Let's discuss about current DCT from a QA perspective

07 November 2024

Japan Society of Quality Assurance (JSQA)
GCP Subcommittee
Terumi Mitsumori

RQA International QA Conference 2024

Discussion points in the Panel

- What is the implementation status of DCT?
- Is DCT going well/not going well?
- What are challenges/issues regarding DCT implementation and reliability assurance?

in your region/regulatory landscape

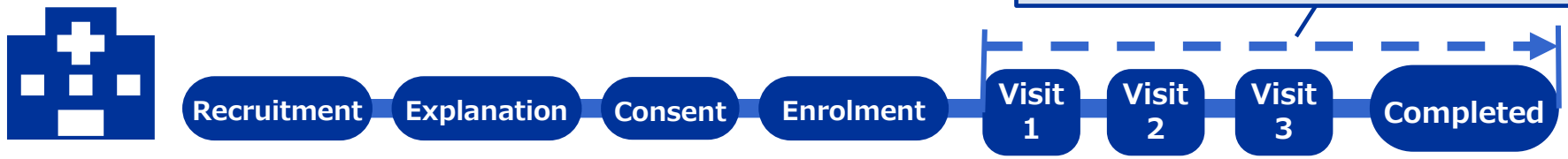
Background of the Study by JSQA Study Group and purpose of discussion

While Decentralized Clinical Trials (DCTs), which minimize patients visits medical institutions when participating in clinical trials, are becoming popular mainly in Europe and the United States, active discussions on DCTs in Japan started between 2018 and 2019. We discussed challenges in promoting DCTs from the perspective of minimum requirements for quality assurance in order to ensure that DCTs would be common practice in Japan and all stakeholders involved in the clinical trials can benefit from them.

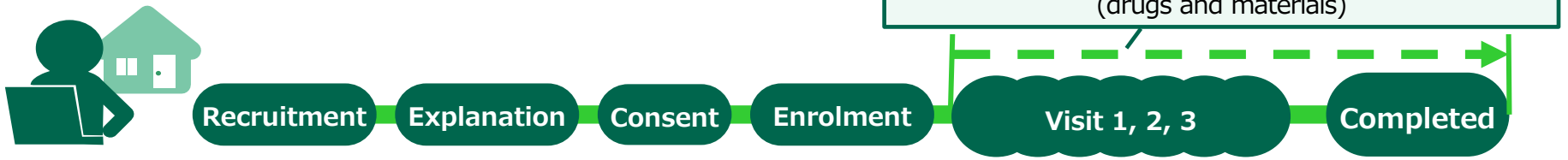
We, the JSQA Study Group, have compiled a checklist of items to consider when auditing/being audited studies in which a typical DCT solution is applied.

What is a DCT?

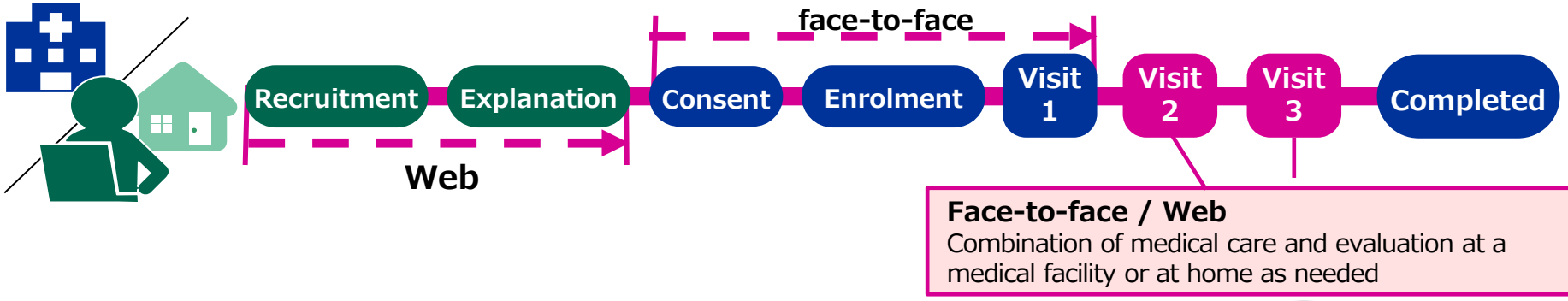
【Conventional Clinical Trial : All face-to-face】



