

DIGITAL HEALTH TECHNOLOGIES IN DECENTRALISED CLINICAL TRIALS – A REGULATORY PERSPECTIVE

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1. Abstract

Background: Digital health technologies (DHTs) are increasingly used in decentralised clinical trials (DCTs) for remote data acquisition, monitoring and generation of digital endpoints. However, differences in regulatory approaches may affect their validation, data integrity, privacy and acceptance in clinical research.

Aim: To comparatively assess the regulatory frameworks governing DHTs in clinical trials in the United States, European Union and India, with emphasis on their application in decentralised clinical research.

Methods: A qualitative, multi-jurisdictional comparative regulatory assessment was conducted using primarily official regulatory and governmental documents from the United States, European Union and India, with peer-reviewed literature used as supporting scientific and regulatory evidence. Regulatory requirements were compared across predefined domains, including DHT selection and validation, digital endpoints, data integrity, privacy, cybersecurity, interoperability and decentralised-trial requirements. An India-focused regulatory gap analysis was performed.

Results: The United States demonstrated a relatively explicit DHT-specific regulatory approach, while the European Union emphasised qualification, scientific validity and context of use. India's framework was distributed across clinical-trial, ethical, telemedicine, data-protection and medical-device provisions. Gaps were identified in consolidated requirements for DHT validation, digital endpoints, interoperability, technology-provider responsibilities and technology-specific data integrity.

Conclusion: India could strengthen DHT-enabled clinical research through a consolidated, risk- and purpose-based framework integrating existing requirements with clearer technology-specific regulatory provisions.

Keywords: Digital health technologies; Decentralised clinical trials; Regulatory framework; Digital endpoints; Data integrity; India.

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2. Introduction

2.1 Evolution of Clinical Trials and Emergence of Digital Health Technologies

Clinical trials have traditionally followed a site-based model, requiring participants to attend designated research centres for recruitment, informed consent, clinical assessments, treatment-related procedures and follow-up. Although this approach provides direct interaction between investigators and participants and facilitates controlled conduct of study procedures, repeated visits may increase participant burden and create accessibility challenges, particularly for individuals who live far from research centres or have difficulty travelling regularly.^{1,2} The development of remote-care approaches and digital technologies gradually enabled selected trial activities to be performed outside conventional research sites. Telemedicine, electronic systems, mobile applications and connected devices allowed certain procedures and data-collection activities to be distributed between research centres and participants' homes or local healthcare settings. This development contributed to hybrid clinical trials, which combine conventional site-based procedures with decentralised elements.^{3,4}

With further incorporation of remote procedures, decentralised clinical trials (DCTs) emerged as an approach in which some or many trial activities can be conducted away from conventional research sites. Depending on the study design, decentralisation may involve remote recruitment, electronic informed consent, telemedicine, home-based assessments, remote monitoring, local healthcare services and remote collection of clinical data. Importantly, decentralisation is not necessarily an entirely site-less model; the extent to which activities are conducted remotely can vary according to the requirements of the trial.^{4,5,6} The transition towards decentralised research was accompanied by the rapid development of digital health technologies (DHTs). Smartphones, wearable sensors, mobile health applications, connected medical devices and other digital platforms enabled health-related information to be collected directly from participants and, in some cases, repeatedly in their usual environments. This expanded the ability of clinical researchers to obtain physiological, behavioural and patient-reported information beyond scheduled site visits.^{7,8} The increasing use of these technologies also introduced new forms of digital measures, biomarkers and endpoints. Unlike

conventional assessments that may provide information only at predefined clinical visits, some DHTs can generate measurements over longer periods and in real-world settings. However, the usefulness of these measurements depends on their technical performance, reliability, validity, usability and suitability for the intended clinical purpose.^{8,9,10} Consequently, the incorporation of DHTs into clinical research has raised regulatory and scientific considerations that extend beyond their technological capabilities. Issues concerning data quality, validation, privacy, security, interoperability and regulatory acceptability have become increasingly important in determining whether digitally generated information can be reliably used in clinical-trial decision-making.^{9,10} Thus, the evolution of clinical trials can be viewed as a progression from predominantly site-centred research towards increasingly flexible, decentralised and technology-enabled models. DHTs have become an important technological component of this evolution, providing new ways of generating and collecting clinical information. Their specific applications within decentralised clinical trials and the regulatory considerations associated with their use are examined in the following sections.

2.2 Types of Digital Health Technologies

Digital health technologies (DHTs) comprise a diverse range of technologies that use software, connectivity and sensors to generate, process and transmit health-related information. In clinical research, they range from mobile applications and wearable devices to connected medical devices, environmental sensors, telemedicine platforms and advanced computational technologies.^{7,8} Wearable and sensor-based technologies, including smartwatches, activity trackers, sensor patches and continuous monitoring devices, can capture physiological and behavioural parameters and support digital biomarkers and endpoints.^{11,12} Their use in clinical trials is expanding across different therapeutic areas.^{11,13} Mobile health (mHealth) technologies include smartphone applications, electronic diaries, digital questionnaires and other software platforms used for participant-generated data, electronic clinical outcome assessments and communication with study teams.^{7,8,14} The regulatory status of such applications depends largely on their intended function and use, particularly where software functions may meet the definition of a medical device.¹⁵ Connected medical devices, such as blood pressure monitors, glucometers, pulse oximeters and spirometers, can electronically record and transmit measurements to smartphones, cloud platforms or clinical databases.^{7,16} Implantable and ingestible technologies can generate physiological or medication-related information but may require additional consideration of safety, device performance and regulatory classification.¹⁴

