A Multi-center Clinical Trial Monitoring System Based on CDISC Standards

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Meet the Speaker

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Seoul National University Hospital, Research professor (2024-current)

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Disclaimer and Disclosures

- The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.

- The author have no real or apparent conflicts of interest to report.

Agenda

1. Considerations in multi-center clinical trial monitoring system
2. Decentralized clinical trials
3. Strategies for implementing CDISC standards

Considerations in multi-center clinical trial monitoring system

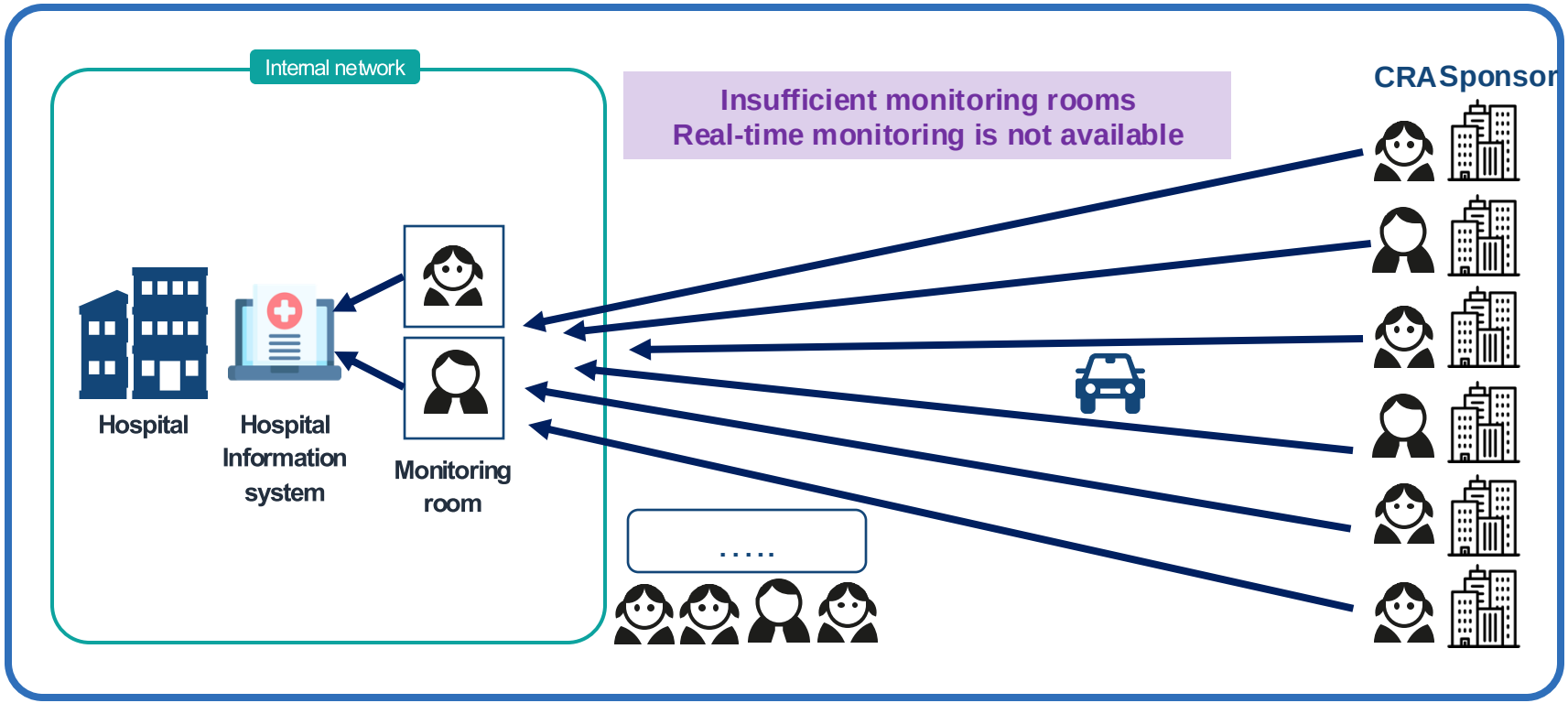
This section will address the current issues and potential solutions for the remote monitoring system.

Monitoring in Clinical Trials

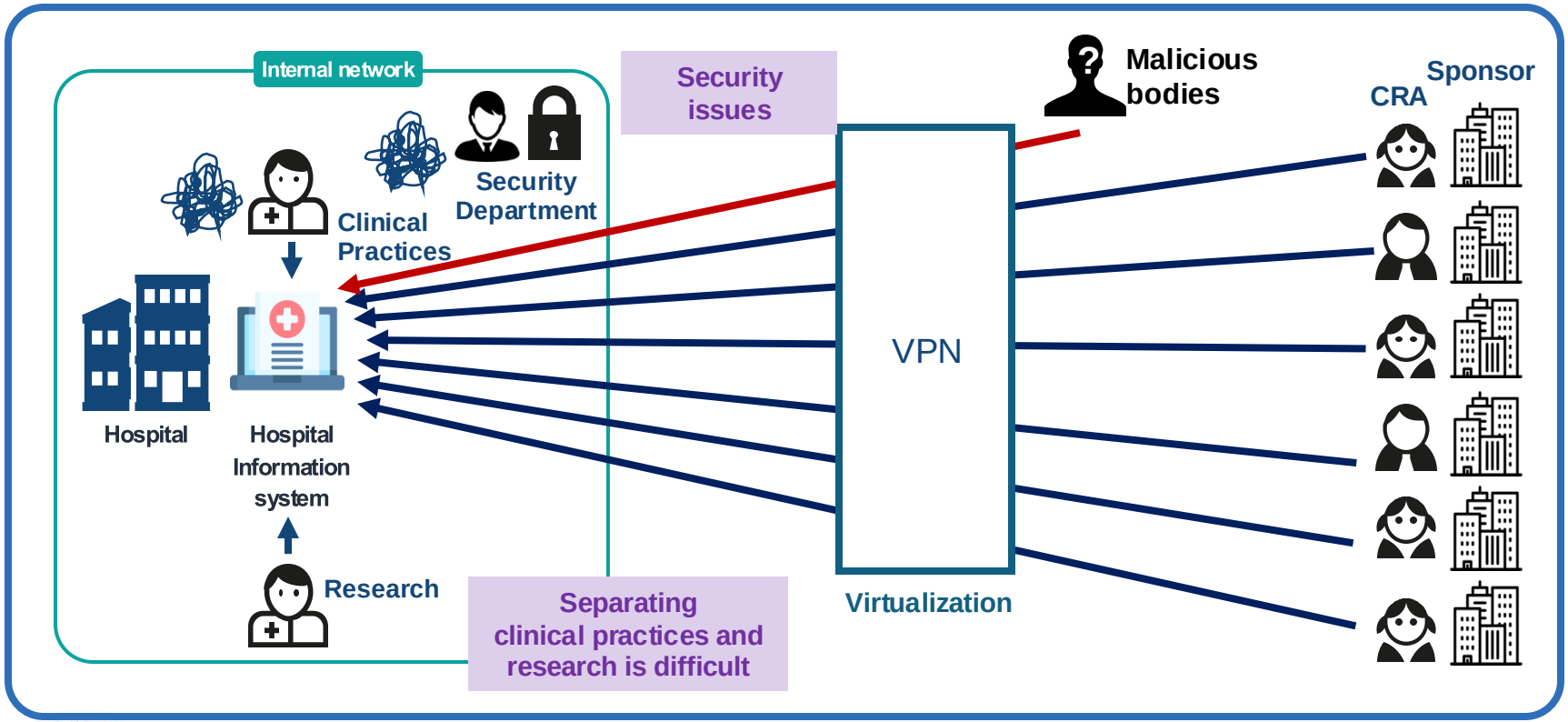
Trial monitoring

- Ensures the reliability of trial results as the trial progresses
- Principal quality control activities
- Performed in relation to the clinical trial activities at the investigator site
- Typically involves considerable manual works

