Clinical Trial Protocol Digitalization: ICH M11 & DDF

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02 Digital Data Flow

01 ICH M11介绍

ICH
harmonisation for better health

ICH M11

Clinical electronic Structured Harmonised Protocol

电子结构化协调的临床方案

指导原则 Guideline

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

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.

模板 Template

ICH
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M11 TEMPLATE

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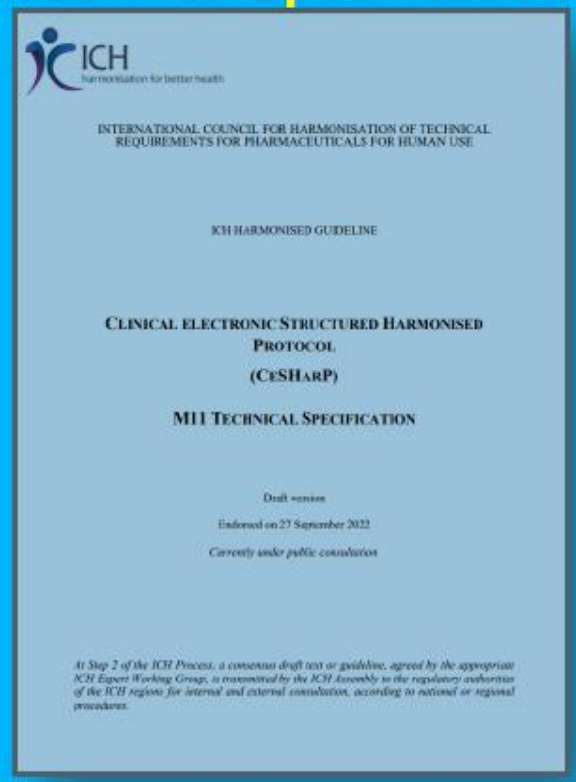
技术规范 Technical Specification



ICH
harmonisation for better health

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ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

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M11 TECHNICAL SPECIFICATION

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背景与目的

- 使用临床试验方案模板有助于申办方或申办方-研究者制定完整、无歧义、组织有序且符合ICH其他指导原则中规定的质量源于设计原则的方案。

- 本指导原则的目的是描述用于制定单独相关文件（ICH地区所有监管机构可接受的ICH M11电子结构化协调的临床方案模板[模板]和技术规范）的一般方案设计原则和方法。
- 模板提供了方案的格式和结构，包括目录、通用标题和内容。
- 技术规范提供了使方案内容能够进行互操作电子交换的一致性、基数和其他技术属性。
- 模板和技术规范具有内置灵活性，并且为版本化文件。

适用范围

- 模板和技术规范适用于临床研究的所有阶段和治疗领域的药物干预性临床试验。

- 干预性试验可能包括但不限于人体药理学研究、探索性研究、确证性研究和批准后研究（参见ICH E8(R1)临床研究的一般考虑）。

- 本指导原则中的术语“药品”和方案模板中的“试验干预”是指任何治疗、预防或诊断制剂，包括药品、生物制品、疫苗、细胞或基因治疗产品（如适用），以及作为药品注册的药物-器械组合产品。

- M11指导原则、模板和技术规范确立了内容放置的通用说明，同时也确立了内容可互操作电子交换的技术属性。

电子结构化协调的临床方案-模板

Clinical Data Science

- 构建通用核心内容-模板设计代表任何药品临床试验的核心信息集。
- 满足利益相关方的需求-模板的结构和内容为存在关联的利益相关方提供了一个框架，以制定、审查和使用方案，其中包括统一的目录、通用章节标题和内容以及通用术语，具有一致性和明确性。
- 定义电子交换的内容-方案内容可以利用当前（例如，电子通用技术文档）和其他未来技术在各方（包括申办方和监管机构）之间进行电子交换。
- 内容重复使用设计-临床方案是丰富的信息来源，可以作为临床试验管理和审查过程的一部分重复使用，除此之外还有多种用处：例如，在临床试验注册处公布以提高临床试验的透明度，还可用于标准化临床试验数据采集。
- 保持灵活性-模板包括建议和可选文本和数据字段，以保持灵活性。保留高级标题结构，而低级部分可以根据需要添加、删除或修改。

