TransCelerate Digital Data Flow (DDF)

DDF IN ACTION

Full Day Event Summary Report

An interactive face-to-face full day event bringing together sponsor companies, clinical solution providers, and key industry stakeholders to exchange knowledge & collaboration on implementing DDF solutions.

Hosted at Johnson & Johnson in New Jersey, USA and Novo Nordisk in Copenhagen, DNK

October 10th, 2024

TransCelerate BIOPHARMA INC.

Envisioning a future with a digitized clinical study protocol with automated data flow and streamlined analytics insights

Enable flexible industry-wide digital interoperability with data standards for protocol

Eliminate manual activities through automation: "Work Smarter Not Harder"

Create a foundation for study design analytics insights and protocol modeling & simulations

EXECUTIVE SUMMARY

DDF in Action day held on October 10, 2024, was a pivotal event showcasing the potential for transforming clinical trials through the adoption of standards and digitalization. Themed "Continuing the Journey, Charting the Future", the event brought together industry leaders, experts, and stakeholders to discuss and share advancements in applying DDF solutions and their impact on clinical trials.

This event was co-located in the United States & Europe and hosted by two sponsor companies, Johnson & Johnson and Novo Nordisk. It was structured to allow simultaneously webcasting of the Keynote & Plenary Session featuring Adoption Stories.

To showcase DDF "in action", three sponsor companies presented adoption stories. All featured the use of the CDISC Unified Study Definitions Model (USDM), applying data standards to technology solutions supporting different scenarios.

The rest of the event was dedicated to other agenda topics, including an overview of CDISC & USDM. In addition, various organizations presented their technical solutions by leveraging DDF solutions through a poster session, followed by a panel discussion where selected solution providers discussed their approaches & challenges.

DDF in Action day highlighted the noteworthy progress made in the digitalization of clinical trial protocols, and the collaborative efforts required to achieve industry-wide interoperability. The event underscored the need for continuous perseverance, stakeholder engagement & shared learnings of implementation efforts for protocol digitization.

Attendees had positive feedback, sharing that attending the event really helped them "connect the dots" and were already looking forward to next year's event.

PARTICIPATING COMPANIES

■ Sponsor Company (blue) ■ Clinical Solution Provider (magenta) ■ Industry Stakeholder (green)
❖ Copenhagen, Denmark ◆ New Jersey, United States

❖ Amgen ❖ Ascendis Pharma ❖◆ Astra Zeneca ❖◆ Bayer

◆ Bristol Myers Squibb ❖◆ CDISC ❖ClinLine

◆ Content Rules ◆CTDN and PFMD ❖ data4knowledge

❖ Devote Consulting ❖ EQTY Lab ◆ EZ Research Solutions

◆ Flatiron Health ◆ Futurpostif Consulting ❖◆ GSK

◆ Johnson & Johnson ◆ Lilly ❖ Medidata ◆ Merck

◆ NNIT ◆ Novartis ❖◆ Novo Nordisk ❖◆ Nurocor

❖◆ PA Consulting ◆ Pfizer ◆ Recursion ◆ Regeneron

❖ Risklick ❖◆ Roche ❖◆ Sanofi ◆ Shionogi

❖◆Sycamore Informatics ◆ TATA Consultancy Services

❖ UCB ❖◆ Veeva

113	18	16	15
Global Attendees	Biopharma Companies	TCB Member Companies	Solution Providers

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CDISC & USDM OVERVIEW

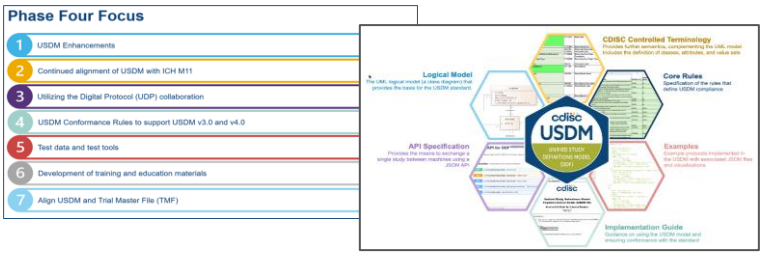
CDISC provided a high-level overview of the Unified Study Definitions Model (USDM), shared information on how USDM, ICH M11 & Utilizing the Digital Protocol (UDP) initiatives are integrated and put forward some USDM use cases.

