CLINICAL TRIAL OPERATIONS AND COMPETITIVENESS

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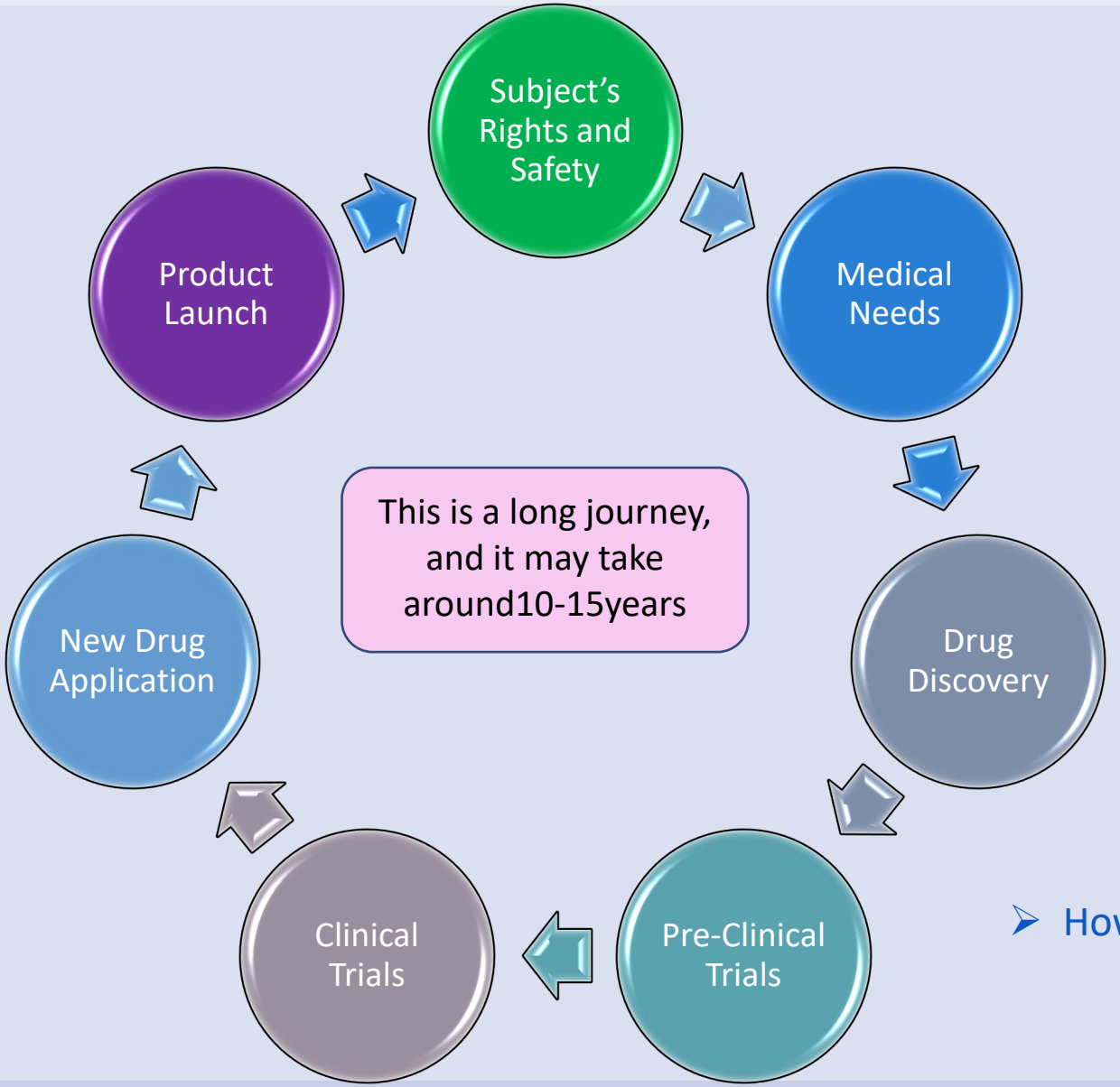
Date:12April2023

Drug Development



- How long can a subject wait?

What are clinical trials?