模板惯例和设计

Clinical Data Science

- 模板在设计时将最重要的执行信息（例如概要、示意图、研究时间表）置于前面。
- 模板通过主体/附录框架进行组织，期中试验特定信息在主体中，而参考资料和更多的一般（非试验特定）信息则在附录中。采用这种组织结构仅仅是因此其在执行过程中具有实用性。
- 附录中的内容与正文中的内容具有同等的重要性和严谨性。
- 尽可能删除不必要的重复。

方案模板目录

迪时 DATA SCIENCE EXPRESS
Clinical Data Science

电子结构化协调的临床方案-技术规范

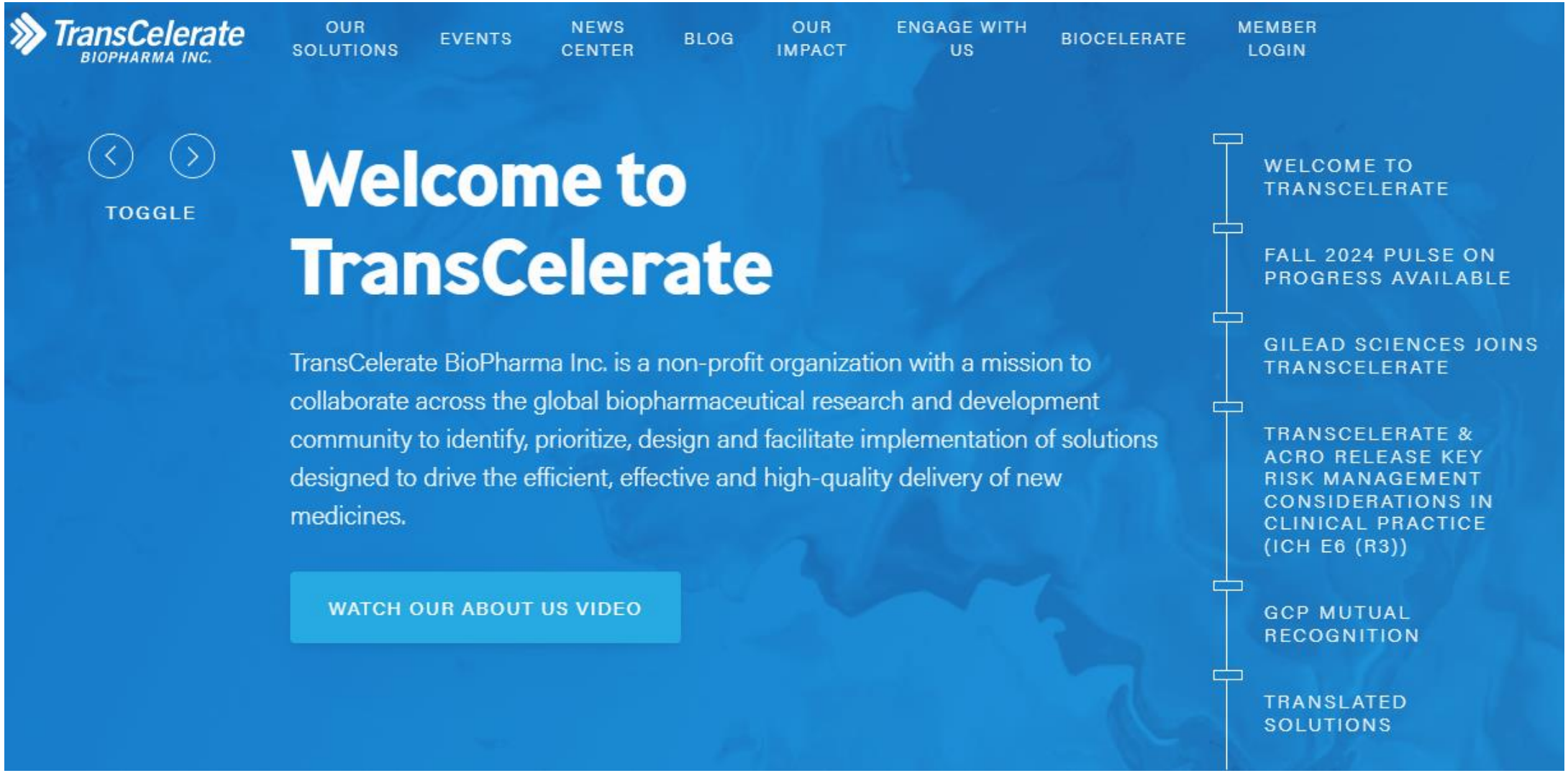
Clinical Data Science

- 改进通用结构化核心内容
- 定义电子交换的内容规范
- 基于规范开发数据模型
- 重点关注相关内容的使用和重复使用
- 使用开放的通用信息交换标准
- 保持技术创新和特定区域使用的灵活性

