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Comparative State-of-the-Art Review

Regulatory Frameworks for Advanced Therapy Medicinal Products (ATMPs): A Comparative Review of FDA, EMA, and CDSCO

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ABSTRACT

Background: Advanced therapy medicinal products (ATMPs) such as gene therapy medicinal products, somatic cell therapy medicinal products, tissue engineered products and combined advanced therapies are one of the fastest growing classes of biological medicines. The biological complexity and individualized manufacturing of these products do not fit well within regulatory systems designed for small-molecule drugs, and the three regulators examined here – the United States Food and Drug Administration (FDA), the European Medicines Agency (EMA), and India's Central Drugs Standard Control Organization (CDSCO) – have each developed distinct legal and procedural routes for this product class.

Aim: To compare the legal basis, institutional architecture, clinical trial oversight, expedited approval pathways, manufacturing and quality expectations, post-approval surveillance needs, and access and reimbursement mechanisms governing advanced therapy medicinal products under the FDA, the EMA, and CDSCO, and examine the extent to which these systems are converging/diverging.

Data Sources: Gray literature from well-acknowledged regulatory and health policy organizations, official publications of FDA, EMA and CDSCO, PubMed and Scopus and Web of Science indexed journals focusing on the content published from 2019 to mid-2026.

Review Methodology: Our approach was narrative and comparative. Peer-reviewed articles, regulatory guidance documents, and health-policy analyzes on ATMP definition, licensure pathway, clinical trial authorization, expedited designation, manufacturing oversight, and reimbursement were identified. These were thematically synthesized and cross-checked against primary regulatory sources where available.

Main Findings: ATMPs are biologics regulated by the FDA under section 351 of the Public Health Service Act by the Center for Biologics Evaluation and Research, with the assistance of the Regenerative Medicine Advanced Therapy designation. The EMA has centrally overseen ATMPs under Regulation (EC) No 1394/2007 via its Committee for Advanced Therapies, a structure currently being reviewed as the European Union completes a broader reform of its pharmaceutical legislation. The Central Drugs Standard Control Organization (CDSCO) oversees cell and gene therapy products along with the Indian Council of Medical Research, the Department of Biotechnology, and the Gene Therapy Advisory and Evaluation Committee under the New Drugs and Clinical Trials Rules, 2019, an arrangement recently strengthened by amendments that put these products under joint central and state oversight. India's approval last year of NexCAR19, a homegrown and much cheaper CAR-T cell therapy, reflects both the maturing Indian pathway and the ongoing global affordability divide.

Conclusion: The FDA and EMA frameworks are demonstrating increasing procedural convergence in quality and comparability expectations, while CDSCO has moved rapidly toward a comprehensive, if still evolving, national framework. Across the three jurisdictions, the principal barriers to equitable patient access to sophisticated therapy medicinal products remain the ability to reimburse and the generation of long-term evidence, rather than scientific review alone before the market.

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Introduction

Biological medicine is a category in itself, advanced therapy medicinal products. These are not synthesized chemical entities but are constructed from genes, cells or tissues with the intent to regulate, repair, replace, add or delete a genetic sequence or to regenerate, repair or replace human tissue.[1] The umbrella term "advanced therapy medicinal product" was created by the European Union in Regulation (EC) No 1394/2007, which combined gene therapy medicinal products, somatic cell therapy medicinal products, tissue engineered products, and combined ATMPs under a single legal category, with oversight given to the Committee for Advanced Therapies at the EMA.[2] The United States has taken a similar but not identical path, treating most of these products as biologics licensed under section 351 of the Public Health Service Act and since 2016 granting a defined subset of them the Regenerative Medicine Advanced Therapy designation created by the 21st Century Cures Act.3 India is a relatively new but fast growing player in this space. Gene and cell therapy products are regulated by CDSCO in collaboration with the Indian Council of Medical Research, Department of Biotechnology and specialized technical committees of CDSCO, mainly through the National Guidelines for Gene Therapy Product Development and Clinical Trials, 2019 and New Drugs and Clinical Trials Rules, 2019.[4]