- **A clinical trial is a carefully designed study that prospectively tests the benefits and risks of an investigational product in human beings.**

- **Data from a clinical trial provide a critical base of evidence for applying an IP in future clinical practice.**

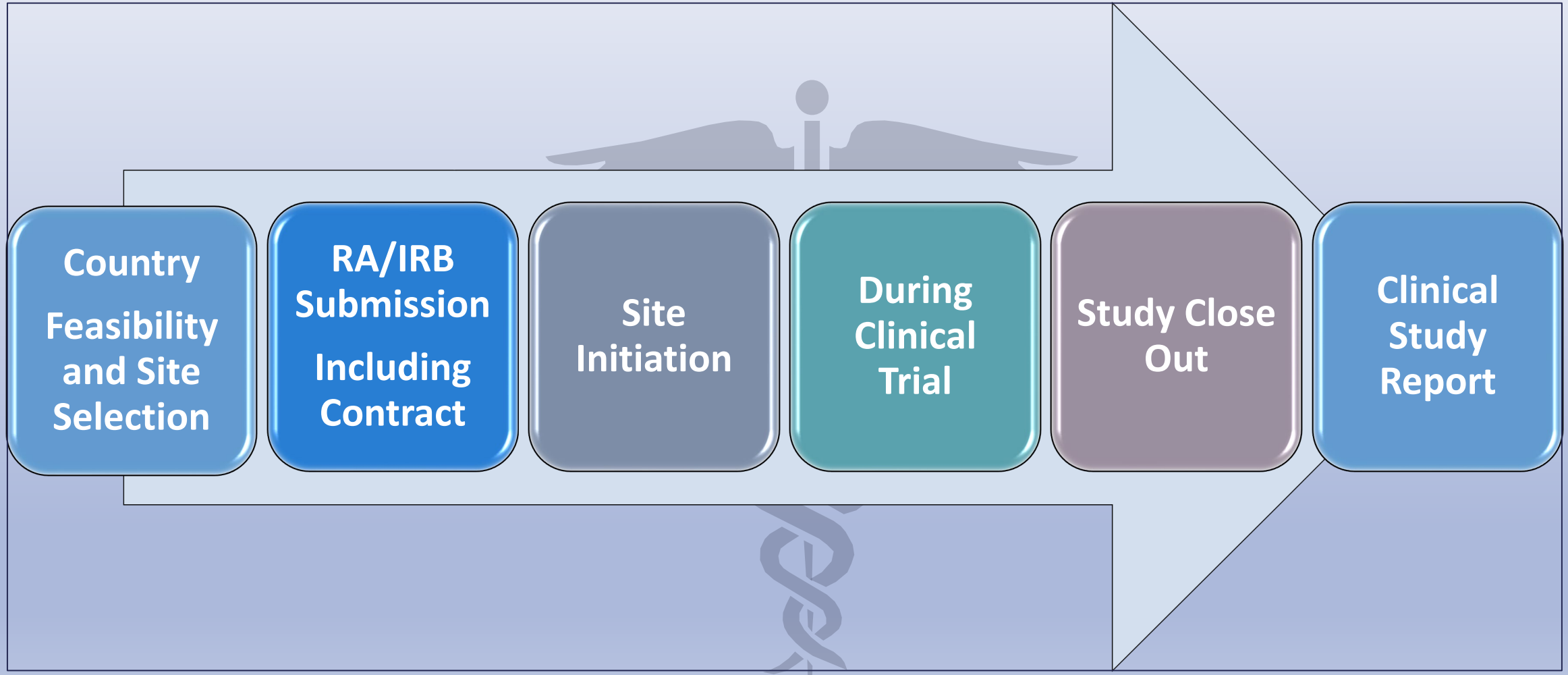
Quality

Speed

Phases of Clinical Development

PHASE	AIM	STUDY POPULATION	NUMBER OF PARTICIPANTS	DURATION (YEARS)
Phase I	First in human safety and tolerability, determines side effects associated with increasing doses	Healthy volunteers or participants who have the disease or condition under study	**Tens**	**~1**
Phase II	Testing of drug on participants to assess efficacy and safety. Assesses short-term safety and ascertains therapeutic dose range (min and mx doses) Must produce data that justifies initiation of Phase III studies	Participants who have the disease or condition under study	**Hundreds**	**~2**
Phase III	Pivotal efficacy and safety for regulatory submission, or to support publications	Target patient population for indication	**Thousands**	**~3**
Phase IV	Post marketing studies delineate additional information including drug risk, benefits and optimal use.	Participants who have the disease or condition under study	**Variable**	**Variable**

Conducting a Clinical Trial



COUNTRY FEASIBILITY

DATA BASE (Internal & External

LOCAL INTELLIGENCE

FEASIBILITY SURVEY

✓ Database presented the site performance for identified potential sites.
- Clinical Research Experience
- Recruitment Performance
- Site Quality Trend

✓ Feasibility Survey
- CDA
- Draft Protocol Synopsis
- Site evaluation

*Carefully review the criteria and procedures are key, and to complete the feasibility survey correctly with estimated potential cases is important to study level

*Timelines is very important which will influence the global level to select the country/site or not

✓ Global Level will review each countries survey and have internal discussion to make final decision

Site Selection
Pre-Study Visit

- Investigators Qualification
- 
- Adequate Resources
- Time Commitment Through Clinical Trial
- The Team Facilities Collaboration
- Space For During a Clinical Trial
- Decentralized Clinical Trial

The Pre-Study Visit (PSV) is a great opportunity to

- Area of interest
- Qualifications
- Patient Pools
- Resources
- Specific site requirement
- IRB requirement/site contract requirement
- The risk of benefit of IP to decide whether to participate or not
- Early identify the protocol design that may differ from clinical practice

Sponsor

Investigator

THE PRE-STUDY VISIT IS AN OPPORTUNITY TO MATCH EXPECTATIONS!