02 Digital Data Flow

TransCelerate

Clinical Data Science



https://www.transceleratebiopharmainc.com/

What is the Digital Data Flow initiative?

Clinical Data Science

- The Digital Data Flow (DDF) initiative aims to modernize clinical trials by enabling a digital workflow that allows for automated creation of study content and configuration of study systems to support clinical trial execution. This initiative will establish a foundation for a future state of automated and dynamic readiness that can transform the drug development process.

BENEFITS

- Eliminate non value-added activities through automation: "Work Smarter Not Harder"
- Enable flexible company and/or industry-wide interoperability by applying clinical protocol standards
- Create foundation for study design analytics insights

Digital Data Flow Initiative Roadmap

Clinical Data Science

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

How We're Enabling Clinical Trial Protocol Digitalization

Clinical Data Science

TransCelerate has collaborated with CDISC and other stakeholders to develop a standard data model for **specifying protocol information,** as well as a **demonstrated way to connect systems** that produce, exchange, or consume this information.

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

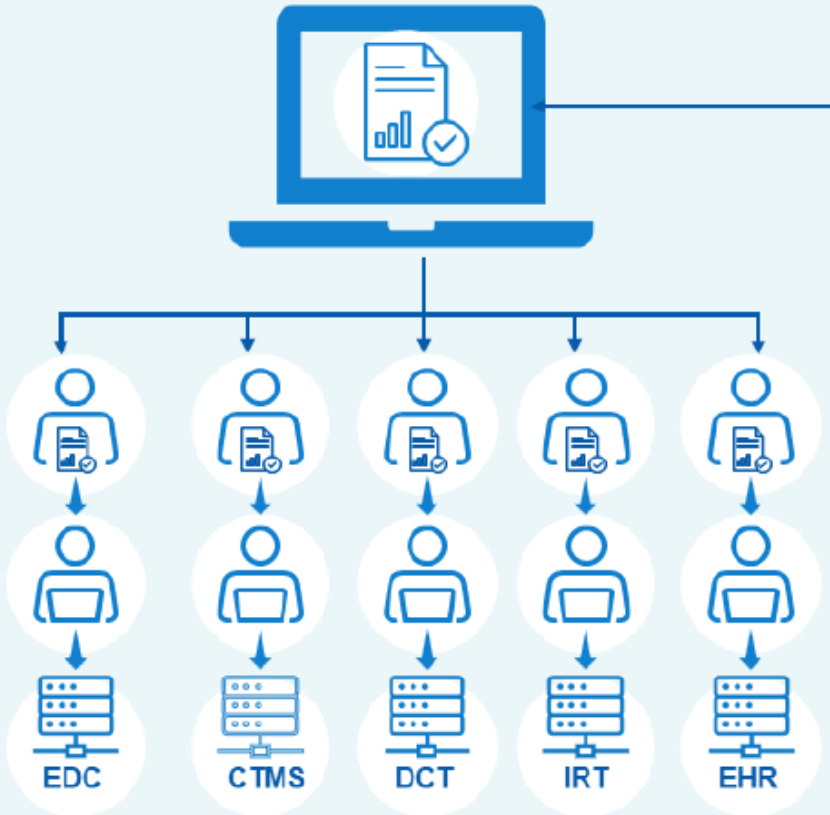
- Vendor-agnostic, platform-independent framework for end-to-end digitalization
- Eventual industry-led governance for long-term sustainability of DDF solutions