USDM Overview

NOTE: Information is readily available on https://cdisc.org/ddf.

Currently CDISC is working Phase 4 of the USDM, focusing on:

- Refining content vs. new content
- Backward compatibility
- Harmonization with ICH M11
- Built-in conformance rules



Alignment Across Other Initiatives

CDISC is partnering with ICH and Vulcan in aligning on standards and clarification on usage of various components. At a high-level:

ICH harmonisation for better health

M11: Focused on protocol structure standards

cdisc TransCelerate BIOPHARMA INC.

USDM: Focused on data standards for protocol elements

VULCAN HL7 FHIR

FHIR: Focused on transmission standards

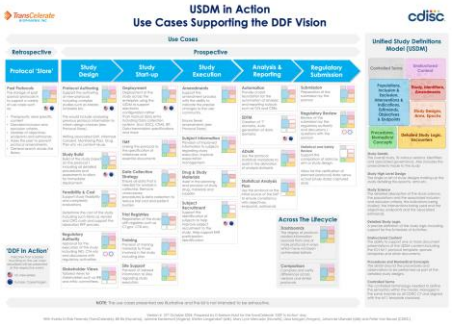
NOTE: See References for links to M11 and UDP

Use Cases for USDM Components

There has been significant interest in the community in understanding potential USDM use cases.

Dave Iberson-Hurst, the USDM product owner at CDISC, shared a graphic that provides some examples featuring key components of the USDM that are used in each use case.

This graphic is available for download here.



ADOPTION STORIES SUMMARY

An exploration of case studies from three sponsor companies on their digital data flow journey

There has been significant interest from the community in learning more about DDF solution adoption stories.

Adoption stories can be a powerful tool to help the community understand the ***possibilities*** through real-life examples and lessons learned.

As each company has different processes, technology ecosystem, and organization structures, when learning about how DDF solutions can be applied successfully, it is highly recommended to:

- Reflect on your company's specific processes, technologies, and structure
- Consider different areas and situations inclusive of an end-to-end data flow, and
- Focus on the greatest value-add for your specific company.

Common Themes Across Adoption Stories

Start Small and Have a Long-Term Plan.

Small Wins and Successes Will Potentially Support Bigger Changes and Better Buy-In.

Iterate & Adjust as Needed.

Getting and Applying End-User Feedback Supports Success and Usage. Design For Your Audience.

Organizational Change Management (OCM) is Critical.

Leadership Support and Alignment is Needed As Well As Time To Adapt.

It Won't be Easy So Don't Wait.

Share the Burden! If It Were Easy, We Would All Be Doing This - There Is Great Potential In Taking the First Steps.

ADOPTION STORIES DETAILS

#1: Digital Schedule of Activities

DDF Solution Application

Creation of Study Definitions Repository (SDR) to better support new studies by digitizing the Schedule of Activities.

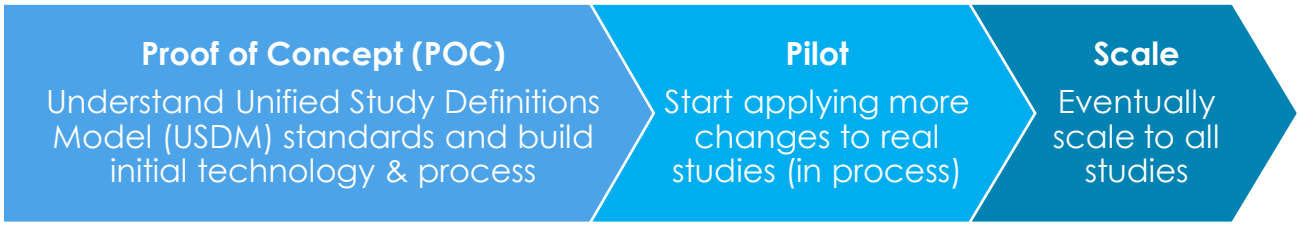
Why Start with Digital Schedule of Activities (DSoA)?

DSoA provides the **biggest impact** with incremental process improvements as well as elimination of "whitespace."

How Was it Done?

"Build a little, test a little, learn a lot" – Adm. Wayne Meyer

High-level three phase approach:



What's Been Done To-Date And What's To Come?

POC

- **Technology:** Created a **Study Definitions Repository (SDR) based on the USDM**
- **Process:** Manual SoA population into SDR based on Natural Language Processing (NLP) pull of SoA information from an authored protocol.

