterogeneity and genetic variability. Meanwhile, r-DNA therapeutics for haematological disorders, diabetes mellitus, and osteoporosis have also gained traction. Technological advances in genome manipulation, improvements in RNA stability, and innovations in delivery vectors have expanded the therapeutic landscape, yet clinical challenges like early biomarker detection and immune evasion by cancer cells continue to drive the demand for more precise, combination-based approaches.

Despite significant progress, challenges still exist in the Indian r-DNA sector. There is a need for more specific regulatory frameworks for products, improved biosimilar evaluation processes, and better skill development programs. Additionally, building non-clinical toxicity testing facilities and strengthening bioinformatics support for genetic data interpretation are vital next steps. Addressing these gaps with government funding, international collaborations, and a focus on affordability and manufacturing capacity will not only boost domestic production but also position India as a global hub for recombinant therapeutics, significantly improving healthcare accessibility across diverse patient populations.

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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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