Recommendations for planning and conducting decentralised clinical trials

Deliverable 14.2

Batuca J, del Álamo M, Lémeret S, Monteiro E
ECRIN, June 2025

This leaflet has been developed as part of the ERA4Health project, co-funded by the European Union under the Horizon Europe Framework Programme. Grant Agreement N° 101095426.

Co-funded by the European Union

Recommendations for planning and conducting decentralised clinical trials

The aim of this booklet is to offer a comprehensive overview of the key aspects of decentralised clinical trials and to provide solutions to the main challenges in developing, implementing and conducting trials with new designs namely decentralised clinical trials (DCTs).

This booklet has been adapted from ERA4Health's original document D14.2 "Recommendation booklet for investigators and sponsors in multi-country investigator initiated clinical studies". References cited in this document can be found at the original source (1).

Co-funded by the European Union

Decentralised clinical trials (DCTs)

Decentralised clinical trials (DCTs) represent a modern approach to clinical research, characterised by the decentralisation of trial operations, where digital health technologies are employed to communicate with study participants and collect data, allowing various trial activities to occur outside of traditional clinical settings.

Decentralised clinical trials, also known as site-less, direct-to-patient, hybrid, remote, or virtual clinical trials, have emerged as a transformative approach in the landscape of clinical trials. This departure from the traditional model, where all study activities are centralised at specific clinical trial sites, signifies a paradigm shift wherein some or all the clinical trial activities transcend the confines of the traditional clinical site, taking place in or closer to participants' homes (2). This innovative approach leverages digital health technologies, such as telemedicine, sensory-based technologies, wearable medical devices, patient-driven virtual health care interfaces and remote methods, including the direct delivery of study drugs and materials to patients' homes. Commonly referred to as decentralisation, this shift marks a change from the conventional centralised approach in favour of a more flexible and participant-centric model (3,4).

The overarching goal of DCTs is to alleviate the burdens associated with trial participation, enhance accessibility and recruitment, and improve the generalisability of evidence generated from trials (5). While the concept of DCTs is not entirely new, the clinical trials landscape has witnessed a significant transformation by incorporating decentralised elements such as electronic diaries, wearables, phone calls, and online appointments. The adoption of these elements varies based on factors like the trial type, participant population, targeted disease, participant conditions, medicinal product characteristics, and development stage.

DCTs design and its inherent flexibility offer an extensive range of advantages identified by various authors (3-4,6-10) such as:

- Remote participation: Participants have the choices and flexibility in how they participate in the trial, remotely from their homes or other local settings, aligning with their preferences and schedules, reducing the need for frequent visits to a centralised clinical site.
- Reducing participant burden: By eliminating the necessity for extensive travel and frequent in-person visits, trial participation is more manageable and positively influences retention rates.

- Better participant engagement: The remote nature of DCTs increases participant convenience and comfort, leading to improved engagement, compliance and data quality.
- Geographic diversity: Remote participation enables a more diverse and broader range of study participants, contributes to greater diversity and inclusivity and potentially makes the results more representative of real-world scenarios.
- Enhance recruitment process: Removing geographic and logistical barriers improves the recruitment process and study efficiency.
- Incorporation of digital health technologies: Enhances data collection efficiency, enables real-time monitoring, often without imposing additional tasks on participants and facilitates seamless communication between participants and researchers.
- Potential reduction in sample size: The integration of digital health tools enables more objective measurement of parameters, facilitating the development of individualised thresholds for measuring treatment effects, and potentially decreasing the required sample size for trials.
- Real time data collection and analysis: Technology allows for the collection of real-time data from patients, providing quick insights for more efficient and timely decision-making during the trial.
- Cost effectiveness: Reducing the need for physical sites and minimising travel expenses results in significant cost savings and makes them an attractive option for sponsors.
- Improve operational efficiency: By streamlining the data collection and reducing the administrative burden, researchers can focus more on data analysis, trial management and providing participants with a positive trial experience.
- Flexible trial designs: Enables the adaptation to evolving circumstances, offering built-in resilience to external factors and disasters.