Environmental and passive sensing technologies, including motion, location-based and contactless sensors, can collect behavioural and physiological information with limited active participant input.^{8,17} Telemedicine platforms enable remote communication and clinical interactions between participants and healthcare professionals or study personnel.^{7,8} DHTs may also be integrated through smartphones, connected devices, cloud platforms and application programming interfaces, allowing data from multiple sources to be combined.^{7,8} Such integration increases the importance of interoperability, data integrity, cybersecurity and privacy. Artificial intelligence and machine-learning technologies can further support the processing and analysis of digitally generated information, but introduce considerations related to algorithm performance, reliability, bias, transparency and validation.^{7,8,18}

2.3 Role of Digital Health Technologies in Decentralised Clinical Trials

DHTs support decentralised clinical trials by enabling remote data acquisition, electronic patient-reported outcomes, continuous or frequent monitoring, telemedicine and integration of information from multiple digital sources. These applications can extend trial activities beyond conventional research sites and reduce reliance on repeated site visits.^{7,11,16} However, their use introduces regulatory considerations related to technology suitability, validation, data integrity, privacy, cybersecurity, interoperability and participant accessibility. These considerations form the basis of the comparative regulatory assessment conducted in this study.

2.4 Regulatory Framework for DHTs in Clinical Trials

2.4.1 United States

In the United States, the regulatory framework for digital health technologies (DHTs) used in clinical investigations is primarily supported by the U.S. Food and Drug Administration (FDA) through DHT-specific guidance and existing regulatory requirements applicable to clinical investigations, medical devices, electronic systems and drug-development tools. The FDA's Digital Health Technologies for Remote Data Acquisition in Clinical Investigations guidance provides recommendations on the selection, use and oversight of DHTs for remote data acquisition in clinical investigations.¹⁶ The US framework also addresses the use of digitally derived measures and clinical endpoints and provides mechanisms for regulatory engagement and qualification of novel drug-development tools.^{20,21} DHTs may also be incorporated into decentralised clinical trials (DCTs), where applicable clinical-trial requirements and participant-protection provisions continue to apply.²²

2.4.2 European Union / European Medicines Agency

In the European Union (EU), DHT use in clinical research operates within the broader clinical-trial framework established by Regulation (EU) No 536/2014, together with guidance and regulatory mechanisms developed by the European Medicines Agency (EMA), European Commission and other relevant bodies.²³ EMA has established mechanisms for regulatory engagement and qualification of digital methodologies, including digital endpoints, digital biomarkers, electronic clinical outcome assessments, wearable technologies and mobile applications used in medicinal-product development.^{24,25} The EU framework also includes recommendations addressing decentralised clinical-trial elements, including electronic informed consent, home-based trial procedures, investigational medicinal-product delivery, data management and monitoring.²⁷ The regulatory requirements applicable to DHTs may also depend on their intended purpose and classification under other relevant EU legislation, including the medical-device framework.²⁴

2.4.3 India

In India, the regulatory framework governing DHT-enabled clinical research is distributed across multiple regulatory, ethical, telemedicine, data-protection and medical-device instruments. The New Drugs and Clinical Trials Rules (NDCTR), 2019 provide the primary framework for clinical-trial conduct, including requirements relating to clinical-trial permission, Ethics Committee oversight, informed consent, investigator responsibilities, safety reporting and participant protection.^{28,29} The ICMR National Ethical Guidelines provide additional requirements concerning ethical oversight, informed consent, privacy and confidentiality, while specific guidance is also available for artificial intelligence in biomedical research and healthcare.^{30,31} The Telemedicine Practice Guidelines, 2020 are relevant where remote clinical interactions form part of decentralised research.³² Data-protection requirements are addressed through the Digital Personal Data Protection Act, 2023 and associated rules, while DHTs that fall within the scope of medical-device regulation may also be subject to the Medical Devices Rules, 2017 and applicable CDSCO requirements for medical-device software.^{33–36}

Overall, the three jurisdictions provide regulatory mechanisms relevant to the use of DHTs in clinical research, although these mechanisms differ in their organisation, scope and degree of specificity. The United States and European Union have developed dedicated mechanisms addressing DHTs and digitally derived measures, whereas relevant Indian requirements are distributed across multiple regulatory instruments.^{16,20,23–36} These

differences provide the basis for the comparative assessment of DHT selection, validation, digital endpoints, data integrity, privacy, cybersecurity, interoperability and other regulatory domains presented in the subsequent sections.

3. Methods

3.1 Study Design

A qualitative, multi-jurisdictional comparative regulatory assessment was conducted to examine the regulatory requirements governing the use of digital health technologies (DHTs) in clinical trials in the United States, European Union and India, with particular emphasis on their application in decentralised clinical trials (DCTs). A predefined analytical framework was used to systematically assess and compare regulatory provisions across key domains relevant to DHT-enabled clinical research.

3.2 Research Question

The study addressed the following research question: What are the similarities and differences in regulatory requirements governing DHTs in clinical trials in the United States, European Union and India, and what regulatory gaps can be identified in the Indian framework for DHT-enabled decentralised clinical research?

3.3 Regulatory Data Sources

The analysis was based primarily on official regulatory and governmental documents from the United States, European Union and India. Relevant documents issued by the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), European Commission, Heads of Medicines Agencies (HMA), Central Drugs Standard Control Organisation (CDSCO), Indian Council of Medical Research (ICMR), Ministry of Health and Family Welfare (MoHFW) and Ministry of Electronics and Information Technology (MeitY) were examined. Relevant peer-reviewed literature was used as supporting scientific and regulatory evidence.

3.4 Analytical Framework and Data Analysis

Regulatory requirements were systematically mapped across predefined domains: DHT selection and fitness for purpose, validation, remote data acquisition, digitally derived endpoints, data integrity and reliability, privacy and data protection, cybersecurity, interoperability, participant safety and protection, ethical oversight, remote clinical interactions, decentralised clinical-trial requirements, technology-provider responsibilities, regulatory consultation and qualification, and digital accessibility and inclusion.

