CDISC SHUG 2024
“跟进新标准”

有临医药

eProtocol 进展、路径、挑战和应用场景

By 张子豹

CDISC上海用户群研讨会
2024-12-06

目录

1. **系统回顾**：行业对临床研究方案（clinical protocol）进行规范/标准/数字化的努力，并尝试分析其策略和挑战
2. **重点介绍**：CDISC’s Unified Study Definitions Model (USDM) , TCB’s Digital Data Flow (DDF)
3. **个人分享**：e-Protocol和DDF可能的应用场景和影响

回顾1：ICH – E6 R1 (1996) to R3 (2019)

有临医药

INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED TRIPARTITE GUIDELINE

GUIDELINE FOR GOOD CLINICAL PRACTICE
E6(R1)

Current *Step 4* version
dated 10 June 1996

(including the Post Step 4 corrections)

This Guideline has been developed by the appropriate ICH Expert Working Group and has been subject to consultation by the regulatory parties, in accordance with the ICH Process. At Step 4 of the Process the final draft is recommended for adoption to the regulatory bodies of the European Union, Japan and USA.

回顾：ICH – M11 (2018-now), Step 4 (2024-2025?)

有临医药

M11 Clinical electronic Structured Harmonised Protocol (CeSHarP)

M11 EWG　**Clinical electronic Structured Harmonised Protocol (CeSHarP)**

This topic was endorsed by the ICH Management Committee in November 2018. This new guideline is proposed to provide comprehensive clinical protocol organisation with standardised content, with:

- A Template which presents the format and structure of the protocol, including the table of contents, common headers, and contents;
- A Technical Specification which presents the conformance, cardinality, and other technical attributes that enable the interoperable electronic exchange of protocol content.

Rapporteur: Dr. Ronald Fitzmartin (FDA, United States)

Regulatory Chair: Dr. Noemie Manent (EC, Europe)

Date of *Step 2b*: 27 September 2022

Status: *Step 3*

Public consultation dates:

ANVISA, Brazil - Deadline for comments by 6 March 2023

EC, Europe - Deadline for comments by 26 February 2023

FDA, United States - Deadline for comments by 21 February 2023

HSA, Singapore - Deadline for comments by 28 February 2023

Health Canada, Canada - Deadline for comments by 17 February 2023

MHLW/PMDA, Japan - Deadline for comments by 17 March 2023

NMPA, China - Deadline for comments by 15 March 2023

SFDA, Saudi Arabia - Deadline for comments by 15 February 2023

Swissmedic, Switzerland - Deadline for comments by 26 February 2023

TFDA, Chinese Taipei - Deadline for comments by 28 February 2023

Guideline

- M11 Draft Guideline
- M11 Template
- M11 Technical Specification

Endorsed Documents

- M11 Concept Paper
- M11 Business Plan
- M11 Work Plan

WG Presentations / Trainings

- M11 Step 2 Presentation

WG list

ICH工作办公室

首页 > ICH指导原则征求意见 > ICH指导原则征求意见详情

关于公开征求ICH《M11：临床电子结构化协调方案（CeSHarP）》指导原则草案意见的通知

2023-01-06

ICH《M11：临床电子结构化协调方案（CeSHarP）》指导原则现进入第3阶段区域公开征求意见阶段。按照ICH相关章程要求，ICH的监管机构成员需收集本地区关于第2b阶段指导原则草案的意见并反馈ICH。

M11指导原则草案的英文原文和中文译文见附件，现就该指导原则内容及中文译文向社会公开征求意见。

社会各界如有相关建议，请于2023年3月15日前通过联系人电子邮件反馈我中心。

联系人：赵建中、何春俐

邮箱：zhaojzh@cde.org.cn, hechl@cde.org.cn

附件：1.【英文】ICH M11电子结构化协调的临床方案指导原则（草案）

2.【中文】ICH M11电子结构化协调的临床方案指导原则（草案）

3.【英文】ICH M11电子结构化协调的临床方案模板（草案）

4.【中文】ICH M11电子结构化协调的临床方案模板（草案）

5.【英文】ICH M11电子结构化协调的临床方案技术规范（草案）

6.【中文】ICH M11电子结构化协调的临床方案技术规范（草案）

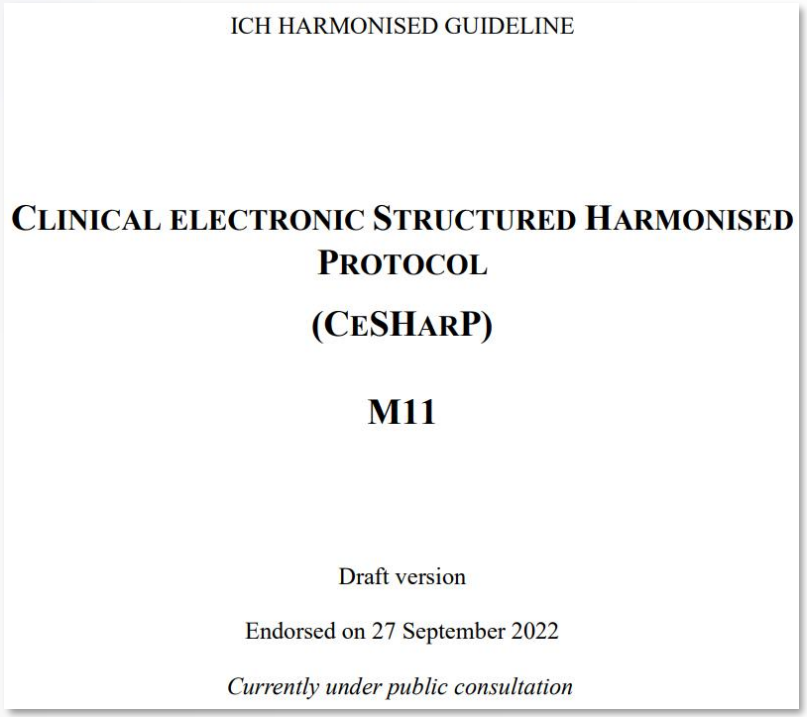
国家药品监督管理局药品审评中心

2023年1月6日

回顾：ICH – M11 Clinical electronic Structured Harmonised Protocol (CeSHarP)

有临医药

Guideline (7pp)



ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CESHARP)