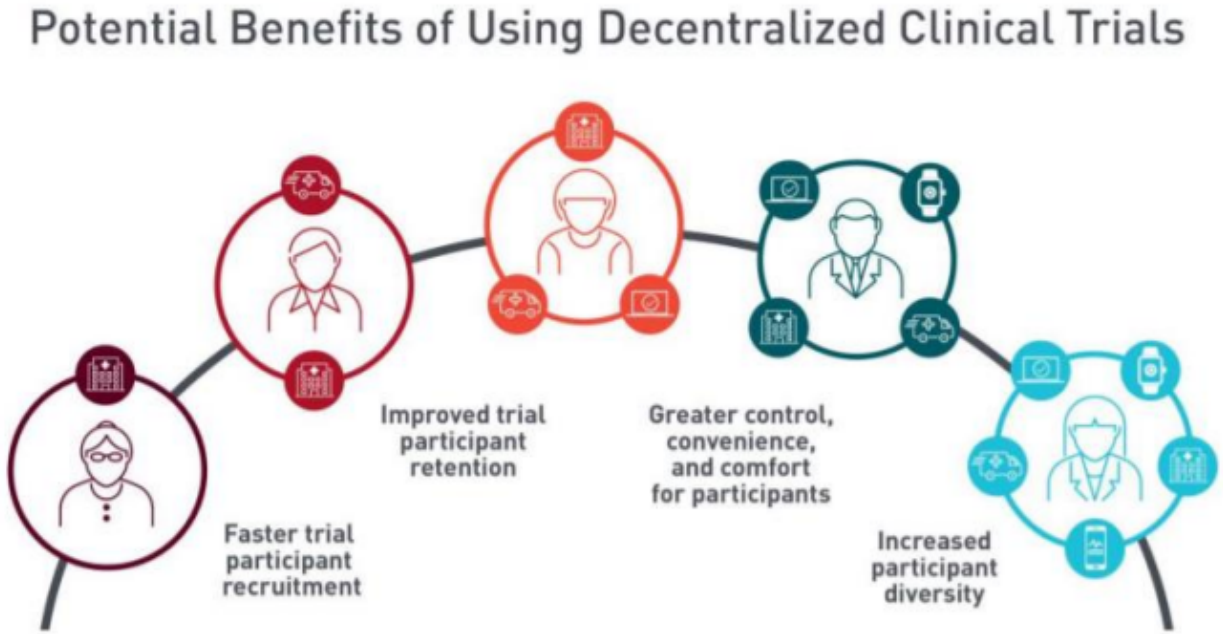
Facilitating and Encouraging Innovation

e.g., Decentralized Clinical Trials (DCTs)

A clinical trial where some or all the trial-related activities occur at a location separate from the investigator's location

Potential benefits:

- Patient convenience (avoiding travel to sites, time off work, etc.)
- Improved inclusivity (patients with mobility, cognitive and economic challenges)
- Ability to study patients in widespread locations (rare or sporadic diseases)



FDA Will Issue a Guidance on DCTs

https://ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_DCT_Recs.pdf

Traditionally, clinical trials have been conducted at specific clinical trial sites, to which patients had to travel to. The aim of DCTs is to make it easier for patients to participate in clinical trials by reducing the need to travel to central trial sites. This approach has the potential to make clinical trials available to a wider demographic of participants and reduce drop-out rates.

Decentralisation is enabled by the advancement of digital tools, telemedicine and more mobile and local healthcare. It includes aspects such as home health visits, remote monitoring and diagnostics, direct-to-patient shipment of study drugs and electronic informed consent.

Exhibit 1

Decentralized clinical trials meet patients where they are.

