# "Digital tools and methods to facilitate clinical trials in Japan"

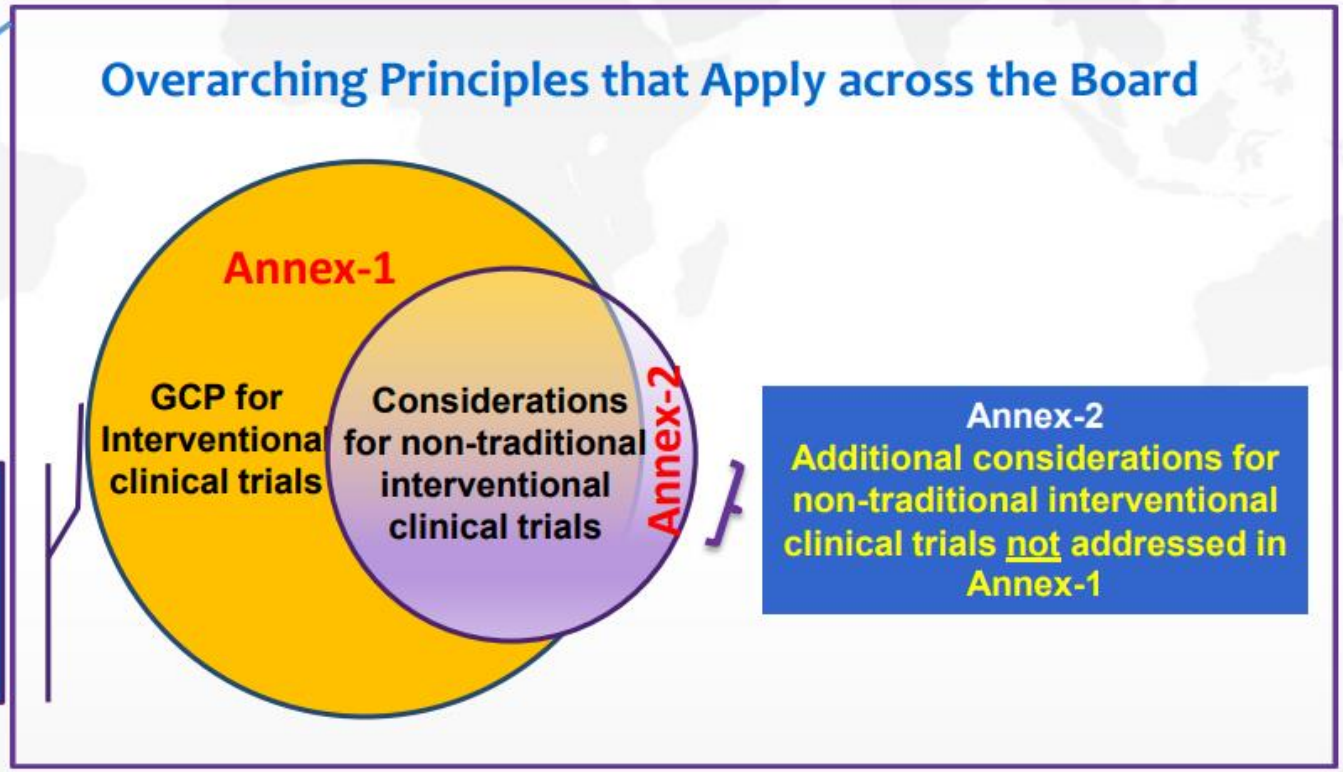
OGATA Akiko, Ph.D
Division Director, Division of Asia I,
Office of International Program, PMDA

10th Joint Conference of Taiwan and Japan on Medical Products Regulation
20th October 2022

ICH harmonisation for better health

# ICH E6(R3) GCP Principles

Draft Principles published in April 2021




**Annex-1**
Reflects the concepts in E6(R2) (with updates and refinements as needed)

**Annex-2**
Additional considerations for non-traditional interventional clinical trials not addressed in Annex-1

Source :The 43rd ICH Immediate Report Meeting (July 7, 2021)

# Decentralized Clinical Trials evolved with COVID-19 pandemic

**Sponsors**

Restrictions on visits to medical institutions

Refrain from any nonessential and non-urgent outings

**Patients**

Limit visits to medical institutions

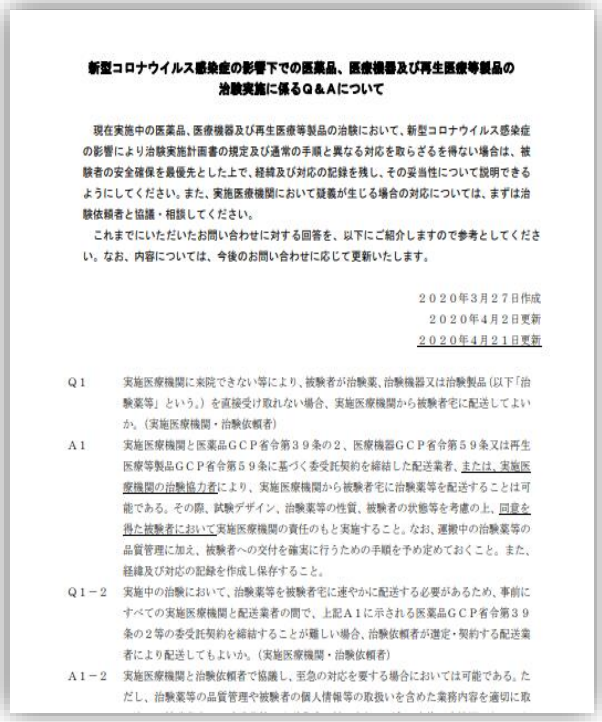
## Utilize ICT tools

Remote SDV
(Source Document Verification)