M11

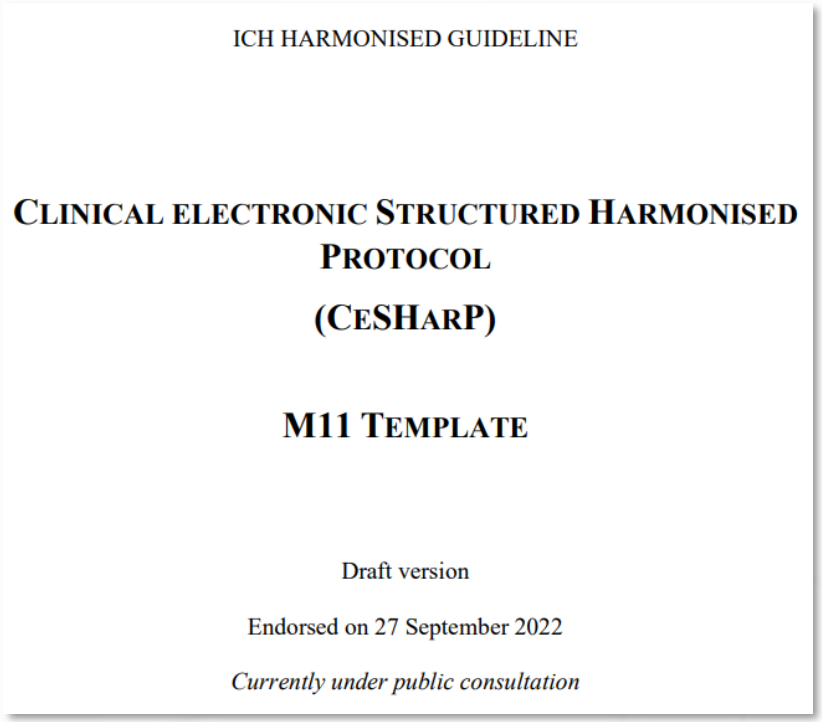
Draft version

Endorsed on 27 September 2022

Currently under public consultation

Defines the background, purpose, scope and principles

Template (54pp)



ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CESHARP)

M11 TEMPLATE

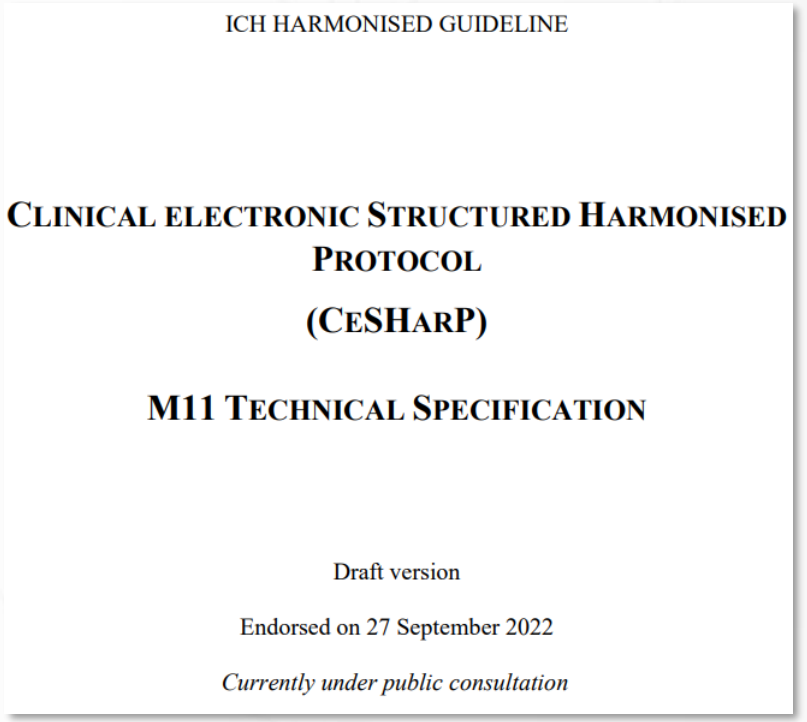
Draft version

Endorsed on 27 September 2022

Currently under public consultation

The specification of the Protocol Document Template that contains embedded data elements

Tech Spec (344pp)



ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CESHARP)

M11 TECHNICAL SPECIFICATION

Draft version

Endorsed on 27 September 2022

Currently under public consultation

Provides a set of data element definitions aligned with the template specification

回顾：ICH – M11 eProtocol TEMPLATE & Tech Spec

有临医药

Table of Contents

1 PROTOCOL SUMMARY

No text is intended here (header only).

1.1 Protocol Synopsis

The protocol synopsis is a short summary of the key points of the trial.

No text is intended here (header only).

Primary and Secondary Objectives and Endpoints

Include a copy of the Objectives/Endpoints Table including primary and secondary endpoints only from Section 3 of the protocol and follow all the same instructions. Not all trials will have a complete estimand. Do not include exploratory endpoints in the synopsis.

[Primary and Secondary Objectives and Endpoints]

Overall Design

Several key aspects of the trial design are summarised below.

Intervention Model:	[intervention model]	**Population Type:**	[population type]
Control:	[control]	**Population Diagnosis or Condition:**	[diagnosis or condition]
Active Comparator:	[comparator]	**Population Age:**	Minimum: [minimum age] – Maximum: [maximum age]
Trial Intervention Assignment Method:	[intervention assignment method]	**Site Distribution:**	[geographic scope]

Briefly state the following:

- Intervention model (for example, single group, parallel group, cross-over, factorial, sequential).
- Control (for example, placebo, active comparator, low dose, historical, standard of care, sham procedure, or none [uncontrolled]).
- Active comparator, if applicable; indicate N/A if not applicable.
- Trial intervention assignment method (for example, randomisation, stratification, or both). Do NOT state block size. If assignment to intervention is by randomisation, describe when randomisation occurs relative to screening.

Term (Variable)	Intervention Model
Data Type	Pick List
Topic, Value or Header	D
Definition	
User Guidance	Intervention model (for example, single group, parallel group, cross-over, factorial, sequential, other)
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Protocol Summary
Relationship (reference to high level conceptual model)	
Value	Single group, parallel group, cross-over, factorial, sequential, other
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Control
Data Type	Pick List
Topic, Value or Header	D
Definition	
User Guidance	Control method (for example, placebo, active comparator, low dose, historical, standard of care, sham procedure, or none [uncontrolled])
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Protocol Summary
Relationship (reference to high level conceptual model)	
Value	placebo, active comparator, low dose, historical, standard of care, sham procedure, or none [uncontrolled]
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

回顾2 – CDISC Protocol相关标准

Protocol相关标准：

- SDTM.TDM (v1.0, 2004 to v2.1, 2024)
- BRIDG (v1.0, 2007 to v5.3.1, 2019)
- PRM (v1.0, 2009)
- USDM (v1.0, 2022 to v4.0, 2024)

回顾 – CDISC PRM (Protocol Representation Model)