Clinical-trial designs

Fully decentralized		Hybrid		Fully centralized
All trial procedures are conducted virtually, enabled by digital technologies and supply delivery	Less complex trial procedures that don't require in-person visits (eg, vital signs, electrocardiograms) are conducted via telehealthcare, remote data collection, or direct-to-patient supply	Less complex trial procedures that require in-person visits (eg, injections) are conducted via mobile clinicians or alternative sites (eg, mobile clinics, retail sites)	Complex trial procedures (eg, complex screening protocols, cell therapy, magnetic resonance imaging) are conducted via research sites (eg, academic medical centers) or local hospitals	All trial procedures are conducted at a research site (eg, academic medical center)

McKinsey & Company

DCT (Decentralized Clinical Trial)

- **Study participant visit :**
  - ✓ eConsent
  - ✓ TeleHealth
  - ✓ Home Visit, Mobile Clinical
  - ✓ Study drug direct to participant, Clinical Trial Pharmacy
  - ✓ Participant self sample collection
  - ✓ Local labs
  - ✓ …
- **Study data collection :**
  - ✓ Wearable biosensors devices, Apps
  - ✓ E-diary
  - ✓ …
- **Study data monitoring (Virtual monitoring – SDV/SDR):**
  - ✓ eSource (data transfer from institution EMR to sponsor database)
  - ✓ EMR direct access (from outside of institution)
  - ✓ Uploading source into secured cloud
  - ✓ Webex, Video call showing sources on screen or via webcam or shared control
  - ✓ …

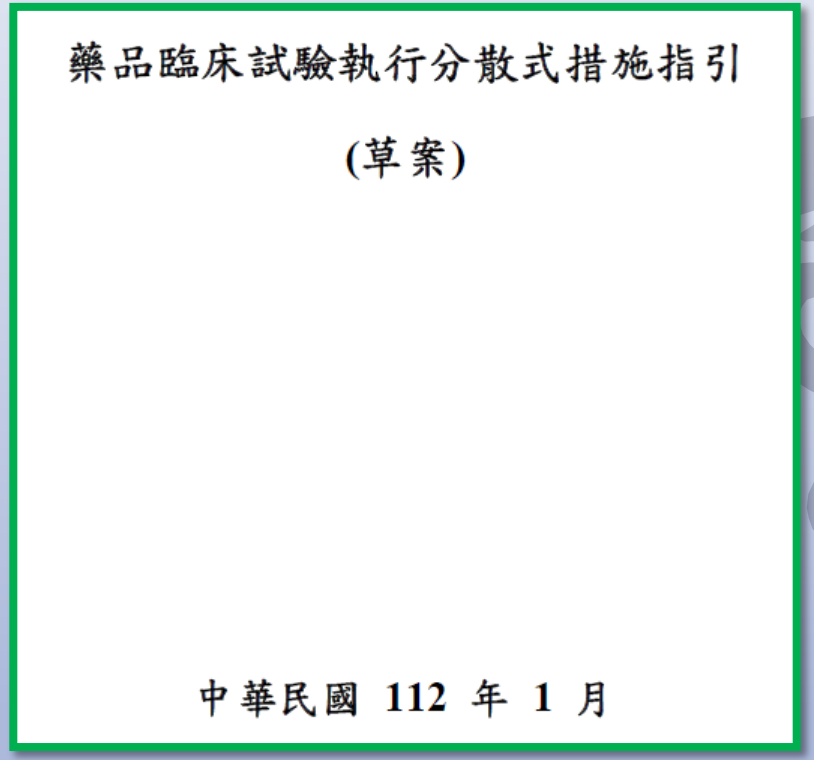
Mobile clinics are the latest decentralized site innovation and an alternative to the traditional clinical trial study site. They offer increased convenience and flexibility for participants while reducing the travel burden. In addition,

Insert the lumbar-worn device into the belt clip button-side first and push down to secure. To remove the device, hold the back of the belt clip and pull the corner of device to release from the clip.

Smart blister pill pack

DCT (DECENTRALIZED CLINICAL TRIAL)

TFDA 草案

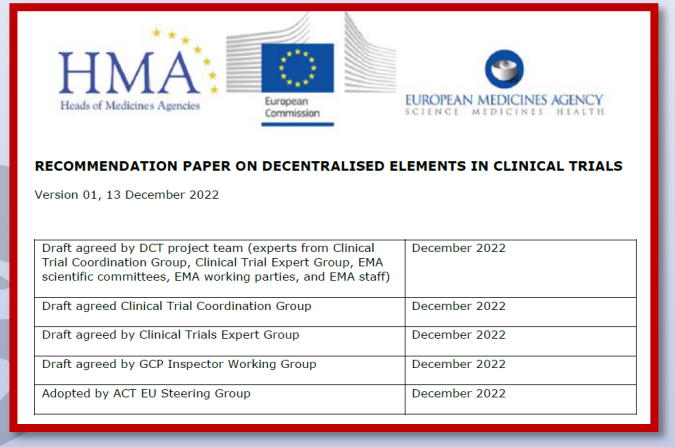


藥品臨床試驗執行分散式措施指引

(草案)

