Global Regulatory Handbook of Decentralized Clinical Trials

Version 1.2 March 2024

Tigermed DCT Solutions | Decentralized Clinical Trials

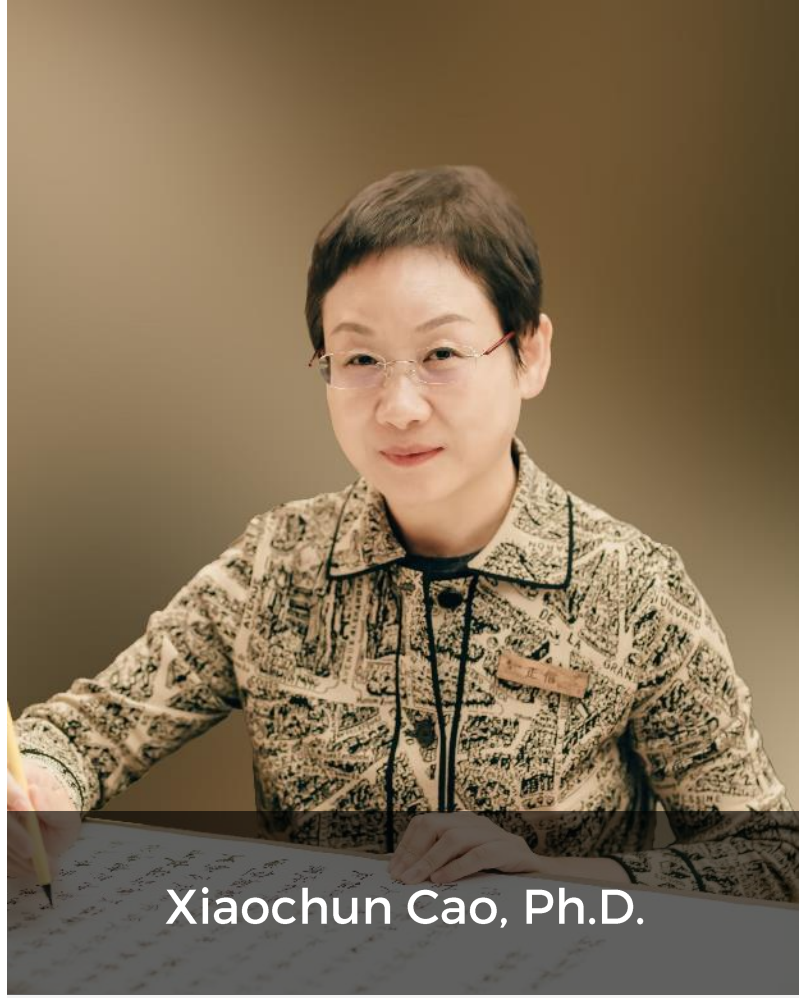
Preface

Clinical trials play a crucial role in the research and development of biomedicine, the advancement of medicine, and human health. Dating back to the famous James Lind's Royal Navy scurvy trial, which originated the "520 International Clinical Trials Day," clinical trials have undergone over 200 years of development. While the concepts, methodologies, and technological tools of clinical trials have become increasingly advanced, they have also become more complex. The burden on clinical trial participants has grown, and their experience has become less favorable.

In recent years, countries and regions worldwide have been proposing new models for "patient-centric" clinical trials. These aim to ensure that the voices of clinical trial participants are more valued and incorporated into trial protocols. The goal is to conduct trial-related activities in non-traditional clinical research centers, efficiently collect remote data using digital technology, enable researchers to conduct televisits or visits at locations convenient for participants, and facilitate drug to patient delivery. These advancements aim to significantly improve the convenience, comfort, and compliance of clinical trial participants, ultimately enhancing the quality of clinical trials and reducing the costs associated with pharmaceutical research and development.

As a comprehensive Contract Research Organization (CRO) in the biopharmaceutical industry, Tigermed is dedicated to innovation in service and building health, with a customer-centric approach. Tigermed's Decentralized Clinical Trial (DCT) solution can be tailored to the unique needs of global clients, providing highly adaptive and flexible solutions and technological platforms. This, in turn, reduces costs, enhances quality, and ensures outstanding delivery.

Let us work together, hand in hand, to drive the development and transformation of clinical trials, contributing to the pursuit of human health!



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Co-founder, Executive Director, President

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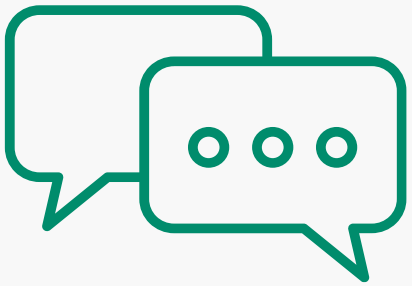

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Tigermed Group

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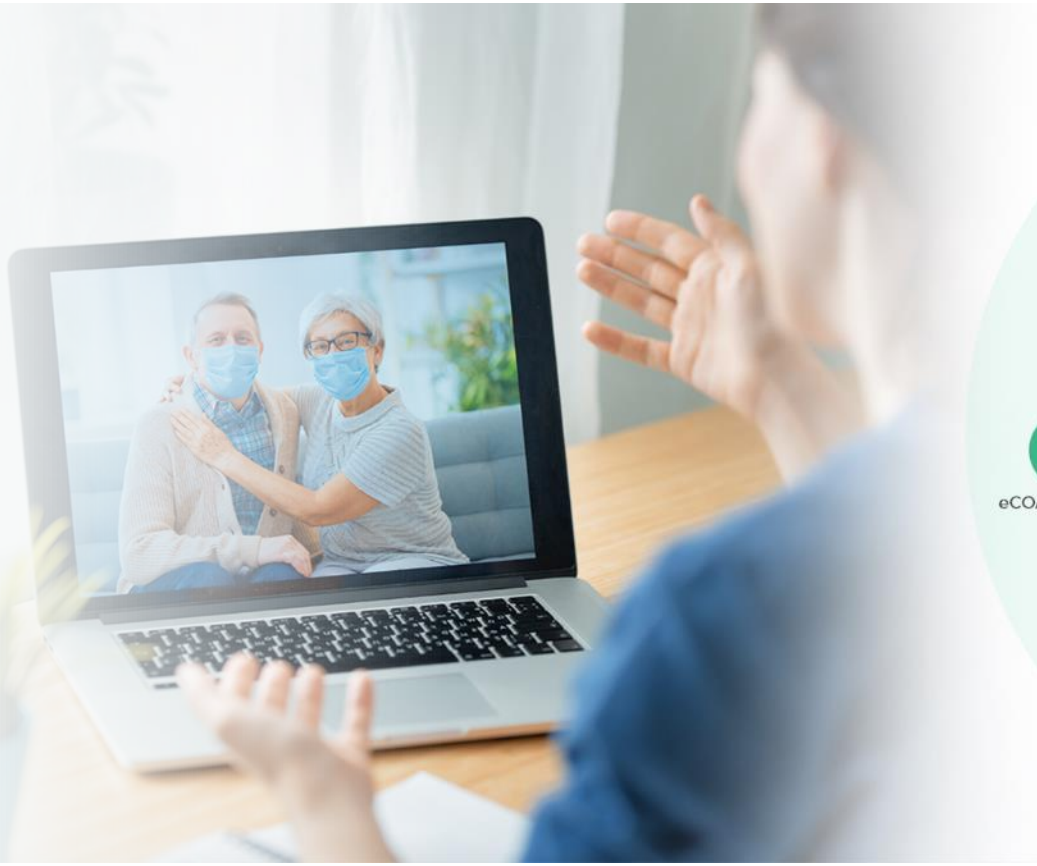
Delivering a Wide Range of Virtual and Hybrid Approaches to Decentralized Clinical Trials