DCTs are not an all-or-nothing method, as decentralisation can be of varying degrees. DCTs, whether operating fully decentralised (with no physical attendance at a clinical trial site) or adopting a hybrid model (combining conventional and decentralised elements), offer a pragmatic trial concept. By integrating participant-centred design with innovative technologies, DCTs strive to make clinical trials more broadly accessible. Teleconsultation visits have proven to be effective, demonstrating the positive participants' reception of decentralisation in both conventional and decentralised settings (11). As technology, infrastructure, and knowledge continue to advance, the evolution of DCTs is becoming indispensable to the future of clinical research.

In 2007, the Food and Drug Administration (FDA) and Duke University established the Clinical Trials Transformation Initiative (CTTI) to identify and promote quality and efficacy of clinical trials. In 2018, the CTTI issued recommendations on DCTs in the United States (12).

DCTs are especially useful in cases that make travel difficult for the patient, either for clinical conditions (e.g., neuromuscular diseases), or logistical barriers, when research sites are far from the patient's home (as often occurs in case of rare diseases), leading to the emergence of several others DCTs in various fields such paediatric (14), diabetes (15,16), rare diseases (17), cardiology (18), and chronic pain (10). However, the DCTs design gains particular relevance in scenarios where traditional, site-based trials face challenges, as exemplified by the importance and usefulness of digital tools and decentralised procedures during COVID-19 pandemic in both healthcare settings and in clinical trials (19-24).

The increasing use of digital tools within clinical trials, accentuated by the lessons from the COVID-19 pandemic, emphasises the importance of embracing the decentralised elements, whether individually or in combination, into clinical trial designs. Numerous initiatives and projects have been launched globally (see Table 1) to develop comprehensive recommendations and tools for defining and operationalising DCTs. This context emphasises the necessity for Regulatory & Ethical Authorities to provide further recommendations regarding the introduction of decentralised elements in the conduct of clinical trials. Notably, various recommendations and guidance documents for modernisation of clinical trials, specifically dedicated to DCTs, have been issued at the USA, the European Union and the country-specific levels as outlined in Table 2.

Name	Entities involved	Objectives	Website /Publication
Clinical Trials Transformation Initiative (CTTI)	Food and Drug Administration (FDA) and Duke University	(1) identify perceived and actual legal, regulatory, and practical barriers to conducting DCTs and (2) identify opportunities to clarify and inform policies that affect the implementation of DCTs	www.ctti-clinicaltrials.org
Accelerating Clinical Trials in the EU (ACT EU) Initiative Decentralised Clinical Trials Task Force	European Commission the Heads of Medicines Agencies (HMA) and the EMA, experts from regulatory bodies, ethics committees, investigators, Good Clinical Practice Inspectors, patient organisations, and health-care professionals	EU and European Economic Area harmonised approach on the use of decentralised elements to increase the accessibility of clinical trials by bringing the trial to the patient, thereby including a more diverse and remote population	https://accelerating-clinical-trials.europa.eu/index_en
Decentralised Trials and Research Alliance (DTRA)	Non-profit multistakeholder initiative (50 international organisations, including the FDA and patient advocacy group)	To promote decentralised trials by establishing clear goals and recommendations, such as defining common nomenclature, promoting best practices, and facilitating education and information sharing	https://www.dtra.org/
TransCelerate	Non-profit BioPharma organisation	Training and tools	https://www.transceleratebiopharmainc.com
Digital Medicine Society (DMS)	Community of Digital Medicine Society	Recommendations and training	https://myscrs.org/
Trials@Home	Public-private partnership funded through the Innovative Medicines Initiative Grant no. 831458	Develop recommendations and tools for the definition and operationalisation of DCTs in Europe	https://trialsathome.com

Table 1: Initiatives and projects that have an interest in decentralised trials (DCTs).