TransCelerate Digital Data Flow (DDF) Ambition

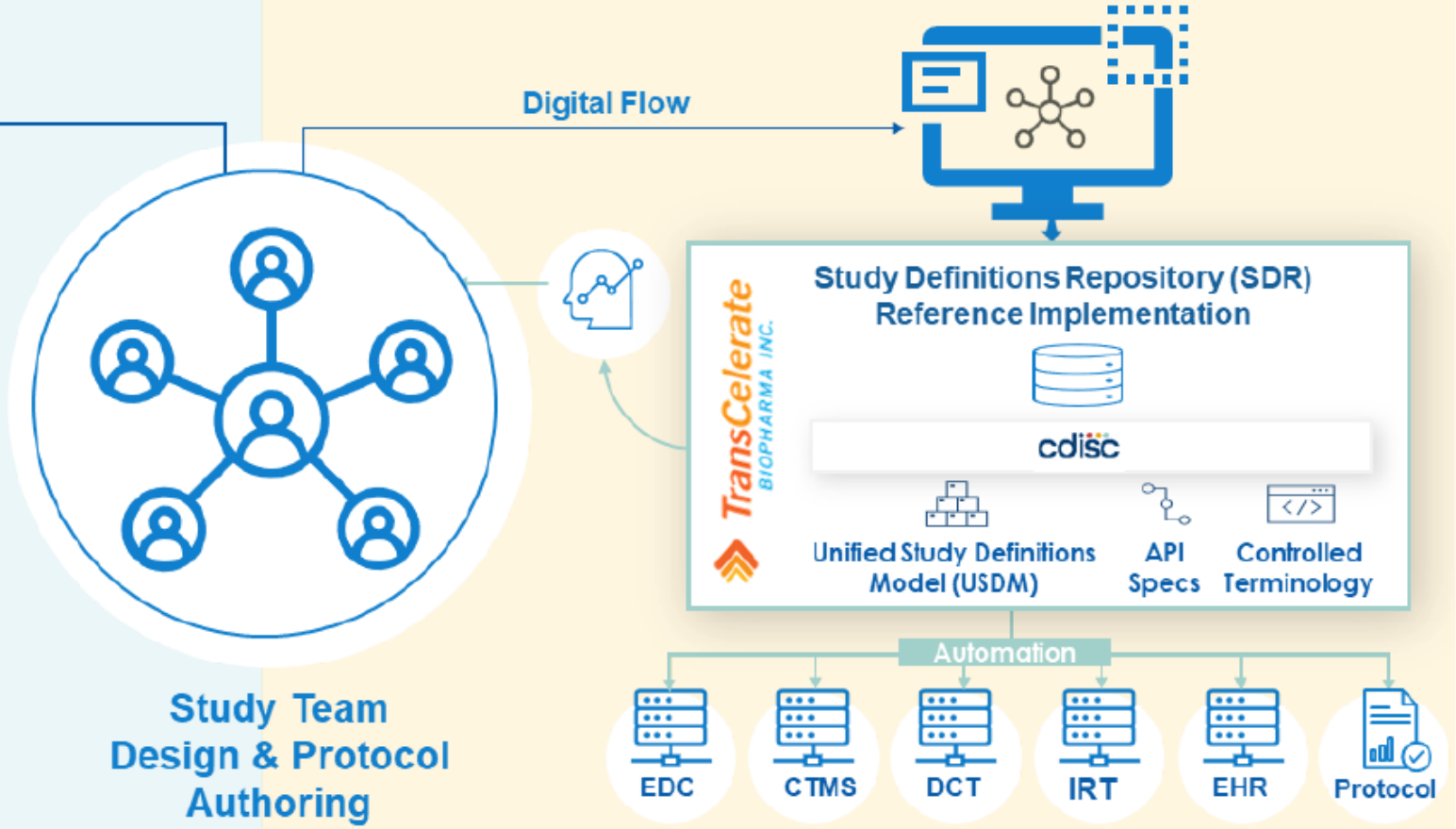
Write Once, Read Many

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

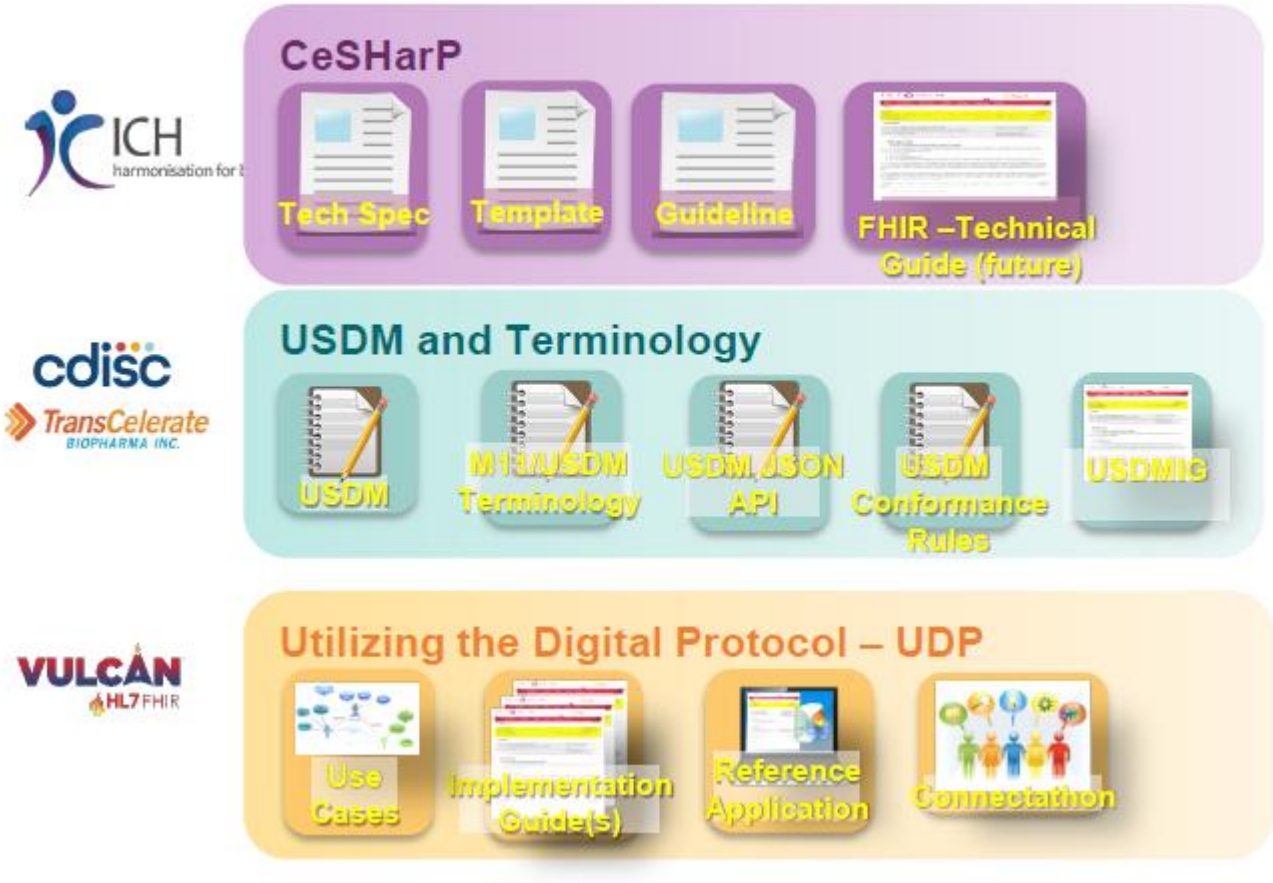
TODAY: Document-based paradigm for protocol creation, interpretation, and transcription into consuming systems



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



ICH M11 and Vulcan Utilizing Digital Protocol (UDP)



- ✓ Data driven Protocol
- ✓ Standardized data model with CDISC / USDM common terms, definitions and formats
- ✓ Facility to exchange the protocol information using multiple formats: DOCX, PDF JSON and FHIR.