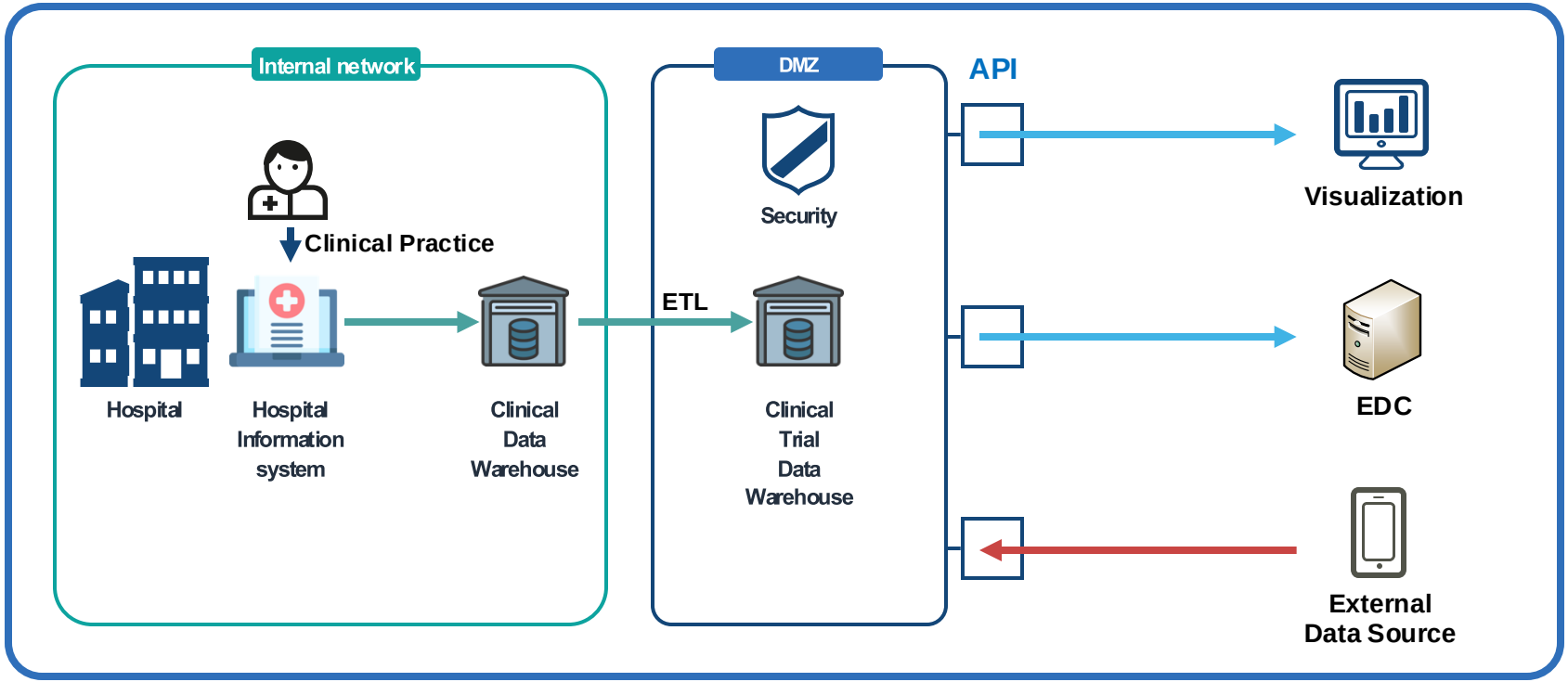
Current status in Korea



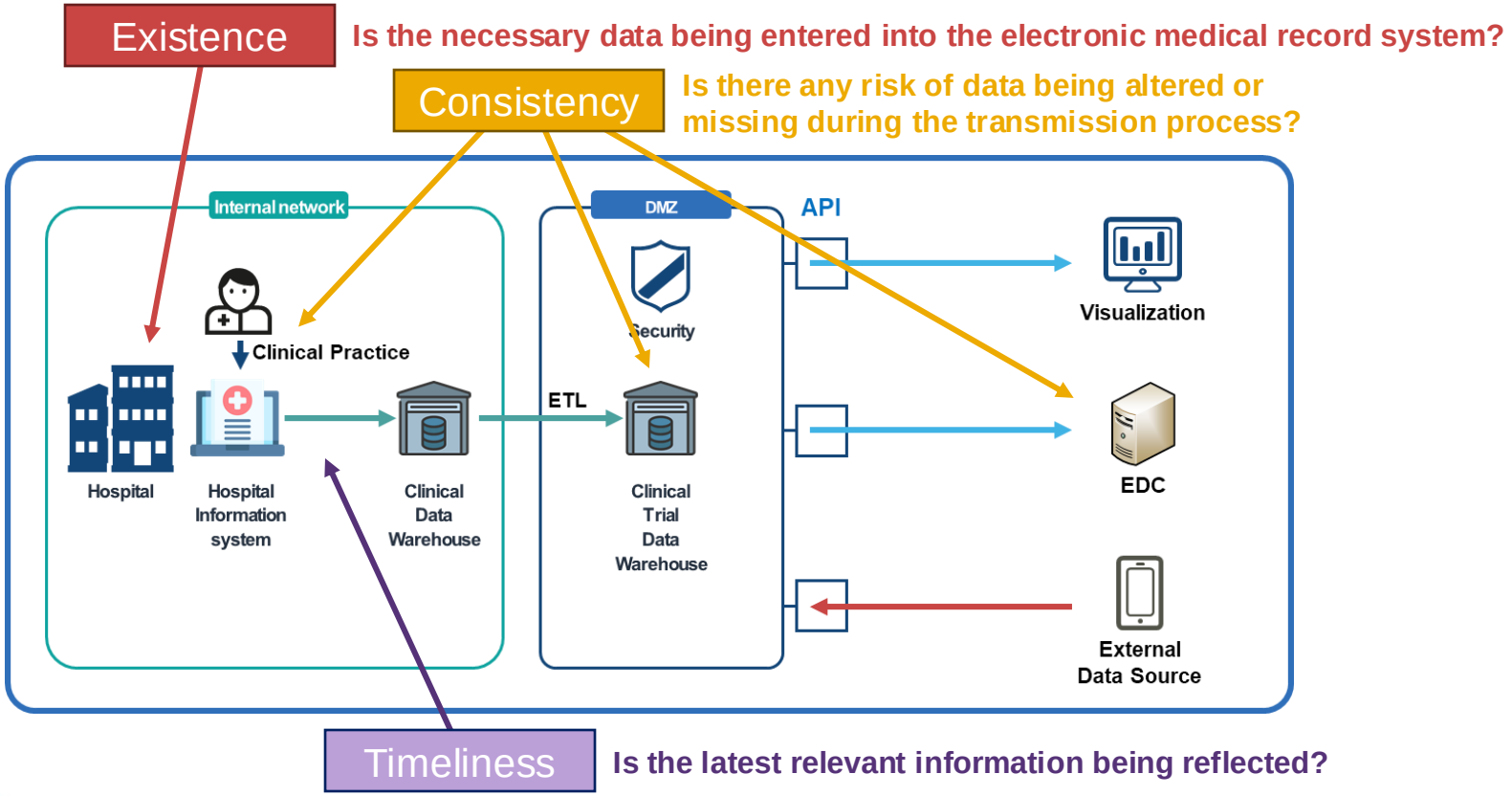
Solution 1: Direct access



Solution 2: Data warehouses-based systems



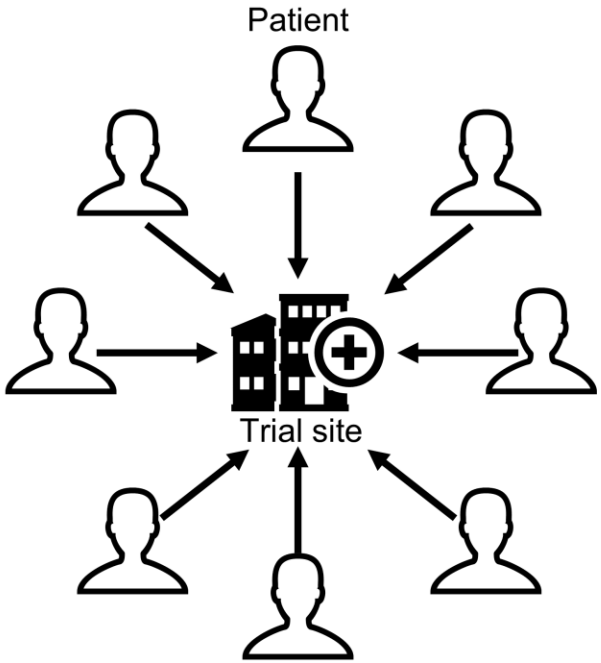
Key considerations



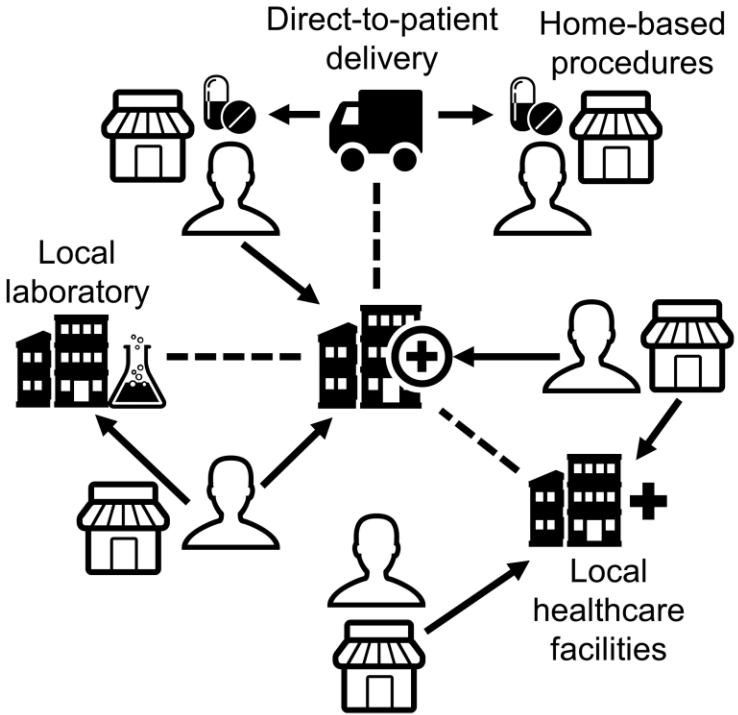
Decentralized clinical trials

This section will discuss the expected changes in trial monitoring in the era of decentralized clinical trials.

Decentralized Clinical Trials (DCTs)



Conventional clinical trial



Decentralized clinical trial

Remote monitoring in DCTs

ICH E6 (R3) Guideline for Good Clinical Practice

3.11.4.1 Investigator Site Monitoring

(a) Monitoring may be performed in relation to the clinical trial activities at the investigator sites (e.g., including their pharmacies and local laboratories, as appropriate). The frequency of monitoring activities should also be determined based on identified risks. Monitoring activities and their frequency should be modified as appropriate using knowledge gained.

(b) This monitoring activity may be performed on-site or remotely depending on the nature of the activity and its objectives.