200+ Clinical trials incorporate elements of DCT

30%+ Tigermed's on-going clinical trials incorporating DCT elements

30% The cost has been discounted by 30%

40% The efficiency has been boosted by 40%



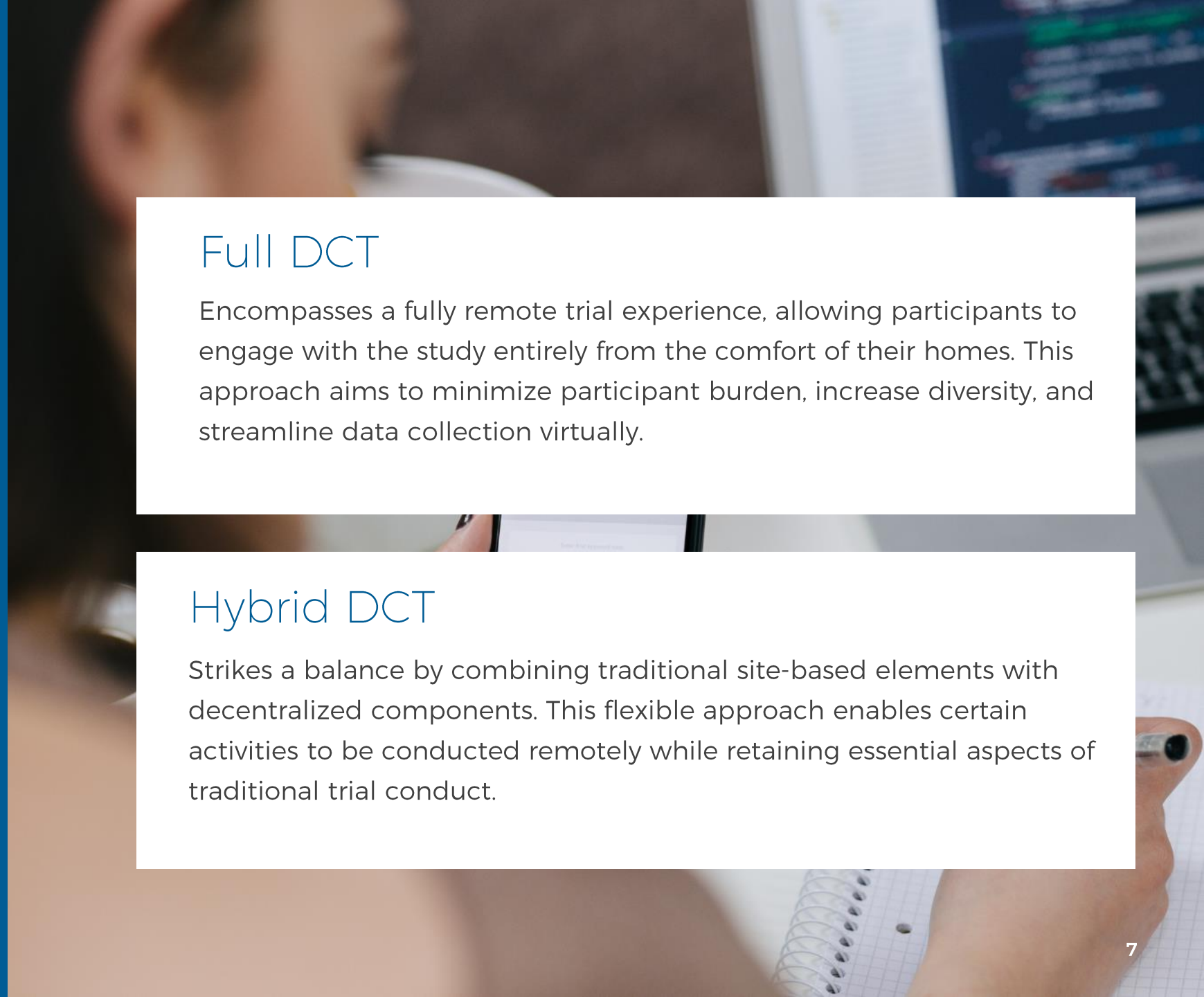
Decentralized Clinical Trials

Decentralized Clinical Trials

Decentralized Clinical Trials, often abbreviated as DCTs, represent a paradigm shift in the traditional conduct of clinical research. These trials leverage digital tools and remote methods to facilitate the collection of data, reducing or eliminating the need for physical visits to clinical trial sites. The primary goal is to enhance participant engagement, inclusivity, and overall efficiency in the research process.

Full DCT and Hybrid DCT

In the realm of DCTs, two primary models emerge:



Full DCT

Encompasses a fully remote trial experience, allowing participants to engage with the study entirely from the comfort of their homes. This approach aims to minimize participant burden, increase diversity, and streamline data collection virtually.

Hybrid DCT

Strikes a balance by combining traditional site-based elements with decentralized components. This flexible approach enables certain activities to be conducted remotely while retaining essential aspects of traditional trial conduct.

DCT and Traditional Clinical Trials

	DCTs	Traditional Clinical Trials
Remote Data Collection	• Relies on digital tools for data collection, allowing participants to contribute data from their homes through wearable devices, mobile apps, and other remote monitoring technologies.	• Often requires participants to visit physical trial sites for data collection, posing logistical challenges and potential barriers to participation.
Patient Engagement	• Fosters increased patient engagement by offering the convenience of remote participation, potentially leading to better retention rates and more diverse participant pools.	• Involves on-site visits, which can be time-consuming and inconvenient for participants, potentially impacting enrollment and retention.
Geographical Diversity	• Facilitates participation from a broader geographic range, promoting diversity in the study population.	• Typically limited to participants who can easily access the physical trial site, potentially leading to a less diverse participant pool.

Common Elements (Components) in DCTs

Electronic Informed Consent (eConsent) / Remote Consent

Electronic informed consent refers to using digital media such as text, images, video, audio, and websites to provide information to potential subjects and obtain their written consent through smart devices like smartphones, tablets, or computers. This process includes information communication, questioning related to the trial, and signing the informed consent form (ICF).

Electronic Clinical Outcome Assessment (eCOA)

A broader term that includes ePRO and other electronic methods of collecting clinical outcome assessment (COA) data, such as clinician-reported outcomes, observer-reported outcomes, and performance outcomes.

Electronic Patient-Reported Outcome (ePRO)

A method of collecting patient-reported outcome (PRO) data electronically, often through the use of a computer or mobile device. ePRO can help to reduce data errors, improve data quality, and increase patient compliance.

Electronic Patient Diary (eDiary)

A type of ePRO that collects patient-reported data over time, often through a series of questions or prompts. e-Diaries can help to capture patient experiences in real-time and provide more accurate and detailed data.