Name	Guidance/ recommendation
CTTI	Clinical Trials Transformation Initiative (CTTI) recommendations: decentralised clinical trials. September 2018 (38). Apostolaros M, et al. Legal, regulatory, and practical issues to consider when adopting decentralised clinical trials: recommendations from the clinical trials transformation initiative. (39).
United States Food and Drug Administration (FDA)	Decentralised Clinical Trials for Drugs, Biological Products, and Devices Guidance for Industry, Investigators, and Other Stakeholders, May 2023 (40).
EC/HMA/EMA	EC/HMA/EMA Recommendation paper on decentralised elements in clinical trials, December 2022 (41). Al M et al Decentralised Clinical Trials Task Force. Decentralised elements in clinical trials: recommendations from the European Medicines Regulatory Network (42).
European Medicines Agency	EMA Guideline on computerised systems and electronic data in clinical trials. March 2023 (43).
The Danish Medicines Agency	Guidance on the implementation of decentralised elements in clinical trials with medicinal products. May 2021 (44).
Swedish Medical Products Agency	Decentralised and virtual interventional clinical trials. Published June 2021, updated December 2022 (45).
SwissMedic and SwissEthics	Decentralised clinical trials (DCTs) with medicinal products in Switzerland 2021 (37).
Canadian Remote Access Framework for Clinical Trials (CRAFT)	CRAFT Recommendations Sundquist S et al CRAFT-A proposed framework for decentralised clinical trials participation in Canada. (46)
Trials@Home	D1.1 First set of recommendations for RDCTS (to be implemented in the pan-EU pilot RDCT); 2020 (47). WP2 – TECH. D2.1 Glossary of terms and definitions used 2020 (48).
Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard (MRCTCENTER)	Comprehensive DCT checklist and use recommendations as a reference document (25).
Digital Medicine Society (DMS)	DCT best practices and recommendations (26).

Table 2: Recommendations and guidance published on decentralised trials (DCTs).

Recommendations for decentralised clinical trials

Regulatory and ethical considerations

Favouring the use of harmonised terminology

- The standardisation of terminology provides a clear and common language, facilitating effective communication among stakeholders engaged in the planning, execution, and oversight of DCTs.

Establishing a unified and robust regulatory framework within the EU for DCTs (28, 36)

- Given the multifaceted nature of DCTs, the legal and regulatory requirements must be sought from broader sources, including Regulation (EU) 536/2014 for clinical trials on medicinal products for human use, Regulation (EU) 679/2016 (GDPR) for personal data protection, Regulation (EU) 745/2017 for medical devices, ISO standards (13485/2016 and 14155/2020), and the ICH GCP E6 (R2), currently under revision to better accommodate technological advances and provide more flexible approaches to clinical trial delivery, and applicable Good Manufacturing Practice (GMP) provisions, applicable Good Distribution Practice (GDP) principles.

Mitigating the risk of ethics committee rejection or assessment delays (2, 27, 29):

- The study protocols and the cover letter of the clinical trial application submitted to regulatory authorities and ethics committees should comprehensively detail the operational features of the study, particularly focusing on the decentralised elements planned in the clinical trial. This proactive approach aims to offer transparency and clarity, addressing potential ethical concerns and streamlining the regulatory review process.
- Provide information regarding which tasks are conducted when, by whom, and in which setting (e.g. at the clinical site, at the trial participant's home, etc.), the potential involvement of additional service providers, the data processing, the communication flow, trial overseeing and ultimately the rights, safety, dignity and well-being of the trial participants and reliability of the trial data.

Ensuring participant privacy / confidentiality (3, 30, 31):

- Adopting new technologies that prioritise data integrity and consider the ethical, regulatory, privacy, and data standards.
- These technologies must adhere to the principles of privacy by design and privacy by default, ensuring the required guarantee that the technology is solely based on European servers and technical assistance. This guarantees that the mandatory levels of data security during collection, transmission and/or storage, and similarly against improper or fraudulent use of data are maintained throughout the study.
- Conducting a privacy impact assessment can be useful to identify technical vulnerabilities and tailor safeguards to the type of data collected.
- State-of-the-art encryption should be implemented to minimise the risk of breaches.
- Pseudonymisation and anonymisation, along with other privacy-preserving approaches, such as data minimisation and access controls, play a pivotal role in safeguarding electronic data against unauthorised access, tampering, or loss.
- Establishing stopping rules and other harm mitigation mechanisms is crucial in the event of data breaches or other technical failures affecting data security.
- These safeguards should be clearly described in the study protocol, allowing the assessment by ethics committees.

Implementing eConsent/ eSignature for collecting informed consent (14, 16, 27):

- eConsent's flexibility accommodates both paper and diverse electronic signature methods, preventing discrimination against participants who cannot or prefer not to use certain technologies.
- eConsent may include multimedia components such as images, audio, video, diagrams, reports, call-out boxes and electronic signatures methods, all designed to enhance and facilitate the consenting process. This electronic approach enriches the consenting process, offering participants a more interactive and comprehensive understanding.
- Investigators and monitors need to uphold the same accountabilities, ensuring that the integrity of the informed consent process remains paramount throughout the study.