Telemedicine
Wearable devices

# Q&A on Management of Clinical Trials during COVID-19 Pandemic


Initially published on 27 March, 2020



**新型コロナウイルス感染症の影響下での医薬品、医療機器及び再生医療等製品の治験実施に係るQ&Aについて**

現在実施中の医薬品、医療機器及び再生医療等製品の治験において、新型コロナウイルス感染症の影響により治験実施計画書の規定及び通常の手順と異なる対応を取らざるを得ない場合は、被験者の安全確保を最優先とした上で、経緯及び対応の記録を残し、その妥当性について説明できるようにしてください。また、実施医療機関において疑義が生じる場合の対応については、まずは治験依頼者と協議・相談してください。

これまでにいただいたお問い合わせに対する回答を、以下にご紹介しますので参考としてください。なお、内容については、今後のお問い合わせに応じて更新いたします。

2020年3月27日作成
2020年4月2日更新
2020年4月21日更新

Q1　実施医療機関に来院できない等により、被験者が治験薬、治験機器又は治験製品（以下「治験薬等」という。）を直接受け取れない場合、実施医療機関から被験者宅に配送してよいか。（実施医療機関・治験依頼者）

A1　実施医療機関と医薬品GCP省令第39条の2、医療機器GCP省令第59条又は再生医療等製品GCP省令第59条に基づく委受託契約を締結した配送業者、または、実施医療機関の治験協力者により、実施医療機関から被験者宅に治験薬等を配送することは可能である。その際、試験デザイン、治験薬等の性質、被験者の状態等を考慮の上、同意を得た被験者において実施医療機関の責任のもと実施すること。なお、運搬中の治験薬等の品質管理に加え、被験者への交付を確実に行うための手順を予め定めておくこと。また、経緯及び対応の記録を作成し保存すること。

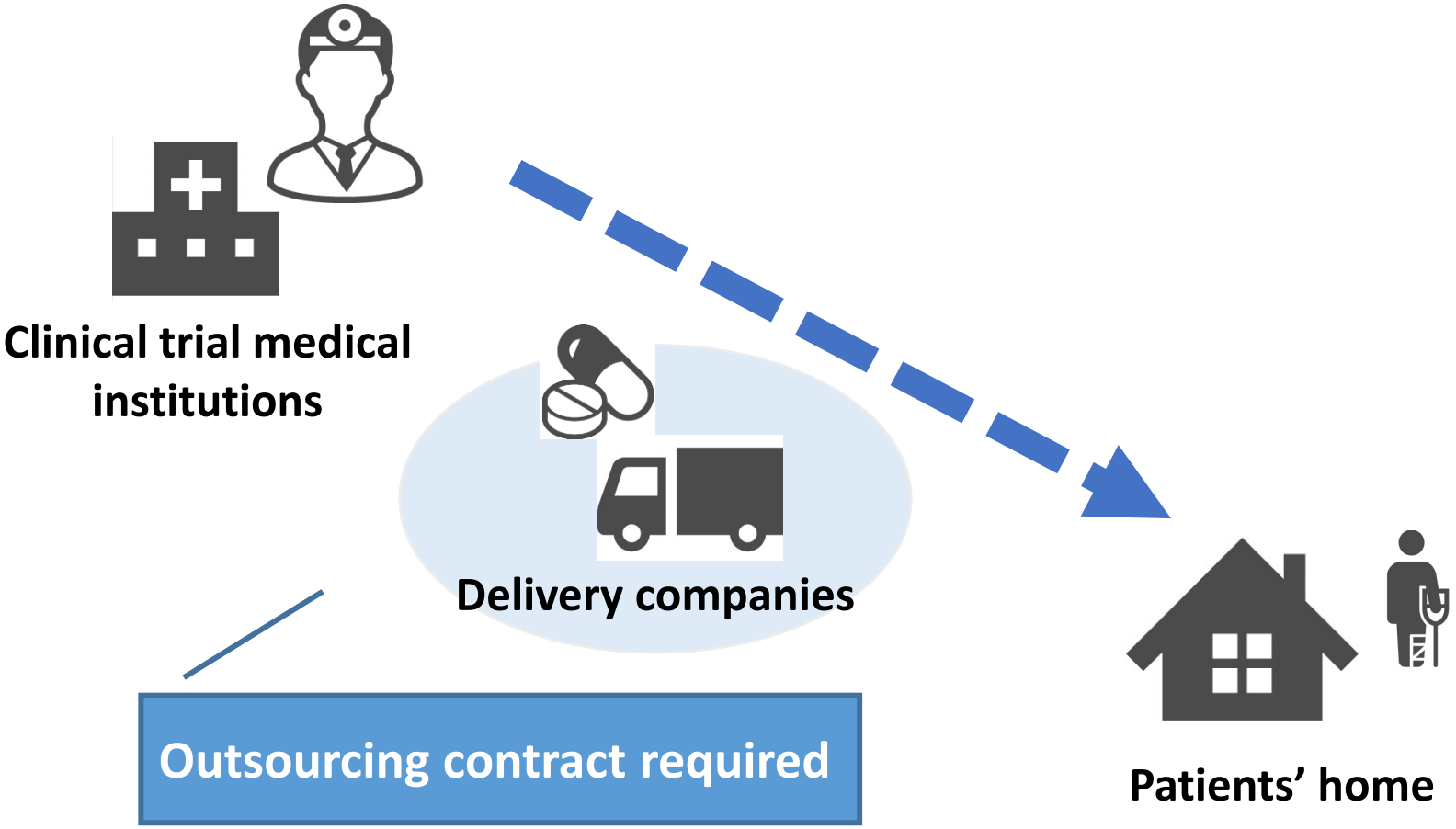
Q1－2　実施中の治験において、治験薬等を被験者宅に速やかに配送する必要があるため、事前にすべての実施医療機関と配送業者の間で、上記A1に示される医薬品GCP省令第39条の2等の委受託契約を締結することが難しい場合、治験依頼者が選定・契約する配送業者により配送してもよいか。（実施医療機関・治験依頼者）

A1－2　実施医療機関と治験依頼者で協議し、至急の対応を要する場合においては可能である。ただし、治験薬等の品質管理や被験者の個人情報等の取扱いを含めた業務内容を適切に取