Drug to Patient (DTP)

A clinical trial model where the investigational drug is delivered directly to the participant's home or a designated location, rather than requiring them to travel to a trial site. DTP can help to reduce participant burden and improve trial enrollment.

Telemedicine

The use of technology, such as videoconferencing, to provide medical care or consultations at a distance. Telemedicine can be used in clinical trials to facilitate remote study visits or monitoring.

Local Health Care Provider (HCP)

A healthcare professional or facility located near a trial participant's home or workplace or go to subject's house, who can provide medical care or support during a clinical trial. Local healthcare providers can be enlisted to help with trial-related procedures, such as blood draws or ECGs, and to provide medical care in the event of an adverse event.

Wearable Device

A device that can be worn on the body, often with sensors that collect physiological or activity data. Wearable devices can be used in clinical trials to collect objective data on participant health and behavior.

Risk-Based Monitoring (RBM)

A monitoring strategy that focuses on the most critical data and processes in a clinical trial, based on risk assessments. RBM can help to reduce monitoring costs and increase the efficiency of clinical trials.

Remote Monitoring

It refers to the use of technology and tools to oversee and manage clinical trial activities without the need for physical presence at the trial site. This approach allows for the collection, review, and analysis of clinical trial data from various locations, including the participants' homes, through the use of electronic systems and communication technologies.

Overview of Global Regulatory Requirements in DCTs

(up to December, 2023)

All regulations or guidelines pertaining to DCTs released up to December, 2023, from 19 regions across APAC, America, and EMEA were thoroughly reviewed.

Permissible DCT Methods (Elements/ Components) per Region/Country

The permissible DCT methods in clinical trials suggest that there are corresponding regulations and/or guidance in each country/region, released until December 2023.

Asia Pacific

Overview of Global Regulatory Requirements in DCTs
(up to December, 2023)

🟢 Regulation Allowed 🟠 No Regulations Found 🔴 Regulations Not Allowed

		eConsent	E-Signature	ePRO/eCOA/eDiary	Drug-to-Patient (DTP)	Telemedicine	Local Health Care Provider (HCP)	Wearable Device	Remote Monitoring/SDV
• China	Chinese Mainland	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢
	Hong Kong China	🟠	🟠	🟠	🟠	🟠	🟠	🟠	🟠
	Taiwan China	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢
• APAC (out of SEA)	Australia	🟢	🟢	🟠	🟠	🟢	🟠	🟠	🟢
	Japan	🟢	🟢	🟢	🟢	🟢	🟢	🟠	🟢
	South Korea	🟢	🟢	🟢	🟠	🟠	🟠	🟢	🟠
• APAC- SEA	Indonesia	🟠	🟠	🟠	🟠	🟠	🟠	🟠	🟠
	Malaysia	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢
	Philippines	🟠	🟠	🟠	🟠	🟠	🟠	🟠	🟠
	Singapore	🟢	🟢	🟠	🟢	🟢	🟢	🟠	🟢
	Thailand	🟠	🟠	🟠	🟠	🟠	🟠	🟠	🟠
	Vietnam	🟠	🟠	🟠	🟠	🟠	🟠	🟠	🟠

America and EMEA

Overview of Global Regulatory Requirements in DCTs
(up to December, 2023)

● Regulation Allowed ● No Regulations Found ● Regulations Not Allowed

		eConsent	E-Signature	ePRO/eCOA/eDiary	Drug-to-Patient (DTP)	Telemedicine	Local Health Care Provider (HCP)	Wearable Device	Remote Monitoring/SDV
• North America	USA	●	●	●	●	●	●	●	●
• Latin America	Argentina	●	●	●	●	●	●	●	●
	Brazil	●	●	●	●	●	●	●	●
• EMEA	Europe (Spain, Italy, Poland)	●	●	●	●	●	●	●	●
	UK	●	●	●	●	●	●	●	●
	South Africa	●	●	●	●	●	●	●	●

Region Summary per Allowed DCT Methods (Elements/ Components)

The permissible DCT methods imply that there are reflected regulations and/or guidance found in each country/region.

	APAC	America	EMEA
eConsent & E-Signature	Australia, China, China-Taiwan, Japan, South Korea, Singapore	USA, Argentina, Brazil	Europe (Spain, Italy, Poland), UK, South Africa
eCOA	China, China-Taiwan, Japan, South Korea	USA, Argentina	Europe (Spain, Italy, Poland), UK, South Africa
DTP	China, China-Taiwan, Japan, South Korea, Singapore	USA, Argentina	Europe (Spain, Italy, Poland), UK, South Africa
Telemedicine	Australia, China, China-Taiwan, Japan, South Korea, Singapore	USA, Argentina, Brazil	Europe (Spain, Italy, Poland), UK, South Africa
Local Health Care Provider	Australia, China, China-Taiwan, Japan, South Korea, Singapore	USA, Argentina, Brazil	Europe (Spain, Italy, Poland), UK, South Africa
Wearable Device	China, China-Taiwan, South Korea	USA, Argentina	Europe (Spain, Italy, Poland), UK, South Africa
Remote Monitoring	Australia, China, China-Taiwan, Japan, Singapore	USA, Argentina, Brazil	Europe (Spain, Italy, Poland), UK, South Africa

Key DCT Regulatory Reference by Countries

In this section, you will find only the key DCT regulations or guidance from 2019 to the end of December, 2023.

Asia Pacific

Key DCT Regulatory Reference by Countries

China

	Document Name	Type	Category	Status (Active, Amended, Draft, Retired)	Effective Date
Chinese Mainland	Technical guidelines for implementation of patient-centric clinical trials (Interim)	Guideline	Clinical Operation-DCT	Active	27 Jul, 2023
	Principles for the Application of Decentralized Clinical Trials in Clinical Development of Rare Disease Drugs (Seek for comments)	Guideline	Clinical Operation-DCT	Draft	24 Nov, 2023
	Technical Guidelines for Patient-Centric Clinical Trial Design (Interim)	Guideline	Trial Design	Active	27 Jul, 2023
	Patient-Centric Clinical Trial Benefit-Risk Assessment Technical Guidelines (Interim)	Guideline	Quality	Active	27 Jul, 2023
	Guidelines for Centralized Monitoring and Statistics of Drug Clinical Trials (Interim)	Guideline	Technology & Statistics	Active	01 Dec, 2021
	Guidelines for the Application of Patient-Reported Outcomes in Drug Clinical Development (Interim)	Guideline	Technology-ePRO	Active	01 Dec, 2021
	Guidelines for drug clinical trial management during the COVID-19 epidemic (Interim)	Guideline	Clinical Operation-COVID-19	Active	01 Jul, 2020
	Electronic Signature Law of the People's Republic of China	Regulation	e-Signature	Active	01 Apr, 2019
Hong Kong China	The Personal Data (Privacy) (Amendment) Ordinance 2021	Regulation	Privacy	Amended	08 Oct, 2021
	Guidelines for All Registered Medical Practitioners	Guideline	Medical Practice	Active	Dec, 2019
Taiwan China	Guideline for Implementing Decentralized Clinical Trials	Guideline	Clinical Operation-DCT	Active	13 Jun, 2023
	Guidelines for the Application of Digital Health Technologies in Conducting Remote Data Collection for Drug Clinical Trials (Draft)	Regulation	Technology-eCOA, ePRO, Wearable Device	Draft	15 May, 2023
	Guidelines for the Use of Computerized Systems and Electronic Data in Drug Clinical Trials (Draft)	Guideline	Technology	Draft	15 May, 2023
	Guidelines for Using Electronic Health Records in Clinical Research	Guideline	Technology- EMR	Active	26 Nov, 2022
	Measures for the production and management of electronic medical records in medical institutions (Amendment)	Regulation	Technology-EMR	Active	18 Jul, 2022
	Recommendations and Principles for Conducting Drug Clinical Trials During the Period of COVID-19 Pandemic & FQA (Amendment)	Guideline	Clinical Operation-COVID-19	Active (Applicable during COVID-19 Pandemic period)	25 Jun, 2021