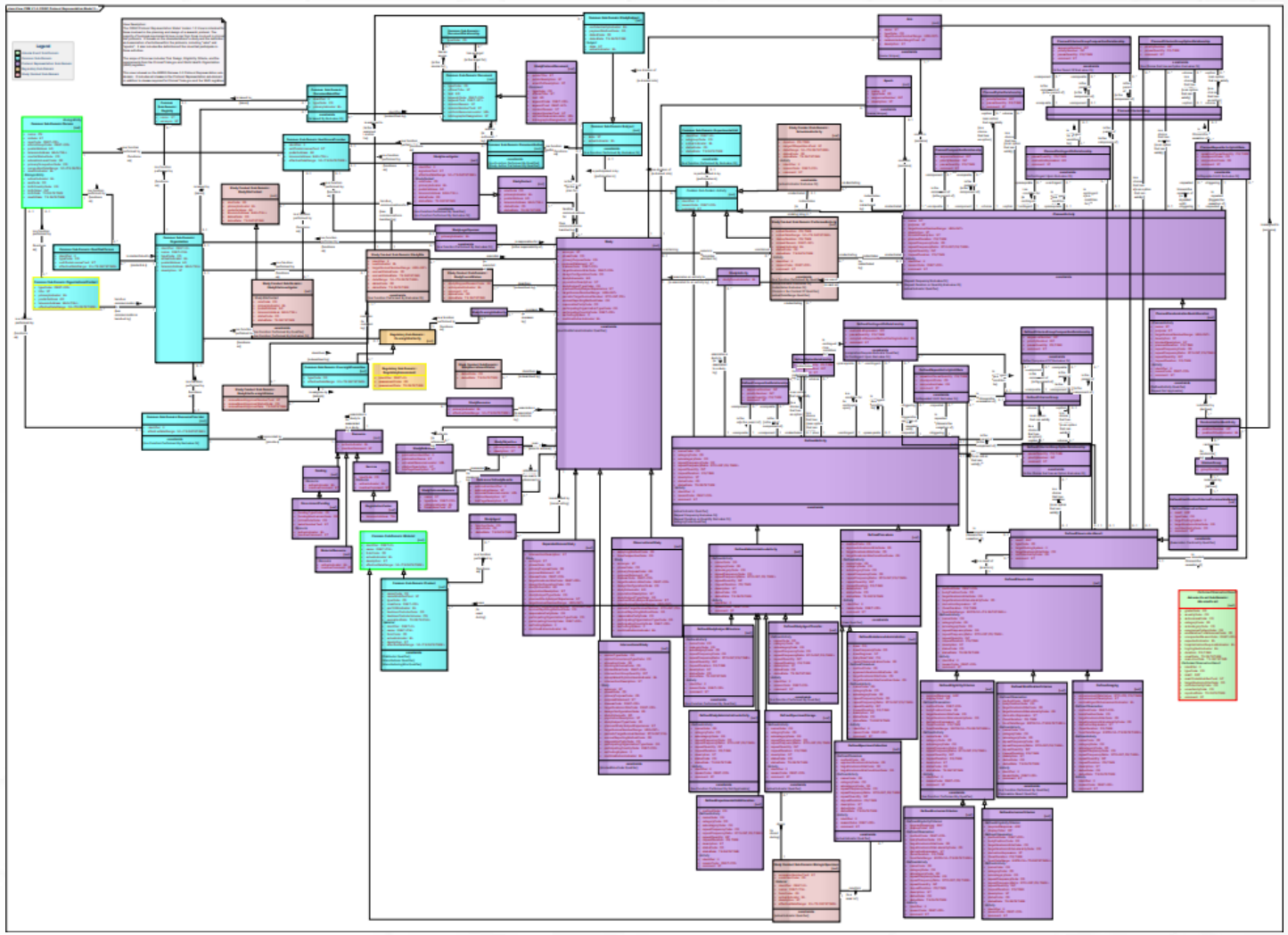
CDISC

The Protocol Representation Model
Version 1.0

Prepared by:

The CDISC Protocol Representation Group (PRG)

 27/Jan/2010



CDISC New Strategic Goal

Expand and enable standards driven automation across the end-to-end study information lifecycle from study design through results
(CDISC will expand and realize the original 360 vision)

Expand & Connect

Expand, Connect, and Digitalize our Standards

Enable & Automate

Reduce Variability, Enable Interoperability, and Increase Automation

Engage & Adopt

Focus on Community Needs

Deliver Business Value

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

End to End Study Information Lifecycle

Standards driven automation across the research information lifecycle

Collection ← Tabulation ← Analysis ← Endpoints ← Protocol

Design & Build

Data Sources

Collection → Integration → Tabulation → Analysis → Endpoints → Report

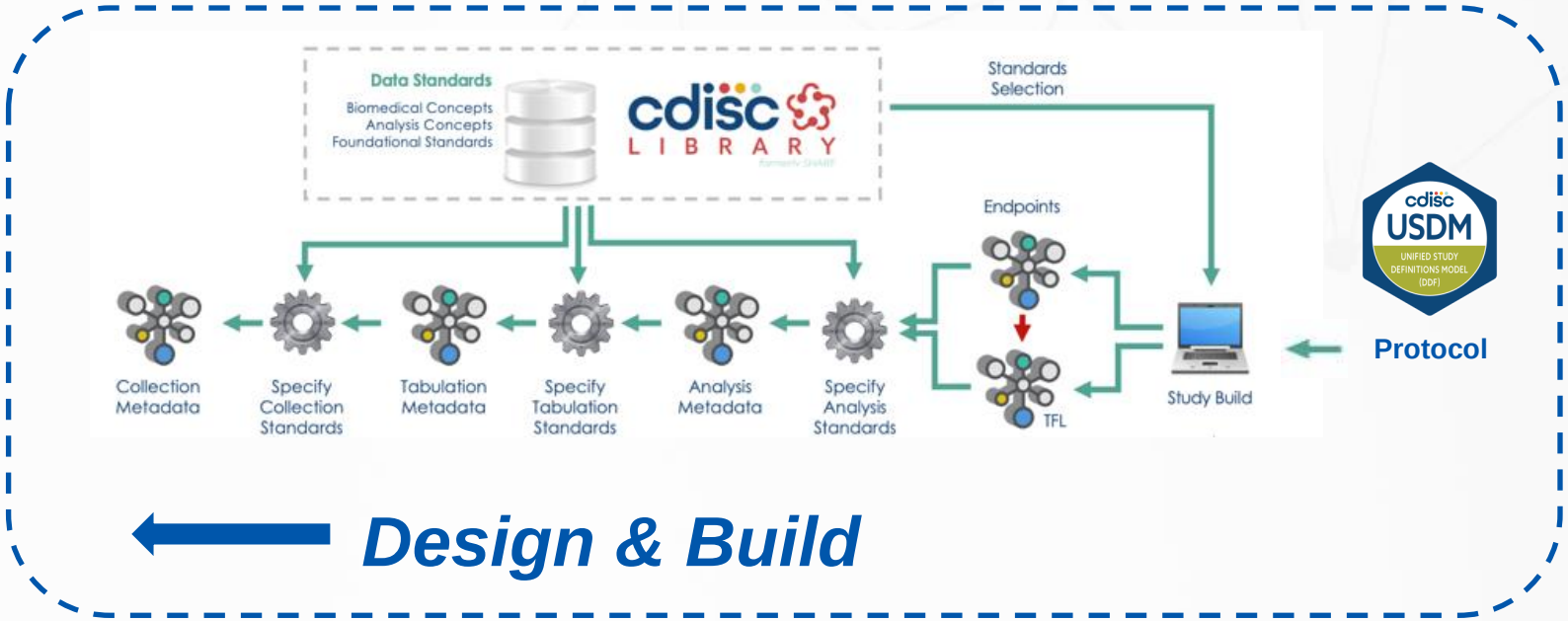
Execution

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

E2E Standards Driven Automation

有临医药

Expand and enable standards driven automation across the end-to-end study information lifecycle from study design through results