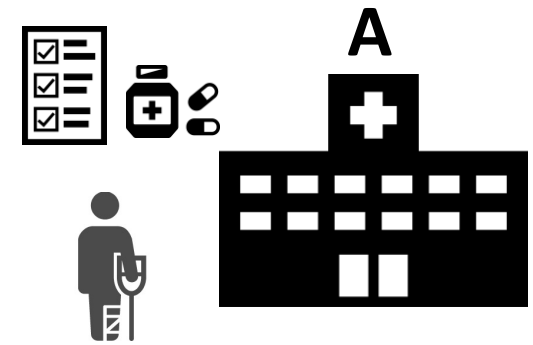
- Protection for safety of the subjects
- Decision to continue trials
- Ensuring reliability of data
- Quality assurance and Delivery of Investigational drugs
- Contracts of outsourcing
- Obligation of Principal Investigator and Responsibilities of medical institutions
- Institutional Review Board
- Monitoring and Deviation
- Record of circumstance and response

https://www.pmda.go.jp/files/000235164.pdf
https://www.pmda.go.jp/english/int-activities/0002.pdf

# Enables Shipments of investigational medical products directly to patients' homes

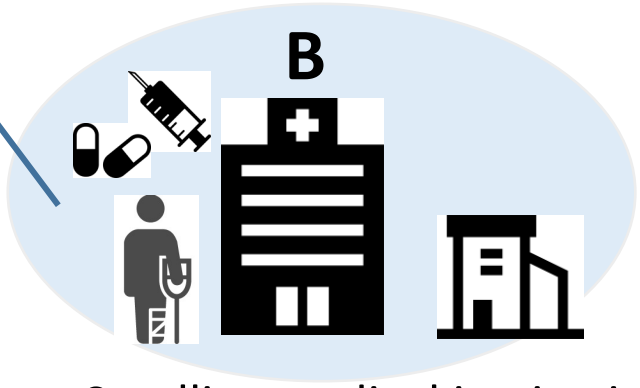


# Enables investigational administration and blood collection for testing on Satellite medical institutions



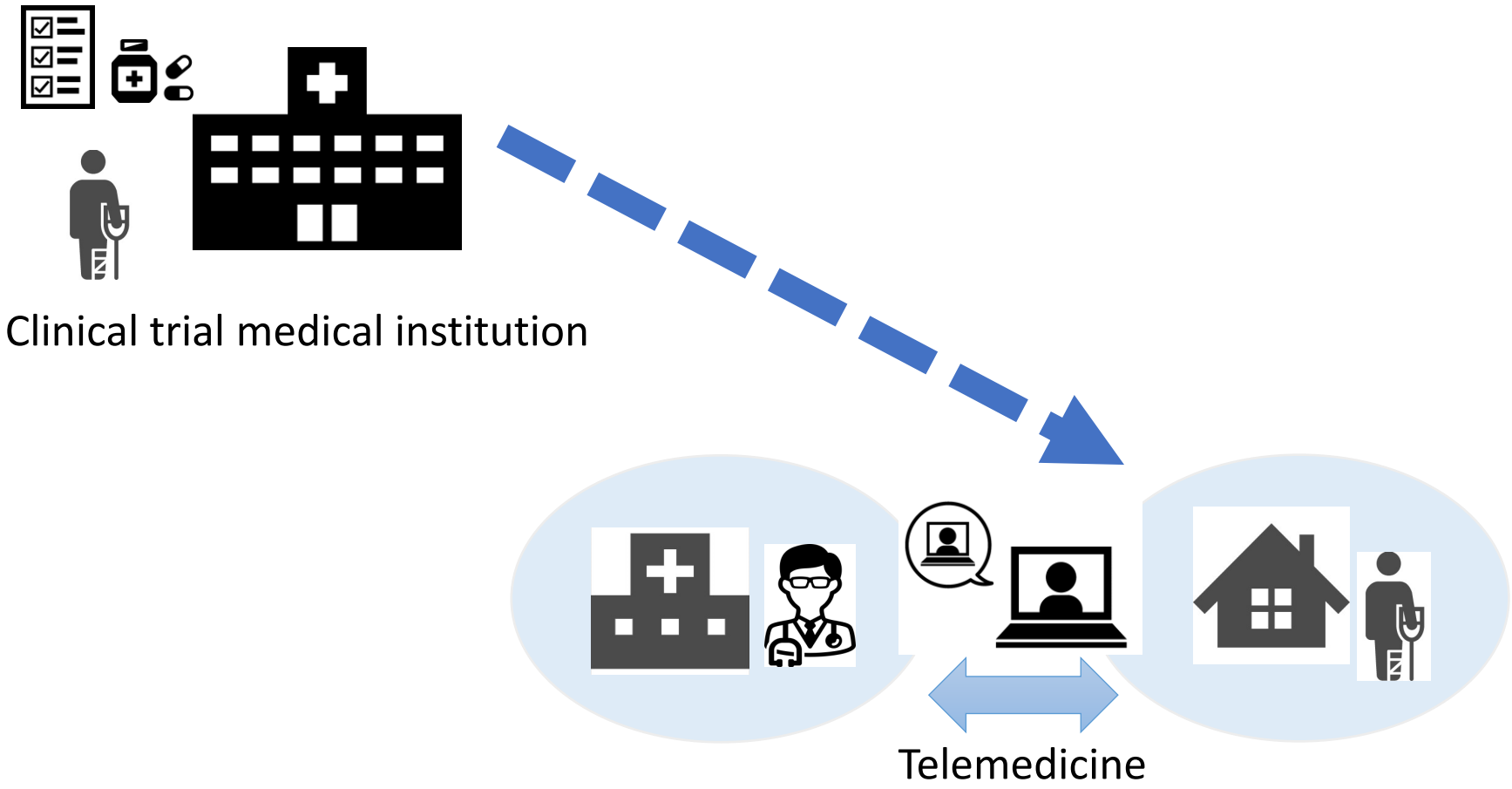

Clinical trial medical institution

**Contract with sponsor required**

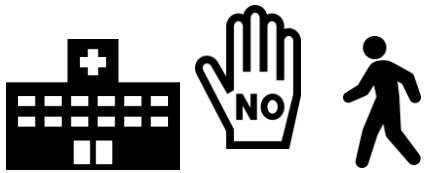



Satellite medical institutions

# Enables Clinical Trials with telemedicine

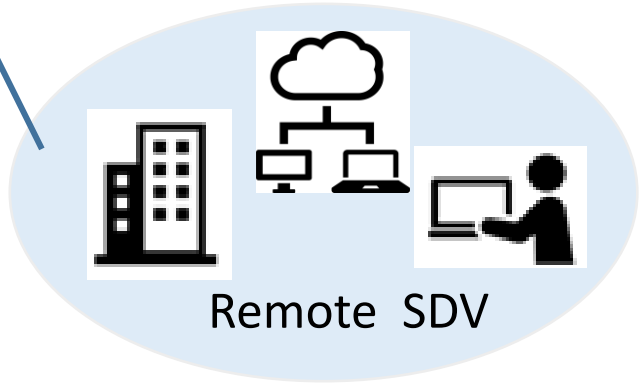


# Remote SDV (Source Document Verification)




Restrictions on visits
to medical institutions

- **Risk assessment of not conducting on-site monitoring**
- **Records of the reasons and correspondence**



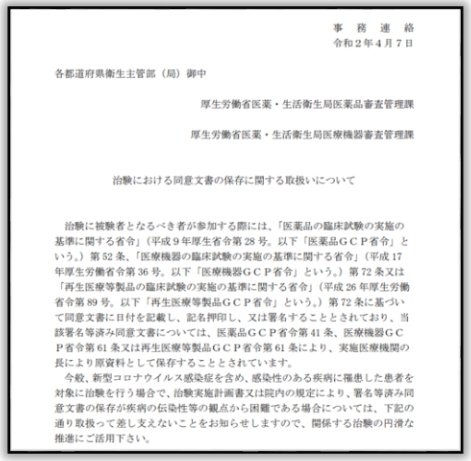
# Electronic-Informed Consent in Clinical Trials will be an option in clinical trials soon

## To accerelate subject enrollment to clinilal trials

- Informed consent by video conference system
- Obtaining a signature to Informed consent forms by electronic methods (e.g. Digital sign by tablet)

## Notification will be issued, and the following points will be explained:

- Basic concept (securing subjects' human rights and safety, scientific quality, and reliability etc.)
- Points to consider (Identify verification, procedures etc.)



事 務 連 絡
令和２年４月７日

各都道府県衛生主管部（局）御中

厚生労働省医薬・生活衛生局医薬品審査管理課

厚生労働省医薬・生活衛生局医療機器審査管理課