(c) Monitoring may include secure, remote, direct read-only access to source records, other data acquisition tools and essential record retention systems.

Remote monitoring in DCTs

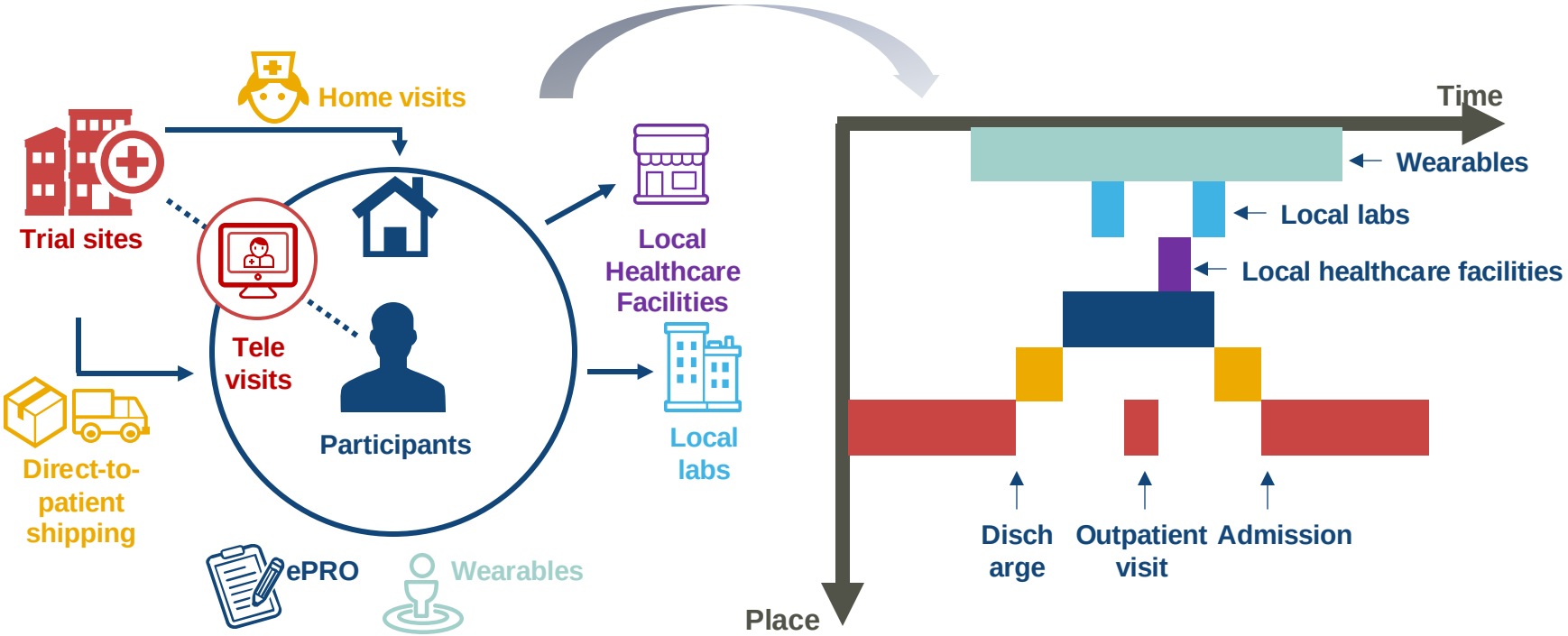
ICH E6 (R3) Guideline for Good Clinical Practice

- Annex-2

The proposed development of Annex 2 will include additional considerations on how GCP principles may be applied across a variety of trial designs and data sources, where applicable. This will include:

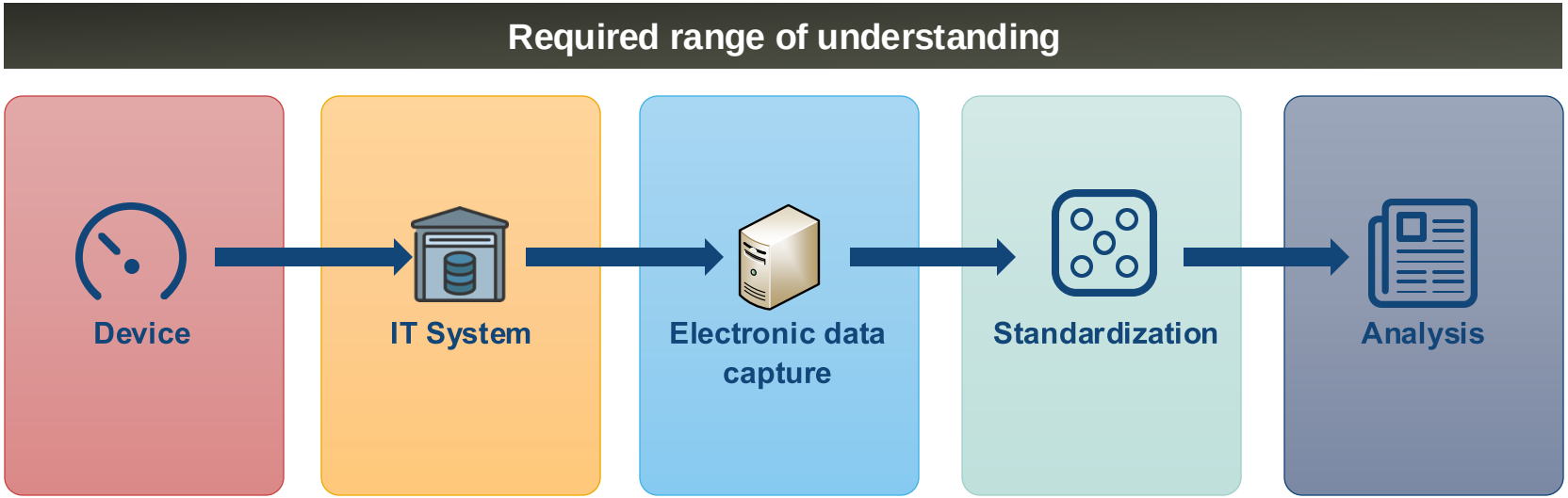
1- Decentralised elements, where some or all trial-related activities occur at locations other than traditional clinical trial sites, such as patient homes, mobile trial units, or local clinics, and data collection may occur remotely.
2- Pragmatic elements, reflecting trials that closely resemble routine clinical practice.
3- Real-world data (RWD) sources[2], for example, the use of registries, electronic health records (EHR), hospital data, pharmacy and medical claims data or wearables.