Pilot (In Process)

- **Technology:** **Build automation** to push Study Design directly into SDR, auto-extraction of DSoA from SDR for the protocol
- **Process:** Eliminate manual entry into SDR; leverage platforms for Study Design into SDR.

Ultimate Vision: **End-to-end digitization** from protocol authoring to clinical study report (CSR) generation

Learnings & Key Takeaways

Things can get complicated very fast. Consider the following:

- Build a roadmap, **start small** with realistic & achievable instantiations, and continue to **iterate and adapt** as you go
- Execute on **continuous stakeholder alignment**, awareness and education
- **Allow enough time** for both the organization and people to adjust to changes

#2: Digitization of Existing Protocols

DDF Solution Application

Creation of Study Definitions Repository (SDR) to store and contain historical protocols, with an interface for searching stored content.

Why Start with Digitizing Existing Protocols?

Delivers tangible business value without first implementing a digital Study Builder. By first creating a **"protocol data hub"** based on USDM standards, value is added in the existing study design process through digital querying capabilities of historical protocol content.

How Was it Done?

A **multi-year plan** for an overall "Digitized Protocol Environment" was envisioned, with several interconnective components that could be developed in phases.

What's Been Done To-Date And What's To Come?

Ultimate Vision

Have a **digital Study Designer platform with automation capabilities**

Learnings & Key Takeaways

- **Cross-functional leadership understanding and buy-in** is important since implementation of the platform and usage are done by different groups (i.e. clinical business functions and informatics/digital/technology functions).
- **Did not wait** and used an earlier version of the USDM (version 2). USDM was later updated to incorporate extensions suggested from the work in building the "digital hub."
- To unlock the power of both data and technology requires **collaboration** between experts, **courage** as leaders to drive and inspire a shift in mindset, and **conviction** in our belief that there is a better way to do things

ADOPTION STORIES DETAILS CONT'D

#3: A Study Builder

DDF Solution Application

Creation of sharable open-source code used to develop a Study Builder with a Study Definitions Repository (SDR) to enable the digitalization of new protocols.

Why Start with a Study Builder?

As the existing Metadata Repository (MDR) was reaching end of life, business decisions were made to **expand the MDR to be an SDR**, align the MDR with the USDM, and create capabilities for data entry and interoperability.

How Was it Done?

A **multi-year plan** for an overall "One Digital Data Flow" was envisioned, with an integrated IT landscape and replacing/updating systems that in parallel have reached end-of-life.

What's Been Done To-Date And What's To Come?

"MVP"

- A Study Builder application with a web-based user interface
- MDR/SDR – central repository for study specific data
- Application Programming Interface (API) layer – interoperability components

"Next Release" (in process)

Expansion of capabilities and usability components

Ultimate Vision

Enable digital data flow from **protocol development to submission and beyond**.

Learnings & Key Takeaways

People	Process	Technology
• **Aligning across organizations** is critical • **Involving end users early** in development better ensures adoption • Ensure that **sufficient resources** are available	• May need to support **interim parallel processes** • Identify & **share business values** & outcomes • **Consider cross-functional alignment & ownership** of implementation	• "Documents to digital" will **require a lot of effort** but great potential • Focus on **small releases & adjust agilely** based on user feedback • **Ensure technology** is not a barrier to adoption (i.e. performance)

CLINICAL SOLUTION PROVIDER SHOWCASE DETAILS

A poster session where clinical solution providers shared different protocol digitization technology solutions.

NOTE: TransCelerate does not endorse, certify or recommend any solution provider or product. All adoption or use of any solution, deliverable, standard, technology, product, or vendor is purely voluntary.

Clinical solution providers' attendance at the event varied by location. Providers and their posters were selected based on an open call for abstracts. The criteria for selection included:

- Information about how the USDM and DDF Solutions, such as the SDR or SDR Reference Implementation, have been applied in practice to achieve protocol digitization
- Demonstrated ability (i.e. in a production environment) for downstream efficiencies related to protocol digitization and availability in the DDF Solution Directory

Review potential Clinical Solution options in the **DDF Solution Directory**

https://transcelerate.github.io/ddf-directory/directory/directory.html

Making Protocol Content Machine Readable via Standards & Markup Language

The solution demonstrates content reuse for machine readable content. It takes a protocol and applies XML markups to create "data elements" leveraging the USDM to create the structure and tags.