Asia Pacific

Key DCT Regulatory Reference by Countries

	Document Name	Type	Category	Status (Active, Amended, Draft, Retired)	Effective Date
Australia	Privacy Act 1988 (Amendment)	Regulation	Privacy	Amended	21 Oct, 2023
	NSW Health Guidance Document COVID-19 and Clinical Trials (Version 2)	Guideline	Clinical Operation-COVID-19	Active	09 Sep, 2020
	National Standard Operating Procedures for Clinical Trials, including Teletrials, in Australia	Guideline	Clinical Operation	Active	25 Feb, 2021
	Australian Clinical Trials Alliance: COVID-19: Guidance on clinical trials for institutions, HRECs, researchers and sponsors	Guideline	Clinical Operation-COVID-19	Active	25 Mar, 2020
	Guide to providing telephone and video consultations in general practice	Guideline	Technology	Active	01 Mar, 2020
	Telehealth video consultations guide	Guideline	Technology	Active	01 May, 2019
Japan	Act on the Protection of Personal Information (Amendment)	Regulation	Privacy	Amended	01 Apr, 2023
	Points to be noted regarding explanations and consent using electromagnetic methods in clinical trials and post-marketing clinical studies	Guideline	Technology-eConsent	Active	30 Mar, 2023
	Regulation on Electronic Signatures and Certification Services (Amendments)	Regulation	e-Signature	Amended	17 Jun, 2022
	Amendments to the Guidance on the Enforcement Standards for Clinical Trials of Pharmaceuticals	Guideline	Technology-DTP	Active	30 Jul, 2021
	Q&A Regarding the Conduct of Clinical Trials for Pharmaceuticals, Medical Devices, and Regenerative Medical Products under the Influence of COVID-19 (Amendment)	Guideline	Technology-DTP, Home Health Care	Amended	26 May, 2020
	Handling of the Storage of Informed Consent Documents in Clinical Trials.	Guideline	Technology-eConsent, Telemedicine	Active	07 Apr, 2020
South Korea	Medical Law Enforcement Regulations (Ministry of Health and Welfare) (Amendment)	Regulation	Technology- Telemedicine, Local Health Care Provider	Amended	15 Mar, 2023
	Law on Implementing Regulations of the Medical Device (Prime Minister's Decree): Prime Minister Ordinance No. 1841	Regulation	Technology-Wearable Device	Active	19 Dec, 2022
	Clinical Trial Practice Standards for Pharmaceutical Products (related to Article 30(1))	Guideline	Technology-DTP	Active	21 Jul, 2022
	Law on the Prevention and Control of Infectious Diseases	Regulation	Technology-Telemedicine	Active	19 Oct, 2021
	55-Year Comprehensive Plan for the Development of Clinical Trials	Guideline	Technology-eCOA, ePRO	Active	Aug, 2019
	Electronic Transactions Act 2010 (Amendment)	Regulation	e-Signature	Amended	01 Feb, 2023
Singapore	Personal Data Protection Act 2012 (Amendment)	Regulation	Data Protection	Amended	01 Oct, 2022
	Guidance on the Conduct of Clinical Trials in Relation to the COVID-19 Situation	Guideline	Clinical Operation-COVID-19	Active	26 Aug, 2022
	Clinical Trials Guidance- Electronic Consent (version 3)	Guideline	Technology	Active	01 Oct, 2021
Malaysia	Malaysia Decentralized Clinical Trial (DCT) Guidance Document (version 1.0)	Guideline	Clinical Operation-DCT	Active	Jul, 2023

America

Key DCT Regulatory Reference by Countries

- North America
- Latin America

	Document Name	Type	Category	Status (Active, Amended, Draft, Retired)	Effective Date
USA	Digital Health Technologies for Remote Data Acquisition in Clinical Investigations Guidance for Industry, Investigators, and Other Stakeholders	Guideline	Technology- eCOA, Wearable Device	Active	Dec, 2023
	Submitting Clinical Trial Datasets and Documentation for Clinical Outcome Assessments Using Item Response Theory	Guideline	Technology- eCOA	Active	Nov, 2023
	Submitting Patient Reported Outcome Data in Cancer Clinical Trials	Guideline	Technology- eCOA	Active	Nov, 2023
	21 CFR parts 11, 45, 50 and 56, 312, 812	Regulation	Technology- eSignature, DTP, Local Health Care Provider, Wearable Device	Amended	23 Oct, 2023
	Decentralized Clinical Trials for Drugs, Biological Products, and Devices (Draft)	Guideline	Clinical Operation-DCT	Draft	23 May, 2023
	Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations Questions and Answers Guidance for Industry (Draft)	Guideline	Technology-eConsent, eSignature, eCOA	Draft	Mar, 2023
	Enforcement Policy for Non-Invasive Remote Monitoring Devices Used to Support Patient Monitoring During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency (Revised) Guidance for Industry and Food and Drug Administration Staff	Guideline	Clinical Operation- COVID-19	Active	Oct, 2020
Argentina	Good Practices for Telemedicine – Disposition 581	Guideline	Clinical Operation-Telemedicine	Active	18 Mar, 2022
	Good Practices for Telemedicine - Guidelines	Guideline	Clinical Operation-Telemedicine	Active	Nov, 2021
	National Telemedicine Law (Draft)	Regulation	Technology-Telemedicine	Draft	Jun, 2020
	Conduct of Clinical Trials During the COVID-19 Public Health Emergency (ANMAT): 25-Mar, 2020	Guideline	Clinical Operation- COVID-19	Active	25 Mar, 2020
Brazil	Recommendations for ICF during COVID-19_Local RA ANMAT	Guideline	Technology-eConsent	Active	20 Mar, 2020
	Clinical Trials and Pandemic, Nota Técnica N°05/2023/SEI/COPEC/GGMED/DIRE2/ANVISA (Amendment)	Guideline	Clinical Operation- COVID-19	Amended	May, 2023
	eICF and Biobank: Ofício Circular N° 23/2022/CONEP/SECNS/DGIP/SE/MS	Guideline	Technology-eConsent, eSignature	Active	17 Oct, 2022
	Telemedicine Resolution: Resolução CFM N° 2.314	Guideline	Technology-Telemedicine	Active	20 Apr, 2022
	Telemedicine Ordinance No. 467	Regulation	Technology-Telemedicine	Active	20 Mar, 2020