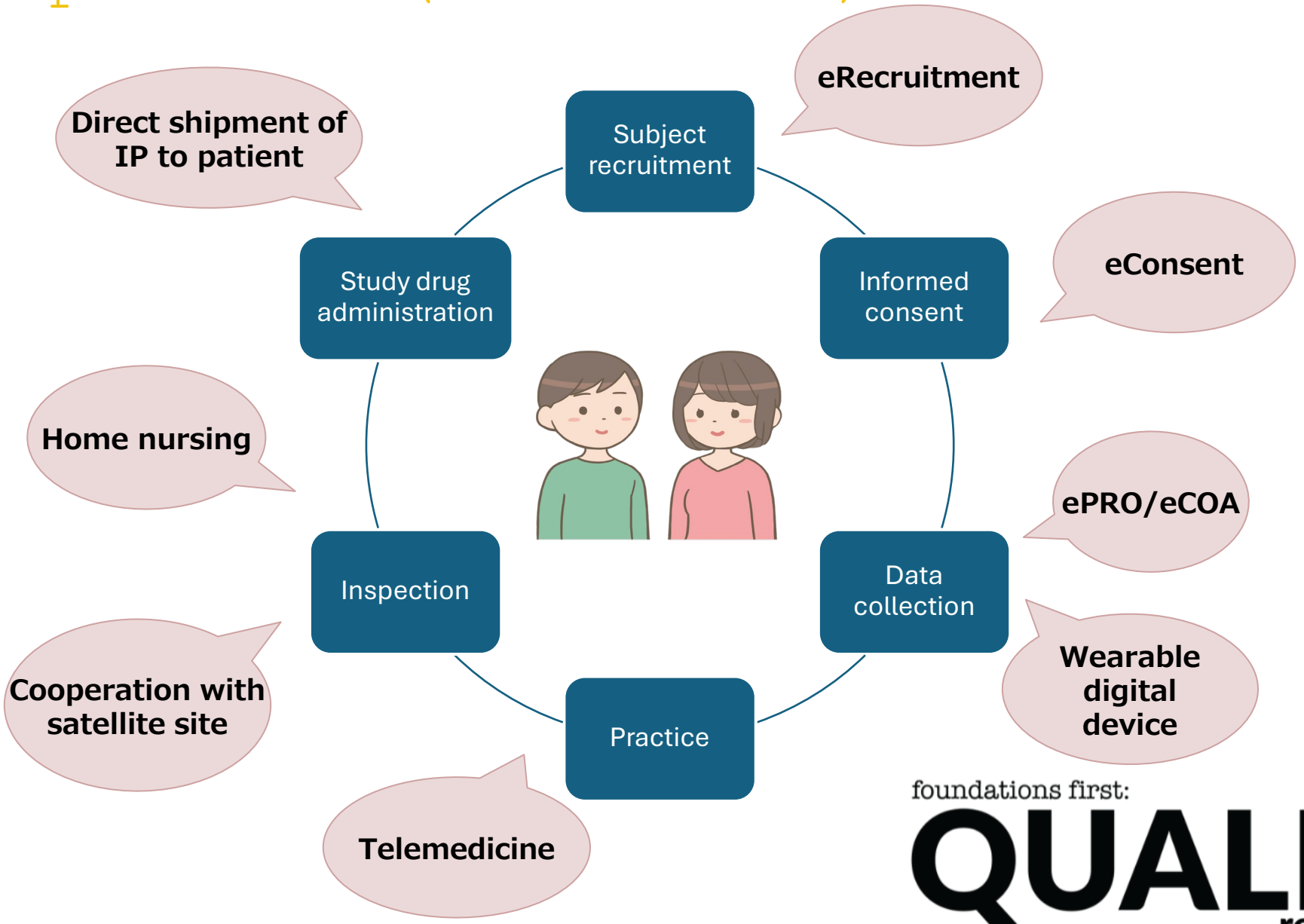
【Decentralized Clinical Trial: All Web】



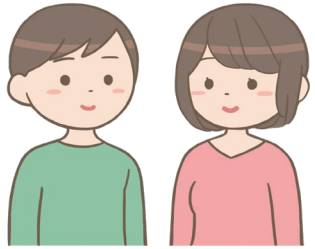
【Clinical trials that do not rely on medical office visits (DCT, hybrid) 】



DCT Components (Solutions)



DCT Components (**Key** Solutions)



- Subject recruitment
  - eRecruitment
  - Direct shipment of IP to Patient
- Informed consent
  - **eConsent**
- Data collection
  - ePRO/eCOA
  - Wearable digital device
- Practice
  - **Telemedicine**
- Inspection
  - **Cooperation with satellite sites**
- Study drug administration
  - **Home nursing**