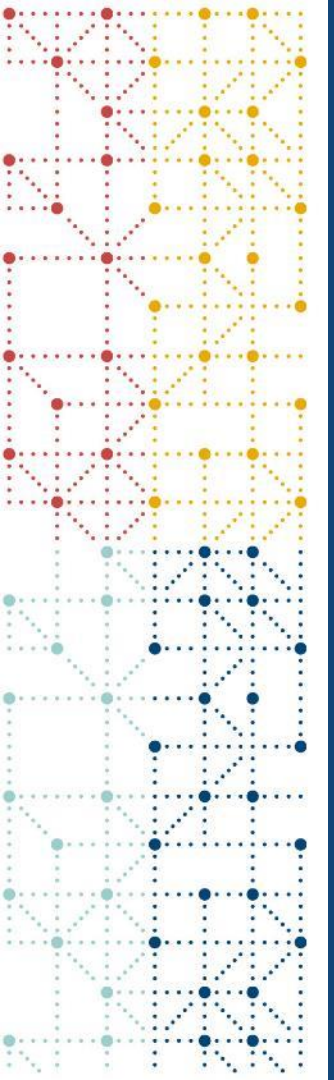
Data integrity issues in DCTs



Chain of validation DCTs

More comprehensive understanding of data is required





Strategies for implementing CDISC standards

This section will discuss how CDISC standards can be implemented in multi-center clinical trial monitoring.

Why CDISC in DCTs?

Expand & Connect

- Embrace and adopt digital study design
- Expand and connect standards across the clinical research information lifecycle
- Define clear pipeline for integration of new data sources

Enable & Automate

- Develop ready to use implementation standards
- Create open-source technology enabled standards
- Establish and manage a conformance framework

Engage & Adopt

- Establish a continuous feedback loop across the CDISC community
- Shift focus to producers/consumers needs and lower the barrier to use
- Prioritize communication to enable our stakeholders

- **Digital health technologies are widely used in DCTs**
- **DCTs require multi-stakeholder collaboration**

https://www.cdisc.org/cdisc-roadmap

What “standards” would be used?