EMEA

Key DCT Regulatory Reference by Countries

	Document Name	Type	Category	Status (Active, Amended, Draft, Retired)	Effective Date
EMA	Guideline on computerised systems and electronic data in clinical trials	Guideline	Technology-DCT method, eConsent, eCOA, IRT	Active	07 Sep, 2023
	Recommendation Paper on Decentralized elements in Clinical Trials	Guideline	Clinical Operation-DCT	Active	13 Dec, 2022
	The EU general data protection regulation (GDPR)	Regulation	Data Protection	Active	25 May, 2018 (Application)
Italy	Clinical trials' management in Italy during the COVID-19 (coronavirus disease 19) emergency	Guideline	Clinical Operation- COVID-19	Active (Applicable during COVID-19 Pandemic Emergency)	17 Sep, 2020
Spain	Code of Conduct Regulating the Processing of Personal Data in Clinical Trials and Other Clinical Research and Pharmacovigilance Activities	Regulation	Clinical Operation- Data Privacy	Active	01 Feb, 2022
UK	Clinical trials applications for Coronavirus (COVID-19)	Guideline	Clinical Operation- COVID-19	Amended	23 Feb, 2022
	Managing clinical trials during Coronavirus (COVID-19)	Guideline	Clinical Operation- COVID-19	Amended	16 Nov, 2021
	Guidance on minimising disruptions to the conduct and integrity of clinical trials of medicines during COVID-19	Guideline	Clinical Operation- COVID-19	Amended	13 Nov, 2020
South Africa	Guideline for Electronic Submission of Clinical Trial Documents (Amendments, Bioequivalence Studies, Responses, Notifications, And Serious Adverse Events)	Guideline	Clinical Operation	Amended	05 Sep, 2022
	Oversight and monitoring in Clinical Trials	Guideline	Clinical Operation- RBM & Remote Monitoring	Amended	Aug, 2022
	The South African Good Clinical Practice (GCP) guidelines (Version 3)	Guideline	Clinical Operation-DCT	Amended	17 Jun, 2020
	SAHPRA Policy on Conduct of Clinical Trials of Health Products During the current COVID-19	Guideline	Clinical Operation- COVID-19	Active	25 Mar, 2020

Global Overview of Decentralized Clinical Trial (DCT) Regulations:

A Country-by-Country Summary

The implementation of Decentralized Clinical Trials (DCT) in most countries was driven by the global COVID-19 pandemic. While some regulatory authorities have issued DCT guidelines following the pandemic, there are ongoing drafting processes in certain regions. This section provides a country-specific summary, concentrating on those that have officially released DCT guidelines.

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Asia Pacific

Chinese Mainland

On July 27, 2023, China's Center for Drug Evaluation (CDE) released three guidance documents pertaining to Patient-Centric Clinical Trials (DCTs):

- Technical Guidelines for the Implementation of Patient-Centric Clinical Trials
- Technical Guidelines for Patient-Centric Clinical Trial Design
- Patient-Centric Clinical Trial Benefit-Risk Assessment Technical Guidelines

On November 24, 2023, China's CDE also issued a "Draft for Comments" on the "Technical Guidance Principles for the Application of Decentralized Clinical Trials in the Clinical Development of Rare Disease Drugs," seeking input from the industry.

Going back to December 1st, 2021, two guidelines, namely "Guidelines for the Application of Patient-Reported Outcomes in Drug Clinical Development (Interim)" and "Guidelines for Centralized Monitoring and Statistics of Drug Clinical Trials (Interim)," were released. These guidelines introduced DCT elements, including electronic Clinical Outcome Assessments (eCOA), electronic Patient-Reported Outcomes (ePRO), and risk-based monitoring.

The DCT guideline released in Jul, 2023 places significant emphasis on the importance of thorough planning, ethical considerations, and participant-centric approaches in the implementation of these trials.

Moreover, not all patient-centric clinical trials are suitable for DCT elements, and their adoption should be carefully considered based on specific conditions. The guideline also highlights the importance of incorporating patient perspectives, leveraging digital technologies, ensuring data integrity and privacy, and compensating participants adequately in the evolving landscape of clinical trials. As clinical research embraces innovations, it is crucial to balance the benefits of advanced technologies with privacy protection, data integrity, and the fair treatment of trial participants.

Asia Pacific

Hong Kong China and Taiwan China

Hong Kong China

As of the end of 2023, Hong Kong's regulatory authority has not issued any specific guidance on DCT. The primary framework continues to align with ICH GCP E6 guidelines, allowing activities such as Risk-Based Monitoring (RBM). However, there are no regulations explicitly permitting remote monitoring in Hong Kong. When implementing DCTs, consultation with the Department of Health and Institutional Review Boards (IRBs) is essential.

The Guidelines for All Registered Medical Practitioners, issued in December 2019, introduced telemedicine to medical practitioners. However, there are no detailed regulations or guidelines governing its implementation in clinical trials. In summary, there are no formal guidelines or regulations directly addressing DCTs or providing principles for their conduct. Therefore, any studies intending to incorporate DCT elements should first consult the regulatory authority and IRBs.

Taiwan China

The implementation of Decentralized Clinical Trials (DCT) in Taiwan, spurred by the global COVID-19 pandemic, was guided by recommendations released in April 2020 and updated in June 2021. This led to the adoption of alternatives like Telemedicine and Drug-to-Patient (DTP). Additionally, following the release of the Chinese version of ICH GCP E6 R2 by the Taiwan Food and Drug Administration (TFDA), Taiwan incorporated centralized and remote monitoring.

On June 13, 2023, TFDA officially released a Guideline for Implementing Decentralized Clinical Trials, providing detailed considerations for various aspects of DCTs. Attention to personal data protection, storage, and security is crucial due to various electronic systems involved. Sponsors should have a risk management plan to minimize potential risks, with delegated tasks to external vendors falling under the responsibility of principal investigators.

In summary, DCT guidelines encompass various elements, and their implementation involves complex considerations affecting clinical trial design and execution. Sponsors must conduct a risk assessment based on individual trial plans to determine the feasibility of DCT elements.

Asia Pacific

Australia

As of the end of 2023, Australia's regulatory authority has not issued specific guidance on Decentralized Clinical Trials (DCT). However, guidelines for conducting clinical trials during the COVID-19 pandemic encourage practices such as remote monitoring and the use of e-signatures. Telehealth, equivalent to telemedicine, is introduced in guidelines for medical practitioners, allowing individuals to consult healthcare providers via phone or video calls, as defined by the Australia Government Department of Health and Aged Care.

While there are no specific regulations regarding eConsent, certain guidelines, like the National Standard Operating Procedures for Clinical Trials, including Teletrials, recognize e-Consent as an acceptable method, subject to Sponsor review and approval by the Human Research Ethics Committee (HREC). The widespread use of e-signatures in Australian clinical trials is acknowledged in the National Standard Operating Procedures, emphasizing the importance of documenting consent. Although specific regulations do not explicitly permit the use of electronic Clinical Outcome Assessment (eCOA), past studies have successfully employed eCOA/ePRO/eDiary, following protocol details and HREC approval.

In Australia, it is crucial to develop a comprehensive protocol that incorporates detailed Decentralized Clinical Trial (DCT) elements when contemplating the utilization of DCTs.