Much of the existing comparative literature on ATMP regulation has focused on the transatlantic FDA-EMA relationship and a few well-cited analyzes have helpfully mapped their differing timelines, committee structures and expedited pathways.[1]India has received far less attention, despite a growing manufacturing base, approval of NexCAR19 in 2023 as an indigenously developed CAR-T cell therapy at a fraction of the price of comparable Western products, and a series of regulatory amendments from 2024 to 2026 that tightened joint central-state oversight of cell and gene therapy products.[5,6] Reviews referring to India typically describe its framework at a single point in time, without positioning it against the parallel reforms underway in the European Union, where a wholesale revision of pharmaceutical legislation proposed in 2023 is expected to reshape the role of the Committee for Advanced Therapies, or against the steady expansion of the American Regenerative Medicine Advanced Therapy pathway, which logged its largest annual number of designations in 2025.[7,10] That leaves a gap in synthesis at a time when the three jurisdictions are moving, for different reasons, toward more codified and in some ways more convergent oversight of this product class.

This review addresses this gap by comparing the FDA, EMA and CDSCO frameworks for advanced therapy medicinal products across several linked domains: definition and classification, legal and institutional architecture, clinical trial authorization, expedited development pathways, manufacturing and quality expectations and post-approval surveillance, before moving to the pricing, reimbursement and access questions that increasingly determine whether an approved ATMP reaches the patients who need it. It is more than descriptive. Where the literature allows, the review discusses the relative merits and demerits of each system, notes points of regulatory convergence and divergence and identifies research gaps relevant to future harmonization efforts including those being discussed through the International Council for Harmonization and dedicated global regulatory convergence initiatives.

Major Review

ATMPs: Definitions and Classification in Different Jurisdictions

The three regulators studied here define this product class in ways that overlap, but are not identical. An ATMP is a gene therapy medicinal product, a somatic cell therapy medicinal product, a tissue engineered product or a combined ATMP involving a medical device. The distinction between an ATMP and a conventional cell or tissue product is based on the extent of manipulation of the manufacturing process and whether the product is used for its original, homologous function.[2] The FDA does not use the term ATMP in its own regulations. Instead of using the term "biologics," it differentiates human cells, tissues, and cellular and tissue-based products regulated only under Section 361 of the Public Health Service Act (which includes minimally manipulated products used in a homologous manner) from the more heavily regulated Section 351 biologics (which include cell therapies, gene therapies, and most tissue-engineered products and are reviewed by the Center for Biologics Evaluation and Research).[3] The scientific scope underlying it, viral and non-viral gene transfer, ex vivo and in vivo genome editing and cell-based immunotherapies such as CAR-T, is essentially the same set of technologies. In practice, India's regulatory vocabulary is closer to the American than the European model, talking about gene therapy products and cell and gene therapy products rather than using the EU's combined ATMP terminology.[4,5] A 2022 draft framework by the World Health Organization has tried to bridge this terminological gap by proposing common definitions that countries like India, which are still developing regulatory capacity in this domain, can adopt without having to replicate the entire EU or US legislative apparatus.[28] The practical implication of this classification exercise is significant: the category a product falls into determines whether it is licensed as a biologic, a device-combination product, or a minimally regulated tissue product, and

Table 1: Comparative regulatory architecture for advanced therapy medicinal products under the FDA, EMA, and CDSCO.