The regulatory frameworks of the United States, European Union and India were first assessed within their respective regulatory contexts and subsequently compared across the predefined domains to identify areas of convergence, divergence and jurisdiction-specific requirements. For the India-focused analysis, regulatory provisions were categorised as aligned, partially addressed or not specifically addressed in comparison with the

corresponding principles identified in the US and EU frameworks. The identified gaps were used to formulate recommendations for strengthening the Indian regulatory framework for DHT-enabled clinical research.

4. Results and Discussion

4.1 Regulatory Evidence Analysed

The analysis examined scientific and regulatory evidence addressing digital health technologies (DHTs), decentralised clinical trials (DCTs), digital endpoints, remote data acquisition and regulatory oversight. The primary analytical evidence comprised regulatory and governmental documents issued by the US Food and Drug Administration (FDA), European Medicines Agency (EMA), European Commission, Heads of Medicines Agencies (HMA), Central Drugs Standard Control Organisation (CDSCO), Indian Council of Medical Research (ICMR), Ministry of Health and Family Welfare (MoHFW), Ministry of Electronics and Information Technology (MeitY) and other relevant authorities. Peer-reviewed literature was used as supporting scientific and regulatory evidence.

The analysis showed that DHT regulation is developing alongside the increasing use of decentralised trial elements. However, the three jurisdictions differ considerably in the way digital technologies are incorporated into clinical-trial regulation. The US has developed relatively explicit DHT-specific guidance, the EU has developed a qualification-oriented approach for digital methodologies alongside recommendations for decentralised trial elements, while India relies primarily on provisions distributed across its clinical-trial, ethical, telemedicine, data-protection and medical-device frameworks. This difference formed the basis of the comparative analysis.

4.2 Regulatory Framework for DHTs in the United States

Among the jurisdictions examined, the United States demonstrated the most explicit dedicated regulatory guidance addressing the use of DHTs for remote data acquisition in clinical investigations. The FDA's Digital Health Technologies for Remote Data Acquisition in Clinical Investigations, issued in December 2023, provides recommendations for sponsors and other stakeholders using hardware and/or software technologies to remotely acquire information from participants. The guidance recognises DHTs as tools that can extend clinical-trial data collection beyond conventional research sites and identifies their potential to improve trial efficiency and participant convenience.¹⁶

A central principle of the FDA framework is that the DHT should be fit for purpose. The suitability of a technology is not determined simply by whether it is technically capable of measuring a particular parameter. Instead, the technology's design, intended function, measurement characteristics, target population and role within the clinical

investigation must be considered. The FDA guidance therefore links DHT selection with the level of validation necessary to support interpretation of the data generated during the investigation.¹⁶

This approach is particularly relevant when DHT-generated information is used to develop digitally derived measures (DDMs). FDA's current position is that DHT-derived measures may be used as clinical outcome assessments, biomarkers or components of multicomponent endpoints. The Agency emphasises that development should begin with the clinically meaningful concept being measured rather than with the technology itself. Verification and validation should establish that the technology measures the intended characteristic with appropriate accuracy and precision and that the resulting measure is clinically meaningful for its intended context of use.²⁰

The FDA approach also recognises the importance of usability and participant compatibility. A technically sophisticated device may not be suitable if participants cannot use it consistently or if its physical or operational characteristics lead to poor adherence or data loss. The FDA therefore considers factors such as ease of use, participant instructions, battery life, device characteristics and the possibility of participants using their own devices. These considerations demonstrate that DHT suitability encompasses not only analytical performance but also practical use in the intended study population.³⁹ Another important finding is the close relationship between DHT regulation and the broader FDA framework for decentralised clinical trials. DHTs are one of the mechanisms through which trial procedures and data collection can occur away from conventional research sites. However, decentralisation does not remove the fundamental regulatory requirements applicable to clinical investigations. The FDA approach instead requires sponsors to determine whether a particular decentralised element is appropriate for the study while maintaining appropriate oversight, participant protection and data reliability. This is consistent with comparative analysis of FDA and EMA DCT guidance, which found patient safety and data integrity to be common considerations in determining the suitability of decentralised elements.⁴⁰

The US framework therefore demonstrates a technology-specific but risk- and purpose-based regulatory approach. Its strength lies in the availability of dedicated guidance addressing remote DHT data acquisition and the increasing regulatory attention to digitally derived measures. At the same time, the continuing development of FDA resources demonstrates that DHT regulation remains an evolving area, particularly for novel measures and emerging technologies. The current FDA framework therefore provides a useful reference model for

countries developing regulatory approaches to DHT-enabled clinical research.^{2,16,39}

4.3 Regulatory Framework for DHTs in the European Union

The European Union follows a somewhat different regulatory model. Rather than relying on a single comprehensive DHT-specific clinical-trial guidance document, the regulatory approach combines the broader EU clinical-trial framework with EMA qualification and scientific-advice mechanisms for digital technology-based methodologies and recommendations concerning decentralised trial elements.

The EMA's Questions and Answers: Qualification of Digital Technology-Based Methodologies to Support Approval of Medicinal Products specifically recognises digital measures, digital biomarkers, digital endpoints and electronic clinical outcome assessments within the qualification framework. The document indicates that when a digital methodology may influence the benefit–risk assessment of a medicinal product, relevant aspects of the technology and the evidence supporting its use may be considered by EMA.²⁴

A particularly important feature of the EU approach is its emphasis on context of use and scientific validity. For example, where a wearable device is used to generate a clinical variable intended to contribute to a regulatory decision, EMA considers aspects such as reliability, accuracy, sensitivity to change, technical and clinical validity, compliance and clinical relevance. In contrast, technical aspects that fall outside the Agency's medicinal-product remit may need to be addressed through the appropriate regulatory pathway for the device itself.²⁴ This separation between the methodology used to generate evidence and the regulation of the underlying technology is an important characteristic of the European approach.