Asia Pacific

Japan

As of the end of 2023, the regulatory authority in Japan, PMDA, has not officially released guidelines for Decentralized Clinical Trials (DCTs), plans to draft such guidelines have been discussed during communications with PMDA. The Q&A Regarding the Conduct of Clinical Trials for Pharmaceuticals, Medical Devices, and Regenerative Medical Products under the Influence of COVID-19 introduces various DCT elements, including DTP, Local Health Care Provider, Remote Monitoring, and Risk-Based Monitoring.

Notably, the Points to be noted regarding explanations and consent using electromagnetic methods in clinical trials and post-marketing clinical studies, released on Mar. 30, 2023, officially endorses the use of eConsent, detailing its requirements. Furthermore, the e-Signature has been discussed, referencing the Regulation on Electronic Signatures and Certification Services (Amendments) on Jun 17, 2022, with an earlier introduction of e-Signature in the Use of Electromagnetic Records and Electronic Signatures in Applications for Approval or Permission for Medical products, etc. (ES/EM guideline) Annex on Apr 1, 2005.

The Points to be noted regarding explanations and consent using electromagnetic methods in clinical trials and post-marketing clinical studies also includes provisions for eCOA/ePro. However, there is currently no specific guidance on telemedicine and wearable devices. During the DIA annual meeting in Jun 2023, a PMDA officer officially confirmed the drafting of a DCT guidance, although the release date remains uncertain.

Consultation with PMDA is recommended before the official release of the DCT guidance in Japan, if there are plans to implement DCTs in Japan.

Asia Pacific

South Korea

The same as the majority countries in APAC, As of the end of 2023, Ministry of Food and Drug Safety (MFDS) has not issued specific guidance on Decentralized Clinical Trials (DCT). The details of eConsent requirements was addressed in the Q&A eConsent (Nov., 2019). The 55-Year Comprehensive Plan for the Development of Clinical Trials released in Aug 2019 mentioned eCOA, but there is no specific regulation mentioned about eCOA and ePRO, however, past studies have successfully employed eCOA/ePRO/eDiary, following protocol details approved by MFDS and IRBs. Wearable device was included in the Law on Implementing Regulations of the Medical Device (Prime Minister's Decree): Prime Minister Ordinance No. 1841, which was released on 19 Dec., 2022.

Although some regulations such as Medical Law Enforcement Regulations (Ministry of Health and Welfare) mentioned the Telemedicine, but the telemedicine is very limited in South Korea, and there is no clear guideline mentioned the telemedicine in clinical trials. The aforementioned medical law also mentioned the home visit, but there is also no clear guideline for using local health care provider in clinical trials. Electronic prescriptions are currently accepted in South Korea, however there is no clear guideline or regulation mentioned the drug shipped to subjects could be implemented, but during the COVID-19 pandemic period, the guideline of Clinical Trial Considerations for COVID-19, release on Mar, 2020, mentioned DTP in some situations.

Same as Japan, consultation with MFDS is recommended, if there are plans to implement DCTs in South Korea.

Asia Pacific

Singapore

In Singapore, the Guidance on the Conduct of Clinical Trials in Relation to the COVID-19 Situation, released on Aug. 26, 2022, mentions various DCT elements such as eConsent, DTP, Telemedicine, Local Health Care Providers (HCP), and remote monitoring. Additionally, the Clinical Trials Guidance- Electronic Consent (version 3), released on 01 Oct., 2021, provides details on eConsent and eSignature.

However, specific guidance for eCOA, including ePRO and wearable devices, is not available. Although there are no explicit regulations permitting the use of electronic Clinical Outcome Assessment (eCOA), past studies have successfully employed eCOA/ePRO/eDiary, following protocol details approved by the Health Sciences Authority (HSA).

Therefore, it is confirmed that several DCT elements, including eConsent, DTP, Telemedicine, Local Health Care Providers (HCP), and remote monitoring, can be implemented in Singapore. The recognition of eCOA is contingent on including detailed procedures in the protocol, which must be approved by the HAS.

Asia Pacific

SEA(Philippines, Malaysia, Indonesia, Vietnam and Thailand)

The implementation status of Decentralized Clinical Trials (DCTs) remains unclear in the South East Asia (SEA) region as of June 30, 2023, with no released guidelines or reflected regulations, except for Malaysia. It is advisable to consult with regulatory authorities in the Philippines, Indonesia, Vietnam, and Thailand when considering the implementation of DCTs in these countries.

In Malaysia, a Decentralized Clinical Trial (DCT) Guidance Document (version 1.0) was issued in July 2023. The document comprehensively covers eConsent & eSignature, DTP, Trial-related Procedures at Home (including local Health Care Provider services), and Data Collection in DCTs. The guidance explicitly mentions eCOA, ePRO, and wearable devices under the data collection section, and it addresses remote monitoring as well. Although there is no dedicated section providing detailed information on telemedicine, it is referenced in the guidance. Therefore, the guidance suggests that the majority of DCT elements are permissible in Malaysia.

America

USA

In September 2018, the Clinical Trials Transformation Initiative (CTTI) released recommendations on Decentralized Clinical Trials (DCTs). These recommendations cover not only an overview of DCT and protocol design of DCTs, but also aspects like investigator oversight. Furthermore, the document addresses specific elements of DCT, including Telemedicine, the Drug Supply Chain concerning direct-to-trial participant Investigational Medicinal Product (IMP) shipment, and remote safety monitoring.

In 2023, the US FDA released several guidance documents related to Decentralized Clinical Trials (DCT). Noteworthy among these are the "Digital Health Technologies for Remote Data Acquisition in Clinical Investigations Guidance for Industry, Investigators, and Other Stakeholders", "Submitting Clinical Trial Datasets and Documentation for Clinical Outcome Assessments Using Item Response Theory", and the "Decentralized Clinical Trials for Drugs, Biological Products, and Devices (Draft)." Some DCT elements, including telemedicine, eConsent, remote monitoring, and Direct-to-Patient (DTP), may have been introduced during the COVID-19 Public Health Emergency in the "Conduct of Clinical Trials of Medical Products" and its Q&A since 2020. For the successful implementation of Decentralized Clinical Trials in the United States, the DCT guidance provided in the "Decentralized Clinical Trials for Drugs, Biological Products, and Devices (Draft)" is deemed essential.

In conclusion, the FDA's guidance on DCTs provides a comprehensive framework for conducting clinical trials with several decentralized elements. By addressing key considerations in trial design, remote visits, digital technologies, roles and responsibilities, informed consent, investigational products, packaging, safety monitoring, and software usage, the guidance ensures flexibility, participant convenience, and adherence to regulatory requirements. Emphasizing proper training, coordination, and monitoring, the guidance aims to facilitate the successful implementation of DCTs while maintaining data integrity and participant safety.

America

Argentina

In Argentina, specific guidelines for Decentralized Clinical Trials (DCTs) are not available. However, the "Conduct of Clinical Trials During the COVID-19 Public Health Emergency (ANMAT)," released on March 25, 2020, provides some information on the incorporation of DCT elements, such as eConsent and remote monitoring. Additionally, a guideline on Good Practices for Telemedicine, published in November 2021, outlines the implementation details of telemedicine in clinical trials and medical practices.