Parameter	*FDA (United States)*	*EMA (European Union)*	*CDSCO (India)*
Governing legislation	Public Health Service Act, Section 351; 21st Century Cures Act (2016)	Regulation (EC) No 1394/2007; Directive 2001/83/EC, Annex I Part IV	New Drugs and Clinical Trials Rules, 2019; National Guidelines for Gene Therapy Product (2019); Drugs Rules, 1945 (amended 2024–2026)
Lead scientific body	Center for Biologics Evaluation and Research, Office of Therapeutic Products	Committee for Advanced Therapies (CAT)	CDSCO / Drugs Controller General of India, with Gene Therapy Advisory and Evaluation Committee (GTAEC) and Review Committee on Genetic Manipulation (RCGM)
Product terminology	Section 351 biologics; cellular and gene therapy products	Advanced therapy medicinal products (gene therapy, somatic cell therapy, tissue engineered, combined ATMP)	Gene therapy products; cell and gene therapy products
Clinical trial authority	FDA reviews and authorizes trials directly (IND)	National competent authorities of member states, via EU Clinical Trials Regulation	CDSCO, with GTAEC no-objection certificate and Institutional Ethics Committee approval
Key expedited pathway	Regenerative Medicine Advanced Therapy (RMAT) designation	PRIority MEdicines (PRIME) scheme	GTAEC scientific advice; SUGAM/ NSWS digital portal review
Long-term follow-up	Up to 15 years for integrating vectors, per FDA guidance	Risk Management Plans (RMPs), case by case	Minimum 5 years mandated; up to 10 years recommended post-commercialization

this in turn governs the clinical evidence, manufacturing oversight, and post-approval obligations that follow.

Legal and Institutional Framework

In the United States, Investigational New Drug applications and Biologics License Applications for cell and gene therapy products are reviewed by the Center for Biologics Evaluation and Research, including the Office of Therapeutic Products. Licensure is granted under Section 351 of the Public Health Service Act.[1,3] A defining feature of the American system is that the FDA itself authorizes and actively monitors clinical trials through the IND mechanism, something the EMA doesn't do directly.[1] Within the European Union, the Committee for Advanced Therapies (created by Regulation (EC) No 1394/2007 and in force since December 2008) was established as the scientific body for the assessment of ATMP quality, safety and efficacy, prior to a decision on a marketing authorization by the European Commission, while clinical trials are now authorized at the level of individual member states, increasingly harmonized by the Clinical Trials Regulation and its associated information system.[1,2] This structure is currently under active revision. In April 2023 the European Commission proposed a new Regulation and a new Directive intended to replace much of the existing pharmaceutical legislation, including the ATMP regulation. In December 2025 EU institutions agreed to a further reform, which will merge the Committee for Advanced Therapies with the Committee for Medicinal Products for Human Use, thus making EMA's governance structure for this product class more streamlined.[10,11] In India, the Central Drugs Standard Control Organization (CDSCO) headed by the Drugs Controller General of India is the central regulatory authority for cell and gene therapy products but it does not work alone. The Indian Council of Medical Research and the Department of Biotechnology jointly oversee biosafety and ethical review through the Review Committee on Genetic Manipulation. The Gene Therapy Advisory and Evaluation Committee provides specialized scientific input and a no-objection certificate before CDSCO's own evaluation under the New Drugs and Clinical Trials Rules, 2019.[4,5] Between 2024 and 2026, an amendment to the Drugs Rules, 1945, has extended joint central and state oversight of CAR-T cell therapies, gene modification and gene replacement products, and animal tissue-derived products – previously the purview of the central government for recombinant DNA products and vaccines – a change the government has described as an attempt to create uniform regulatory standards across India's federal system.[6] Table 1 shows the resulting comparative architecture.

Clinical Trial Authorization and Oversight

The pathway from laboratory concept to first-in-human study differs markedly in complexity across the three systems. In the United States, a single IND submission to the FDA, subject to a default 30-day review, initiates human testing, with the agency retaining direct authority to place trials on clinical hold at any stage.[1,3] The European Union's Clinical Trials Regulation has consolidated what