中華民國 112 年 1 月

Facilitating Decentralised Clinical Trials in the EU | European Medicines Agency (europa.eu)



HMA Heads of Medicines Agencies

European Commission

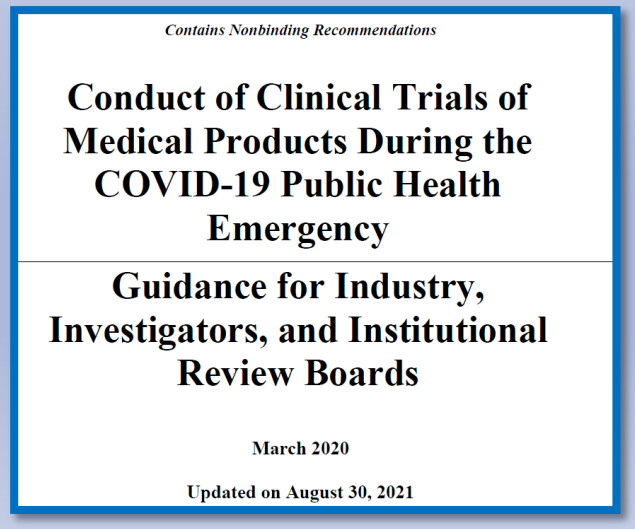
EUROPEAN MEDICINES AGENCY SCIENCE MEDICINES HEALTH

RECOMMENDATION PAPER ON DECENTRALISED ELEMENTS IN CLINICAL TRIALS

Version 01, 13 December 2022

Draft agreed by DCT project team (experts from Clinical Trial Coordination Group, Clinical Trial Expert Group, EMA scientific committees, EMA working parties, and EMA staff)	December 2022
Draft agreed Clinical Trial Coordination Group	December 2022
Draft agreed by Clinical Trials Expert Group	December 2022
Draft agreed by GCP Inspector Working Group	December 2022
Adopted by ACT EU Steering Group	December 2022

FDA Guidance on Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency | FDA



Contains Nonbinding Recommendations

Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency

Guidance for Industry, Investigators, and Institutional Review Boards

March 2020

Updated on August 30, 2021

Even It wasn’t yet confirmed if site will be selected or not during Pre-Study Visit

But being readiness will help speed up the process and your International Competitiveness ~

Submission timelines

Asia-Pacific Country Regulatory Timeline

Figure 15: Regulatory Timelines for Clinical Trials by Location, Asia-Pacific, 2020

Source: Novotech

Asia-Pacific Clinical Trials - White Paper - Frost & Sullivan (frost-apac.com)

Challenges for submission-Taiwan

- Obtain all study documents (including local language translation estimation time) including signature package from PIs. (1M-1.5Months)
- Contract negotiation with PIs and institution as early as possible
- Contract can be negotiated in parallel with IRB submission, but for some hospitals, the sealing process ~~is~~ can only be started after IRB approval. (additional 2-3 weeks)