治験における同意文書の保存に関する取扱いについて

治験に被験者となるべき者が参加する際には、「医薬品の臨床試験の実施の基準に関する省令」（平成９年厚生省令第28号。以下「医薬品ＧＣＰ省令」という。）第52条、「医療機器の臨床試験の実施の基準に関する省令」（平成17年厚生労働省令第36号。以下「医療機器ＧＣＰ省令」という。）第72条又は「再生医療等製品の臨床試験の実施の基準に関する省令」（平成26年厚生労働省令第89号。以下「再生医療等製品ＧＣＰ省令」という。）第72条に基づいて同意文書に日付を記載し、記名押印し、又は署名することとされており、当該署名等済み同意文書については、医薬品ＧＣＰ省令第41条、医療機器ＧＣＰ省令第61条又は再生医療等製品ＧＣＰ省令第61条により、実施医療機関の長により原資料として保存することとされています。

今般、新型コロナウイルス感染症を含め、感染性のある疾病に罹患した患者を対象に治験を行う場合で、治験実施計画書又は院内の規定により、署名等済み同意文書の保存が疾病の伝染性等の観点から困難である場合については、下記の通り取扱って差し支えないことをお知らせしますので、関係する治験の円滑な推進にご活用下さい。

# Ensuring Data Reliability on DCT

## Additional considerations

### Expansion of involved stakeholders

System vendors, satellite medical institutions/home-visit medical treatment, delivery companies, administrators of self-testing devices, etc.

### Responsibilities

Responsibilities of Investigator and medical institution, Ensuring patients' compliance, etc.

### New issues

Grasp of implementation status, Information flow, Information security, contract/arrangements between stakeholders, availability of vender services in participating countries/regions, etc.

**Additional guidance are under consideration**

- Investigate actual cases of DCT
- Collect information of guidance in overseas counties

# Remote GCP Inspections

**Notification on Remote GCP inspections published in May 2020**

https://www.pmda.go.jp/files/000235011.pdf

**Notification on the method of remote GCP inspections published in Nov 2020**

https://www.pmda.go.jp/files/000237602.pdf

- Implementation policy
- Procedure
- Consideration for preparing evidence material
- Consideration for web conference system


Revised

**Notification on the method of remote GCP inspections published in May 2022**

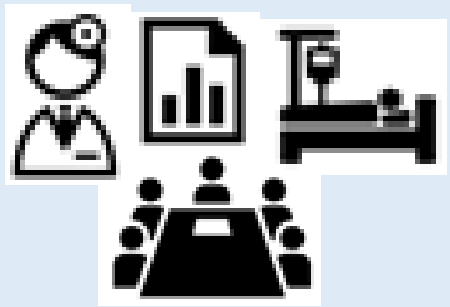
https://www.pmda.go.jp/files/000247964.pdf

- Submission through the gateway system
- Points to be considered in preparation of documentation