was once a fragmented, member-state-by-member-state process into a harmonized submission through the Clinical Trials Information System, though the EMA's own scientific review through the Committee for Advanced Therapies is formally distinct from this national-level trial authorization.[1,2] India's process is comparatively layered. A prospective sponsor typically requires sequential approvals from an Institutional Biosafety Committee, the Review Committee on Genetic Manipulation for preclinical and biosafety aspects, a no-objection certificate from the Gene Therapy Advisory and Evaluation Committee, formal clinical trial approval from CDSCO on Form CT-04 under the New Drugs and Clinical Trials Rules, 2019, and site-level clearance from a CDSCO-registered Institutional Ethics Committee.[4,5] This layered structure has historically drawn criticism for its length and the number of agencies involved, but recent digitization initiatives, including CDSCO's 2025 rollout of clinical research organization registration and site and investigator change notifications for cell and gene therapy products through the SUGAM online portal, indicate a deliberate move toward procedural consolidation without removing the underlying scientific checkpoints.[1,2] All three systems require Good Clinical Practice training for investigators and, in India, specific GCP or ICH-GCP certification is an explicit prerequisite for staff conducting gene therapy product trials.

Expedited and Accelerated Development Pathways

Each jurisdiction has built a mechanism to accelerate development of therapies addressing serious unmet medical need, though the legal basis and eligibility criteria differ enough that direct one-to-one comparison is difficult. The FDA's Regenerative Medicine Advanced Therapy designation, created by the 21st Century Cures Act in December 2016, offers sponsors the benefits of Fast Track and Breakthrough Therapy designation combined with more frequent, senior-level interaction with the agency, and is available once preliminary clinical evidence suggests a product may address an unmet need in a serious condition.[3] Uptake was modest for several years, averaging under fourteen designations annually between 2017 and 2023, before rising sharply as the cell and gene therapy pipeline matured, reaching forty-three designations in 2024 and a record forty-eight in 2025.[7] The EMA's parallel mechanism, the PRIority MEdicines scheme introduced in 2016, shares the underlying objective of earlier patient access but rests on a different legal basis and different qualifying criteria than the American Breakthrough Therapy programme, a divergence that the two agencies have partly addressed since late 2016 by jointly tracking parallel designation requests and comparing review outcomes.[1] India does not yet operate a single named expedited designation comparable to RMAT or PRIME. Instead, acceleration is achieved procedurally, through early GTAEC scientific advice, prioritized Subject Expert Committee review, and, increasingly, digital portal submission that shortens administrative turnaround, an approach that is less formally codified but has nonetheless allowed products such as NexCAR19 to move from pivotal trial completion to marketing authorization within roughly a year.[5,17]

Manufacturing, Quality, and Comparability

Chemistry, manufacturing, and controls requirements for ATMPs are widely regarded as the area of greatest technical convergence between the FDA and the EMA, even though full alignment has not been achieved. The FDA issued draft guidance on manufacturing changes and comparability studies for human cellular and gene therapy products in July 2023 and on potency assurance in December 2023, and by January 2026 had signaled a more flexible risk-based approach to chemistry, manufacturing, and controls for cell and gene therapies, while stressing that flexibility does not equate to reduced scientific rigor.[10] The EMA's own unified guideline on the quality, non-clinical, and clinical requirements for investigational ATMPs came into effect on 1 July 2025, six years after its initial adoption, and industry commentary has described it as evidence of substantial, though incomplete, convergence with FDA expectations, particularly regarding comparability and potency assessment.[14] Good manufacturing practice for advanced therapies in the European Union is now consolidated within Volume 4 of the rules governing medicinal products in the EU, developed jointly by the EMA and national authorities.[15] In India, cGMP certification of manufacturing infrastructure by CDSCO is mandatory, and for autologous cell products such as CAR-T therapies, rigorous documentation of chain of identity, confirming that modified cells are returned to the correct patient, and chain of custody, tracking the product from collection through infusion, is expected, with additional cold-chain validation required for centrally manufactured or imported products.[7] NexCAR19 illustrates an alternative model to this last requirement: because ImmunoACT manufactures the product domestically under CDSCO-certified cGMP conditions, the logistical and regulatory burden of international cold-chain transport that complicates access to imported CAR-T products in India is substantially reduced.[5,17]