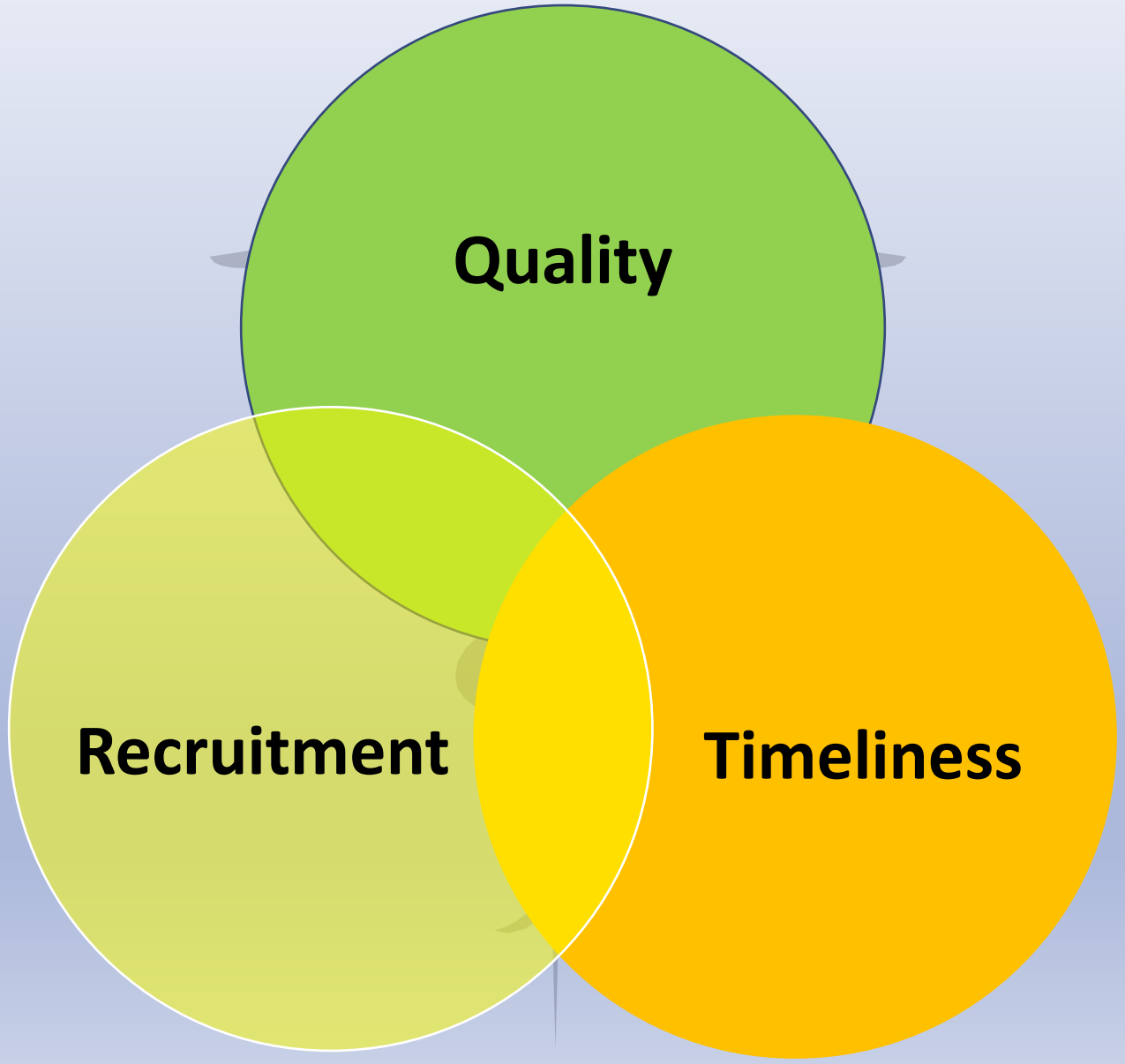
Site Initiation Visit

Site Initiation Visit (Site ready for enrolment)

Approval for study site	Staff Qualification and Facility	Timelines and Process discussion
Written of RA / IRB approval	Study Training completion	Review study timelines and site recruitment goals
Contract Fully Executed	IP on site	Safety definitions and reporting process review
Import License	Signature and delegation log completion	Data entry timelines
Others License (NCC..etc)	Site Facilities (quality control/ calibration)	Monitoring Space
Biosafety Approval	Study Materials ready on site	
	Documents Storage	

READY FOR RECRUITMENT

During Clinical Trial



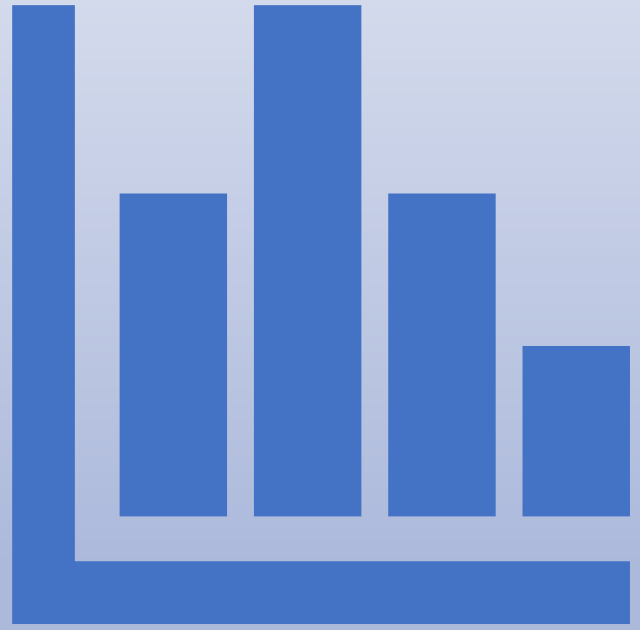
During Clinical Trial

- ✓ Recruitment
  - Know the inclusion/exclusion criteria
  - Personal patients
  - Referrals
  - Consider previous experience with advertising
- ✓ Retention
  - Understand participants needs
  - Don't forget families and care partners
  - Provide incentives for participants
  - Provide easy tools and materials to participants
- ✓ Data Collection (ALCOACCEA)
  - Accurate source and on time data entry to be done correct at once
- ✓ Be Ready for audit, inspection

The delay recruitment and delay data entry brings the delay of drug development to patient's