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

回顾3 – TCB：Common Protocol Template (CPT)

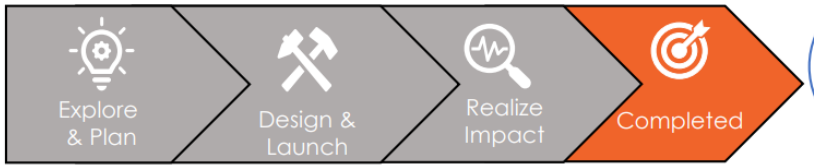
有临医药

Clinical Content & Reuse (CC&R)

Formerly Common Protocol Template (CPT)

Create a common template suite for clinical trial information to ease interpretation and use, enable downstream automation of clinical processes and align to industry data standards

Project Life Cycle Phase:



Benefits:

- Develops harmonized format and streamlined content of key clinical trial documents
- Enables content reuse to downstream documents and registries
- Enables ease of review & interpretation
- Enables end-to-end use of metadata and traceability
- Improves access to protocol information
- Increases quality of clinical development

Solutions:

TransCelerate Clinical Template Suite (CTS) (2015-2024):
Basic Word Edition of the CPT(2015), SAP & CSR editions added in 2018

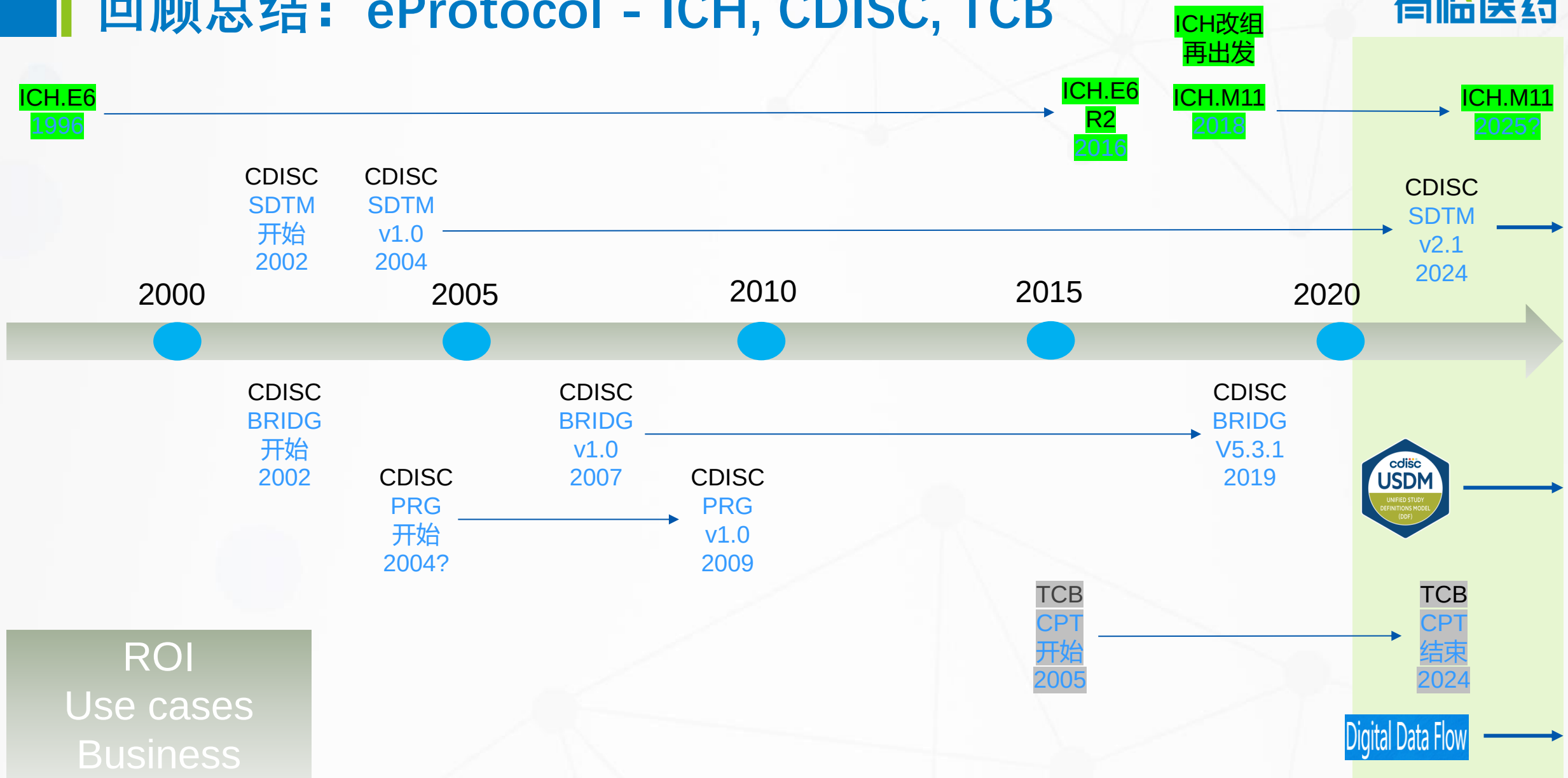
eCPT (2015-2024), eSAP, and eCSR (2019-2024):
Technology-enabled versions of the Clinical Template Suite.

CTS Implementation Toolkit (2015-2024):
Support materials for evaluation and implementation of solutions

Innovation & Collaboration
Procedures Library White Paper (2022), SoA Point of View Blog (2024), TransCelerate/ACRO: CSR Points to Consider for Disrupted Clinical Trials (2023), Master Protocol Design Considerations (2024)