# GCP on-site inspection and document-based inspection

## Medical institutions

Implementation System Records



Data collection
IRB
Medical records

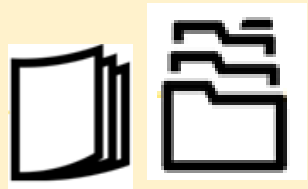
## Sponsors

Implementation System Records

CRF, EDC, DDC
Data Management,
Analysis

## Application Dossier

**CSR**
(Clinical Study Report)

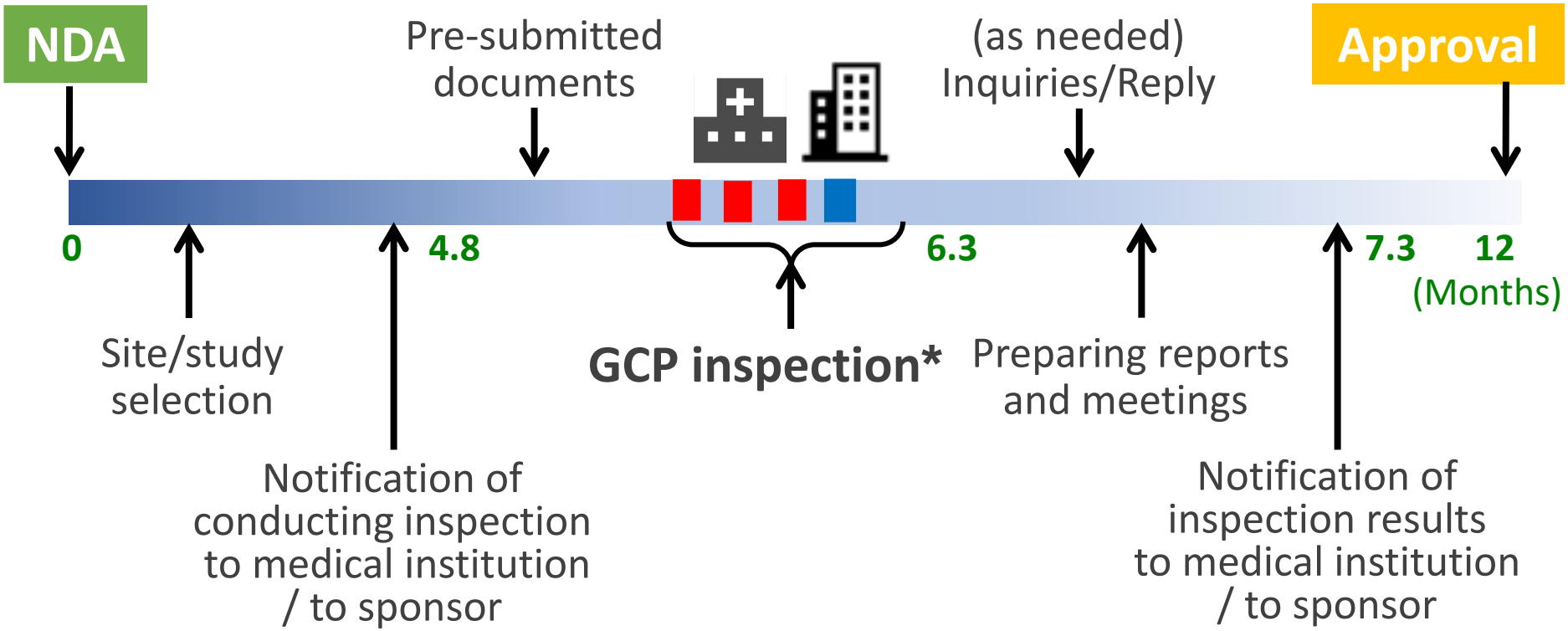


IRB: Institutional Review Board
CRF: Case Report Form
EDC: Electronic Data Capture
DDC: Direct Data Capture