Japan Society of Quality Assurance

foundations first:
QUALITY reconstructed

Japanese regulations and guidelines for **key** solutions

	Referenced law	J-GCP	Referenced guidelines and guidelines	Other references, guidelines, etc.
eConsent	○		○ **(For Clinical Trials)**	○
Telemedicine	○		○ (For general medical care)	○ **(For Clinical Trials)**
Cooperation with satellite sites			○ (For general medical care)	○ **(For Clinical Trials)**
Home nursing	○		○ (For general medical care)	

There are no specific regulations or guidelines focused on each solution other than eConsent.

foundations first:
QUALITY
reconstructed

Japanese guideline for eConsent

Japan Society of Quality Assurance

Points to Consider for Informed Consent Using Electromagnetic Means in Clinical Trials and Post-marketing Clinical Trials

Basic principles

1. On the premise that an explanation, questions, and answers, etc. related to the clinical trial are provided at the same level as a conventional face–to–face setting under the responsibility of the investigator and sub–investigator, it is possible to explain/obtain consent using electromagnetic means.
2. An explanation/obtainment of informed consent using electromagnetic means should be conducted after establishing a necessary information and communication system, operating procedures, etc. based on the following points.

Points to consider

1. Method of identification (identification, authentication)
2. Places and conditions for explaining/obtaining informed consent
3. Procedures for explaining/obtaining informed consent
4. Requirements for electronic signatures, etc.
5. Provision of written information/informed consent form and related matters
6. Handling of documents

PSEHB/PED Notification No. 0330-6 PSEHB/MDED Notification No. 0330-1 March 30, 2023

Japanese regulations and guidelines for **other** solutions

	Referenced law	J-GCP	Referenced guidelines and guidelines	Other references, guidelines, etc.
Direct shipment of IP to patient		○		
eRecruitment			○ (For COVID-19 treatment drug)	○1 ○2 (For Clinical Trials)
ePRO/eCOA	○		○ (For Clinical Trials)	
Wearable digital device	○		○ (For Clinical Trials)	

These solutions are relatively widespread in Japan, as there are notifications and reference guidelines related to clinical trials.

Japanese guideline relating to Telemedicine

Points to consider for the evaluation of efficacy and safety using information collected as electromagnetic records by information and communication devices in clinical trials and post-marketing clinical trials

September 20, 2024

Positioning of this guidance

In clinical trials, it is possible to collect data from subjects and evaluate efficacy and safety using information collected as electromagnetic records by information and communication devices.*

This guidance summarizes the points to keep in mind when doing so.

*Information and communication devices: Devices capable of collecting information as electromagnetic records and transmitting information through telecommunications lines. There are devices that are solely used for communication and devices with communication functions, such as video chat systems, mobile devices, and wearable devices.

Points to consider

1. Efficacy and safety evaluation via video chat system
2. Collecting data using mobile devices, wearable devices, etc. and evaluating efficacy and safety
3. Ensuring the safety of subjects
4. Reliability assurance for information and communication devices
5. Security measures
6. Instructions for use

DCT Checklist by JSQA Study Group

※Organize issues and points to consider when implementing DCT, focusing on eConsent, Televisits, collaboration with Satellite Sites and Home Nursing.