回顾总结：eProtocol - ICH, CDISC, TCB

有临医药



ROI
Use cases
Business

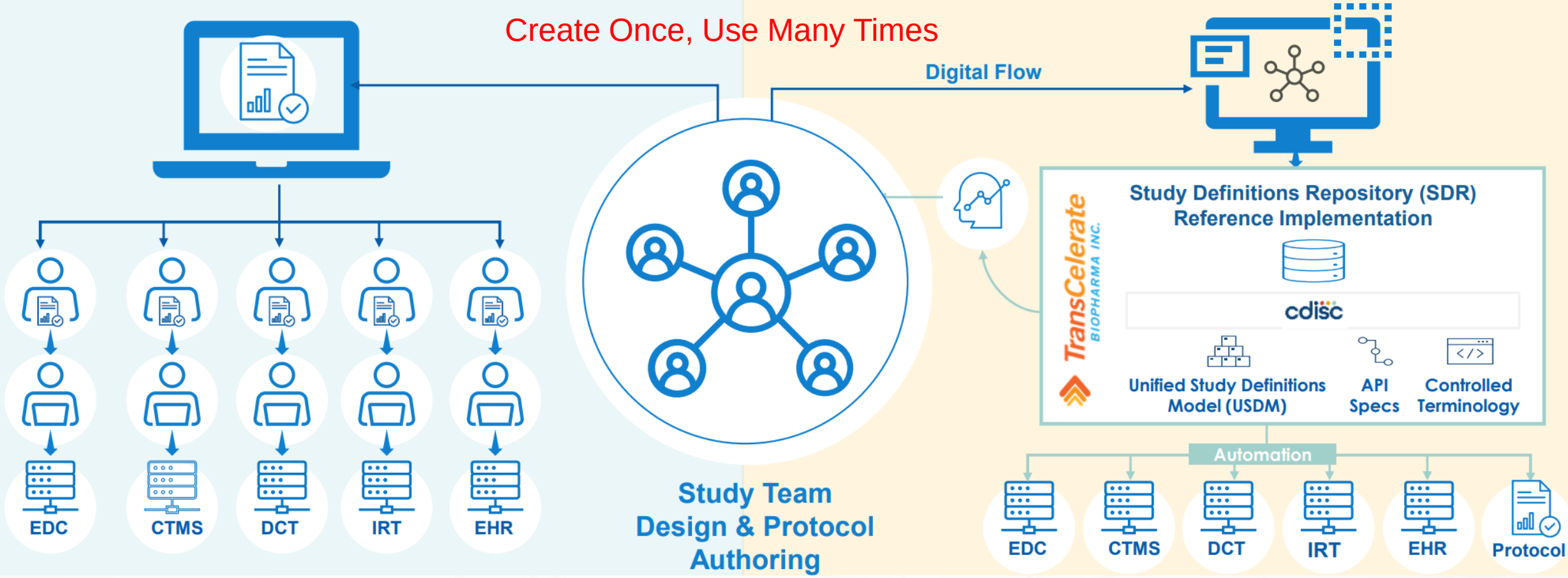
TCB Digital Data Flow (DDF) Initiative

有临医药

TODAY: Document-based paradigm for protocol creation, interpretation, and transcription into consuming systems

TOMORROW: Digital paradigm for protocol creation, with fully automated data flow and interoperability between systems

Create Once, Use Many Times



Source: https://www.transceleratebiopharmainc.com/assets/digital-data-flow-solutions/

TCB DDF Initiative Three Key Principles

有临医药

Engage with critical stakeholders

- Sponsors
- Solution Providers
- CROs
- Health authorities
- Clinical study sites

Development of clinical protocol standards

- CDISC
- ICH M11
- CC&R initiative (Common Protocol Template)
- Vulcan HL7 FHIR

Encourage development of technical solutions

- Vendor-agnostic, platform-independent framework for end-to-end digitalization
- Eventual industry-led governance for long-term sustainability of DDF solutions

TCB DDF Initiative Roadmap

有临医药

Introduce clinical trial protocol standards

- Partnered with CDISC for standards development (USDM)
- USDM encapsulates all sections of a protocol allowing for the generation of an entire protocol document

Introduce reference implementation for end-to-end digitalization

- Study Definitions Repository (SDR) Reference implementation of a novel central component to manage data flow
- SDR open-source code available on a public GitHub site for use and feedback by the open-source community

Introduce mechansims for industry adoption

- Toolkits development
- Solutions forum
- Community meetings
- Other efforts (not exhaustive)

Setup a long-term sustainable governance model for DDF

- Industry-run governance model

eProtocol – Industry Collaboration

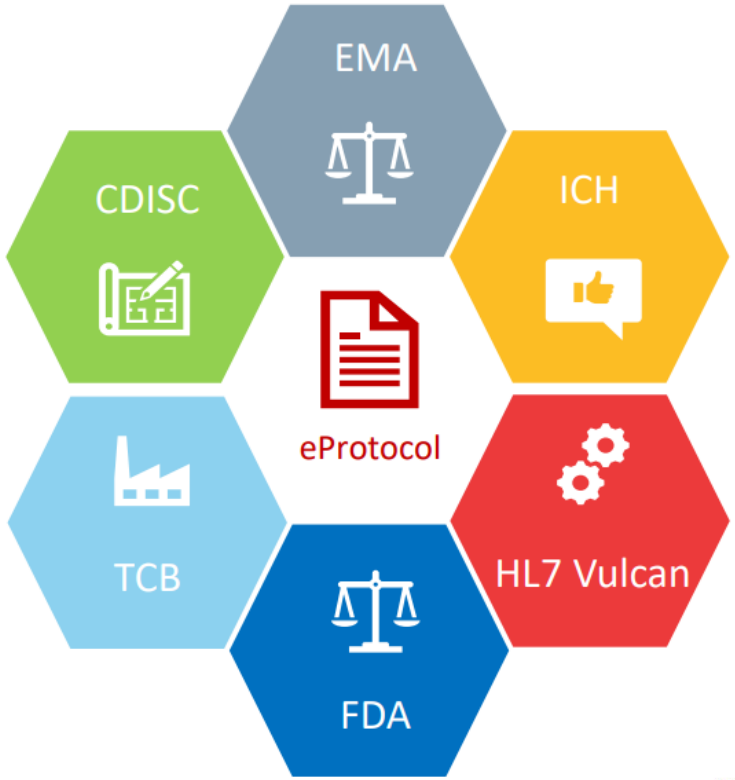
有临医药

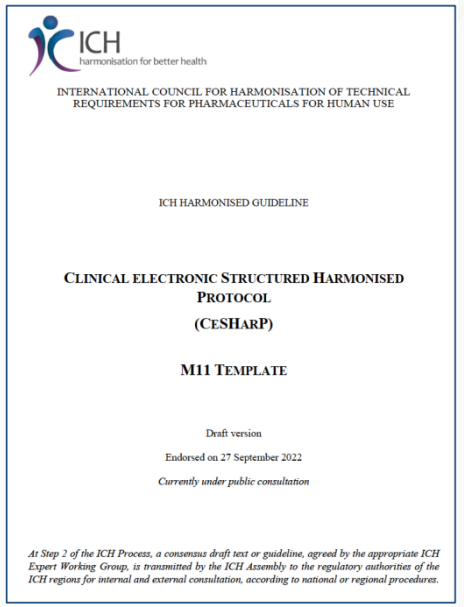
cdisc

Unified Study Definitions Model (USDM) Reference Architecture

TransCelerate's Study Definitions Repository (SDR)

TCB Digital Data Flow





ICH
harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL
(CESHARP)

M11 TEMPLATE

Draft version

Endorsed on 27 September 2022

Currently under public consultation

At Step 2 of the ICH Process, a consensus draft text or guideline, agreed by the appropriate ICH Expert Working Group, is transmitted by the ICH Assembly to the regulatory authorities of the ICH regions for internal and external consultation, according to national or regional procedures.