Foundational

BRIDG

SEND

CDASH

SDTM

SDTMIG

ADaM

Analysis Results

Tobacco IG

QRS

Medical Devices

Data Exchange

CTR-XML

Dataset-JSON

Dataset-XML

Define-XML

LAB

ODM

RDF

SDM-XML

Terminology

Glossary

Controlled Terminology

NSV Registry

Digital Data Flow

USDM

Therapeutic Areas

Alphabetical

By Disease Area

Published User Guides

Trial Master File

TMF Reference Model

Exchange Mechanism

Standards

Standards Timeline

In Development

Public Reviews

Standards in Development

CDISC 360

CORE

CDISC Biomedical Concepts

Digital Health Technologies

TIG eSubmission Pilot

CDISC Library

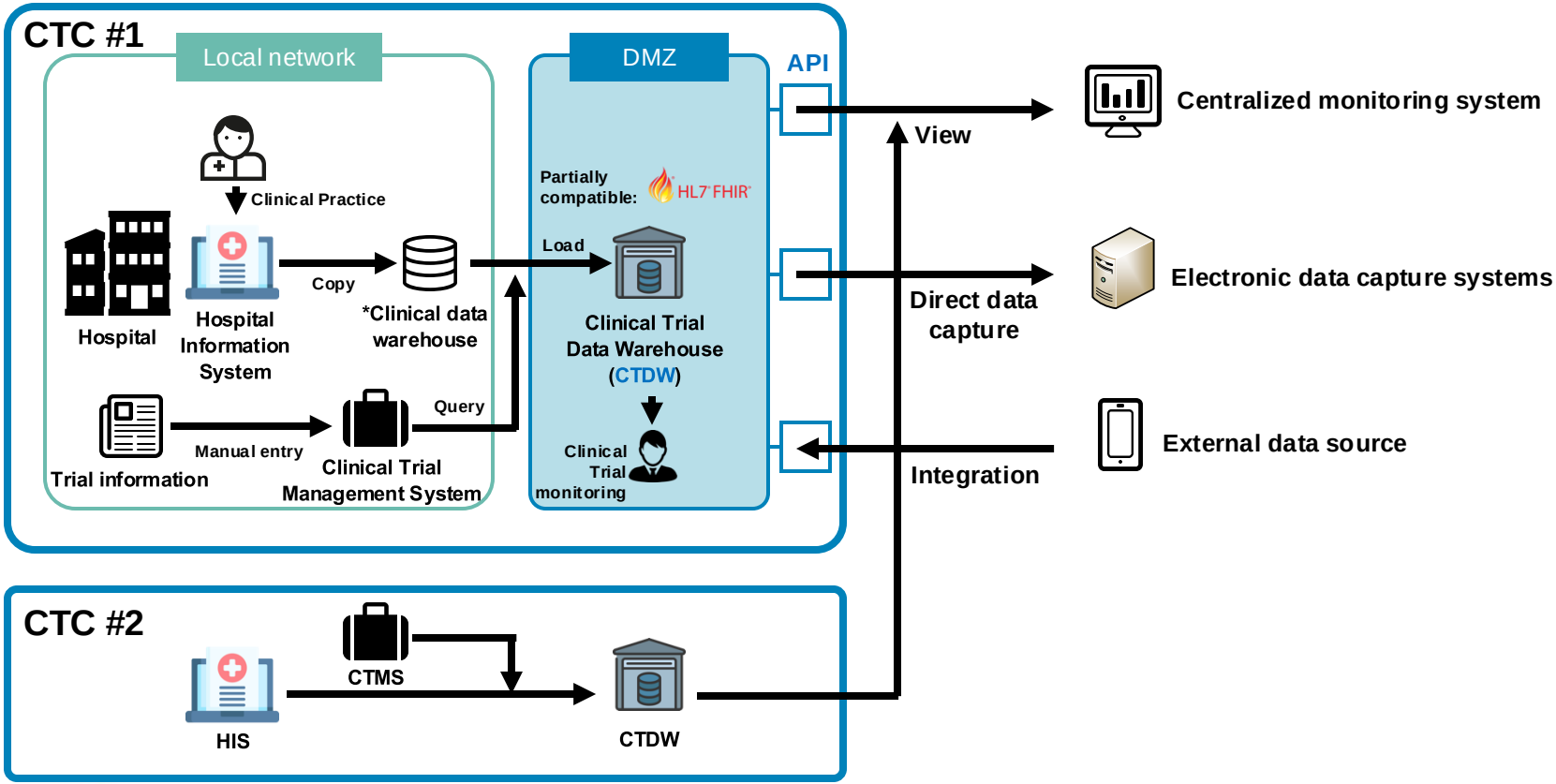
CDISC Library

Real World Data

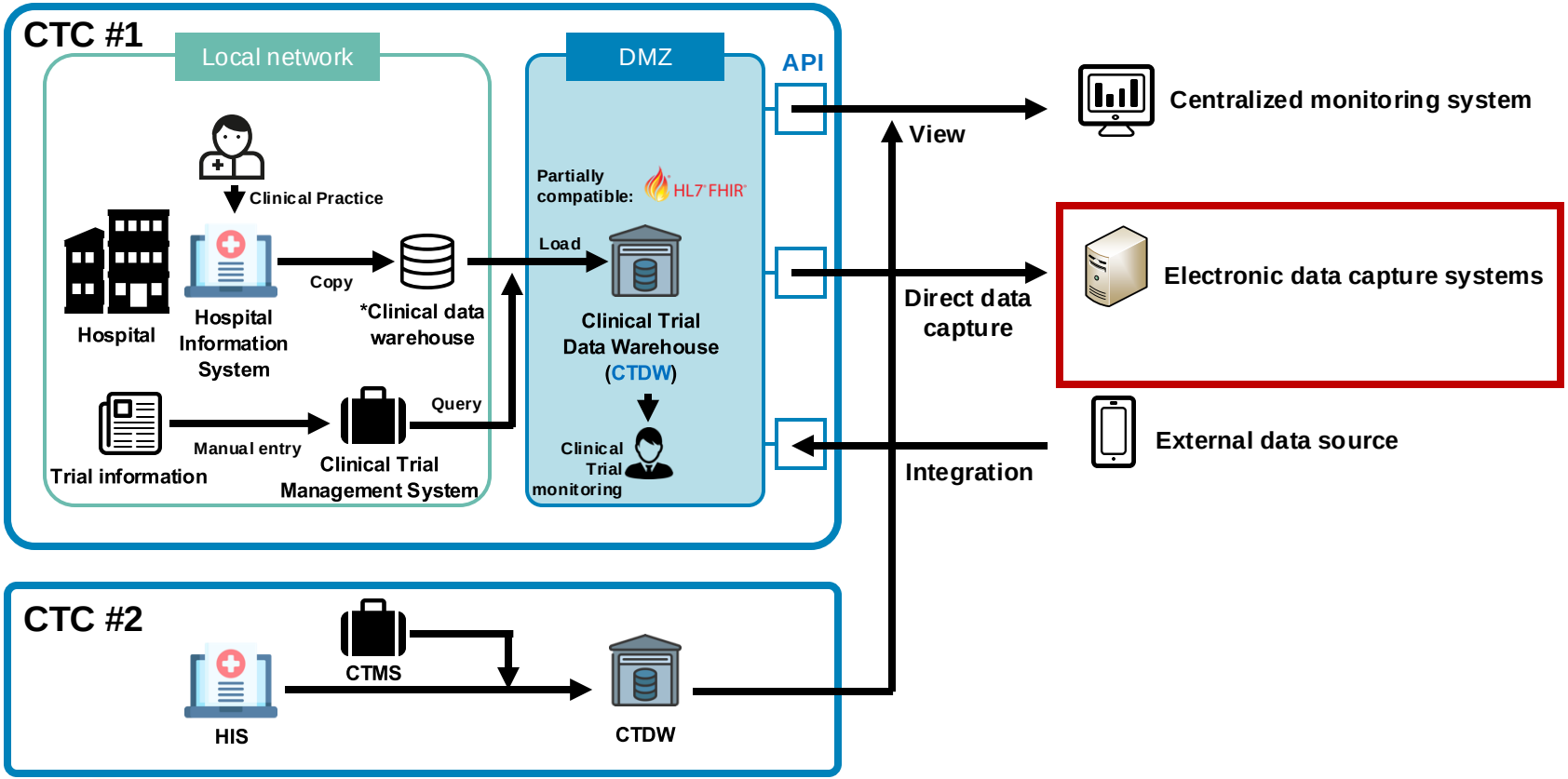
FHIR-CDISC

Vaccine Administration

DECENT project @SNUH



1) Electronic data capture



SDTM

- **During COVID-19**

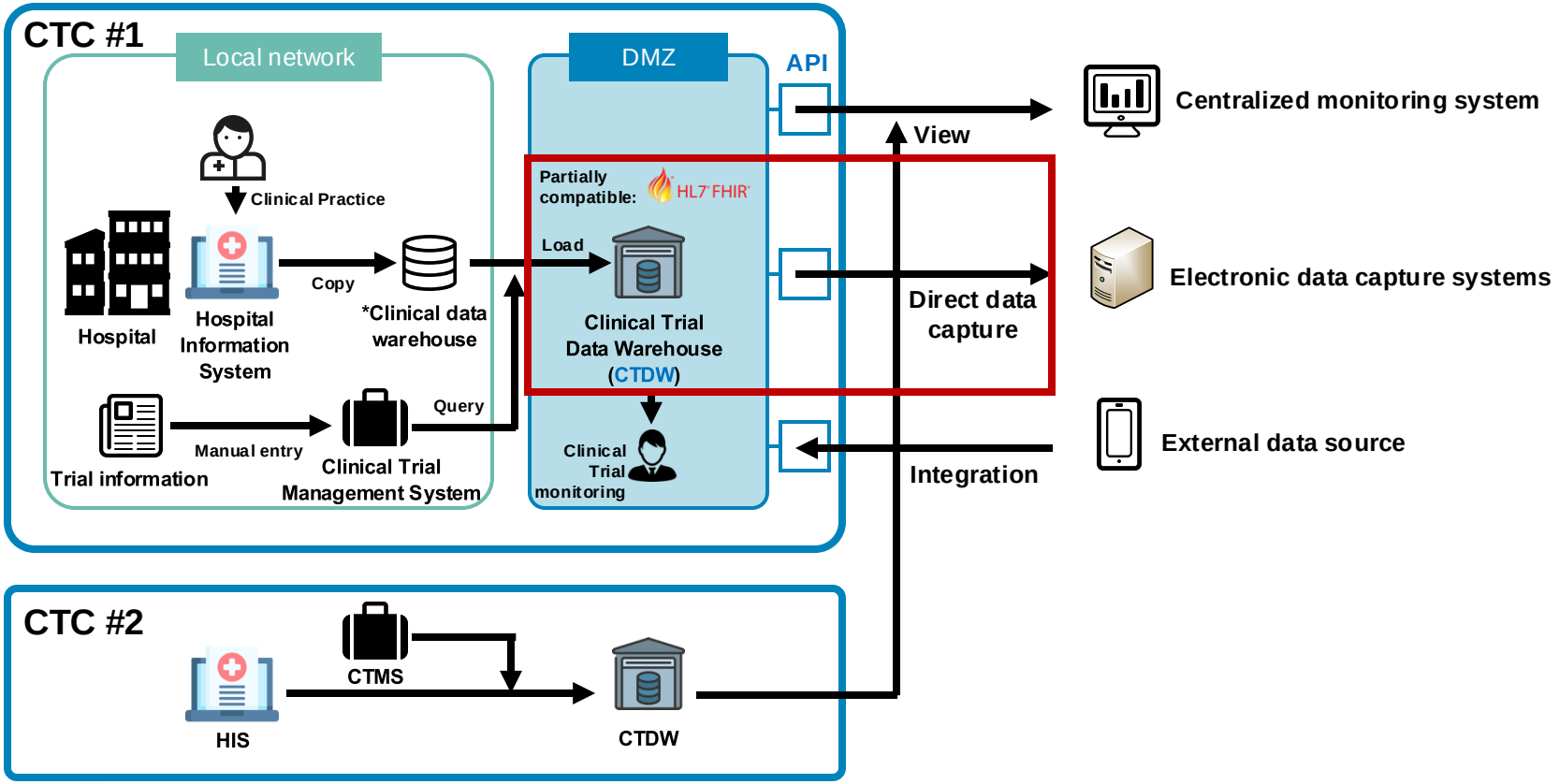
(…) including information about missed visits and about contacts that might not be conventionally thought of as visits, such as phone calls, would be useful

- Subject Visit (SV) as an events domain (SDTMIG v3.4)

SVREASOC	Reason for Occur Value	The reason for the value in SVOCCUR. If SVOCCUR="N", SVREASOC is the reason the visit did not occur.
SVCNTMOD	Contact Mode	The way in which the visit was conducted. Examples: "IN PERSON", "TELEPHONE CALL", "IVRS".
SVEPCHGI	Epi/Pandemic Related Change Indicator	Indicates whether the visit was changed due to an epidemic or pandemic.
VISITDY	Planned Study Day of Visit	Planned study day of VISIT. Should be an integer.

https://www.cdisc.org/kb/articles/subject-visits-and-covid-19

2) Direct data capture



FHIR-CDISC Joint Mapping

Convert data between HL7 FHIR and CDISC standards

- HL7 FHIR is commonly used in clinical systems
- CDISC is commonly used to submit clinical trial data for analysis and regulatory approval