Post-Approval Surveillance and Long-Term Follow-Up

Because many ATMPs, particularly integrating gene therapy vectors and genetically modified cell products, carry theoretical risks that may only become apparent years after administration, all three regulators mandate extended follow-up beyond conventional pharmacovigilance. The FDA requires long-term follow-up, in some cases extending to fifteen years for products using integrating vectors, and has required Risk Evaluation and Mitigation Strategies for several approved cell and gene therapy products.[3,18]

Table 2: Selected landmark advanced therapy medicinal product milestones across the three jurisdictions.

Product	*Jurisdiction / Year*	*Category*	*Notes*
Tisagenlecleucel (Kymriah)	FDA, 2017	CD19 CAR-T cell therapy	First FDA-approved CAR-T therapy, for relapsed/ refractory paediatric and young adult B-cell ALL
Axicabtagene ciloleucel (Yescarta)	FDA, 2017	CD19 CAR-T cell therapy	Approved for relapsed/refractory large B-cell lymphoma
Voretigene neparvovec (Luxturna)	FDA 2017; EMA 2018	In vivo AAV2 gene therapy	First in vivo gene therapy approved in both jurisdictions, for RPE65-mediated retinal dystrophy
Alipogene tiparvovec (Glybera)	EMA 2012 (withdrawn 2017)	Gene therapy	First EU-approved gene therapy; withdrawn by manufacturer for lack of commercial demand
Onasemnogene abeparvovec (Zolgensma)	FDA 2019; EMA 2020	AAV9 gene therapy	Approved for spinal muscular atrophy; adopted under managed access agreements in several EU markets
Atidarsagene autotemcel (Libmeldy)	EMA 2020	Ex vivo gene-modified stem cell therapy	Reimbursement secured via Beneluxa joint negotiation (2024) for metachromatic leukodystrophy
Idecabtagene vicleucel (Abecma) / similar	EMA, extended indications 2024	BCMA CAR-T cell therapy	Illustrates continued CAT-recommended indication expansion for CAR-T products
NexCAR19 (actalycabtagene autoleucel)	CDSCO, October 2023	Humanized CD19 CAR-T cell therapy	India's first indigenous CAR-T product; developed by ImmunoACT with IIT Bombay and Tata Memorial Centre

A safety signal identified across marketed CD19-directed and BCMA-directed CAR-T products, linking treatment to rare secondary T-cell malignancies, prompted a 2024 FDA safety communication and labelling updates, underscoring the practical importance of these long-term obligations.[18] In the European Union, Risk Management Plans are the primary post-authorization surveillance instrument, with a recent scoping review identifying eighteen such plans covering eighteen approved ATMPs, compared with a smaller number of FDA-approved REMS documents over the same period.[18] India's National Guidelines for Gene Therapy Product Development and Clinical Trials mandate a minimum of five years of clinical follow-up for all gene therapy trial participants, with up to ten years recommended once a product reaches commercialization, and a dedicated paediatric follow-up study for NexCAR19 recipients is under way at Tata Memorial Centre in parallel with its adult commercial use.[4,17]