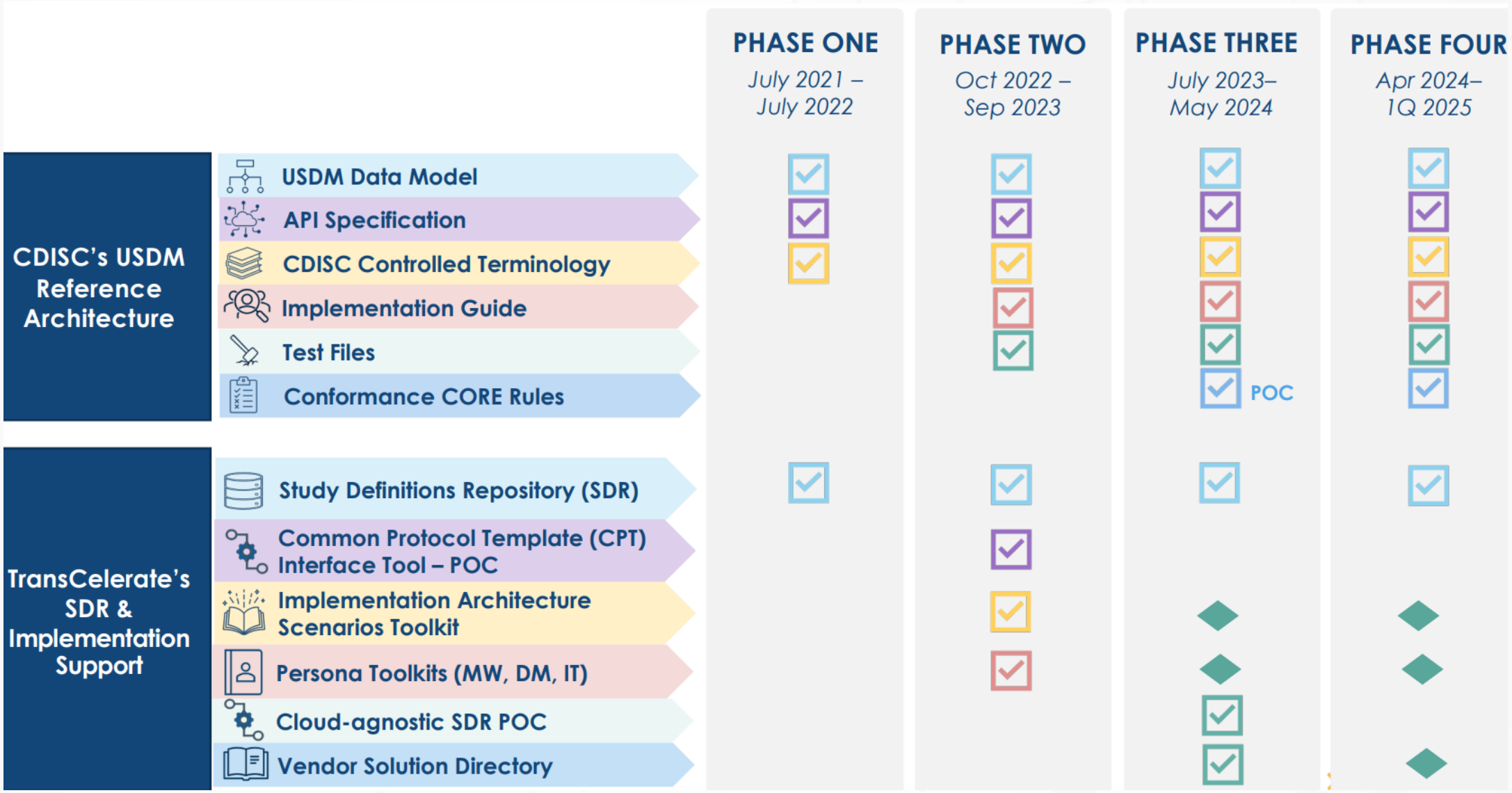
PROJECT PRISM

A Regulatory Cloud Collaborative Initiative

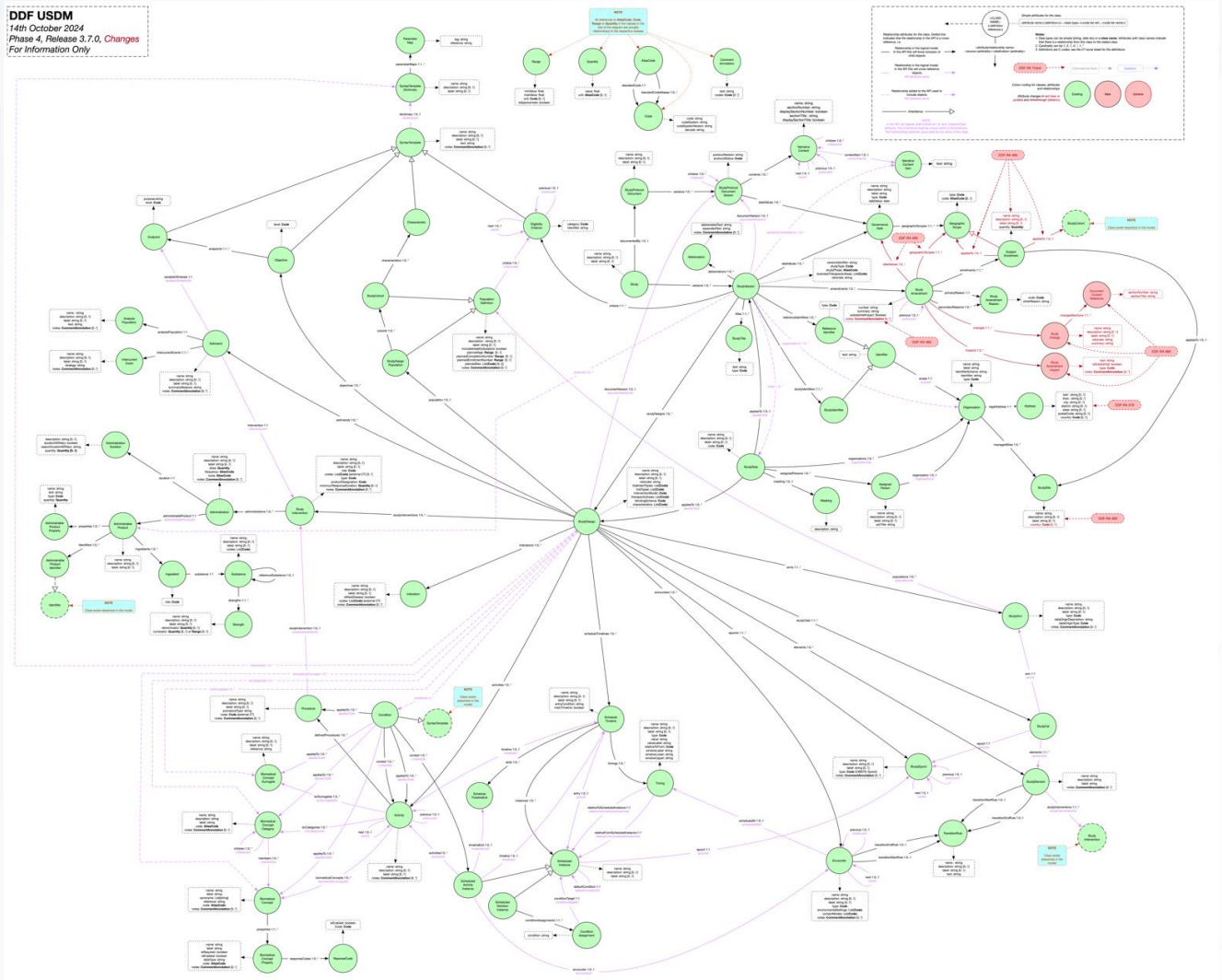
precisionFDA Regulatory Information Service Module
FDA-Industry Research Collaboration Agreement
(Public-Private Partnership)