Digital Data Flow

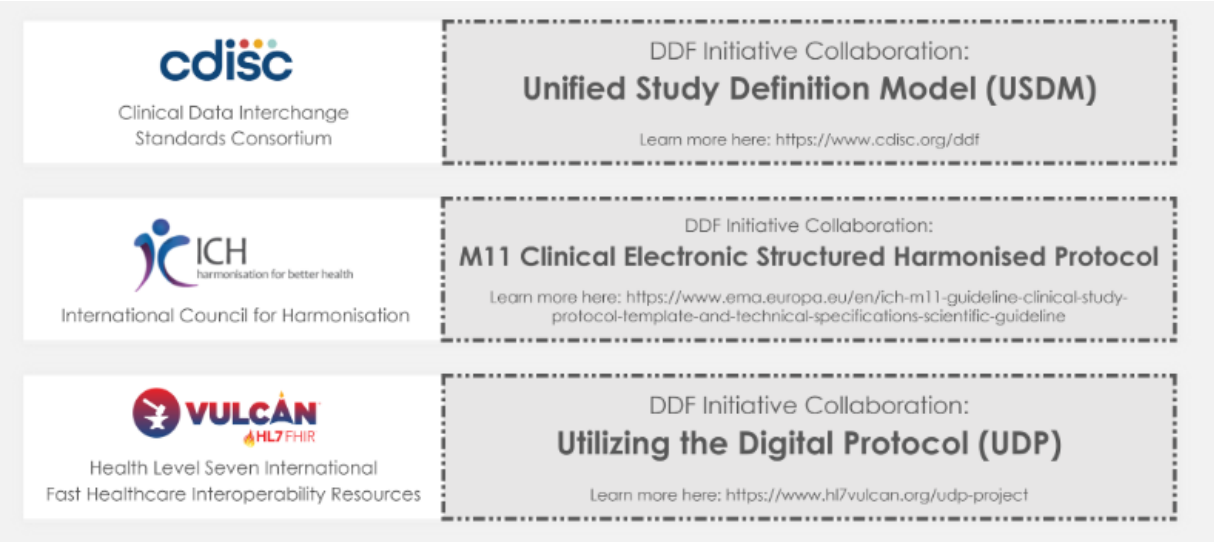
Clinical Data Science

Data Standards Collaborations Collaborating Across Initiatives

Currently, multiple initiatives are focusing on different aspects of protocol digitization.

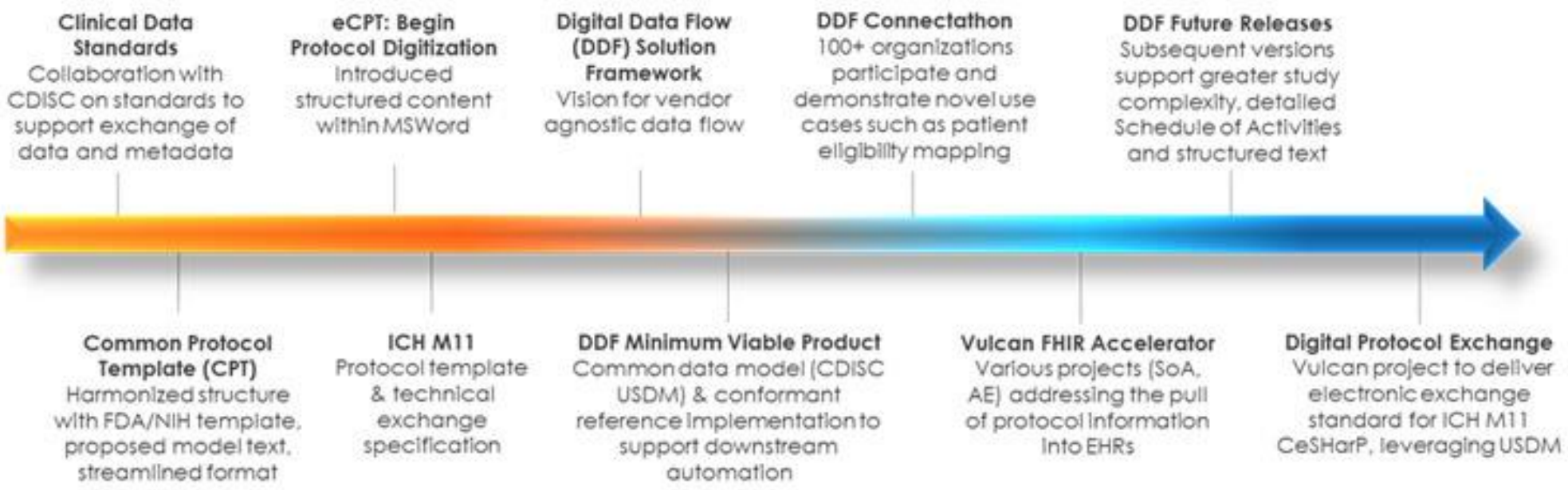
By aligning on content and working together, the collaboration across these initiatives amplifies the value of a Digital Protocol.