No.23C04 別添資料

DCTチェックリスト

※ eConsent、オンライン診療、近隣医療機関（治験実施医療機関外の医療機関）との連携と訪問看護にフォーカスして、DCT実施の際の課題、留意点を整理

作成者：一般社団法人 日本QA研究会 GCP部会 第2分科会（電子） Aグループ

作成日：2024年2月

カテゴリ	規制要件	カテゴリ・工程	治験依頼者・CROの立場から		医療機関・SMOの立場から		JSQAとしての見解
			DCTを適用したい場合の課題	DCTを適用する際の留意事項（チェック項目）	DCTを適用したい場合の課題	DCTを適用する際の留意事項（チェック項目）	
eConsent	<日本> ・「人を対象とする生命科学・医学系研究に関する倫理指針」（2021年3月23日発出）により医学系研究ではeConsentが可能 ・治験及び製造販売後臨床試験における電磁的方法を用いた説明及び同意に関する留意点について（薬生薬審発0330第6号、薬生機審発0330第1号 令和5年3月30日） ・薬物、機械器具又は加工細胞等に係る治験の計画の届出に関する質疑応答集（Q＆A）について（事務連絡、令和5年3月30日） ・オンライン診療の適切な実施に関する指針（平成30年3月（令和5年3月一部改訂）） 治験責任医師等は、情報通信システム、汎用サービスの適切な利用 のため、「オンライン診療指針」のV.2.（5）．1）を参照すること。 ・参照すべき規制 ※ER/ES指針：「医薬品等の承認又は許可等に係る申請等における電磁的記録及び電子署名の利用について」（厚生労働省 平成17年4月1日 薬食発第 0401022号） ※e文書法：「民間事業者等が行う書面の保存等における情報通信の技術の利用に関する法律」（平成16年法律第149号）と「民間事業者等が行う書面の保存等における情報通信の技術の利用に関する法律の施行に伴う関係法律の整備等に関する法律」（平成16年法律第150号） ※電子署名及び認証業務に関する法律（平成12年法律第102号） ※ 21 CFR part 11 (FDA regulations regarding electronic records and electronic signatures) ・参照文書：「医療機関への来院に依存しない臨床試験手法の活用に向けた検討 －日本での導入の手引き－」（日本製薬工業協会・医薬品評価委員会臨床評価部会 2021年7月作成）	対面での同意説明・取得 -説明は紙で取得は電子 -説明も取得も電子 （-説明は電子で取得は紙）	①eConsentの実装経験がない	① □参照となる各種ガイドラインを読み込む。動画等が説明文書に含まれる場合は治験届に添付が必要となるため、動画等は説明文書に含まれるのか、参考資料として説明文書に含まれないか取り扱いを明確にしておくこと	①eConsentを使用した同意説明・同意取得の手順及び資料（同意書原本）の保管方法について、施設の規定がない	① □自施設におけるeConsent及び電磁的記録（同意書原本の取り扱い）に関する手順書の作成 □同意書（写）の提供方法について依頼者に確認する	ガイダンスから外れる又はガイダンスにない運用でeConsentを適用とする場合は規制当局へ事前相談が必要であるが、ガイダンスに則っていれば事前の相談は不要で適用可能である。 実施にあたっては、周到な事前準備、特にサービスプロバイダと事前に十分協議・確認が必要であり、施設の手順やインフラが整っており、eConsent使用に理解が得られていなければならず、システムトラブルや被験者の要望に応じて紙も準備する必要がある。 電子(動画を用いた)説明は、様々な年齢層で受け入れられるものと考えるが、文章を読む事や対面で担当医師やCRC説明される事よりも理解が遠くなる可能性等も考えられる。動画の内容や構成等の改善も必要ではあるが、選択、対面での補足等も行いながら電子での説明を導入することを推奨したい。また、電子での署名についてはすでに様々な場面において導入が進んでいる事もあり、治験での同意についても今後取り入れるべく推奨するものとする。
			②施設からeConsent使用について理解（メリット）が得られない	② □被験者、医療機関、依頼者社内へのeConsent導入メリット、操作方法などの理解促進のための活動を検討する □eConsentによる同意取得プロセスについて依頼者、医療機関双方の関係者が正しく理解するためのトレーニングの実施とマニュアルの準備を行う □必要に応じて被験者向けのマニュアルを準備する □施設スタッフからの問い合わせやトラブル時のサポート体制を構築する	②施設のICFフォーマットを使用したい	② □施設選定時に施設のICFフォーマットの使用可否について依頼者に確認する	
			③IRBの事前レビュー（ヒアリング）時に必要なもの・情報が揃わない	③ □IRBによりeConsentに関するビデオや音声、Webサイトを含めた全ての資料が審査され、同意取得プロセスについて承認が得られているかを確認する （動画等が説明文書に含まれるか、参考資料とみなして説明文書に含まれないかの取り扱いを明確にしておくこと）	③eConsentによる同意取得の経験不足・プロセスの理解不足	③ □被験者対応を行うための施設手順に関する施設スタッフへのトレーニング	
			④eConsentセットアップ完了まで時間がかかる	④ □施設のICFフォーマットの使用の可否及び使用可能な場合にセットアップまでのプロセスやタイムラインを確認する （ICF改訂時や複数のICF（任意も含めて）がある場合、メインと合わせて準備し、メインと同様に対応・確認する）	④eConsent使用時のテクニカルな問題（インターネット環境、ITシステム/デバイスの不具合や使用方法についての不明点）に対して懸念がある	④ □eConsent使用時のテクニカルな問題に関する問い合わせ先を依頼者に確認しておく	
			⑤使用するITシステム/デバイス（サービスプロバイダ）によって仕様が異なるが、使用経験がないと何をどう確認・準備してい	⑤ □使用するITシステム/デバイス（サービスプロバイダ）が決	⑤ 患者さんがeConsentを使いたくない、使うのが難しい	⑤ □被験者への説明資料を依頼者とともに準備する	

DCT Checklist

eConsent

Points to consider when auditing/being audited in the study of applied eConsent

- **<Sponsor>**
  - Confirm that the IRB reviewed and approved the informed consent process in using eConsent including all materials related to eConsent, such as videos, etc.
  - Check the specifications whether the device to be used complies with applicable regulatory requirements.
  - Discuss in advance with the service provider about the procedures and documents that need to be prepared, such as manuals for medical institutions and study subjects, and how to deal with system troubles.
  - When explaining and obtaining consent remotely, it is necessary to prepare appropriate communication methods, such as video calls and confirm any measures for obtaining consent after confirming that the subject sufficiently understands (question flag function, understanding degree test, etc.)