Patient recruitment and retention

- Recognising the diverse preferences of participants is essential in order to offer flexibility in visit methods to accommodate individual comfort and circumstances during a clinical trial.
- Sponsors should provide participants with a wide range of visit methods, including telemedicine (tele-visits with telephone-only or video options), in-home visits, and engagement with local providers. This ensures accessibility and convenience for all participants.

- Building confidence among all stakeholders requires significant investment in education and training for clinicians, research teams, participants, and caregivers. Emphasis should be placed on highlighting how DCTs can enhance the participant experience while maintaining the integrity of the physician-patient relationship (8).

Protocol design or methodological considerations

Ensuring that DCTs are suitable to answer the research question

- Consider adoption of hybrid designs combining conventional and decentralised elements. These hybrid studies empower sponsors to significantly reduce the number of sites and the frequency with which patients visit them, leveraging technologies and processes that enable virtual trials while maintaining physical locations for specific procedures.
- Consider the need to establish infrastructure and technology to support direct-to-patient supply of IMPs and to guarantee the quality of the medicinal product (13,49).

Guaranteeing the accessibility to and usability of digital health technologies

- In the selection of digital health technologies, beside ensuring alignment with applicable ethical, regulatory, privacy, and data standards, opting for mature, well-tested, validated technology, particularly those designed to be user friendly, with straight forward interfaces built-in tools for easy form completion without additional assistance, and mechanisms for providing feedback to participants and not increasing patient burden is highly recommended (7-9, 32).
- It is critical to understand and incorporate the perspectives of potential research participants in planning clinical trials (33). Conduct smaller, simpler, pre-pilot (or feasibility) studies to assess and test novel hardware and software.
- Careful consideration should be given to potential inconveniences or discomfort associated with wearable devices, and attention to device visibility is essential to maintain patient confidentiality.
- Evaluating the level of support provided by the wearable device's vendor is crucial. An experienced vendor ensures a robust help desk support system for quick problem resolution for both sites and patients.
- Sponsors should prioritise adopting technology that seamlessly aligns with the trial protocol, aiming to simplify the overall trial process. Introducing multiple new technologies and devices within a single trial is discouraging, as each additional element amplifies the perceived burden for participants (8, 9, 11, 32).

Data management

- Establishing a study coordination centre equipped with a sophisticated information technology platform is imperative for operational efficiency, especially considering the logistical complexity inherent to DCTs.
- Taking proactive measures, including mapping data flows, implementing user access controls, addressing data reconciliation, and establishing data standards to facilitate portability and interchangeability among various digital health technologies, thereby ensuring data integrity and quality (34).
- Effective management of data demands a risk-based approach, facilitating the timely identification of technical failures in digital devices and enabling the identification, reporting, and management of adverse events during a trial. This demands comprehensive training and acquisition of knowledge on digital tools for all team members and participants.
- Sponsors may need to anticipate higher costs associated with the management of technological support and remote oversight (hardware, software, dedicated personnel, etc.) (35).