Use Case / Scenario

Standards Leveraged

Retrospective vs. Prospective

Digitization vs. Digitalization

- Artificial Intelligence
- Digitization: Document to Digital
- Markup Language
- RWE
- Common Protocol Template Mapping Tool
- Document Generation
- Prospective: New Studies
- Study Build
- Data Exchange: 1 way or 2 way
- Fast Healthcare Interoperability Resources
- Recruitment
- Study Data Tabulation Model
- Digitalization: Starts as Digital Content
- ICH M11
- Retrospective: Completed Studies
- Unified Study Definitions Model

CLINICAL SOLUTION PROVIDER SHOWCASE DETAILS

Various clinical solutions featuring DDF Solutions

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Standardizing I/E Criteria for Recruitment via Matching Algorithm

The solution demonstrated converting protocol Inclusion/Exclusion (I/E) data into a USDM structure. FHIR was further applied to extend the content to be used on an Electronic Medical Record (EMR)/Electronic Health Record (EHR) platform. Patient matching algorithms were applied on EMR/EHR systems based on structured data.

Use Case / Scenario

Standards Leveraged

Retrospective vs. Prospective

Digitization vs. Digitalization

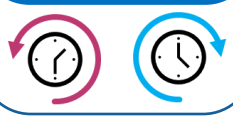
Digital Data Flow from Study Design to SDTM Generation

The solution demonstrated data flow from protocol to Study Data Table Model output, including loading protocol into a USDM structure, aligning the data to biomedical concepts, and extracting data to SDTM, electronic Case Report Forms (eCRF), and XML structures.

Use Case / Scenario

Standards Leveraged

Retrospective vs. Prospective



Digitization vs. Digitalization

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Study Definitions Repository Reference Implementation

The Study Definitions Repository (SDR) Reference Implementation is a working instance of a Study Definitions Repository developed based on the USDM using Microsoft Azure. A proof-of-concept utility tool was also created to show how USDM can be mapped to the TransCelerate CC&R Common Protocol Template (CPT) format with automated population into an eCPT document.

Use Case / Scenario	Standards Leveraged	Retrospective vs. Prospective	Digitization vs. Digitalization
	cdisc USDM, CPT		

Leverage FHIR for Standardized Protocol Content Data Exchange

The solution demonstrates leveraging FHIR for data exchange across various systems. A protocol standardized via USDM is used as a starting point with potential data flow to Electronic Data Capture (EDC), Clinical Trial Management System (CTMS), EHR, Laboratory Information Management System (LIMS) platforms.

Use Case / Scenario	Standards Leveraged	Retrospective vs. Prospective	Digitization vs. Digitalization
	cdisc USDM		

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Leverage Standardized Protocol Content for Real-World Data Analysis

The solution demonstrates using the USDM for structured I/E data from the protocol, and standardizing patient data via JavaScript Object Notation (JSON) to convert and store into an Observational Medical Outcomes Partnership (OMOP)-like database where data can be anonymized for additional analysis.

Use Case / Scenario

Standards Leveraged

Retrospective vs. Prospective

Digitization vs. Digitalization

Study Builder and Document Generation Platform

The solution demonstrates applying the USDM to a Study Builder and document generation platform, with Artificial Intelligence (AI) and automation. The solution supports outputs into other core documents (i.e. Statistical Analysis Plan, Consent forms, SoA, and operational documents such as Billing Plan, Protocol Summary, etc.)

Use Case / Scenario

Standards Leveraged

Retrospective vs. Prospective

Digitization vs. Digitalization

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CLINICAL SOLUTION PROVIDER SHOWCASE DETAILS

Various clinical solutions featuring DDF Solutions

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Open-Source Code for Study Builder Solution

The solution demonstrates an open-source study builder and SDR platform leveraging the USDM for data standards. Use of APIs show full connectivity to a variety of different systems.

Use Case / Scenario

Standards Leveraged

Retrospective vs. Prospective

Digitization vs. Digitalization

Study Designer/Builder with Workflow Capabilities

The solution demonstrates a core suite of integrated standards-driven study builder applications that covers USDM study elements, clinical authoring and SoA-based specimen management plans. The solution also enables workflow driven API integration with an SDR.