**On-site inspections**

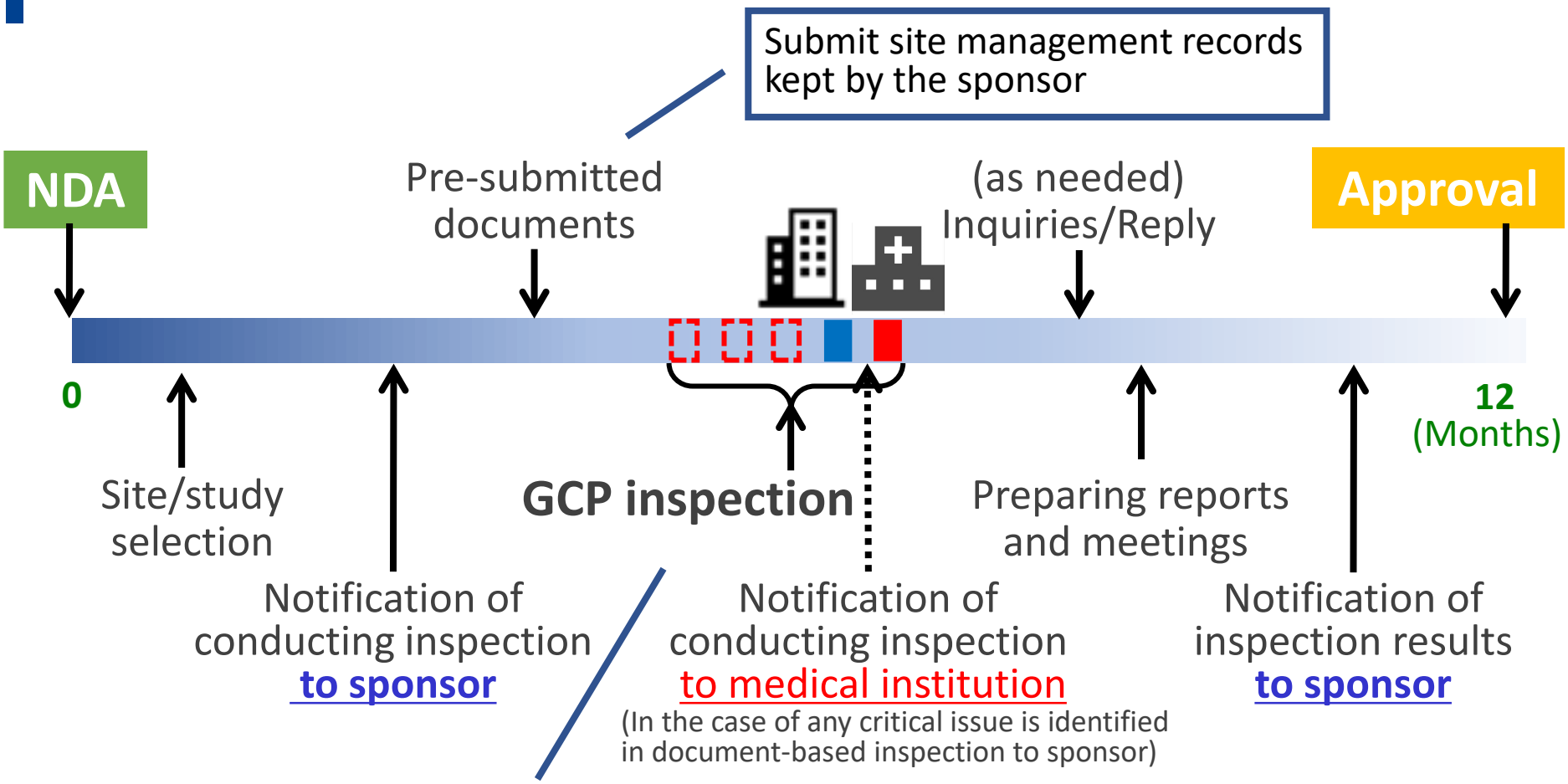
**Document-based inspections**

# Conventional GCP inspection

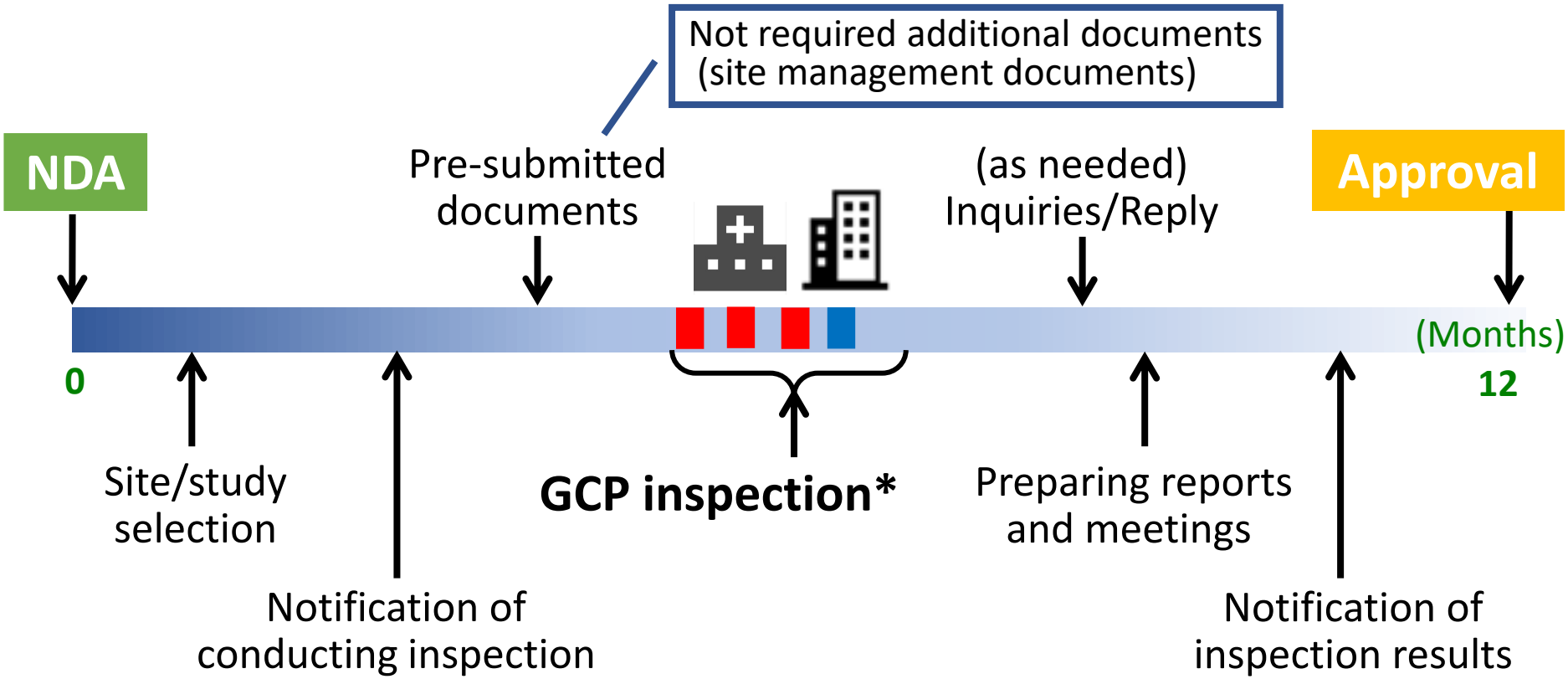



* Medical institutions (on-site inspection) → Sponsor (on-site inspection)

# Remote GCP inspection during the COVID-19 pandemic



# New approach for GCP inspections for medical institutions (in case of visiting medical institutions)




* Medical institutions (on-site inspection)

→ Sponsor (remote inspection, for the time being)

# Procedure for Remote GCP inspection

**Pre-examination of pre-submitted documents**

## On-site inspection

(1 - 3 business days)

1. Examine documents
2. Identify concerns
3. Issue inquiries, request additional documents
4. Examine additional documents

## Remote inspection

**Connectivity test of the cloud system**

(Cloud, CD/DVD available)

**Request for submission of documents**
**(13 business days before Main-inspection)**

PMDA
- Send requests

Applicant/Sponsor
- Upload requested documents(copy)

PMDA
- Review documents uploaded to cloud
- Issue inquiries

Cloud

Applicant/Sponsor
- Respond to inquiries
- Upload additional documents

**Pre-inspection**
**(10 business days)**
1. Examine documents
2. Identify concerns
3. Issue inquiries, request additional documents