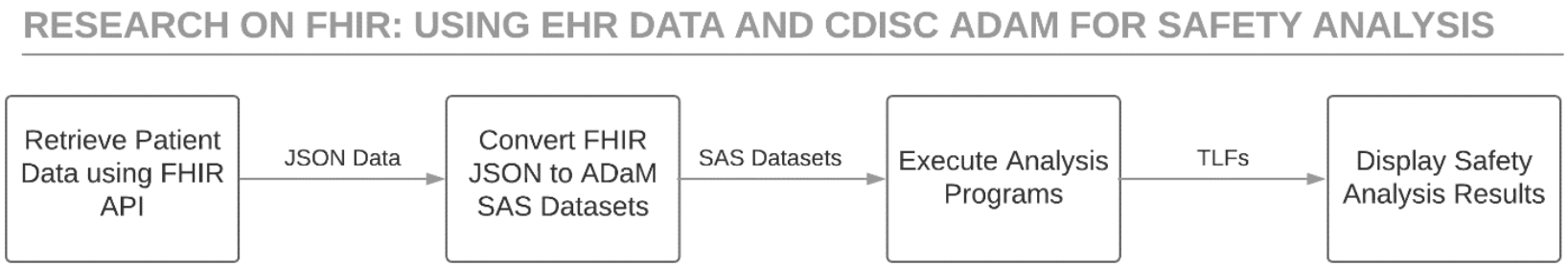
FHIR to CDISC Joint Mapping Implementation Guide
1.0.0 - STU 1

- Allow trial-driven data capture to occur directly inside clinical systems rather than separate clinical trial management solutions, leveraging technologies like SMART on FHIR.
- Can support the creation of case report forms (CRFs) that link to data elements defined using FHIR resources and profiles.

ADaM

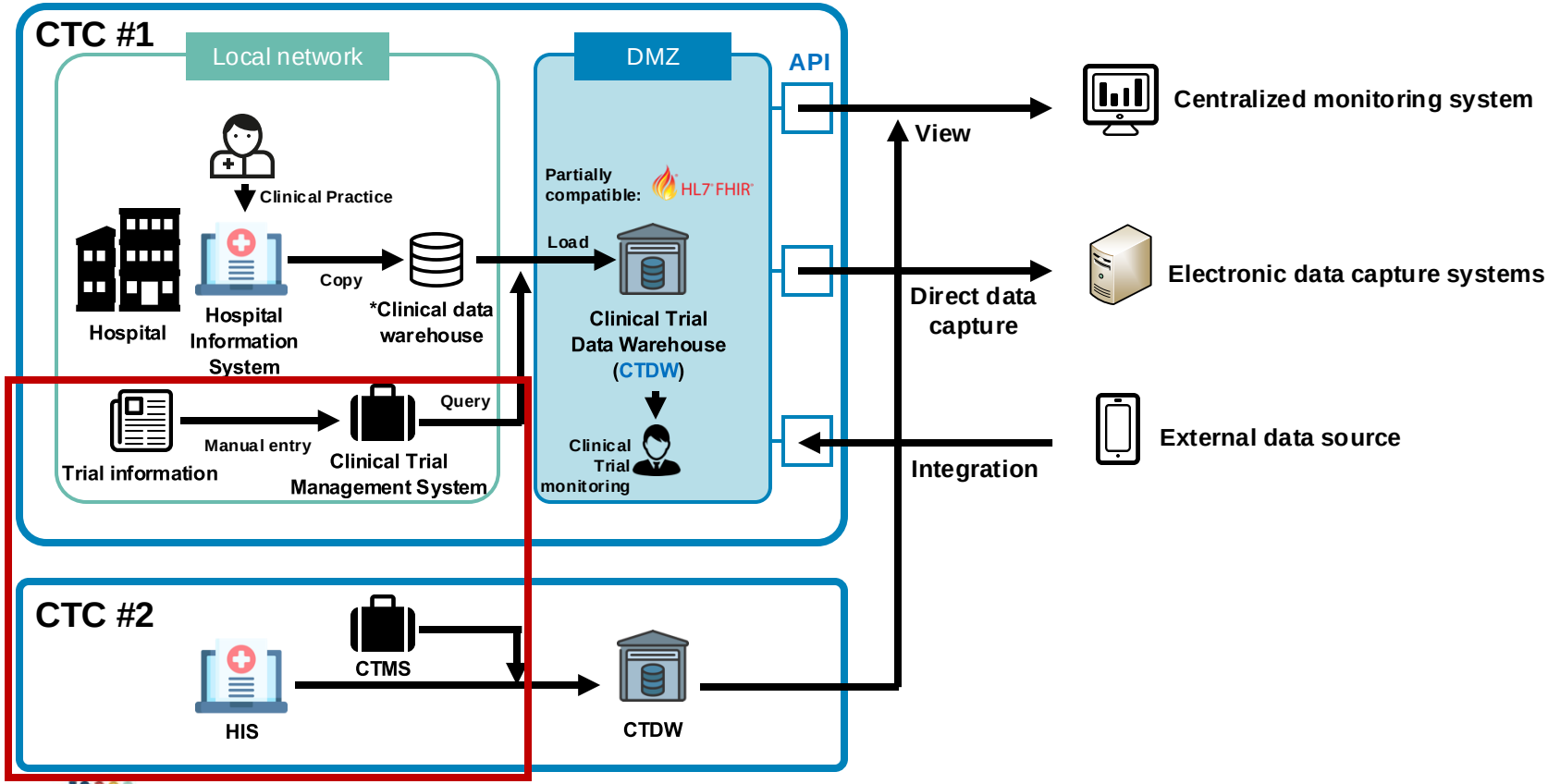
Specifies data and metadata structures to support the efficient generation and replication of analyses

- Mapping from the FHIR standards to ADaM
- Can streamline the data flow from data collection to analysis



https://www.cdisc.org/kb/articles/use-fhir-clinical-research-electronic-medical-records-analysis

3) Trial information



Clinical Trial Management System

Key infrastructure that manages trial conducts

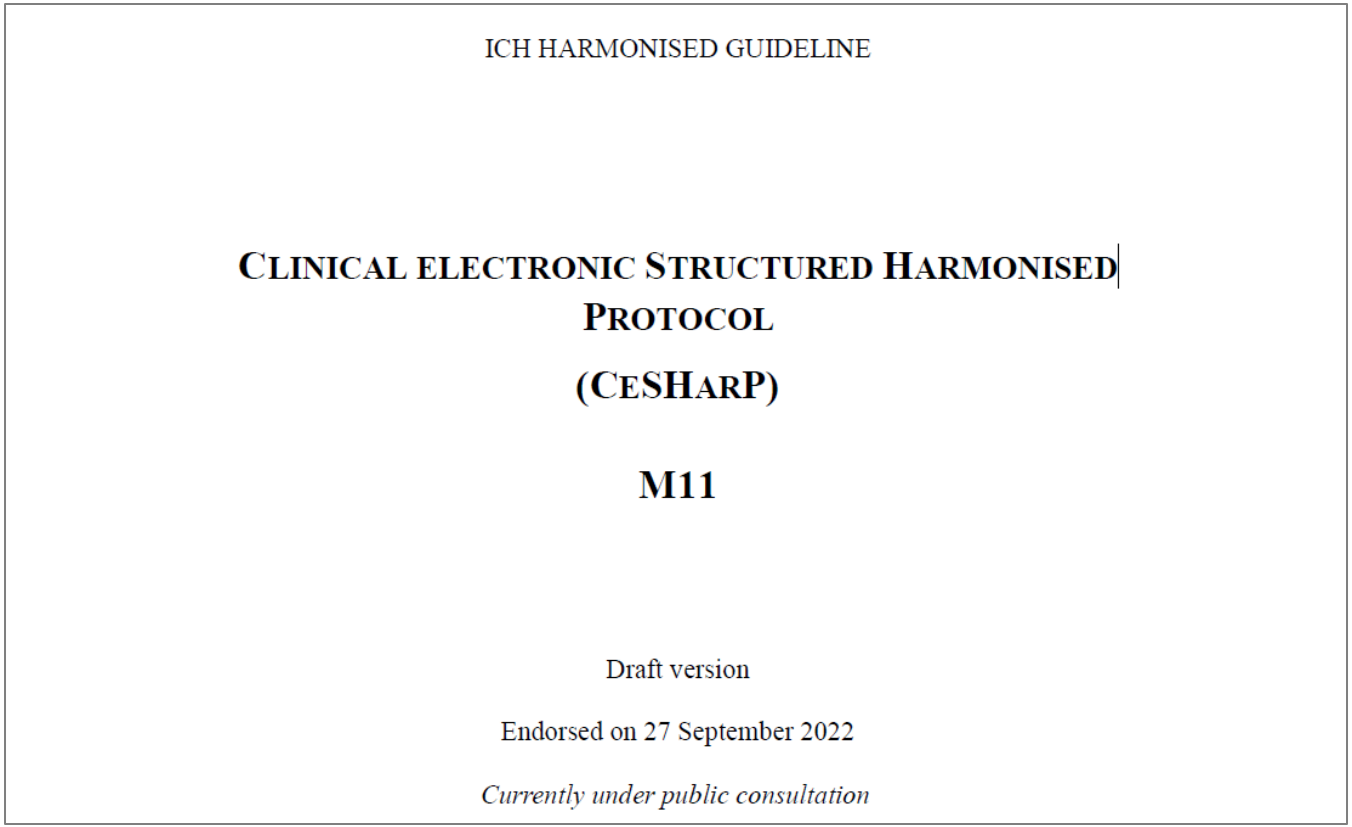
Requires machine-readable information from study protocols