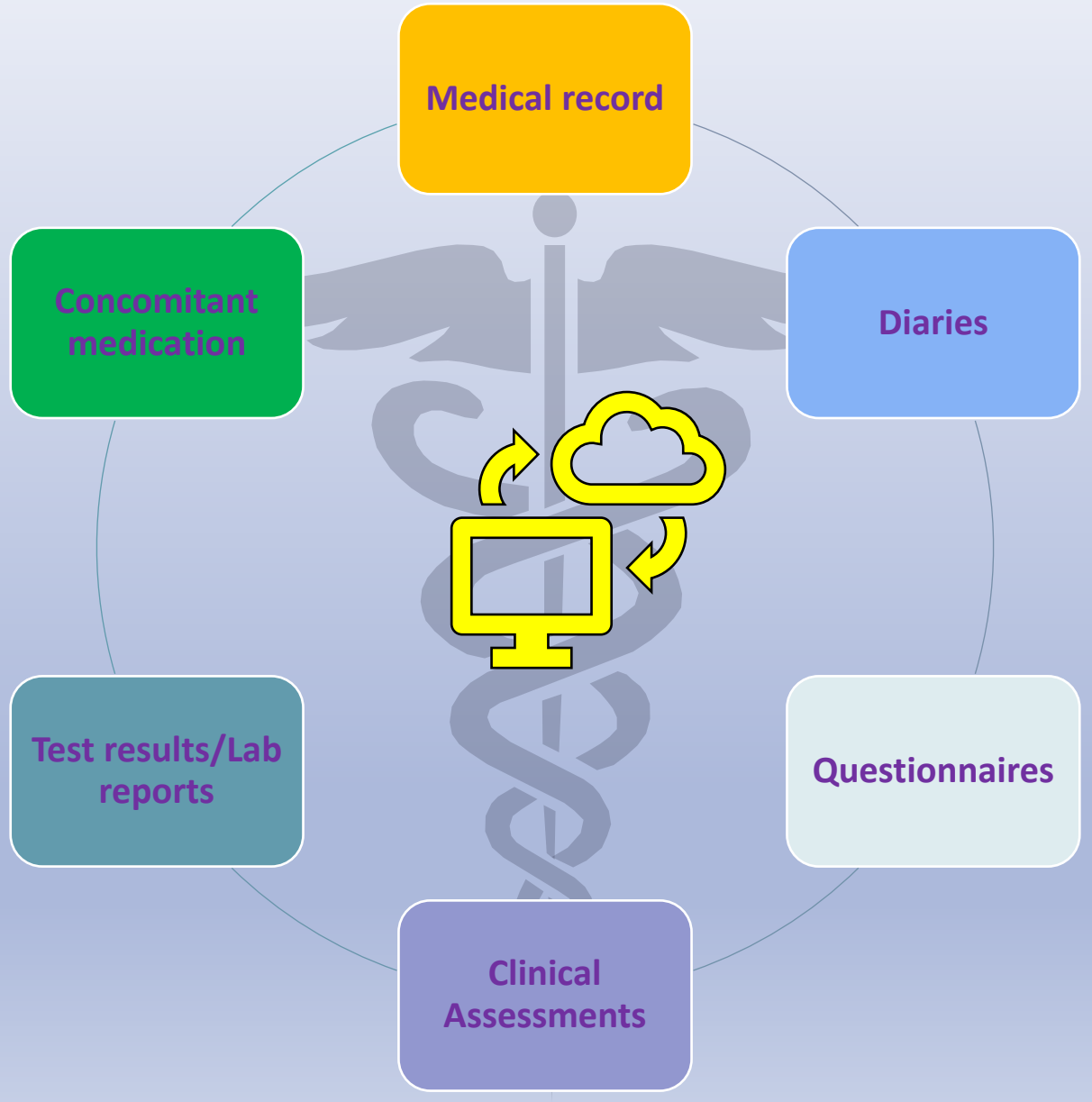
If it's not written down, it didn't' happen

"Well, if you don't have time to do it right, what makes you think you'll have time to do it over?"