Use Case / Scenario

Standards Leveraged

Retrospective vs. Prospective

Digitization vs. Digitalization

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Study Designer and MDR with Data Exchange Capabilities

The solution demonstrates a Study Designer platform with a Metadata Repository (MDR) aligned to the USDM. The solution has the ability to leverage AI/Machine Learning (ML) for exports to STDM, EDC, etc.

Use Case / Scenario	Standards Leveraged	Retrospective vs. Prospective	Digitization vs. Digitalization
			

AI-Enabled Auto-Generation of Protocol Datasets

The solution demonstrates Trial Design dataset automation. The solution leverages AI/ML to extract PDF protocols into an SDR, where the data can be used for future study designs.

Use Case / Scenario	Standards Leveraged	Retrospective vs. Prospective	Digitization vs. Digitalization
			

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CLINICAL SOLUTION PROVIDER SHOWCASE

Panel session summary

Several clinical solution providers were selected via attendee anonymous voting to participate in a panel discussion after the open poster session.

The New Jersey and Copenhagen locations involved different solutions based on attendance and participation.

The following are some key takeaways from both locations.

USDM Standards

"Locking" the next version to allow for true backward compatibility is key for scaling technology solution development.

Custom Approaches

Each company has their own goals and technology ecosystem. Focus on company's priorities to get started.

Continued Expansion

There is room for additional standards extensions, such as Therapeutic Area data or create IE/ endpoints/ objectives libraries.

Cross-Industry Partnership

TransCelerate DDF Initiative has allowed for great pharma industry, solution provider & regulatory collaboration, which ultimately benefits patients.

Standards Benefits & Value

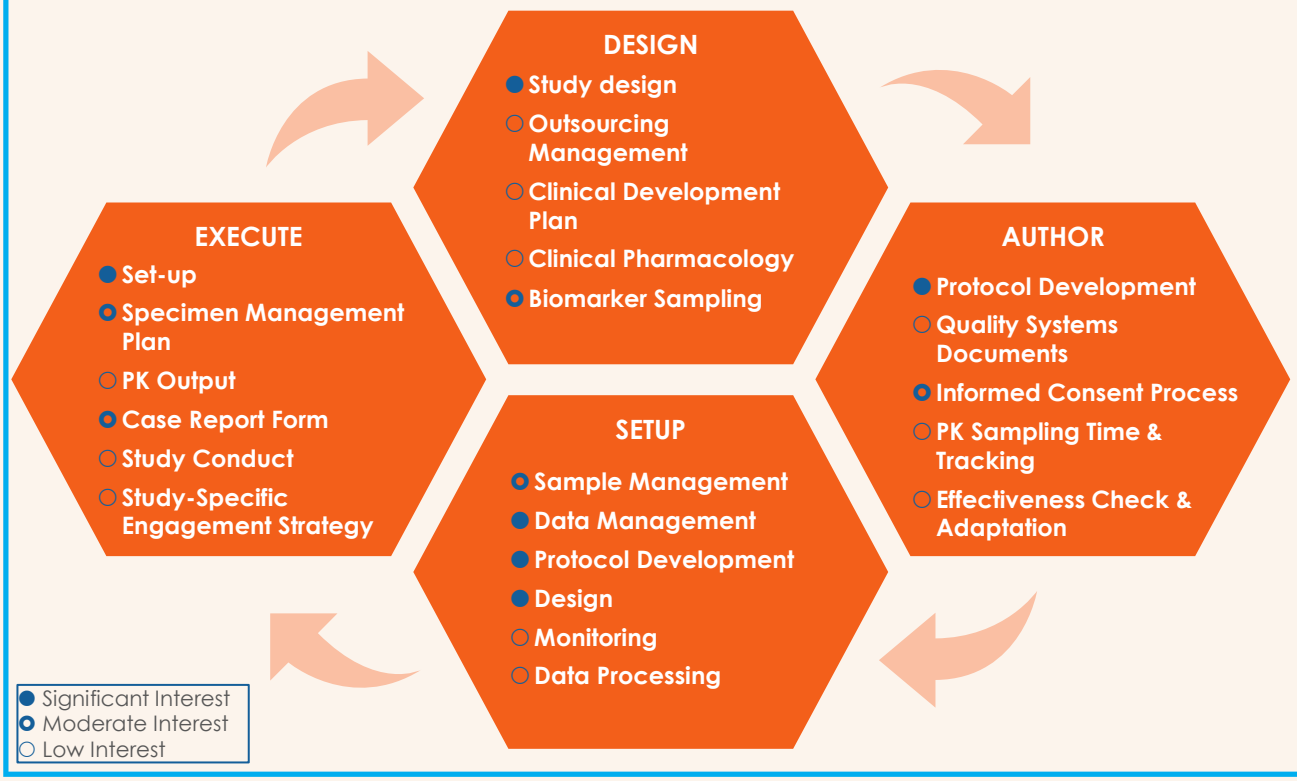
USDM can really support automation, including AI, by increasing machine learning opportunities and allowing greater data reuse and connectivity.