The EMA qualification system also provides an opportunity for early regulatory engagement. The Agency can provide qualification advice and scientific advice during the development of novel methodologies, allowing developers to discuss the scientific rationale and supporting evidence before the methodology becomes central to a clinical-development programme. This is particularly relevant for DHT-derived endpoints, where uncertainty may exist regarding the clinical meaning and validation of a new digital measure.²⁵

Evidence from the EMA's own experience supports the importance of this approach. Jadoenathmisier et al. reviewed DHT-related Qualification Opinions, Qualification Advice and Scientific Advice procedures from 2013–2022 and found that accelerometers, glucose monitors and smartphones were among the most frequently proposed technologies. The regulatory feedback emphasised validation, precision and a clearly defined context of use, demonstrating that the scientific acceptability of

the measurement remains central to regulatory assessment.²⁶

The EU framework has also continued to develop its approach to decentralised trial conduct. The European Commission's EudraLex Volume 10 currently identifies a Recommendation Paper on Decentralised Elements in Clinical Trials, developed as a priority action of the ACT EU initiative involving the European Commission, HMA and EMA.²⁷ This development indicates that decentralised trial procedures are increasingly being addressed within the European regulatory environment rather than being treated solely as experimental trial practices.

A direct comparison of FDA and EMA approaches found substantial convergence in their emphasis on patient safety and data integrity when assessing decentralised elements. However, differences exist in the way the regulatory information is structured and communicated.⁴⁰ The EMA approach places considerable emphasis on qualification and scientific advice for novel digital methodologies, whereas the FDA has issued dedicated guidance specifically addressing remote DHT data acquisition.

Thus, the EU approach can be characterised as a qualification- and evidence-oriented model, where the regulatory acceptability of a DHT-derived measure depends strongly on its scientific validity, reliability and defined context of use. This provides an important reference for India, particularly in relation to the development and regulatory acceptance of novel digital endpoints.

4.4 Regulatory Framework for DHTs in India

In contrast to the more specific DHT mechanisms identified in the US and EU, the Indian regulatory framework is distributed across several regulatory and policy instruments. The principal framework for clinical trials involving new drugs and investigational products is the New Drugs and Clinical Trials Rules (NDCTR), 2019, administered by CDSCO. The Rules establish requirements for clinical-trial permissions, Ethics Committee oversight, informed consent, investigator responsibilities, safety reporting and related participant protections.²⁸

The analysis found that the NDCTR provides an important foundation for clinical-trial oversight but does not function as a consolidated framework specifically addressing the selection, validation and regulatory acceptance of DHTs used for remote data acquisition or digitally derived endpoints. This distinction is important: the absence of a dedicated DHT chapter or guidance should not be interpreted as meaning that DHT use is unregulated. Rather, DHT-enabled research must currently operate within the broader regulatory requirements applicable to clinical investigations and any additional requirements triggered by the nature of the technology.

Ethical governance is supported by the ICMR National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, which address informed consent, privacy, confidentiality, participant welfare and Ethics Committee review. ICMR has subsequently issued the Ethical Guidelines for Application of Artificial Intelligence in Biomedical Research and Healthcare (2023), which provides additional ethical considerations for AI-related applications in biomedical research.^{30,31}

Remote clinical interactions introduce another layer of regulation. The Telemedicine Practice Guidelines, 2020 establish a framework for registered medical practitioners providing healthcare through telemedicine. Although these guidelines were developed for clinical care rather than specifically for DCTs, they are relevant where teleconsultation becomes part of a decentralised clinical-trial procedure.³² This illustrates the broader characteristic of India's regulatory model: individual components of a technology-enabled clinical trial may be governed by different regulatory instruments.

Data governance represents another important component. The Digital Personal Data Protection Act, 2023 establishes the legal framework for processing digital personal data in India, while the Digital Personal Data Protection Rules, 2025 provide the associated implementation framework. The Rules were notified in November 2025 and include a phased commencement structure.^{33,34} For DHT-enabled trials, this framework is particularly relevant because wearable devices, mobile applications, connected devices and remote monitoring platforms can generate and transmit substantial quantities of participant-related information.

Where DHTs constitute or incorporate medical-device software, an additional regulatory layer applies. CDSCO regulates medical-device software under the Medical Devices Rules, 2017, and CDSCO issued a draft guidance document in October 2025 specifically addressing medical-device software, including its scope, classification, standards, technical documentation and quality-management requirements.³⁶ This demonstrates that India is progressively developing technology-specific regulatory material, although the medical-device software framework does not by itself constitute a comprehensive framework for all DHTs used in clinical trials.

The literature also indicates that the regulatory fragmentation observed in the documentary analysis has practical consequences. Moka et al. reported that India's transition towards digital clinical trials is associated with regulatory uncertainties, ethical concerns, infrastructure limitations and participant-related barriers. Their review also identified difficulties related to data security, patient

engagement, technology integration and preparedness of Ethics Committees.³⁷

Recent stakeholder evidence further supports this finding. Biswas and Dalal examined perspectives from Indian clinical research site professionals and reported that hybrid DCTs were more common than fully decentralised trials. Their findings identified limited digital literacy and regulatory uncertainty among important barriers to broader implementation.³⁸ These findings are particularly relevant because they indicate that regulatory uncertainty is not merely a theoretical gap identified through document comparison; it may influence how decentralised approaches are implemented in actual Indian clinical research settings.