Case Study: CAR-T Cell Therapy Approvals in Comparative Perspective

Chimeric antigen receptor T-cell therapies offer a useful lens through which to view these three systems side by side, because comparable products have now been evaluated, and in most cases approved, by all three regulators. The FDA authorized the first CD19-directed CAR-T products in 2017 through the standard Biologics License Application pathway, several benefiting from Breakthrough Therapy designation, and the EMA subsequently authorized comparable products through its centralized procedure, with the Committee for Advanced Therapies continuing to recommend expansion of CAR-T indications, including for multiple myeloma, in more recent assessments.[10] India's regulatory trajectory culminated in October 2023, when CDSCO granted marketing authorization to NexCAR19, a CD19-targeted, humanized CAR-T cell therapy developed by ImmunoACT, a company incubated at the Indian Institute of Technology Bombay, in collaboration with Tata Memorial Centre.[17,18] The approval rested on a multi-center Phase I/II pivotal trial of just over sixty patients with relapsed or refractory B-cell lymphomas and leukemia, reporting an overall response rate of approximately sixty-seven to seventy percent and a comparatively favourable safety profile, notably a lower reported incidence of neurotoxicity than has been described for some murine-antibody-derived Western products, an outcome attributed to the construct's humanized antigen-binding domain.[17,19] The therapy was priced in the region of thirty to fifty thousand US dollars, against roughly four hundred thousand dollars for comparable therapies in the United States at the time.[19] This case illustrates two points relevant to the wider comparison. First, CDSCO was willing to grant marketing authorization on a smaller pivotal dataset than would typically support an FDA Biologics License Application or an EMA centralized marketing authorization, reflecting both an urgent domestic clinical need and confidence built through sustained GTAEC and CDSCO engagement across the product's decade-long academic-to-commercial translation. Second, the price differential achieved through domestic development and manufacturing offers a concrete illustration of how regulatory approval and genuine patient access, discussed further below, are related but distinct achievements.

Pricing, Reimbursement, and Access

Regulatory approval of an ATMP does not, by itself, guarantee that patients can obtain it, and the three jurisdictions have adopted markedly different strategies for closing this gap. In the United States, oncologic gene therapies approved by mid-2023 were priced between roughly sixty-five thousand and four hundred seventy-five thousand dollars, while non-oncologic gene therapies ranged from approximately six hundred thirty thousand to three and a half million dollars, prompting the Centers for Medicare and Medicaid Services to launch a Cell and Gene Therapy Access Model in 2023, which began state-by-state rollout in January 2025 and by 2026 involved more than thirty states in outcomes-based multistate agreements covering gene therapies for sickle cell disease.[24,25] In the European Union, national Health Technology Assessment bodies, now increasingly coordinated through the joint clinical assessment process established under Regulation (EU) 2021/2282, rely heavily on managed entry agreements to manage the uncertainty and budget impact of ATMPs; a recent analysis found that essentially all single-dose gene therapies available in Italy, the United Kingdom, France, Germany, and Spain were reimbursed under outcomes-based managed entry agreements, arrangements that add an average of roughly one and a half years to reimbursement negotiations and whose confidential terms have been criticized for limiting cross-country transparency and comparability.[22] The contrasting fates of two European gene therapies illustrate the stakes involved: Libmeldy secured coordinated reimbursement through the Beneluxa joint negotiation initiative in early 2024, while Glybera, the first gene therapy ever to receive EU marketing authorization, was withdrawn by its manufacturer in 2017 after failing to achieve commercially viable adoption despite regulatory approval.[14] India's experience with NexCAR19 points toward a different route to affordability, namely reducing the underlying cost of development and manufacture through domestic production rather than negotiating discounts on an already high list price, an approach that has drawn interest from other low- and middle-income countries seeking similar models.[19] This concern for global equity is not unique to India: a 2024 multinational analysis coordinated in part by Indian health ministry researchers documented a persistent translational gap between the countries where gene therapies are developed and the countries, disproportionately low- and middle-income, that bear the greatest burden of the diseases these therapies treat, arguing that local manufacturing capacity, workforce training, and government commitment are as important to genuine access as regulatory approval itself.[26]