Points to consider when auditing/being audited in the study of applied eConsent

<Medical Institution>

- It is necessary to establish procedural documents for electromagnetic records (handling of the original consent form) to enable the use of eConsent.
- When explaining and obtaining consent, secure a location where the privacy is protected without any problems in the internet environment.

<Common by Sponsor and Medical Institution>

- it is necessary for both the investigators and the subjects to confirm each other's identity using the identification documents.
- It is desirable that specifics to authenticate the identity of the person signing the electronic signature will be established in the information communication system

eConsent: JSQA Study Group's opinion

eConsent can be applied when established guidelines are followed! Furthermore, it is recommended that both processes for providing and obtaining informed consent be performed remotely. However…

- Thorough advance preparation is needed, and prior sufficient consultation and confirmation is needed especially when dealing with service providers.
- Facility protocol and proper infrastructure must be established, and an understanding on the use of eConsent is mandatory.
- Paper versions of all consent forms must be prepared for times of system error and for when requested by subjects.
- It is also perceived that use of electronic explanations (via video) can result in a weaker understanding, therefore, supplementary accommodations must also be made available as needed .
- Extensive and careful attention to detail is necessary for confirming the subject's identity, level of understanding, and their current situation when using fully-remote eConsent.
- While it is considered possible to acquire eConsent remotely from the first encounter, preparations must be made to have methods ready for directly communicating with subjects, including video calls and excluding voice-only real-time communication.

DCT Checklist

Telemedicine

Points to consider when auditing/being audited in the study of applied Telemedicine

＜Preliminary consideration by both the sponsor and the medical institution conducting the trial and provisions in the study protocol＞

- When planning study protocol, thoroughly consider whether endpoints for safety and efficacy can be appropriately evaluated by reflecting the limitations in telemedicine.
- Stipulate in the study protocol how to document clinical trial related medical records at the medical institution conducting the clinical trial (items observed through telemedicine, including records of deviations, etc.).
- Determine how to manage the subject's visit when requiring any medical treatment due to AE/SAE.
- Stipulate the benefits of telemedicine and the handling of the disadvantages that may result from it for patients and their families, etc., in the study protocol and ICF beforehand.

Telemedicine: JSQA Study Group's opinion

- Thorough analysis is to be performed for each individual clinical trial, and it is thought that revisions will be necessary, as proper countermeasure review will be needed for stakeholders and regulatory authorities when issues arise. In that event, individuals will also refer to related notices for telemedicine with regard to standard medical treatment.
- It is recommended to refer to case studies as they relate to telemedicine.
- It is thought that there will need to be a feasibility analysis, and both sponsors and medical institutions participating in clinical trials will have a mutual reconciling regarding cost of compensation/reimbursements for expenses incurred, telemedicine medical itemization surcharges, and infrastructure cost burden necessary for telemedicine.

DCT Checklist

Satellite Sites / Home Nursing

Satellite site: A medical institution located close to the patient's home that performs clinical trial-related practices for the patient based on the instructions of, or in cooperation with, the clinical trial site.

Points to consider when auditing/being audited in the study of applied Satellite Sites/Home Nursing

<Common items among Sponsor, medical institution and satellite site>

- Clarify the clinical trial implementation system and the scope of work whether the contract between sponsor and medical institution is executed in accordance with J-GCP
- Select and confirm the selection records of home nursing stations. If the home nursing vendor is not involved, consult with the medical institution if their cooperation is available.
- Establish appropriate structure of clinical trial implementation that utilizes satellite sites, home nursing, home nursing vendors, etc., and to clarify the roles and responsibilities of each party.
- Consider and develop procedural documents (e.g., emergency procedure, procedures for home administration, procedures for receiving and storing investigational drugs, etc.) that need to be supplemented with the current procedure.
- The sponsor provides necessary training and ensures that staff in home nursing station* receive training by the sponsor or medical institution or satellite sites.