4.5 Comparative Regulatory Analysis

The comparative assessment demonstrated that the United States, European Union and India share common regulatory objectives, particularly with respect to participant safety, clinical-trial oversight and reliability of clinical data. However, substantial differences were observed in the degree of regulatory specificity and the mechanisms used to address DHTs. The comparison across the major regulatory domains is presented in Table 2.

Table 2. Comparative regulatory assessment of digital health technologies in clinical trials in the United States, European Union and India

Regulatory domain	United States – FDA	European Union – EMA/EU	India – CDSCO/ICMR and related frameworks	Comparative finding / implication for India
Regulatory scope for DHTs	FDA has specific guidance addressing DHTs used for remote data acquisition in clinical investigations.	DHTs are addressed through EMA's qualification of digital technology-based methodologies and broader EU clinical-trial mechanisms.	No single consolidated DHT-specific clinical-trial framework; requirements are distributed across NDCTR 2019, ethical, data-protection, telemedicine	US and EU provide more explicit DHT-related regulatory mechanisms, whereas Indian requirements are distributed across multiple

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			and medical-device provisions.	regulatory instruments.
DHT selection	Select ion should consider the intended use, characteristics of the technology and the clinical-trial context.	Selection is linked to the scientific validity and intended context of use of the digital methodology.	General clinical-trial and device requirements apply, but specific DHT-selection criteria are not consolidated.	India could establish explicit fit-for-purpose criteria for DHT selection.
Fitness for purpose	Explicitly emphasised when determining whether a DHT is appropriate for a clinical investigation.	Strongly linked to context of use and scientific validity.	No equivalent consolidated pathway was identified in the reviewed regulatory framework.	A dedicated fit-for-purpose approach could reduce uncertainty for Indian sponsors.
Validation	Requires appropriate verification and validation according to the intended use and	Validation and reliability are important components of qualification of digital methodologies.	Validation requirements may arise from applicable clinical-trial or medical-device provisions but	DHT-specific validation requirements are an important regulatory gap for India.

	measurement.		are not consolidated specifically for DHTs.	
Remote data acquisition	Specifically addressed in FDA's 2023 DHT guidance.	Supported through digital methodologies and decentralised trial approaches.	Can be incorporated through existing clinical-trial and telemedicine provisions, but without a dedicated DHT remote-data framework.	FDA provides dedicated regulatory guidance addressing remote DHT data acquisition.
Digital endpoints	FDA recognises digitally derived measures and provides considerations for their development and use.	EMA has an established qualification mechanism for novel digital methodologies and experience with DHT-derived endpoints.	No equivalent consolidated pathway specifically for qualification of DHT-derived clinical endpoints.	Digital endpoint qualification is a major area for Indian regulatory development.
Data integrity	Reliability, accuracy and appropriate data acquisition are central considerations in	Scientific validity, reliability and precision are important considerations.	General clinical-trial and data-governance requirements apply.	Common principle across jurisdictions, but India could provide more DHT-specific

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	DHT use.			requirements.
Privacy and data protection	Applicable privacy and clinical-trial data requirements govern DHT-generated information.	GDPR provides a comprehensive framework for personal-data protection.	DPDP Act 2023 and DPDP Rules 2025 provide the principal digital personal-data framework.	India has a dedicated data-protection framework, but its interaction with DHT-enabled clinical trials requires further clarification.
Cybersecurity	Cybersecurity considerations apply to digital health technologies and clinical-trial data systems.	Data protection and security requirements apply within the EU regulatory environment.	Data-protection requirements exist, but DHT-specific cybersecurity expectations within clinical trials are not consolidated.	India could establish clearer technology-specific cybersecurity expectations.
Interoperability	FDA recognises the importance of supporting technologies and reliable transmission	Digital methodologies require reliable generation and handling of data within the intended context of use.	Relevant requirements are distributed across different systems and frameworks.	Interoperability and standardisation require greater regulatory clarity in India.

	n of DHT-generated data.			
Participant protection	Decentralised elements must maintain participant safety and appropriate clinical oversight.	Patient safety is a major consideration in decentralised trial approaches.	Participant protection is addressed through NDCTR and ICMR ethical requirements.	Strong convergence exists across jurisdictions regarding participant protection.
Ethics oversight	Ethics /IRB requirements continue to apply to decentralised and DHT-enabled trials.	Ethics requirements remain part of EU clinical-trial governance.	ICMR ethical guidelines and Ethics Committee requirements provide the principal framework.	India has an established ethical foundation; DHT-specific operational guidance could strengthen implementation.
Telemedicine / remote clinical interaction	Remote interactions can form part of decentralised trial conduct subject to applicable requirements	Remote trial activities are incorporated within the EU decentralised-elements approach.	Telemedicine Practice Guidelines provide a framework for remote clinical interactions.	India has a relevant framework, but it was not developed specifically for clinical trials.