Toward Regulatory Convergence

Despite their structural differences, the three systems examined here are moving, unevenly, toward greater alignment. The International Council for Harmonisation's S12 guideline on nonclinical biodistribution considerations for gene therapy products, finalized in 2023 and adopted by both FDA and EMA, is one concrete example of technical harmonization achieved through a multilateral standard-setting body rather than bilateral negotiation.[1] The FDA and EMA have jointly tracked parallel Breakthrough Therapy and PRIME designation requests since 2016, comparing review outcomes even where the two schemes' underlying legal criteria differ.[1] India's own guidelines were, from the outset, explicitly framed with reference to FDA and EMA precedent, positioning the Indian framework less as an independent system built from first principles and more as an adapting one that draws deliberately on established international practice while tailoring specific requirements, such as the layered biosafety and ethics review structure, to domestic institutional capacity.[4] At the multilateral level, the World Health Organization's 2022 draft global regulatory framework for cell and gene therapy products, and a September 2024 workshop convened by the Reagan-Udall Foundation for the FDA together with the FDA and the Gates Foundation specifically to discuss regulatory convergence for low- and middle-income country access, using sickle cell disease as

Table 3: Comparative advantages and limitations of the FDA, EMA, and CDSCO frameworks for advanced therapy medicinal products.

Jurisdiction	*Advantages*	*Limitations*
FDA	Direct agency oversight of clinical trials allows early, iterative dialogue; RMAT designation has scaled rapidly with pipeline growth; recent CMC flexibility eases early-phase development	Very high list prices persist even after approval; access still depends heavily on payer-specific coverage decisions and the new, still-maturing CMS Cell and Gene Therapy Access Model
EMA	Centralized procedure gives a single scientific opinion across the EU; unified 2025 clinical-stage ATMP guideline improves consistency; strong post-authorization Risk Management Plan infrastructure	Clinical trial authorization remains partly national; reimbursement is fully decentralized, producing wide intra-EU disparities and lengthy managed entry agreement negotiations
CDSCO	Demonstrated capacity to support genuinely novel domestic development at substantially lower cost, as shown by NexCAR19; joint ICMR/DBT/GTAEC review adds specialized scientific input	Multi-agency, layered approval structure remains more procedurally complex than a single-agency model; long-term outcome and health-economic data from India remain comparatively limited

a model condition, both signal growing recognition that harmonization efforts can no longer be confined to the United States and the European Union alone if the benefits of this therapeutic class are to reach the majority of the world's population.[28]

Future Perspectives

Several trends are likely to shape ATMP regulation over the coming several years. The planned integration of the Committee for Advanced Therapies into the Committee for Medicinal Products for Human Use, agreed in principle in December 2025, will test whether the European Union can preserve the specialized scientific expertise that CAT has developed since 2007 while simplifying its governance structure.[11] In the United States, continued growth in RMAT designations suggests that the FDA's expedited infrastructure will face increasing throughput pressure, which may in turn accelerate the shift toward the more flexible, risk-based chemistry, manufacturing, and controls expectations signaled in early 2026.[10] India's recent extension of joint central-state oversight to CAR-T, gene editing, and xenograft products under the amended Drugs Rules, 1945, is likely to be followed by further guidance clarifying how this joint framework interacts with the existing GTAEC and RCGM structures, and by continued expansion of digital submission infrastructure.[6],[12] Across all three jurisdictions, the rise of in vivo genome-editing therapies, which raise distinct nonclinical and long-term follow-up questions not fully anticipated by guidance written primarily for viral vector gene addition or ex vivo cell products, will likely require dedicated updates to existing frameworks. Finally, continued multilateral engagement through the World Health Organization and cross-agency workshops focused specifically on low- and middle-income country access suggests that future regulatory convergence efforts will increasingly need to include countries such as India not merely as recipients of established FDA and EMA practice but as active contributors to global regulatory science.