Bibliography

1. D14.2 Recommendation booklet for investigators and sponsors in multicountry IICS WP14. Available at: https://era4health.eu/results/deliverables.php.
2. Apostolaros M, et al. Legal, Regulatory, and Practical Issues to Consider When Adopting Decentralized Clinical Trials: Recommendations from the Clinical Trials Transformation Initiative. Ther. Innov. Regul. Sci. 2020;54:779–787. doi: 10.1007/s43441-019-00006-4.
3. Van Norman GA. Decentralized Clinical Trials: The Future of Medical Product Development? JACC Basic Transl Sci. 2021 Apr 27;6(4):384-387. doi: 10.1016/j.jacbts.2021.01.011.
4. Iersel TV, Courville J, Doorne CV, Koster RA, Fawcett C. The Patient Motivation Pyramid and Patient-Centricity in Early Clinical Development. Curr Rev Clin Exp Pharmacol. 2022;17(1):8-17. doi: 10.2174/1574884716666210427115820.
5. Khozin S, Coravox A. Decentralized Trials in the Age of Real-World Evidence and Inclusivity in Clinical Investigations. Clin Pharmacol Ther. 2019;106:25–27.
6. Perry B, Geoghegan C, Lin L, McGuire F, Nido V, Grabert BK, et al. Patient Preferences for Using Mobile Technologies in Clinical Trials. Contemp Clin Trials Commun. 2019;15:100399.
7. Moseson H, Kumar S, Juusola JL. Comparison of Study Samples Recruited with Virtual Versus Traditional Recruitment Methods. Contemp Clin Trials Commun. 2020 Jun 17;19:100590. doi: 10.1016/j.conctc.2020.100590.
8. Goodson N, Wicks P, Morgan J, Hashem L, Callinan S, Reites J. Opportunities and Counterintuitive Challenges for Decentralized Clinical Trials to Broaden Participant Inclusion. NPJ Digit Med. 2022 May 5;5(1):58. doi: 10.1038/s41746-022-00603-y.
9. de Jong AJ, van Rijssel TI, Zuidgeest MGP, van Thiel GJMW, Askin S, Fons-Martínez J, et al. Opportunities and Challenges for Decentralized Clinical Trials: European Regulators' Perspective. Clin Pharmacol Ther. (2022) 112:344–352. doi: 10.1002/cpt.262811.
10. Rogers A, De Paoli G, Subbarayan S, Copland R, Harwood K, Coyle J, Mitchell L, MacDonald TM, Mackenzie IS; Trials@Home Consortium. A systematic review of methods used to conduct decentralised clinical trials. Br J Clin Pharmacol. 2022 Jun;88(6):2843-2862. doi:10.1111/bcp.15205.
11. Dorsey ER, Kluger B, Lipset CH. The New Normal in Clinical Trials: Decentralized Studies. Ann Neurol. 2020 Nov;88(5):863-866. doi: 10.1002/ana.25892.
12. Clinical Trials Transformation Initiative CTTI recommendations: decentralized clinical trials. September 2018.
13. de Jong AJ, Santa-Ana-Tellez Y, Zuidgeest MGP, Grupstra RJ, Jami F, de Boer A, Gardarsdottir H; Trials@Home Consortium. Direct-to participant investigational medicinal product supply in clinical trials in Europe: Exploring the experiences of sponsors, site staff and couriers. Br J Clin Pharmacol. 2023 Dec;89(12):3512-3522. doi: 10.1111/bcp.15850.
14. Blake K, Holbrook JT, Antal H, Shade D, Bunnell HT, McCahan SM, Wise RA, Pennington C, Garfinkel P, Wysocki T. Use of mobile devices and the internet for multimedia informed consent delivery and data entry in a pediatric asthma trial: Study design and rationale. Contemp Clin Trials. 2015 May;42:105-18. doi: 10.1016/j.cct.2015.03.012.