- Trial design
- Participants enrollment
- Study schedules
- Staff management

CTMS system @SNUH

항목 / Unit	1	2	3	4	5	6	7	memo
구분		입원기간	입원기간		입원기간	입원기간	외래기간	
병상시간		전일	오전		전일	오후		
Day	-28 ~ -1	1	2	3	8	9	12	
주요활동	Screening	Full-day	퇴원		Full-day	퇴원	종료방문(PSV)	
식이건수 아침		없음	치료식(1)		없음	치료식(1)		
식이건수 점심		치료식(1)	없음		치료식(1)			
식이건수 저녁		치료식(1)	없음		치료식(1)			
Window	+ 일 - 일	+ 0 일 - 0 일	+ 0 일 - 0 일	+ 일 - 일	+ 0 일 - 0 일	+ 0 일 - 0 일	+ 2 일 - 2 일	

ICH M11: CeSHarP



ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CESHARP)

M11

Draft version

Endorsed on 27 September 2022

Currently under public consultation

ICH M11: CeSHarP

Variability in format and core content among sponsors

- Contributes to inefficiencies and difficulties in searching, reviewing, and assessing clinical trial protocols.

Clinical Electronic Structured Harmonized Protocol

- Ensures harmonized data exchange format acceptable to the regulatory authorities.

USDM

USDM v3.0

- Ability to represent the draft ICH Clinical electronic Structured Harmonised Protocol (CeSHarP) developed by the ICH M11 group in USDM
- Add elements to expand population of SDTM trial design datasets
- Identify elements within USDM that can assist in population of trial planning elements for clinical trial registration in trial registries
- Addition of elements and model amendments required to represent structured study design information for more complex studies, including complex cohort trial designs
- Model enhancements to support use of the USDM and ensure consistency within the model

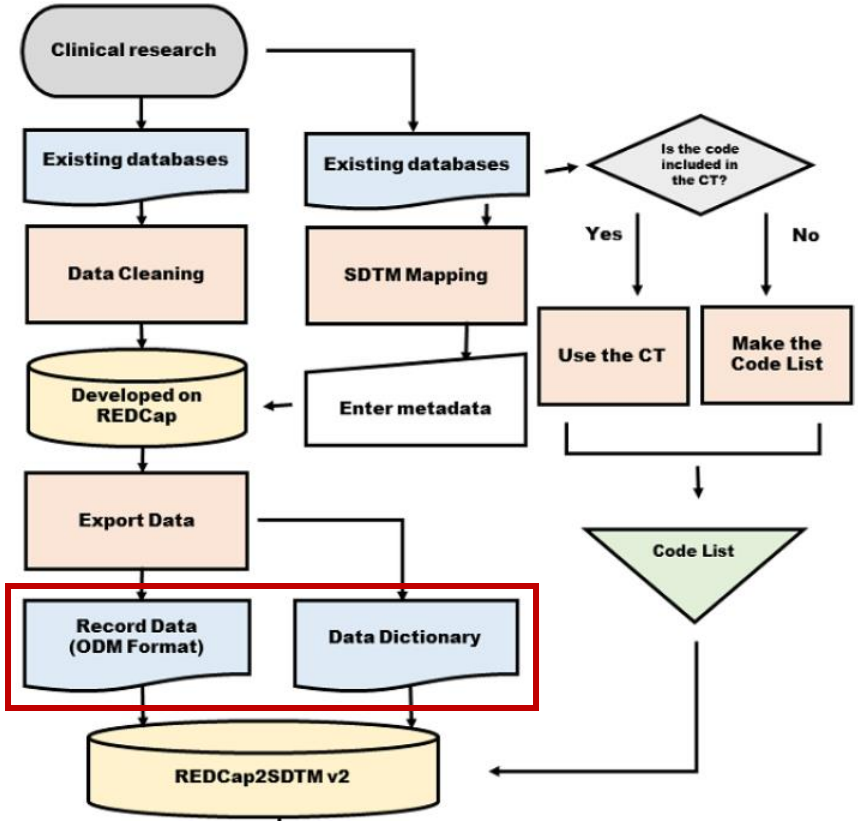
CTMS and CeSHarP

Efficient conversion to ‘machine-readable’ format

Reusable trial designs

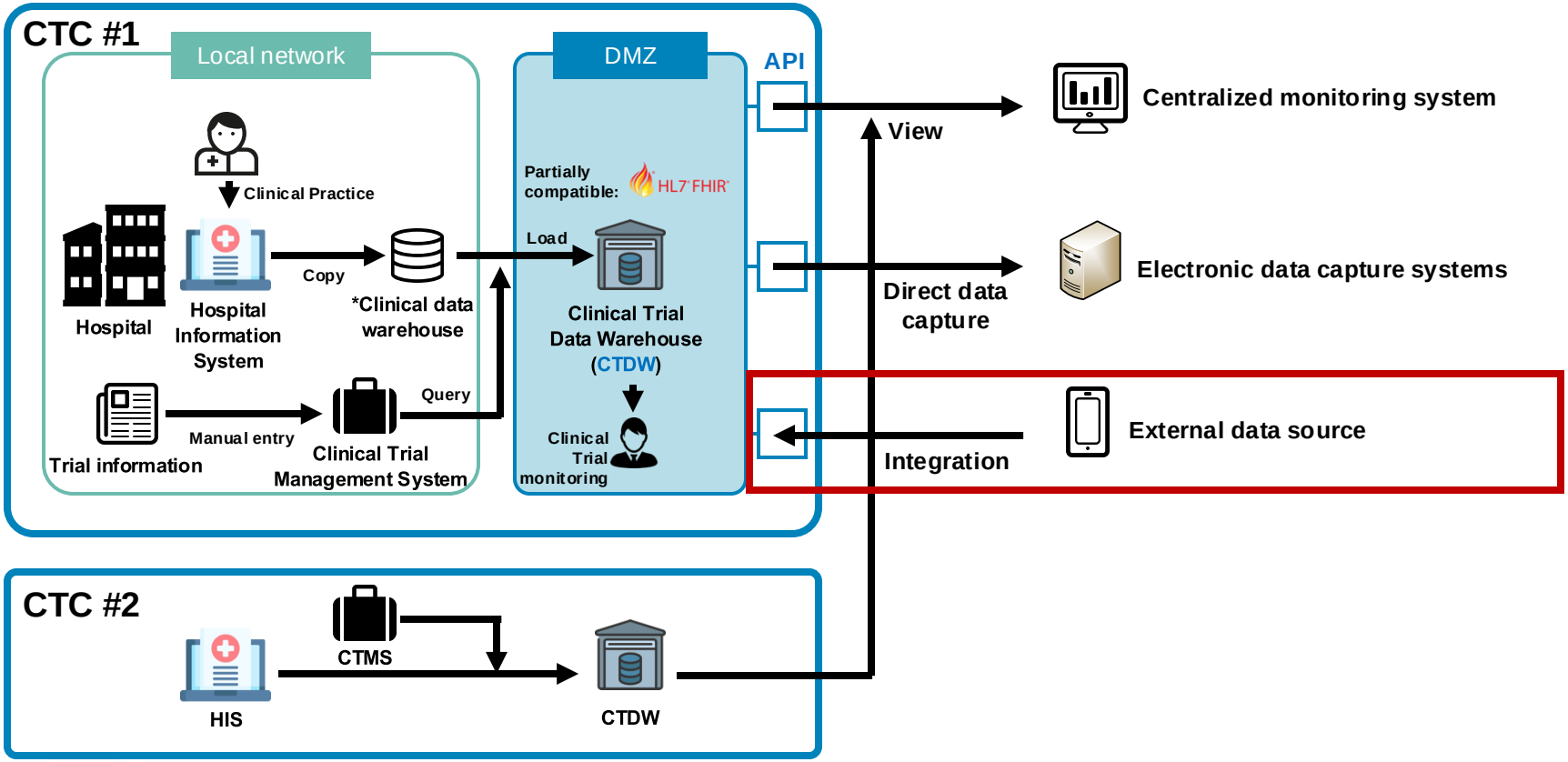
- Most investigators have difficulty in entering trial design in a system