Satellite Sites/Home Nursing: JSQA Study Group's opinion

- Clarify the scope of business and the DCT implementation system. Confirm whether the trial falls under a contract based on Article 13 of the Contract for Clinical Trials or Section 2 of Article 39 of an Outsourcing Contract.
- Thorough analysis is to be performed for each individual clinical trial, and it is thought that revisions will be necessary, as proper countermeasure review will be needed for stakeholders and regulatory authorities when issues arise. Furthermore, refer to the Health Insurance Act, the Long-Term Insurance Care Act, and related notices.
- It is recommended to refer to prior existing case studies as they relate to cooperation with nearby medical institutions and home-visit nursing care services.

Summary of JSQA Study Group's opinion

「Why DCT」

Has the potential to create ideal clinical trial implementation environments for both subjects and sponsors.

「What DCT」

The extent to which DCT is used may also depend on the specialization of the clinical trial (disease, protocol etc.).

「How DCT」

Consider how each trial and investigator site can respond by referring to existing case studies.

「Shape DCT」

Implement feasible components found via accumulated case studies.

「Future DCT」

Create better policies and guidelines by learning from accumulated case studies (including Trial & Error).

Next step in JSQA Study Group

With the introduction of DCT, patients will have more opportunities to participate in clinical trials, and both sponsors and clinical trial sites can expect an acceleration in the trial process.

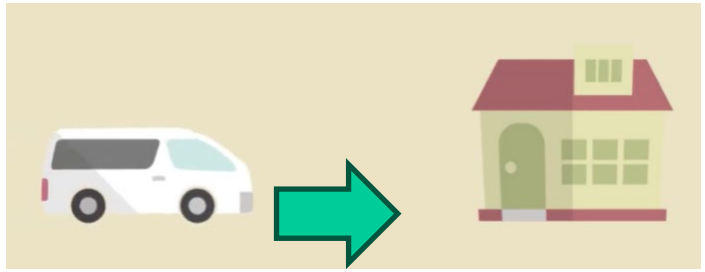
We will continue to explore and implement feasible measures step by step!

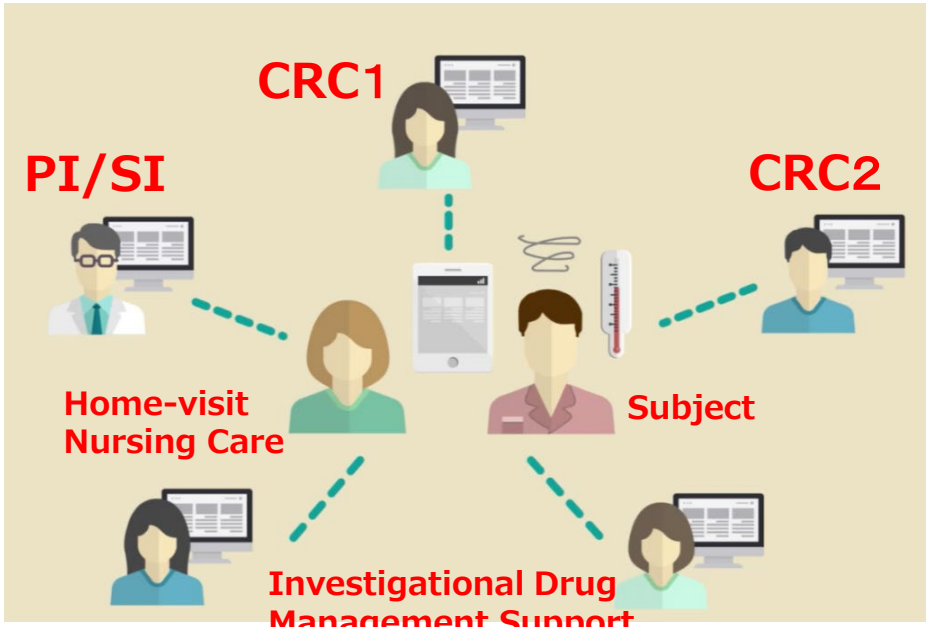
- Refine the DCT checklist to make it more user-friendly and suitable from an audit perspective.
- Conduct user evaluations when using the DCT checklist and performance assessments of DCT to incorporate the results into the checklist.

DCT Model/Clinic

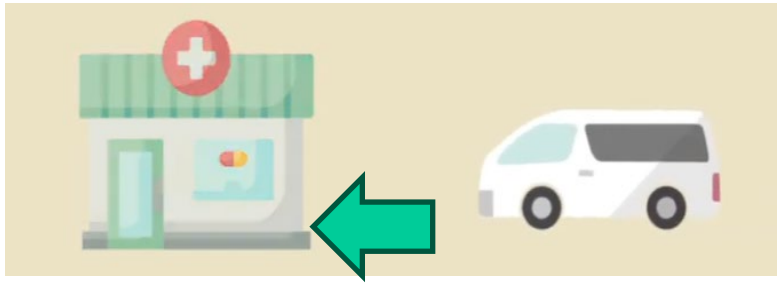
Domestic Clinic DCT Model

(COVID-19 Investigational Drug Clinical Trial)