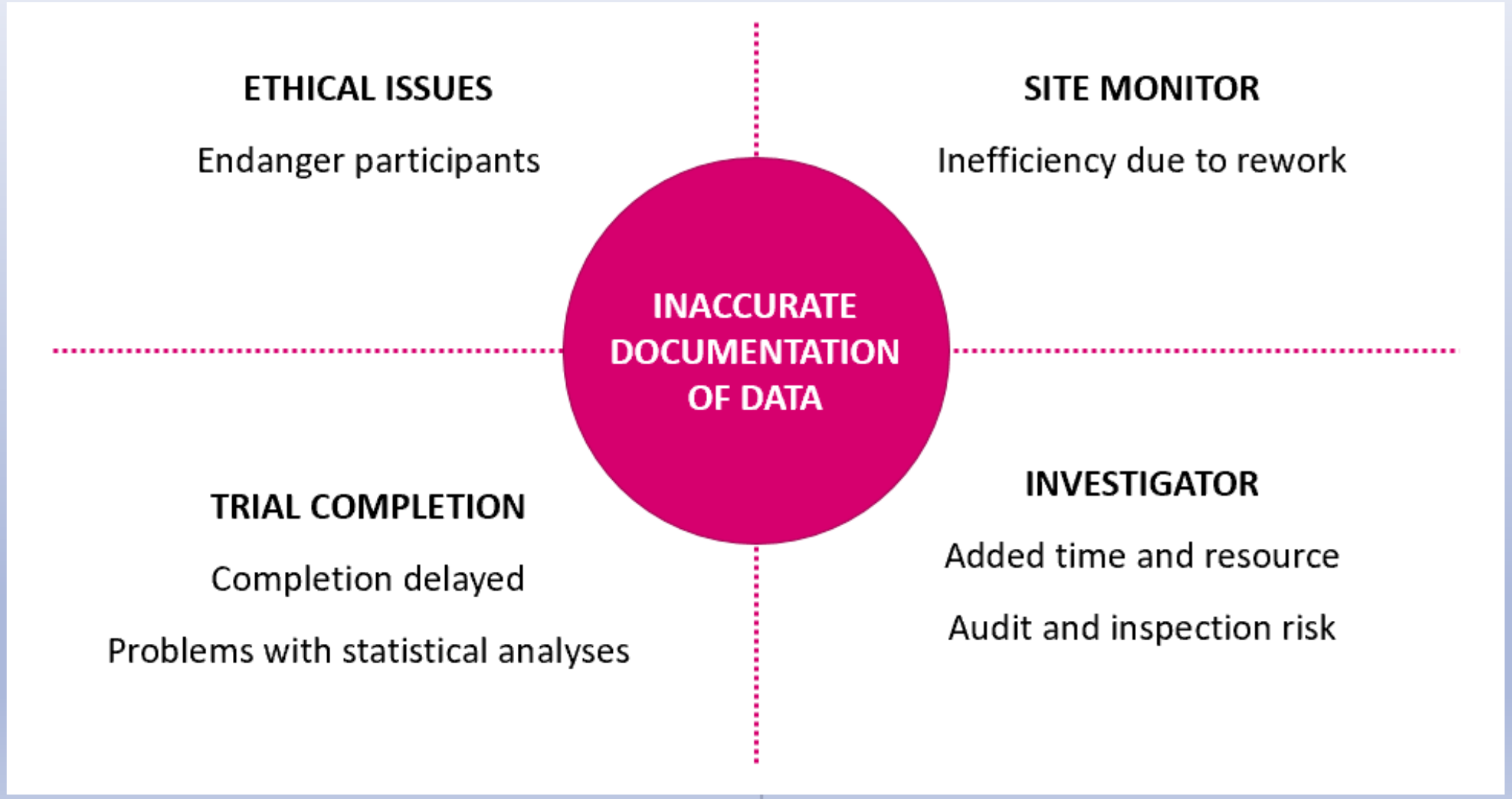


Data Reporting

Data Reporting



Consequences of inaccurate data



Clinical Study Report

- A written description of a trial/study of any therapeutic, prophylactic, or diagnostic agent conducted in human subjects, in which the clinical and statistical description, presentations, and analyses are fully integrated into a single report (ICH E6 1.13)

✓ CSR will support a New Drug Application

✓ New Drug Application will lead to GCP inspections

Take away note

- Key points to increase the clinical trials competitiveness
  - ✓ Regulatory support (e.g.; DCT environment build up)
  - ✓ Institution support to speed up the start up review cycle (IRB/EC and Contract)
  - ✓ Site facility (e.g.; clinical trial space, pharmacy setting, monitoring space..etc) to be flexible and friendly
  - ✓ Good tracked record on recruitment performance
  - ✓ Good quality for data and on time data entry
  - ✓ Investigators awareness and operations staff's resource

A better environment shaping for Taiwan

THANK YOU

for your participation!

Reference:

1. ICH GCP E6
2. FDA Guidance on Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency | FDA
3. Facilitating Decentralised Clinical Trials in the EU | European Medicines Agency (europa.eu)
4. Home - ClinicalTrials.gov
5. Regulatory timelines in the Asia-Pacific – George Clinical
6. KONECT 국가임상시험지원재단
7. Asia-Pacific Clinical Trials - White Paper - Frost & Sullivan (frost-apac.com)