There is no guideline specifically addressing local Healthcare Providers (HCPs) in clinical trials, although relevant regulations may touch upon this aspect in medical practice. While specific guidelines for electronic Clinical Outcome Assessments (eCOA), Direct-to-Patient (DTP), and wearable devices are absent, past studies have successfully utilized these elements following protocol details approved by the National Administration of Drugs, Food, and Medical Technology (ANMAT). Notably, utilizing all electronic systems in any aspects should adhere to the Personal Data Protection Law implemented in October 2020.

In summary, the majority of DCT elements can be conducted in Argentina, but the detailed procedures for each DCT element should be specified in the protocol and informed consent form with the approval from ANMAT.

America

Brazil

Similar to Argentina, Brazil lacks specific guidelines for Decentralized Clinical Trials (DCTs). However, the guideline titled "eICF and Biobank: Ofício Circular N° 23/2022/CONEP/SECNS/DGIP/SE/MS," released on October 17, 2022, grants permission to utilize eConsent in clinical trials and Biobank consents. It emphasizes that the use of eConsent must be justified based on potential benefits and the minimization of risks for research participants.

Both the "Telemedicine Resolution: Resolução CFM N° 2.314," released on April 20, 2022, and the "Telemedicine Ordinance No. 467," released on March 20, 2020, introduced the term "telehealth," akin to telemedicine. To employ telemedicine, physicians must possess a qualified digital signature conforming to the ICP-Brazil standard. The "Clinical Trials and Pandemic, Nota Técnica N° 05/2023/SEI/COPEC/GGMED/DIRE2/ANVISA," released in 2020 and amended in 2023, indicated the use of telemedicine and remote monitoring in clinical trials during COVID-19 period. However, during the implementation of remote monitoring, consistency in defined methods, such as photos, scanned documents, and videos, should be maintained throughout the study.

Although local Healthcare Providers (HCPs) are addressed in medical practice regulations, there is no specific guideline for their involvement in clinical trials. The utilization of home nurse systems is common in Brazil, and past studies have successfully incorporated local HCPs when the protocol specifies detailed procedures approved by regulatory authorities. No specific guidelines or regulations mention electronic Clinical Outcome Assessments (eCOA), Direct-to-Patient (DTP), and wearable devices in clinical trials.

Given the absence of a specific guideline for implementing Decentralized Clinical Trials (DCTs) in clinical trials, it is advisable to seek guidance from regulatory authorities when incorporating DCTs into a specific clinical trial.

EMEA

Europe(Spain, Italy, Poland)

The European Union (EU) is a supranational political and economic union comprising 27 member states primarily located in Europe, including Italy, Poland, and Spain. The European Medicines Agency (EMA) is a decentralized agency of the EU tasked with evaluating, supervising, and regulating medicinal products in the EU.

In December 2022, the "Recommendation Paper on Decentralized Elements in Clinical Trials" was published, delineating the roles and responsibilities of sponsors and investigators, addressing electronic informed consent, Investigational Medicinal Product (IMP) delivery, trial-related procedures at home, and data management and monitoring in a decentralized clinical trial setting. The appendix provides an overview of current national provisions in each Member State (MS) related to these topics.

It's important to note that the national provision appendix serves as guidance only, as offering a comprehensive overview of all scenarios for implementing decentralized elements in a clinical trial is not feasible. MS discretion is crucial in determining the acceptability of certain decentralized elements in a specific clinical trial. Sponsors are encouraged to seek scientific advice from the European Medicines Agency (EMA), specifically the scientific advice working party (SAWP), or national competent authorities (national or simultaneous national scientific advice - SNSA) regarding the use of specific decentralized elements, especially where experience and evidence may be limited. Additionally, sponsors can request a consolidated opinion via the Clinical Trial Coordination Group (CTCG) for regulatory issues of general impact not specific to a particular trial.

As per the recommended paper, most DCT elements, such as eConsent, eSignature, Telemedicine, Direct-to-Patient (DTP), remote monitoring, local Healthcare Providers (HCPs), and wearable devices, can be utilized in a clinical trial. However, feasibility depends on factors like subject type and therapeutic area. The planning of a DCT should carefully consider patient safety, patient and investigator inclusion, and the evaluation of DCT risks and benefits.

Apart from the recommended paper, Italy has a guideline titled "Clinical Trials' Management in Italy During the COVID-19 (Coronavirus Disease 19) Emergency," released on September 17, 2020. In Spain, a regulation titled "Code of Conduct Regulating the Processing of Personal Data in Clinical Trials and Other Clinical Research and Pharmacovigilance Activities," released on February 01, 2022, is also a valuable reference when planning a DCT.

EMEA

UK

Despite the UK no longer being a member of the EU since January 31, 2020, the "Recommendation Paper on Decentralized Elements in Clinical Trials" released by the European Medicines Agency (EMA) remains a valuable reference when implementing Decentralized Clinical Trials (DCTs) in the UK. Three additional guidelines also serve as primary references for DCT implementation in the UK: "Clinical Trials Applications for Coronavirus (COVID-19)," amended on February 23, 2022; "Managing Clinical Trials During Coronavirus (COVID-19)," released on November 16, 2021; and "Guidance on Minimizing Disruptions to the Conduct and Integrity of Clinical Trials of Medicines During COVID-19," released on November 13, 2020.

Basically, similar to EU, most DCT elements, such as eConsent, eSignature, Telemedicine, Direct-to-Patient (DTP), remote monitoring, local Healthcare Providers (HCPs), and wearable devices, can be utilized in a clinical trial in UK, but the implementation is still upon the protocol approval by Medicines and Healthcare products Regulatory Agency (MHRA).

EMEA
South Africa

The South African Good Clinical Practice (GCP) guideline, released on Jun 17, 2020, requires compliance with the International Council for Harmonisation (ICH) guidelines for all clinical trials conducted in South Africa, including Decentralized Clinical Trials (DCTs) and trials using electronic data capture (EDC) systems. The SAHPRA Policy on Conduct of Clinical Trials of Health Products During the current COVID-19, released on Mar 25, 2020, is to ensure that research activities continue to adhere to ethical standards while addressing the unique challenges presented by a pandemic situation. It provides detailed information on various aspects of research, including participant recruitment, informed consent, data collection, analysis, and reporting. The Oversight and monitoring in Clinical Trials, published in Aug, 2022, emphasizes the need for proactive and risk-based monitoring approaches, tailored to the specific characteristics of each clinical trial.

In South Africa, the majority DCT elements, such as eConsent, eSignature, Telemedicine, Direct-to-Patient (DTP), remote monitoring, local Healthcare Providers (HCPs), and wearable devices, can be utilized in a clinical trial. However, protocol should provide the detailed procedures of each utilized DCT element with the approval from the South African Health Products Regulatory Authority (SAHPRA) and ECs.