Research Gaps

This review identifies several gaps warranting further investigation. First, long-term, real-world outcome data directly comparing patients treated under the three regulatory pathways remain scarce, making it difficult to assess whether differences in premarket evidentiary requirements translate into measurable differences in postmarket safety or effectiveness. Second, published, peer-reviewed cost-effectiveness analyses of ATMPs originating from India are limited, in contrast to the substantial health-economic literature now available for European and American products, which constrains evidence-based reimbursement policy design in India and other low- and middle-income settings. Third, the generalizability of Indian pivotal trial data, often derived from cohorts of sixty to seventy participants at a small number of centers, to broader and more diverse patient populations has not been systematically examined. Fourth, the confidential nature of managed entry agreement terms in Europe continues to hinder independent research into their actual effect on patient access and health system sustainability. Finally, the practical operation of regulatory reliance or work-sharing arrangements between CDSCO and stringent regulatory authorities such as the FDA and EMA, which could in principle accelerate Indian review of already-approved Western products, remains underexplored in the published literature.

Clinical Implications

For clinicians involved in ATMP delivery, several practical implications follow from this comparison. Eligibility criteria, labelled warnings, and long-term monitoring obligations differ by jurisdiction and by product, and accurate, jurisdiction-specific patient counselling, including disclosure of the theoretical secondary malignancy risk now flagged for several marketed CAR-T products, is essential to informed consent regardless of where a product was developed or approved.[18] Hospital-based cell therapy programmes, whether operating under FDA, EMA, or CDSCO oversight, must build robust chain-of-identity and chain-of-custody systems, since these are now explicit regulatory expectations in all three jurisdictions rather than optional quality measures. Clinicians in India treating patients with NexCAR19 or similar domestically manufactured products should be aware that CDSCO's mandated five- to ten-year follow-up period is not merely an administrative requirement but a scientific necessity for a therapy class whose long-term risk profile is still being characterized, and that participation in structured follow-up registries strengthens the evidence base supporting continued and expanded access. More broadly, clinicians and health system administrators should recognize that securing regulatory approval for an ATMP in their jurisdiction is a necessary but not sufficient condition for patient access, and that engagement with payers, health technology assessment bodies, or, in India, hospital and government affordability initiatives, is frequently the more decisive determinant of whether an approved therapy actually reaches appropriate patients.

Limitations of Current Evidence

This review has several limitations. It follows a narrative rather than a systematic methodology, and while search terms and source types were defined in advance, formal duplicate screening and quality scoring of individual sources were not performed. The regulatory landscape described here is changing rapidly: the European Union's pharmaceutical legislation overhaul and India's amendments to the Drugs Rules, 1945, were both still being implemented at the time of writing, so some cited

provisions may be superseded or refined before this review reaches publication. For the most recent developments, particularly regulatory actions from late 2025 and 2026, this review has drawn in places on regulatory trade press and organizational publications alongside peer-reviewed literature, reflecting the reality that formal academic publication lags behind regulatory change in this fast-moving field; readers should treat these more recent, less formally peer-reviewed sources with appropriate caution. Finally, heterogeneity in the availability and format of comparability, efficacy, and cost data across the three jurisdictions limited the extent to which quantitative, rather than qualitative, comparisons could be drawn, particularly for India, where published health-economic and long-term outcome data remain comparatively sparse.

Conclusion

The regulatory treatment of advanced therapy medicinal products in the United States, the European Union, and India reflects three distinct institutional histories converging, gradually and imperfectly, on a shared set of scientific expectations. The FDA and EMA, despite differing legal bases, have moved closer together on manufacturing and comparability standards and continue to coordinate on expedited pathway tracking, even as the European Union restructures its own governance of this product class. CDSCO, working jointly with the Indian Council of Medical Research, the Department of Biotechnology, and the Gene Therapy Advisory and Evaluation Committee, has built a functioning national framework capable of supporting genuinely novel domestic development, as demonstrated by NexCAR19, while continuing to adapt its procedures toward greater consistency and speed. Across all three systems, however, the evidence reviewed here points to a common conclusion: the principal barrier standing between an approved advanced therapy medicinal product and the patient who might benefit from it is now less often the premarket scientific review itself than the subsequent question of pricing, reimbursement, and sustained access, a challenge that regulatory convergence alone will not resolve.

Data Availability Statement

No new data were generated or analyzed in the preparation of this review. All data discussed are available within the cited references.

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