Adoption Challenges

Doing everything all at once is too much. Start small, add as you go, and bring stakeholders with you on both the process & technology journey.

EVENT FEEDBACK & KEY TAKEAWAYS

Throughout the event, participants were asked to identify use cases that were of interest. This information will be used to inform future adoption stories & case studies.



Summary of Common Themes

Leadership support is key.

Leaders from different functional lines including clinical business functions and data and technology functions will need to be aligned.

Bring biggest impacted stakeholders in early.

Because data flow starts with Study Design, involving and getting buy-in from those stakeholders is critical.

Need for organizational change management (OCM) can not be underestimated.

Make the case, take the time, mind the effects, and share the burden.

Don't boil the ocean – Focus on something small and doable.

Start small, celebrate & promote wins, and continue to expand with a long-term plan.

QUOTES

(DDF in Action day)"has a **huge value** for industrial development and collaboration."

"Good to hear the **'real life' experience** from other sponsors and their strategy on implementations"

(after we've heard)… "we're going to completely go back and **re-think our strategy**"

"Great to see how **DDF has evolved**"

"Some good **common themes**"

"Very **excited by possibilities** but recognize need to start small"

"…**thoroughly enjoyed** DDF Action Day…"

"It was truly an **eye-opening** experience"

"It was great to have direct access to a small and **focused group** on a game changer like digital data flow"

"The insights provided during the session were incredibly valuable, as they offered practical strategies on how we can consider and **enable adoption** within our own organization."

"Great to know the **implementation challenges, benefits and improvements** going to happen in USDM approach"

"We're looking forward to **next year**!"

CONCLUSION

DDF in Action day convened sponsor companies, clinical solution providers, and key industry stakeholders to forge connections, explore some DDF solution options, and gain valuable insights into protocol digitization.

Based on the feedback regarding the presentations of practical applications of DDF solutions by sponsor companies, interactive networking sessions, and moderated discussions with solution providers, the event was successful in:

- **Connecting** industry peers on the know-how for implementing DDF solutions
- **Sharing** potential pathways from transformative enablers across the industry
- **Creating momentum** through knowledge sharing and networking
- **Imparting** lessons learned through DDF solutions adoption stories

The attendance of the event and enthusiastic engagement throughout the day in both locations demonstrate the growing interest & attention by the life-sciences and pharmaceutical community in protocol digitization.

The DDF Initiative project team is very thankful to all for the active participation, insightful contributions, and collaborative engagement at DDF in Action day.

The smooth facilitation and seamless logistics of a dual continent DDF in Action day event was only made possible by the meticulous planning from members of the DDF Initiative project team, as well as tight coordination and preparation between the DDF Initiative program management office and representatives from the host companies, Johnson & Johnson and Novo Nordisk.

Let's continue this journey together to break the document paradigm through active exploration of potential applications, candid interchange with cross-industry thought partners, and enthusiastic promotion within the clinical development community about the value and benefits of protocol digitalization and Digital Data Flow.

REFERENCES

To learn more about DDF, access the links & QR Codes below.

DDF Website

Primary website for DDF

https://transcelerate.github.io

CDISC DDF Website

Explore & access the USDM

https://cdisc.org/ddf

TCB DDF Initiative

Discover the initiative background

https://www.transceleratebiopharmainc.com/initiatives/digital-data-flow

DDF GitHub Repos

Review & access the SDR Refence Implementation.

https://github.com/transcelerate

To learn more about other related initiatives, access the links & QR Codes below.

ICH M11

Explore & access ICH M11

https://www.ema.europa.eu/en/ich-m11-guideline-clinical-study-protocol-template-and-technical-specifications-scientific-guideline

Utilizing the Digital Protocol (UDP)

Learn more about this umbrella initiative

https://www.hl7vulcan.org/udp-project