PMDA
- Discuss concerns

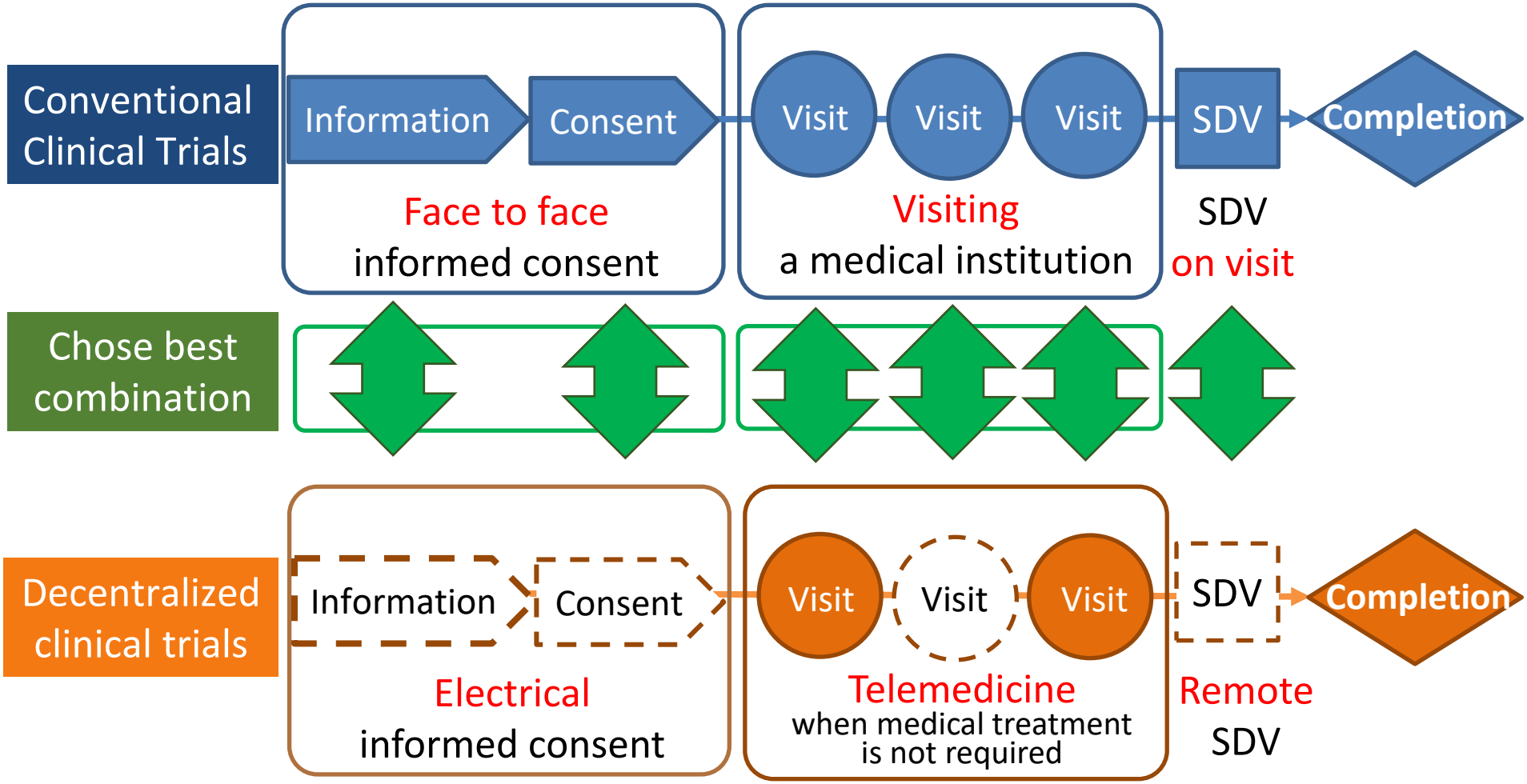
Video conferencing system

Applicant/Sponsor
- Make detailed explanations for concerns

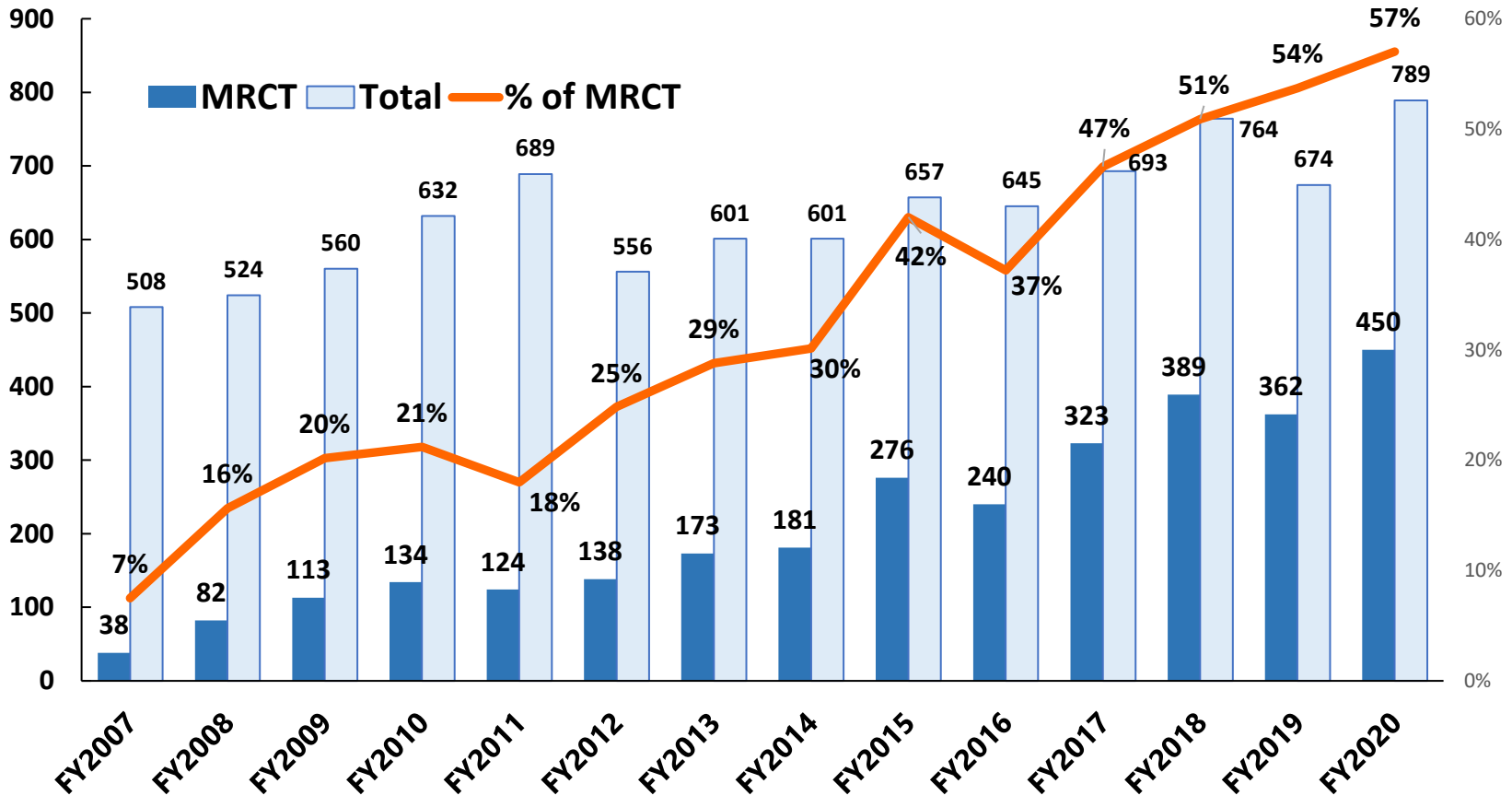
**Main-inspection**
**(1 business day)**
4. Examine additional documents