The DDF Initative is collaborating with the following organizations and initiatives with regards to data standards:

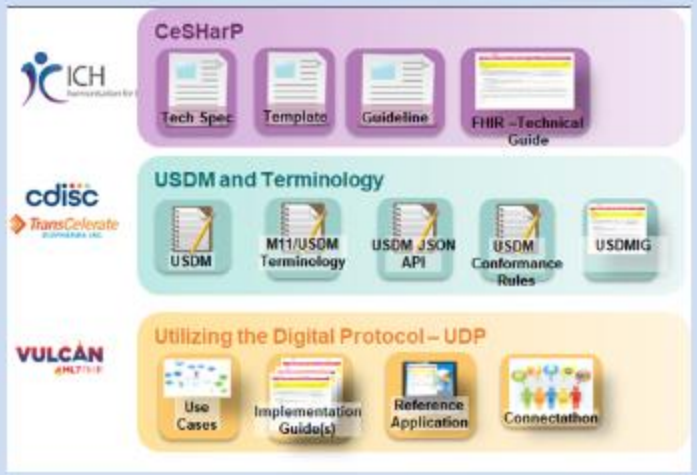


From Common Protocol Template to Digital Protocol Exchange

Clinical Data Science



UDP: Utilizing the Digital Protocol



UDP is a collaborative effort between Vulcan, CDISC and TransCelerate. The Guideline, Template and Technical Specification produced by ICH M11 provide a basis for development of an Information Model and Terminology and a FHIR Implementation Guide.

The protocol is what drives every detail of a clinical trial.

Currently it is managed as PDFs and Word Documents.

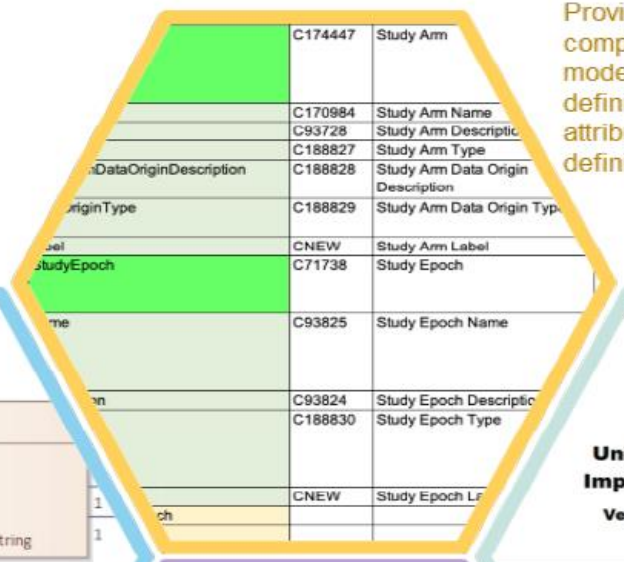
Having a machine processable form of the protocol has huge implications across the board.

UDP — HL7 Vulcan

The USDM Standard

CDISC Controlled Terminology

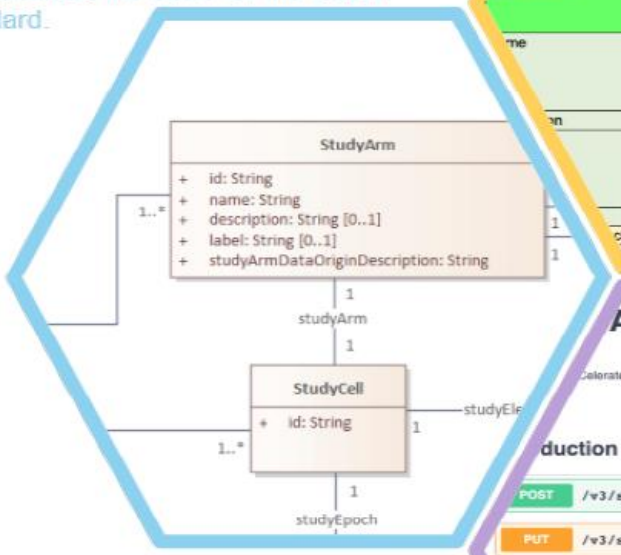
Provides further semantics, complementing the UML model. Includes the definition of classes and attributes along with the definition of value sets