Harmonized data exchange between regulatory agencies



JMIR Med Inform. 2023 Dec 21:11:e46725.

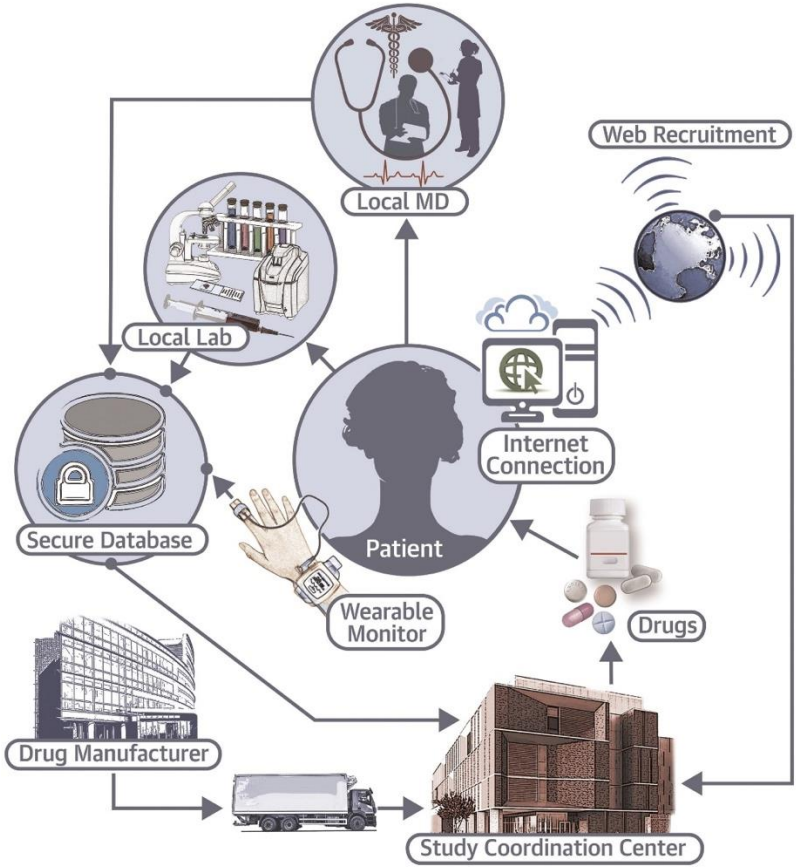
4) External data sources



4) External data sources

DCT elements

- Electronic consent, remote consent
- Direct-to-patient shipping
- Digital data collection
- Remote safety monitoring
- Remote trial monitoring
- Local healthcare facility
- Home visits
- Telehealth



Van Norman G, et al. *J Am Coll Cardiol Basic Trans Science. 2021 Apr, 6 (4) 384–387.*

Digital Health Technologies / QRS

CDISC Digital Health Technologies

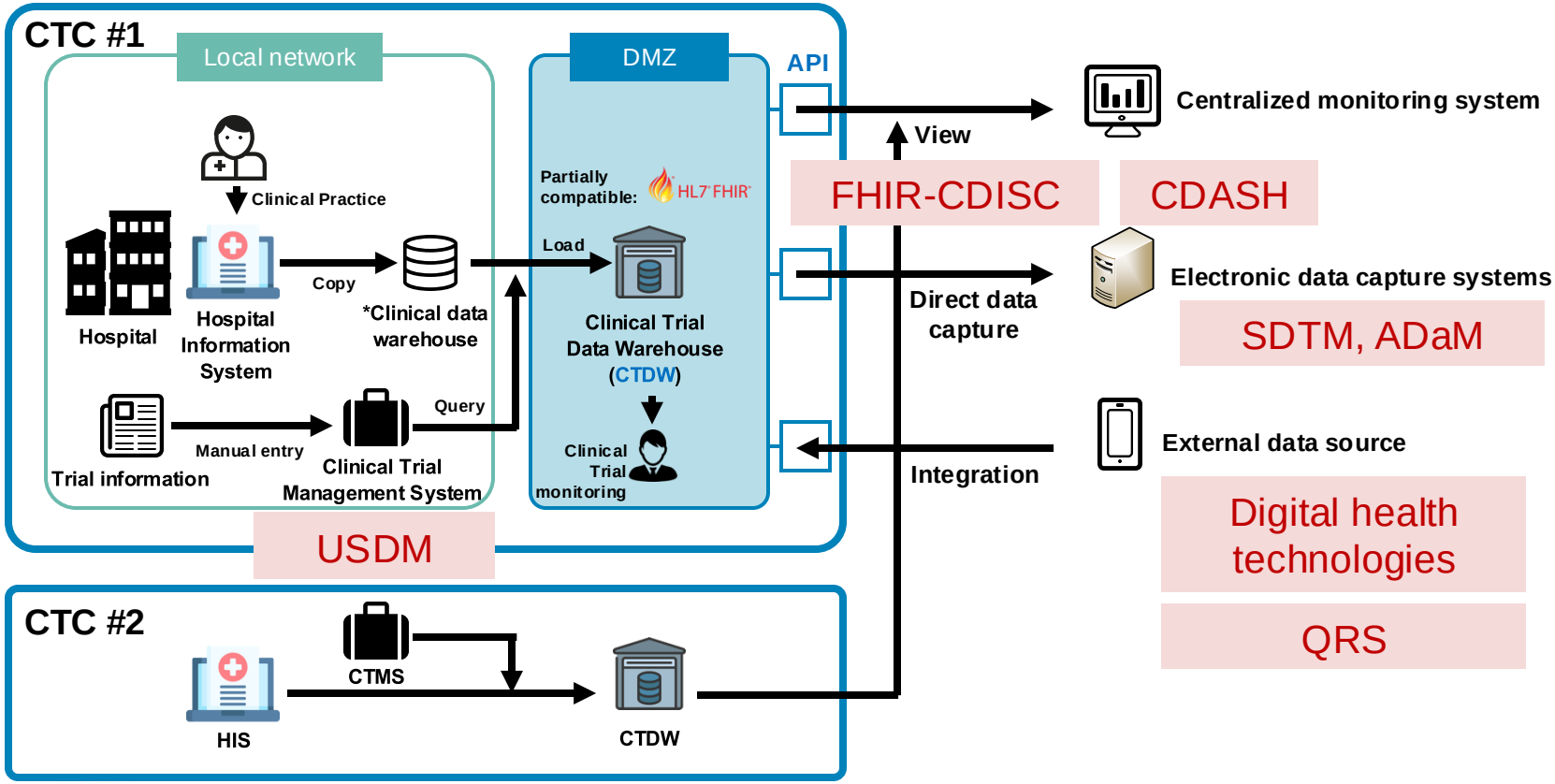
- CDISC and the Digital Medicine Society (DiMe) have partnered to enhance interoperability and comparability of data across different DHTs and accelerate innovation in digital health through shared standards and common semantics.

QRS

- Various ePROs would be used in DCTs
- Questionnaires, Functional Tests, Clinical Classifications and Disease Response

https://www.cdisc.org/standards/in-development/digital-health-technologies

CDISC Landscape in DCTs



Thank You!