DDF Evolution: Phases One to Four

有临医药



CDISC USDM Standard



Controlled Terms

Estimands

Populations

Inclusion & Exclusion

Interventions & Indications

Objectives & Endpoints

Study, Identifiers, Amendments

Unstructured Content

Study Designs, Arms, Epochs

Detailed Study Logic, Encounters

Procedures, Biomedical Concepts

Unified Study Definitions Model (USDM) Phase 4 Graphic, source: https://github.com/cdisc-org/DDF-RA

CDISC USDM Standard – IG

有临医药

cdisc

Unified Study Definitions Model Implementation Guide (USDM-IG)

Version 3.0 (Final)

Prepared by the DDF Team

Notes to Readers

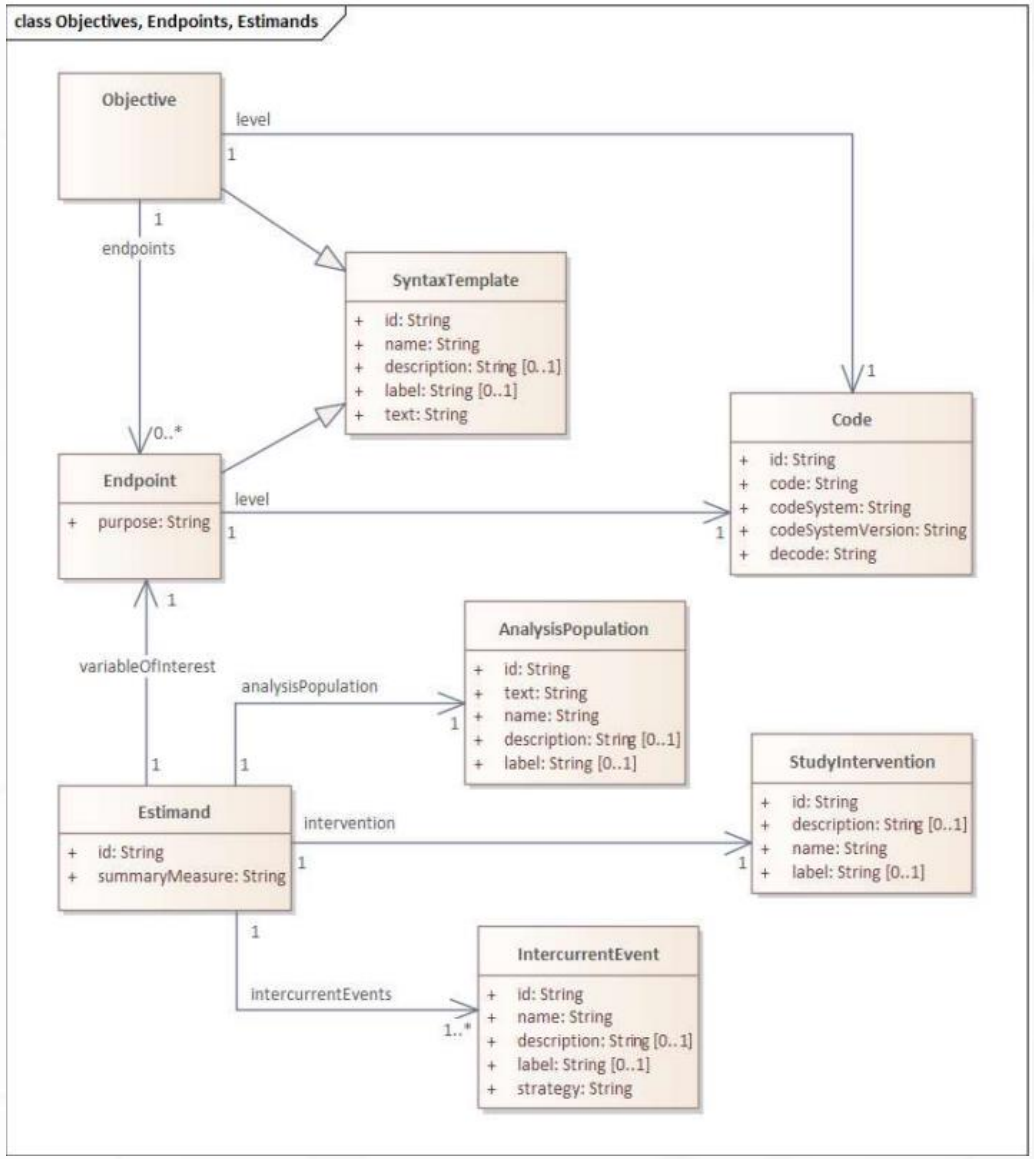
- This is the final Version 3.0 of the Unified Study Definitions Model Implementation Guide (USDM-IG v3.0).

Revision History

Date	Version
Not applicable*	1.0
2023-06-07	2.0 Final
2024-04-16	3.0 Final

*No USDM-IG was developed for USDM Version 1.0.

See Appendix E for Representations and Warranties, Limitations of Liability, and Disclaimers.



DDF & CDISC USDM Resources

有临医药

Overview | What is the USDM | Participate | Webinars | Versions | FAQ | Contact Us

Welcome to Digital Data Flow (DDF) for Clinical Trial Protocols

Digital Data Flow Initiative will help modernize clinical trials by enabling a digital workflow with protocol digitization. This initiative establishes a foundation for a future state of automated & dynamic readiness that can transform the drug development process.

Below are a list of the different websites sourcing specific content and resources. Depending on where you are in the journey, please feel free to explore the different websites and their information.