Regulatory Authority (RA) submission for DCTs

China

	Regulatory Authority Name	Related Guidance or Regulations	Submission Requirements	Submission & Approval Timeline
Chinese Mainland	National Medical Products Administration (NMPA)	Technical guidelines for implementation of patient-centric clinical trials (Interim): 27 July, 2023	When adopting some new technologies, new methods, and new models, it's necessary to communicate with the review agency in a timely manner on the purpose of use, use scenarios, basic information, evaluation and verification data, data of comparative experiments with traditional methods, risk assessment and mitigation measures, etc. 1. Protocol & ICF: Provide the used DCT components & detailed information 2. Risk management and mitigation plan, Data management plan, Pharmacy manual, DHT user manual, Centralized monitoring plan, Remote monitoring plan, and others etc., may be requested upon the review	Approval timeline is same as the traditional trials, but submission preparation timeline may be longer as need to double check all the required information is available
Hong Kong China	Department of Health	Not applicable	Follow the traditional trials	Follow the traditional trials
Taiwan China	Taiwan Food and Drug Administration (TFDA)	Guidelines for Implementing Decentralized Clinical Trials: 13-Jun, 2023	• Utilized DCT components & its detailed information should be provided in the protocol & ICF • A Checklist of DCT in Guidelines for Implementing Decentralized Clinical Trials should be completed along with the detailed information e.g., system, software • A risk management plan should be provided while any DCT component is written in the protocol • TFDA may request additional documents during the review period	Approval timeline is same as the traditional trials, but submission preparation timeline may be longer to include all the required information in the checklist followed the requirements.

Regulatory Authority (RA) submission for DCTs

Asia Pacific

	Regulatory Authority Name	Related Guidance or Regulations	Submission Requirements	Submission & Approval Timeline
Australia	Therapeutic Goods Administration (TGA)	Not applicable	Follow the traditional trials	Follow the traditional trials
Japan	Pharmaceuticals and Medical Devices Agency (PMDA). The PMDA is a government agency under the Ministry of Health, Labour and Welfare (MHLW) and plays a crucial role in the regulation and approval of pharmaceuticals and medical devices in Japan.	Q&A Regarding Clinical Trials of Pharmaceuticals, Medical Devices, and Regenerative Medicine Products under the Influence of COVID-19 Pandemic, 26 May,2020 But the Q&A didn't mention any specific submission approach for DCTs.	Follow the traditional trials	Follow the traditional trials
South Korea	Ministry of Food and Drug Safety (MFDS)	Not applicable	Follow the traditional trials	Follow traditional trials
Indonesia	Badan Pengawas Obat dan Makanan (BPOM)	Not applicable	Follow the traditional trials	Follow traditional trials
Malaysia	National Pharmaceutical Regulatory Agency (NPRA)	Not applicable	Follow the traditional trials	Follow traditional trials
Philippines	Philippines FDA	Not applicable	Follow the traditional trials	Follow traditional trials
Singapore	Health Sciences Authority (HSA)	1. Clinical Trials Guidance- Electronic Consent, Version 3, 01 Oct 2021 2. Guidance on the Conduct of Clinical Trials in Relation to the COVID-19 Situation, 26 Aug 2022	No specific submission requirement but It is ,required to consult with HSA prior to implementation of DCT elements so that they can advise accordingly.	Follow traditional trials, but consultation time prior to HSA submission should considered.
Thailand	Thai Food and Drug Administration (Thai FDA)	Not applicable	Follow the traditional trials	Follow traditional trials
Vietnam	Drug Administration of Vietnam (DAV)	Not applicable	Follow the traditional trials	Follow traditional trials

Regulatory Authority (RA) submission for DCTs

America

		Regulatory Authority Name	Related Guidance or Regulations	Submission Requirements	Submission & Approval Timeline
• North America	USA	U.S. Food and Drug Administration (US FDA)	Decentralized Clinical Trials for Drugs, Biological Products, and Devices (Draft): 23 May, 2023	● Used DCT components & its detailed information should be provided in the protocol & PICF, pharmacy manual (e.g., DTP) and training materials and user manuals for EC submission. ● Risk management plan, a plan for technical assistance, safety management plan, data management plan and verification and validation data (for DHTs) may be required to submit.	Follow traditional trials
• Latin America	Argentina	National Administration of Drugs, Food and Medical Technology (ANMAT)	Not applicable	Follow traditional trials	Follow traditional trials
	Brazil	Agencia Nacional de Vigilância Sanitária (ANVISA) Comissão Nacional de Ética em Pesquisa (CONEP)	Not applicable	Follow traditional trials	Follow traditional trials

Regulatory Authority (RA) submission for DCTs

EMEA

	Regulatory Authority Name	Related Guidance or Regulations	Submission Requirements	Submission & Approval Timeline
Italy	Italian Medicines Agency (AIFA)	Not applicable	EU CTR unified requirements	105 days (10 days of validation, 90 days for review, 5 days for issue decision)
Spain	Spanish Agency for Medicines and Health Products (AEMPS)	Not applicable		
Poland	The Office for Registration of Medicinal Products, Medical Devices And Biocidal Products	Not applicable		
UK	Medicines and Healthcare products Regulatory Agency (MHRA)	Not applicable	Centralized IRAS system	60 days (up to 60 days for review, 10 days for issue decision)
South Africa	The South African Health Products Regulatory Authority (SAHPRA)	• The South African Good Clinical Practice (GCP) guidelines (Version 3) • Guideline for Electronic Submission of Clinical Trial Documents (Amendments, Bioequivalence Studies, Responses, Notifications, And Serious Adverse Events): V3.0, 05 Sep, 2022	E-mail submission	• Monthly submission dates. • Submission can be done up until the day of submission. • Turnaround Time for new applications and within 3 weeks of receipt. • Recommendations would be sent within 10 weeks of the submission due date. • Historical average approval time is 90 days

Conclusion: Navigating the Evolving Landscape of Decentralized Clinical Trials

The regulatory handbook, led by Tigermed DCT Solution with contributions from Tigermed International Business Units and China Clinical Operation Unit, delves into the multifaceted realm of Decentralized Clinical Trials (DCTs). We explored critical facets such as the Full DCT and Hybrid DCT models, and a thorough examination of global regulatory requirements.

Our exploration of the regulatory landscape has unveiled intriguing insights. While some authorities like the United States, Chinese Mainland, and Taiwan China offer detailed DCT guidance, the majority of countries/regions navigate this evolving landscape with frameworks in flux. Notably, some nations lack explicit DCT guidelines, dispersing relevant DCT elements across separate regulations.

A significant revelation stems from our interactions with regulatory authorities. It's evident that many are actively developing comprehensive guidance tailored to decentralized trials, highlighting the dynamic nature of the regulatory landscape and its intrinsic need for adaptation in advancing clinical research methodologies.

Examining submission requirements to Regulatory Authorities (RAs) reveals diverse practices. Unlike Taiwan China's detailed DCT checklist, most countries/regions still adhere to traditional submission requirements even for DCTs, emphasizing the need for a nuanced approach when navigating global regulatory pathways.

Concluding this handbook, the unfolding landscape of Decentralized Clinical Trials presents challenges and opportunities. Stakeholders must stay vigilant, aligning with evolving guidance and engaging with regulatory bodies to shape the future of DCTs. The Tigermed DCT Solution team is committed to this ongoing journey, continuously collecting and updating guidance and regulations from diverse authorities. This ensures the handbook remains a reliable resource, reflecting our dedication to precision, compliance, and the advancement of clinical research.

In essence, this handbook is not just a compendium but a living document, embodying Tigermed DCT Solution's commitment to advancing the frontiers of clinical research.

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