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DCT frame work	FDA issued dedica ted guida nce on condu cting clini cal trials with decent ralised elem ents.	EU has develop ed recomm endatio ns address ing decent ralised elem ents in clinical trials.	No single consolid ated DCT framew ork identifie d; provisio ns are distribut ed across existing regulatio ns.	India has a clear opportu nity to consoli date DCT- related require ments.
Techn ology- provid er respon sibility	DHT spons ors and techno logy provid ers must suppo rt appropri ate techno logy perform ance and data reliabi lity.	Respon sibilitie s depend on the method ology, technol ogy and applica ble regulato ry pathwa y.	Respon sibilities may be distribut ed between spons ors, investig ators and technol ogy/dev ice provider s.	Clearer allocati on of respon sibilitie s could improv e accoun tability in India.
Regula tory consult ation / qualifi cation	FDA provid es opportu nities for regula tory intera ction regard ing DHT develo pment and digital ly derive d	EMA provid es establis hed qualific ation and scientific- advice mechan isms for novel method ologies.	No directly equival ent consolid ated DHT qualific ation pathway identifie d.	Early regulat ory consult ation could be particu larly valuabl e for India.

	measu res.			
Digital literac y / accessi bility	Partici pant usabili ty is consid ered when selecti ng and imple menti ng DHTs.	Usabilit y and feasibili ty contrib ute to the accepta bility of digital method ologies.	Recent Indian stakehol der evidenc e identifie s limited digital literacy as a barrier to DCT implem entation .	Indian guidan ce should address digital includi ng and partici pant capabil ity, not only technol ogy perform ance.
Overall regulat ory approa ch	Explic it, DHT- focuse d and fit- for- purpo se orient ed.	Qualific ation- and evidenc e- oriented , with decent ralised elem ents address ed through EU mechan isms.	Multi- layered and distribut ed across several regulato ry instrum ents.	The compar ison indicat es that regulat ory require ments in India are distrib uted across multipl e instru ments rather than consoli dated within a single DHT- specifi c frame work.

4.5.1 DHT selection and validation

The most pronounced difference concerns the regulatory treatment of DHT suitability and validation. FDA explicitly recommends that DHTs used for remote data acquisition be fit for purpose, considering both their form and function.¹⁶ The FDA's newer discussion of digitally derived measures further distinguishes verification of the technology from validation of its ability to measure the clinical characteristic of interest.²⁰

EMA similarly places emphasis on reliability, accuracy, precision, technical and clinical validity, compliance and context of use when digital methodologies are intended to support medicinal-product development.^{24,26}

In India, these concepts are addressed indirectly through the broader regulatory framework, but the analysis did not identify an equivalent consolidated DHT-specific pathway comparable to the FDA's dedicated remote-data-acquisition guidance or EMA's qualification mechanism. Therefore, validation represents one of the clearest areas where regulatory clarification could strengthen India's framework.

4.5.2 Digital endpoints

Digital endpoints represent another major area of regulatory divergence. DHTs can generate measurements that capture physiological or behavioural characteristics repeatedly in participants' normal environments. However, the regulatory value of such information depends on whether the resulting measure is sufficiently reliable and clinically meaningful.

FDA's current framework recognises digitally derived measures as potential clinical outcome assessments, biomarkers or components of multicomponent endpoints and recommends evidence appropriate to their intended context of use.²⁰ EMA similarly considers digital endpoints and digital biomarkers within its qualification framework and has accumulated experience assessing their proposed use in clinical development.^{24,26}

India does not currently have an equivalent consolidated pathway specifically dedicated to the qualification or regulatory acceptance of DHT-derived clinical endpoints. This does not mean that digital endpoints cannot be used in Indian research; rather, it indicates that greater regulatory clarity regarding their development, validation and acceptance could reduce uncertainty for sponsors and investigators.

4.5.3 Data integrity and reliability

Data integrity is a common regulatory concern across the three jurisdictions, even though the mechanisms differ. FDA explicitly links DHT suitability to the reliability and interpretability of data generated during clinical investigations.^{16,20} The comparative analysis of FDA and EMA guidance identified data integrity as one of the two major principles used by both regulators when assessing decentralised trial elements, the other being patient safety.⁴⁰

The challenge becomes greater when data are collected using multiple devices, software platforms or local healthcare providers. Differences in measurement characteristics, missing observations, device changes and transmission problems can influence the consistency of the resulting dataset. Therefore, the use of DHTs requires not only a

suitable device but also appropriate processes for data collection, transmission, storage and quality control.

For India, this suggests that future DHT guidance should address technology performance and data-quality management across the entire data pathway, rather than focusing only on whether the device itself is approved.

4.5.4 Privacy and cybersecurity

Privacy and data protection form another important regulatory domain because DHT-enabled clinical research can involve continuous or repeated collection of participant-generated information. In the EU, digital health data are handled within the broader data-protection framework, while in India the DPDP Act 2023 and DPDP Rules 2025 form an increasingly important part of the legal environment for digital personal data.^{33,34}

However, the regulatory challenge for clinical trials extends beyond general data protection. DHT-based research may involve multiple actors, including sponsors, investigators, technology vendors, cloud-service providers and other third parties. Therefore, regulatory clarity is needed concerning data access, responsibility for data quality, security measures, retention and transfer across different systems.

The Indian framework is developing in this area, but its interaction with clinical-trial-specific DHT requirements remains an important issue for further regulatory clarification.

4.5.5 Interoperability and integration of data sources

DHT-enabled trials increasingly depend on information generated by multiple sources, including wearable devices, mobile applications, connected medical devices, electronic health records and clinical databases. The value of these data streams depends on their ability to be combined without compromising quality or interpretability.

The FDA's DHT guidance recognises that DHTs may depend on other technologies, including smartphones and communication networks, and therefore recommends consideration of the adequacy of these supporting technologies.¹⁶ In practice, this means that regulatory assessment cannot always be limited to the sensor or application alone.

For India, interoperability is particularly relevant because DHT-enabled trials may involve a mixture of commercial technologies, hospital information systems and sponsor-managed platforms. The absence of a single consolidated DHT clinical-trial framework means that expectations regarding interoperability and standardisation may need to be clarified across different regulatory and operational settings.