Bibliography

15. Mafham MM, Bowman LJ, Haynes RJ, Armitage JM. Streamlined mail-based methods for large randomised trials: lessons learnt from the ASCEND study. Diabetologia. 2020 May;63(5):898-905. doi: 10.1007/s00125-019-05049-8.87.
16. Business Wire. eClinicalHealth announces successful results for an entirely remote online clinical trial. 2016.
17. Krischer J, Cronholm PF, Burroughs C, McAlear CA, Borchin R, Easley E, Davis T, Kullman J, Carette S, Khalidi N, Koening C, Langford CA, Monach P, Moreland L, Pagnoux C, Specks U, Sreih AG, Ytterberg S, Merkel PA; Vasculitis Clinical Research Consortium. Experience With Direct-to-Patient Recruitment for Enrollment Into a Clinical Trial in a Rare Disease: A Web‐Based Study. J Med Internet Res. 2017 Feb 28;19(2):e50. doi: 10.2196/jmir.6798.
18. Steinhubl SR, Waalen J, Edwards AM, et al. Effect of a Home-Based Wearable Continuous ECG Monitoring Patch on Detection of Undiagnosed Atrial Fibrillation: The mSToPS Randomized Clinical Trial. JAMA. 2018;320(2):146-155.
19. Tan AC, Ashley DM, Khasraw M. Adapting to a pandemic—conducting oncology trials during the SARS-CoV-2 pandemic. Clin Cancer Res. 2020; 26(13): 3100–3103.
20. Bagiella E, Bhatt DL, Gaudino M. The Consequences of the COVID-19 Pandemic on Non‐COVID-19 Clinical Trials. J Am Coll Cardiol. 2020 Jul 21;76(3):342-345. doi: 10.1016/j.jacc.2020.05.041.
21. Upadhaya S, Yu JX, Oliva C, Hooton M, Hodge J, Hubbard-Lucey VM. Impact of COVID-19 on oncology clinical trials. Nat Rev Drug Discov. 2020 Jun;19(6):376-377. doi: 10.1038/d41573-020-00093-1.
22. Suman A, van Es J, Gardarsdottir H, Grobbee DE, Hawkins K, Heath MA, Mackenzie IS, van Thiel G, Zuidgeest MGP; Trials@Home Consortium. A cross-sectional survey on the early impact of COVID-19 on the uptake of decentralised trial methods in the conduct of clinical trials. Trials. 2022 Oct 6;23(1):856. doi: 10.1186/s13063-022-06706-x.
23. Gergova VT, Serbezova AH and Sidjmova D. Analysis on decentralized clinical trials in some European countries. Archives of the Balkan Medical Union 2021; 56(4):394-401. doi 10.31688/ABMU.2021.56.4.01.
24. van Dorn A. COVID-19 and readjusting clinical trials. Lancet. 2020 Aug 22;396(10250):523-524. doi: 10.1016/S0140-6736(20)31787-6.
25. MRCTCENTER Comprehensive DCT checklist and use recommendations as a reference document. Available online at: https://mrctcenter.org/resource/irb-ec-considerations-for-dct-review/#qualityprivacysecurity.
26. Digital Medicine Society DCT Best Practices and Recommendations. Available online at: https://myscrs.org/best-practices-and-recommendations/.
27. Petrini C, Mannelli C, Riva L, Gainotti S, Gussoni G. Decentralized clinical trials (DCTs): A few ethical considerations. Front Public Health. 2022 Dec 15;10:1081150. doi: 10.3389/fpubh.2022.

Bibliography

28. Trials@Home Work Package 4 (EAGLE). Deliverable 4.1: Mapping andanalys is of the EU legislation on Remote Decentralised Clinical Trials including legal, regulatory, ethical and stakeholder recommendations for the conduct of the pan-EU pilot 2021.
29. van Rijssel TI, de Jong AJ, Santa-Ana-Tellez Y, Boeckhout M, Zuidgeest MGP, van Thiel GJMW; Trials@Home Consortium. Ethics review of decentralized clinical trials (DCTs): Results 90 of a mock ethics review. Drug Discov Today. 2022 Oct;27(10):103326. doi: 10.1016/j.drudis.2022.07.011.
30. Russell C, Ammour N, Wells T, Bonnet N, Kruse M, Tardat A, Erales C, Shook T, Kirkesseli S, Hovsepian L, Pretorius S. A Pilot Study to Assess the Feasibility of Collecting and Transmitting Clinical Trial Data with Mobile Technologies. Digit Biomark. 2018 Nov 7;2(3):126-138. doi: 10.1159/000493883.
31. Vayena E, Blasimme A, Sugarman J. Decentralised clinical trials: ethical opportunities and challenges. Lancet Digit Health. 2023 Jun;5(6):e390-e394. doi: 10.1016/S2589-7500(23)00052-3.
32. Getz K, Sethuraman V, Rine J, Peña Y, Ramanathan S, Stergiopoulos S. Assessing Patient Participation Burden Based on Protocol Design Characteristics. Ther Innov Regul Sci. 2019 Aug 19:2168479019867284. doi: 10.1177/2168479019867284.
33. Perry B, Geoghegan C, Lin L, McGuire FH, Nido V, Grabert B, Morin SL, Hallinan ZP, Corneli A. Patient preferences for using mobile technologies in clinical trials. Contemp Clin Trials Commun. 2019 Jun 20;15:100399. doi: 10.1016/j.conctc.2019.100399.
34. European Medicines Agency. Guideline on computerised systems and electronic data in clinical trials. 9 March 2023, https://www.ema.europa.eu/en/documents/regulatory□procedural-guideline/guideline-computerised-systems-and-electronic-data-clinical□trials_en.pdf.
35. Betcheva L, Kim JY, Erhun F, Oraiopoulos N, Getz K. Applying Systems Thinking to Inform Decentralized Clinical Trial Planning and Deployment. Ther Innov Regul Sci. 2023 Sep;57(5):1081-1098. doi: 10.1007/s43441-023-00540-2. Epub 2023 Jun 30.
36. EC/HMA/EMA Recommendation paper on Decentralised elements in clinical Trials. December 2022. Available online at: https://health.ec.europa.eu/system/files/2023-03/mp_decentralised-elements_clinical-trials_rec_en.pdf.
37. SwissMedic and SwissEthics Decentralised Clinical Trials (DCTs) with Medicinal Products in Switzerland. (2021). Available online at: https://www.swissmedic.ch/swissmedic/en/home/humanarzneimittel/clinical-trials/clinical-trials-on-medicinal-products/publikationen.htm.
38. Clinical Trials Transformation Initiative CTTI recommendations: decentralized clinical trials. https://ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_DCT_Recs.pdf September 2018.
39. Apostolaros M, et al. Legal, regulatory, and practical issues to consider when adopting decentralized clinical trials: recommendations from the clinical trials transformation initiative. Ther. Innov. Regul. Sci. 2020;54:779–787. doi: 10.1007/s43441-019-00006-4.