	C174447	Study Arm
	C170984	Study Arm Name
	C93728	Study Arm Descriptio
	C188827	Study Arm Type
DataOriginDescription	C188828	Study Arm Data Origin Description
iginType	C188829	Study Arm Data Origin Typ
el	CNEW	Study Arm Label
tudyEpoch	C71738	Study Epoch
me	C93825	Study Epoch Name
n	C93824	Study Epoch Descriptio
	C188830	Study Epoch Type
	CNEW	Study Epoch La
ch		

Logical Model

The UML logical model (a class diagram) that provides the basis for the USDM standard.



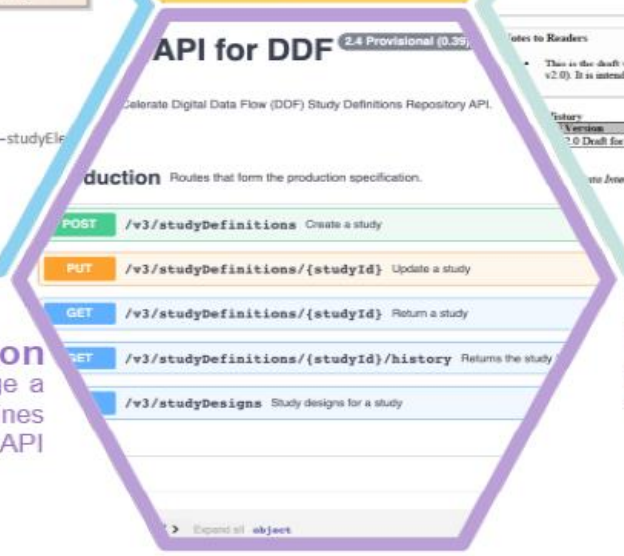
Examples

Example protocols implemented in the USDM with associated JSON files and visualisations

```
tudyArms": [
  {
    "id": "StudyArm_1",
    "name": "Placebo",
    "label": "",
    "description": "Placebo",
    "type": {
      "id": "Code_61",
      "code": "C174268",
      "codeSystem": "http://www.cdisc.org",
      "codeSystemVersion": "2022-12-16",
      "decode": "Placebo Comparator Arm"
    },
    "studyArmDataOriginDescription": "Data collec
    "dataOriginType": {
      "id": "Code_62",
      "code": "C188866",
      "codeSystem": "http://www.cdisc.org",
      "codeSystemVersion": "2022-12-16",
      "decode": "Data Generated Within Study"
    }
  },
  {
    "id": "StudyArm_2",
    "name": "Xanomeline Low Dose",
    "label": "",
    "description": "Active Substance",
    "type": {
      "id": "Code_63",
      "code": "C174267",
      "codeSystem": "http://www.cdisc
      "codeSystemVersion": "2022-12-
```

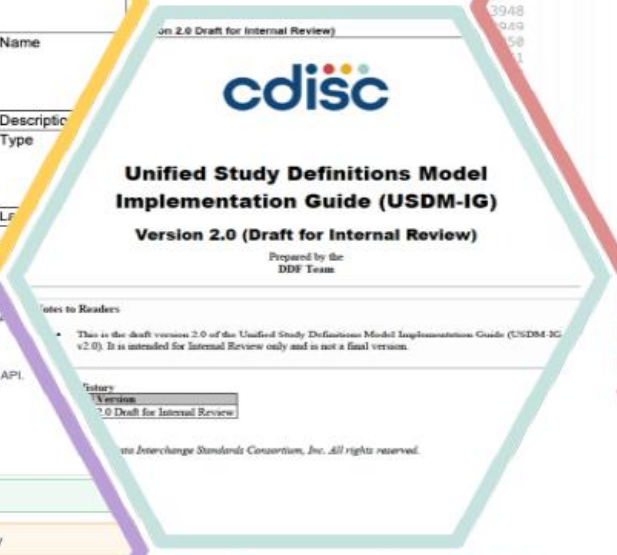
API Specification

Provides the means to exchange a single study between machines using a JSON API



Implementation Guide

Guidance on using the USDM model and ensuring conformance with the standard



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