4.5.6 Participant safety and accessibility

A major area of convergence between the US and EU is the emphasis on participant safety when deciding whether a decentralised element is

appropriate. The FDA–EMA comparison found that both agencies recommend assessing the impact of decentralised elements according to the characteristics and complexity of the trial and the risks associated with the intervention.⁴⁰

At the same time, decentralisation may improve accessibility for individuals who experience difficulty travelling to research centres. DCT literature identifies reduced travel requirements and greater flexibility as important potential advantages. Sinha et al. describe DCTs as approaches intended to reduce the need for participants to travel to trial sites while facilitating remote collection of safety and efficacy data.²

However, accessibility is not automatically achieved through digitalisation. Participants may have differences in digital literacy, internet connectivity, device availability and familiarity with technology. This issue is particularly relevant to India, where recent stakeholder evidence identified limited digital literacy as a barrier to DCT adoption.³⁸ Therefore, a future Indian regulatory framework should address digital inclusion alongside technological innovation.

4.6 Regulatory Gaps and Implications for India

The comparative assessment indicates that the principal issue for India is not the complete absence of regulatory provisions, but their distribution across different regulatory domains. NDCTR 2019 provides the clinical-trial foundation; ICMR guidelines provide ethical oversight; the Telemedicine Practice Guidelines address remote medical interactions; the DPDP framework addresses digital personal data; and medical-device regulations apply to relevant software and devices.^{28,30,31,32,33,34}

The resulting framework can therefore accommodate several components of digital and decentralised research, but it does not provide the same degree of consolidated regulatory direction for DHT-specific clinical-trial questions seen in the US and EU. This distinction is important because sponsors may need to interpret several regulatory instruments simultaneously when determining how a particular DHT should be selected, validated, monitored and incorporated into a clinical investigation.

The first major gap is the absence of a consolidated framework for DHT selection and fitness-for-purpose assessment. FDA has explicitly established this concept for DHTs used in remote data acquisition, while EMA considers the scientific validity and context of use of digital methodologies through its qualification system.^{16,24} A comparable consolidated mechanism could provide Indian sponsors and investigators with clearer expectations before initiating a DHT-enabled trial.

The second gap concerns digitally derived endpoints. The FDA and EMA approaches indicate that regulatory acceptance requires evidence demonstrating that a digital measure captures a

clinically meaningful characteristic and performs adequately for the intended purpose.^{20,24,26} A dedicated Indian pathway for scientific advice or qualification of novel digital endpoints could therefore reduce uncertainty and support the adoption of validated digital measures.

The third gap relates to data governance across multiple technology providers. DHT-enabled trials can involve several organisations that collect, process, transmit or store participant data. Indian stakeholders have reported challenges involving data security and technology integration, suggesting that technical and organisational responsibilities may require greater clarification.³⁷

The fourth gap is interoperability and standardisation. As clinical-trial data increasingly originate from multiple digital sources, regulatory expectations concerning data formats, data transfer, device changes, missing data and integration with clinical databases become increasingly important. A future Indian framework could therefore establish minimum expectations for interoperability and traceability without prescribing a particular technology.

The fifth gap concerns regulatory readiness. de Jong et al. argue that regulators need to respond to innovation in a timely manner while avoiding unnecessary overregulation and suggest exploratory approaches such as regulatory sandboxes to generate evidence regarding innovative trial approaches.⁴¹ This concept may be particularly useful for India because DHT technologies are evolving faster than conventional regulatory cycles. A structured mechanism for early consultation between CDSCO, Ethics Committees, sponsors, investigators and technology developers could allow emerging technologies to be evaluated without waiting for extensive regulatory uncertainty to accumulate.

Table 3. Key regulatory gaps in India and their implications for DHT-enabled clinical trials

Regulatory domain	US/ EU regulatory approach	Regulatory status	Current position in India	Identified regulatory gap	Implication for India
DHT selection and fitness for purpose	FDA explicitly recommends a fit-for-purpose approach, while EMA	Partially addressed	DHT use is addressed through broader clinical-trial and technology-	No consolidated DHT-specific criteria for selecting and assessing	May create uncertainty for sponsors and investigators when deter

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	considers scientific validity and context of use.		related provisions.	suitability of a technology.	mining whether a DHT is appropriate for a particular trial.
DHT validation	FDA provides considerations for verification and validation; EMA evaluates reliability, accuracy, precision and validity within qualification processes.	Partially addressed	Validation requirements may arise from applicable clinical-trial or medical-device requirements but are not consolidated specifically for DHTs.	Absence of a dedicated DHT validation pathway.	Could affect consistency in demonstrating the reliability and suitability of DHT-generated clinical data.
Digitally derived endpoints	FDA provides a framework for digitally derived measures, while EMA has qualification	Not specifically addressed	No equivalent consolidated pathway specifically addressing qualification and regulatory accept	Lack of a defined pathway for development, qualification and acceptance of novel digital	May discourage adoption of innovative digital measures and increase regulatory

	n and scientific-advice mechanisms for novel digital methodologies.		ance of DHT-derived clinical endpoints.	endpoints.	uncertainty.
Data governance and accountability	US and EU approaches consider reliability, appropriate data handling and responsibilities associated with digital data generation and use.	Partially addressed	Data governance is distributed across clinical-trial, ethical and data-protection frameworks.	Responsibilities among sponsors, investigators, technology providers and data processors are not consolidated specifically for DHT-enabled trials.	Greater clarity could improve accountability for data quality, security, storage and transmission.
Interoperability and standardisation	DHT regulatory assessment considers supporting technologies and the reliability	No specifically addressed	DHT data may involve multiple devices, applications, health care systems	No consolidated DHT-specific expectations for interoperability, data formats,	May complicate integration of data from multiple digital sources and affect

	of data generation and transfer.		and sponsors or platforms under different regulatory settings.	transfer and traceability.	data consistency.
Regulatory consultation and readiness	FDA and EMA provide mechanisms for regulatory interaction, including scientific advice and qualification of novel methodologies.	No specifically addressed	No directly equivalent consolidated DHT-specific qualification mechanism was identified.	Limited formal pathway for early regulatory engagement specifically for emerging DHT methodologies.	Early consultation could reduce uncertainty and allow innovative technologies to be evaluated before their wider use.
Digital inclusion and accessibility	Usability and participant compatibility are considered when selecting and implementing DHTs.	Partially addressed	Indian evidence identifies digital literacy and infrastructure-related barriers to DCT implementation.	Limited DHT-specific regulatory consideration of digital literacy, connectivity and participant capability.	Regulatory guidance should consider equitable access along side technological performance.