1. Subject home-visit via DCT car



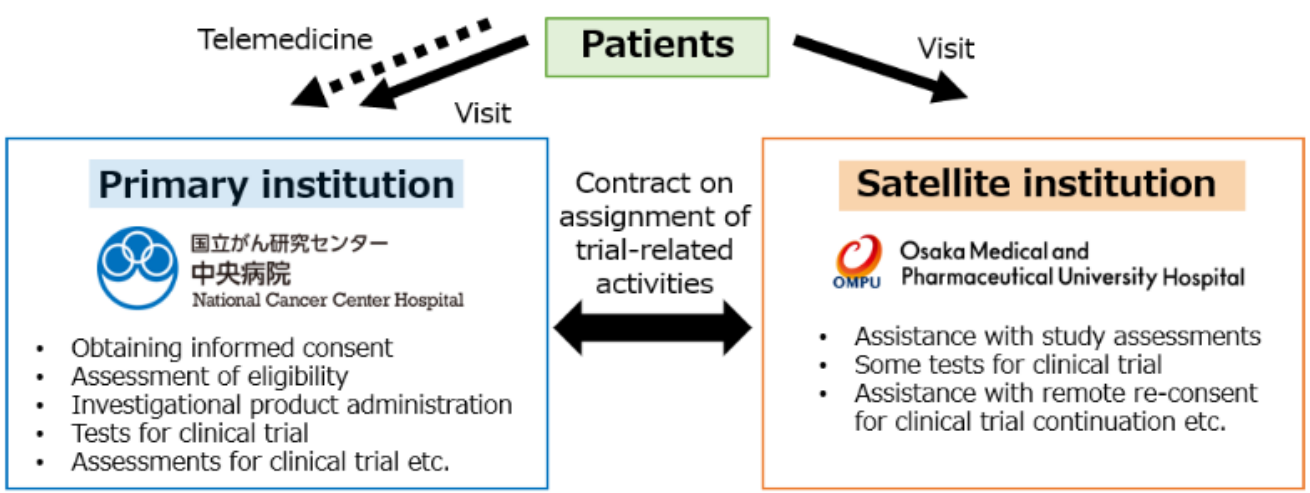
2. Online Conference System:
   - 2-1 Provide & Obtain Written Informed Consent
   - 2-2 Specimen Collection
   - 2-3 Perform Observation & Recording
   - 2-4 Confirm Investigational Drug Administration

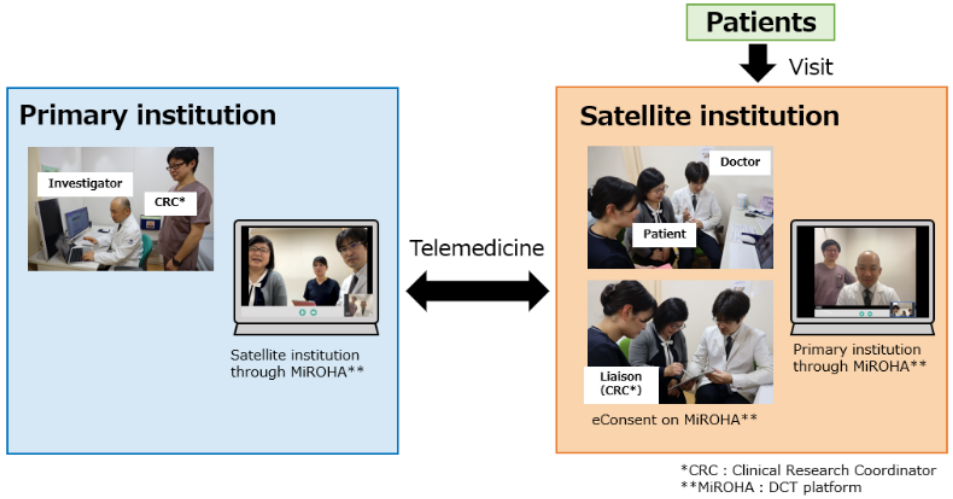
Results are recorded in a timely manner in cloud-based electronic clinical records

Refer to Tokyo center clinic website
https://www.youtube.com/watch?embeds_referring_euri=https%3A%2F%2Ftokyo-center-clinic.studio.site%2F&source_ve_path=Mjg2NjQsMTY0NTAz&feature=emb_share&v=mYAA5Ig4I44

DCT Model/National Hospital

Company-Sponsored Phase I Study in Oncology with a New Decentralized Clinical Trial Structure