→Reduce the number of staff participating in main-inspection

# Image of a clinical trial utilizing ICT technology

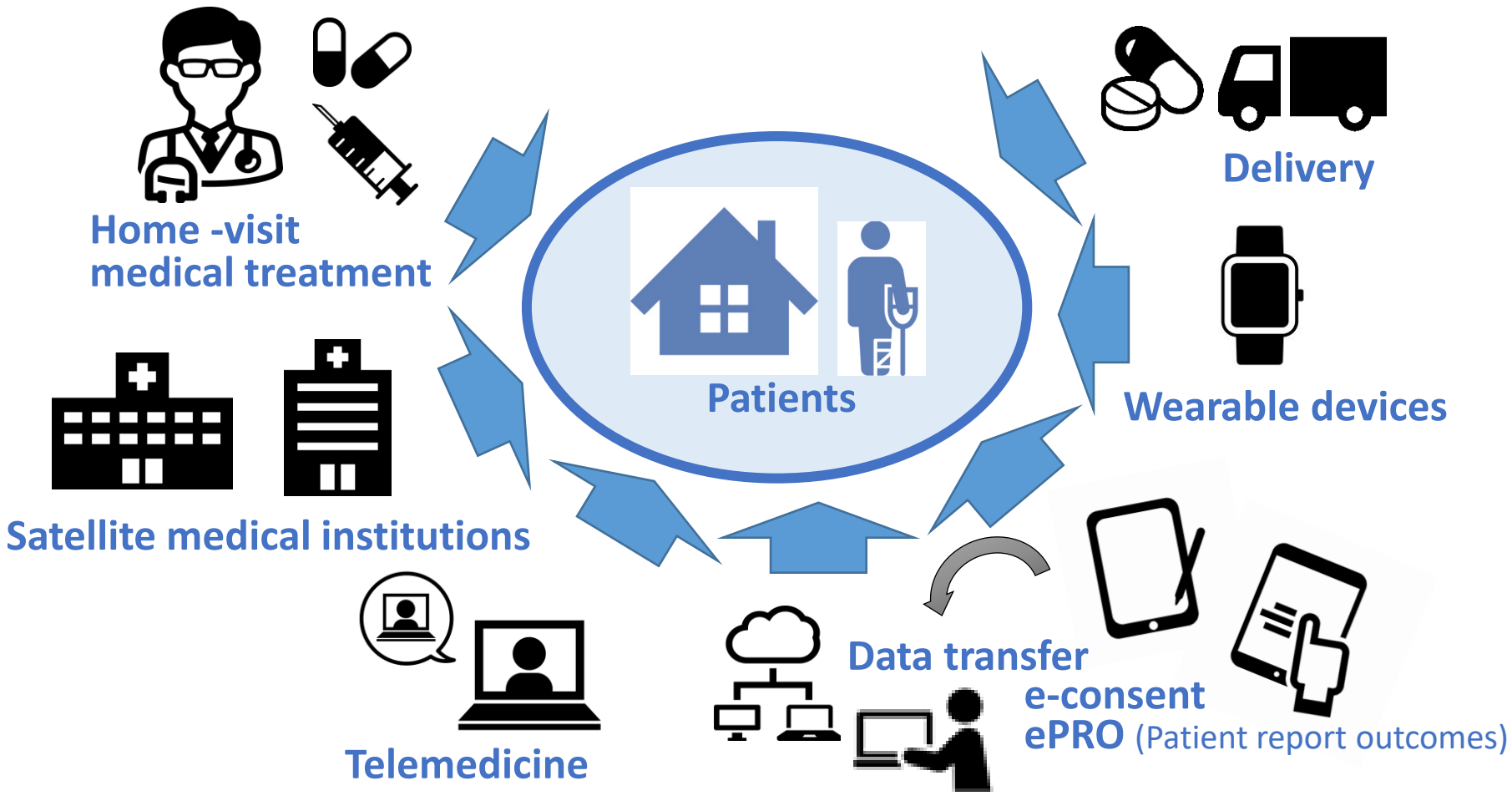


# Trends of MRCT-related Clinical Trial Notifications in Japan




MRCT: March Regional Clinical Trail

# Expectations for efficient clinical trials by utilizing ICT tools



# Thank you for listening