CDISC DDF Website	**DDF Website**	**DDF GitHub Repos**	**TransCelerate DDF Initiative Solutions**
You are here! Learn about and access the Unified Study Definitions Model (USDM) Reference Architecture supporting Digital Protocol Data Standards	As the main website for the DDF initiative, learn and access all resources for DDF solutions	Learn about a technical Reference Implementation of the USDM, the Study Definitions Repository (SDR), and access the supporting codebase	Learn about DDF Initiative background and roadmap
Target Audience: All those interested in data standards	**Target Audience:** All those interested in implementing DDF Solutions	**Target Audience:** All those interested in SDR development	**Target Audience:** All those generally interested in TransCelerate initiatives

https://www.cdisc.org/ddf

DDF Use Cases

有临医药

From machine actionable Protocol authoring to automation of downstream connectivity

Study Design → Study Start-up → Study Execution / Data Acquisition → Analysis & Reporting → Regulatory Submission Enablement

Protocol development to approval

Connectivity to downstream systems

Use cases to improve study design and analytics

- Predictive model - likelihood of Amendments
- Ingestion and mining of retrospective protocol data
- Compute protocol complexity, site burden, etc
- Optimizing Inclusion / Exclusion Criteria
- Determine study feasibility including subject recruitment

Use cases to automate downstream processes and enable E2E traceability

- Setup of data capture systems
- Generation of SDTM Trial Design datasets
- Provision of study information to a Clinical Trial Registry
- Publishing Protocol Data into different document templates/views
- Update CTMS, TMF, and other downstream systems

"As a medical writer, the digitalization of data flows enables me to work faster with my team on one dedicated system, accessing study content in a single digital study design system.

"As a data manager, the digitalization of end-to-end processes from study design to EDC generates structured data that can be leveraged to track outcomes and progress made.

"As a technical expert, the digitalization of data flows reduces tedious manual work freeing up time for more complex projects that cannot be automated (value-added activities focus).

3. e-Protocol潜在应用场景和可能影响

- Protocol Authoring (incl. ICH M11)
  Tools for protocol authoring, review, analysis etc

- Clinical trial registries (ct.gov, CDE临床试验注册平台)
- EDC/IRT
- CTMS/TMF

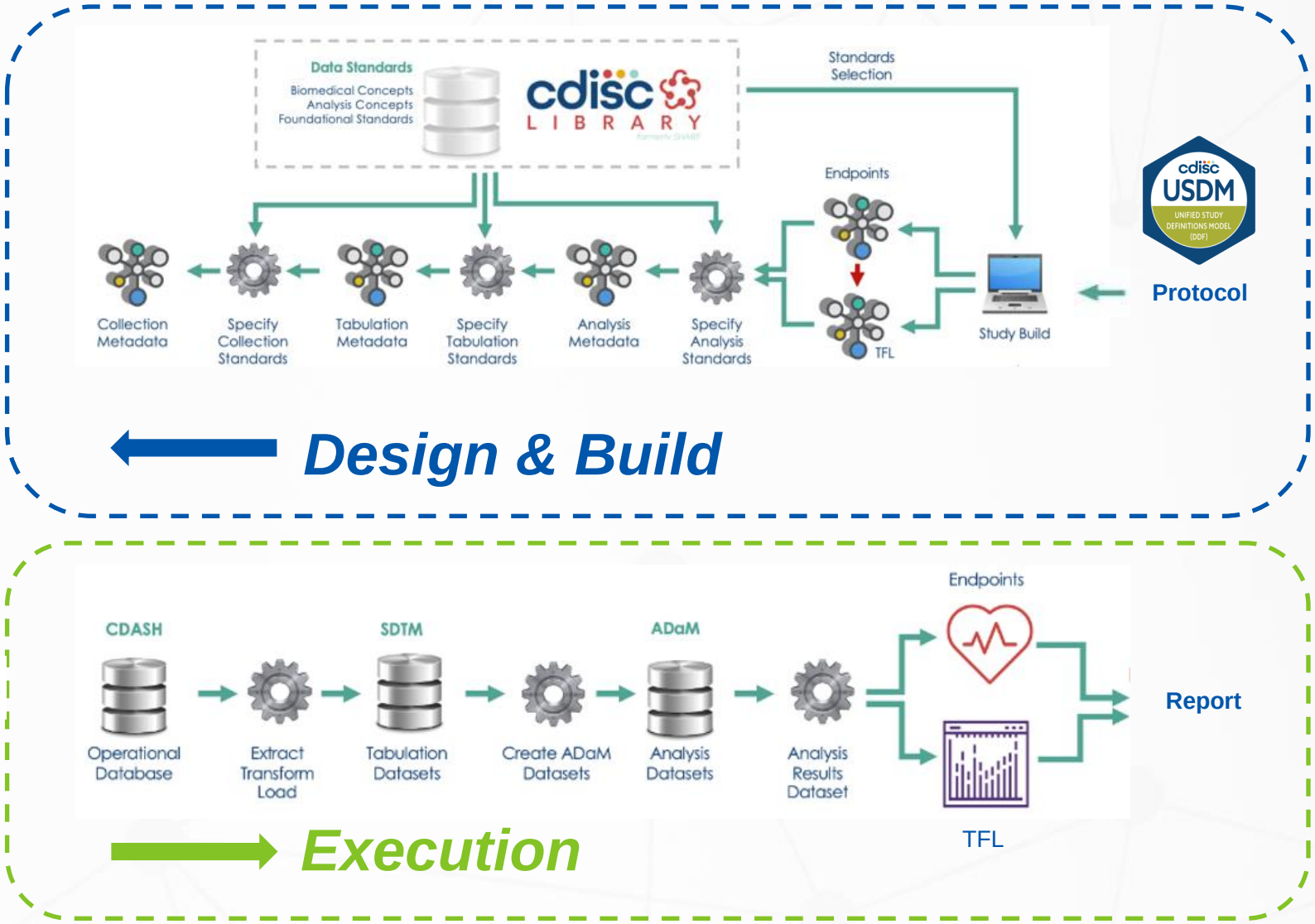
- SDTM.TDM
- Define.XML
- …

Business
Use cases
ROI

CDISC E2E Standards Driven Automation

有临医药

Expand and enable standards driven automation across the end-to-end study information lifecycle from study design through results



Summary – Key Messages

1. Learn hard and think hard - how to put it into business
2. Use cases – need strong evidence for implementation
3. ROI
4. Data – Tools – AI
5. China

Q&A

有临医药

为新药临床提速度　为万千患者谋新生

致力成为**肿瘤·自免·感染·神经·心血管**领域最具专业能力的临床CRO

为新药临床试验提供一体化解决方案

项目经验 **200+**

合作研究者 **2000+**

合作中心 **700+**

服务团队 **500+**

驻地城市 **100+**

有临医药

唯天下至圣，为能聪明睿智，足以有临也

Contact Us

+8621-58301389

bd@union-laboratory.com

www.union-laboratory.com

上海总部

上海市浦东新区育仁路
188弄1号10楼

北京办公室

北京市丰台区南四环西路
186号院汉威国际广场
3期3号楼5M08

南京办公室

南市玄武区苏宁大道
64号3栋1912四维空间
ICC4楼404室

广州办公室

广州市荔湾区中山七路
50号西门口广场办公楼
1105单元

业务咨询

微信公众号

UNION LAIYA · Union Image · 曙研智能 · ClinElite 临英汇 · START

为新药临床提速度　为万千患者谋新生