Refer to National Cancer Center Japan website

[Chugai, NCCH, OMPU and MICIN Start Company–Sponsored Phase I Study in Oncology with a New Decentralized Clinical Trial Structure | National Cancer Center Japan]

Implementation of DCT Solutions in Japan Industries

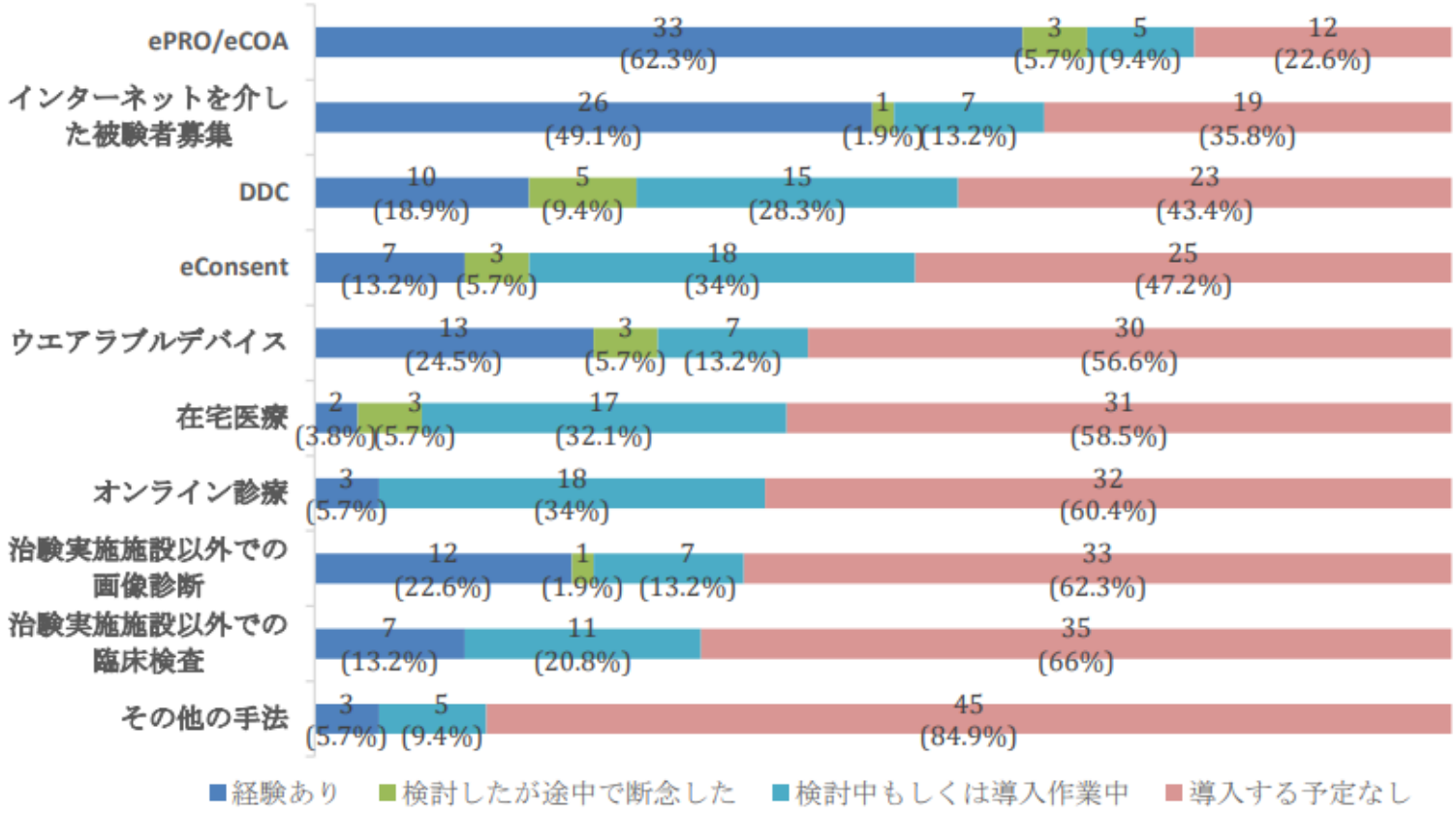


図4-2. DCTに関連する各手法の導入経験

日本製薬工業協会医薬品評価委員会データサイエンス部会資料「DCT におけるデータの流れとその信頼性確保」2022 年 8 月
https://www.jpma.or.jp/information/evaluation/results/allotment/gbkspa00000017ol-att/DS_202208_DCT_f01.pdf

Thank you!

Contact:

terumi.mitsumori@ppd.com