4.7 Implications for Strengthening the Indian Regulatory Framework

The findings suggest that India could strengthen its regulatory environment by developing a consolidated guidance framework specifically addressing DHT use in clinical research while retaining the existing NDCTR, ethical, data-protection and medical-device requirements. Such guidance would not necessarily need to duplicate the FDA or EMA frameworks; instead, it could integrate relevant principles into an Indian context.

First, guidance could establish a risk- and purpose-based approach to DHT selection, requiring sponsors to demonstrate why a particular technology is appropriate for the intended measurement, participant population and trial design. This would be consistent with FDA's fit-for-purpose approach.^{16,20}

Second, India could establish a clearer pathway for regulatory consultation and qualification of novel digital endpoints. The EMA qualification mechanism demonstrates how early scientific engagement can provide regulatory clarity for emerging methodologies.^{25,26}

Third, future guidance could clarify responsibilities among sponsors, investigators, technology vendors and data processors, particularly when commercially available devices or third-party digital platforms are used. This would be particularly important for maintaining accountability for data quality, security and continuity throughout the trial.

Fourth, digital inclusion should be incorporated into DHT implementation requirements. The Indian context requires attention to digital literacy, connectivity, affordability and participant ability to use technology effectively. The finding that limited digital literacy is a reported barrier among Indian clinical-research stakeholders indicates that technological adoption alone may not ensure equitable participation.³⁸

Finally, regulatory development should remain adaptive rather than technology-specific. Because DHTs evolve rapidly, highly prescriptive regulations may become outdated. A principles-based framework supported by regulatory guidance, early scientific advice and periodic updates may provide greater long-term flexibility. This is consistent with the broader concept of regulatory readiness proposed in the DCT literature.⁴¹

Overall, the comparison suggests that India does not need to create an entirely new clinical-trial regulatory system for DHTs. Instead, the more practical approach would be to build on existing frameworks and establish clear, consolidated requirements for DHT selection, validation, digital endpoints, data integrity, privacy, cybersecurity, interoperability and decentralised trial activities. Such an approach could reduce regulatory uncertainty while supporting innovation and maintaining participant protection.

4.8 Limitations

This study has several limitations that should be considered when interpreting its findings. First, the analysis employed a qualitative comparative regulatory approach and therefore did not use quantitative methods or a formally validated scoring system to measure the relative regulatory maturity of the jurisdictions examined. Second, the comparison was limited to the United States, European Union and India; consequently, the findings may not fully represent regulatory approaches adopted in other developed or emerging jurisdictions. Third, the analysis was based primarily on publicly available regulatory documents, guidance, policy materials and published literature, and therefore may not capture unpublished regulatory practices, internal decision-making processes or jurisdiction-specific implementation experiences. Fourth, the regulatory landscape for DHTs and DCTs is rapidly evolving, and subsequent amendments, new guidance or emerging regulatory practices may alter some of the findings presented in this study. Fifth, the study did not include primary data from sponsors, investigators, technology providers, Ethics Committees, regulators or trial participants; therefore, the identified gaps and proposed recommendations have not been empirically validated through stakeholder consultation. Finally, the proposed measures for strengthening the Indian regulatory framework represent recommendations derived from comparative regulatory analysis and should not be considered as tested implementation models. Further research involving stakeholder consultation, empirical assessment and evaluation of implementation feasibility would be valuable for validating and refining the proposed regulatory approach.

5. Conclusion

Digital health technologies are increasingly reshaping the conduct of clinical trials by enabling remote data acquisition, continuous or frequent monitoring, digital endpoints, electronic patient-reported outcomes and other decentralised trial activities. The comparative analysis demonstrated that the United States and European Union have developed more explicit regulatory approaches for the use and evaluation of DHTs in clinical research, particularly in relation to technology suitability, validation, digitally derived measures and scientific assessment.

In contrast, India has relevant regulatory provisions distributed across multiple frameworks, including the NDCTR 2019, ICMR ethical guidelines, Telemedicine Practice Guidelines, DPDP framework and medical-device regulations. These provisions provide an important foundation for DHT-enabled clinical research and participant protection, but they do not collectively provide a consolidated framework specifically addressing DHT selection, fitness for purpose, validation,

digital endpoints, interoperability, cybersecurity and responsibilities of technology providers.

The major regulatory gap identified in India is therefore regulatory fragmentation rather than the complete absence of regulation. The US and EU approaches provide useful reference points for strengthening India's framework, particularly through fit-for-purpose DHT assessment, clearer validation requirements, qualification of digital endpoints and mechanisms for early regulatory consultation. At the same time, these approaches should be adapted to India's regulatory, technological and healthcare environment rather than directly replicated.

A consolidated, risk-based and adaptive regulatory framework for DHT-enabled clinical research could improve regulatory clarity while supporting innovation and maintaining participant safety, data integrity and privacy. Such an approach should also consider interoperability, cybersecurity, technology-provider accountability and digital accessibility. Strengthening these areas would help create a more coherent regulatory environment for the responsible integration of DHTs into clinical trials and facilitate the future implementation of decentralised clinical research in India.

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