Bibliography

40. FDA Decentralized Clinical Trials for Drugs, Biological Products, and Devices Guidance for Industry, Investigators, and Other Stakeholders. May 2023. Available online at: https://www.fda.gov/media/167696/download.
41. EC/HMA/EMA Recommendation paper on Decentralised elements in clinical Trials . December 2022. Available online at: https://health.ec.europa.eu/system/files/202303/mp_decentralised-elements_clinical-trials_rec_en.pdf.
42. Al M, Levison S, Berdel WE, Andersen DZ; Decentralised Clinical Trials Task Force. Decentralised elements in clinical trials: recommendations from the European Medicines Regulatory Network. Lancet. 2023 Apr 22;401(10385):1339. doi: 10.1016/S0140-6736(23)00463-4.
43. EMA Guideline on computerised systems and electronic data in clinical trials. 9 March 2023, March. Available online at: https://www.ema.europa.eu/en/documents/regulatoryprocedural-guideline/guideline-computerised-systems-and-electronic-data-clinicaltrials_en.pdf.
44. Danish Medicines Agency Guidance on the implementation of decentralised elements in clinical with medicinal products. May 2021. Available online at: https://laegemiddelstyrelsen.dk/en/ news/2021/guidance-on-the-implementation-ofdecentralisedelements-in-clinical-trials-with-medicinal-products-is-now-available/ _/media/5A96356760ED408CBFA9F85784543B53.ashx June.
45. Swedish Medical Products Agency Decentralised and virtual interventional clinical trials. Published June 2021 , updated December 2022. Available online 88 at:https://www.lakemedelsverket.se/en/permission-approval-and-control/clinicaltrials/medicinal-products-for-human-use/decentralised-clinical-trials.
46. Sundquist S, Batist G, Brodeur-Robb K, Dyck K, Eigl BJ, Lee DK, Limoges J, Longstaff H, Pankovich J, Sadura A, Sullivan P, Dancey JE. CRAFT-A Proposed Framework for Decentralized Clinical Trials Participation in Canada. Curr Oncol. 2021 Sep 30;28(5):3857-3865. doi: 10.3390/curroncol28050329.
47. Trials@Home D1.1 First set of recommendations for RDCTS (to be implemented in the pan-EU pilot RDCT); 2020. Available online at: https://trialsathome.com/wpcontent/uploads/2020/09/Trials@Home_D1.1-First-set-of-recommendations-for-RDCTs-tobe-implemented-in-the-pan-EU-pilot-RDCT.pdf.
48. Trials@Home WP2 – TECH. D2.1 Glossary of terms and definitions used. 2020. Available online at: https://trialsathome.com/wp-content/uploads/2021/04/D2.1-Glossary-of-termsand-definitions_-2021Update_Final.pdf.
49. Malone M, Ferguson P, Rogers A, Mackenzie IS, Rorie DA, MacDonald TM. When innovation outpaces regulations: The legal challenges for direct-to-patient supply of investigational medicinal products. Br J Clin Pharmacol. 2022 Mar;88(3):1115-1142. doi: 10.1111/bcp.

This booklet has been developed by ECRIN within the context of the ERA4Health project.