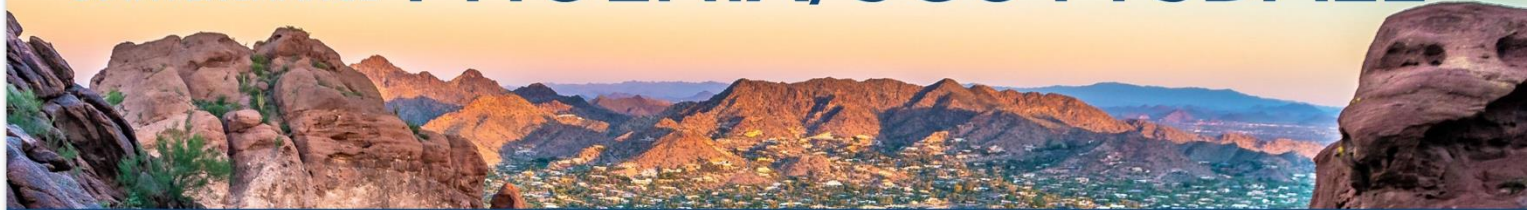




2024 CDISC + TMF
US INTERCHANGE

PHOENIX/SCOTTSDALE



23-24 OCTOBER: CONFERENCE & EXPO | 21, 22, 25 OCTOBER: TRAININGS

DDF and Breaking Down the Document Barrier

Bob Brindle, VP Product Management, Nurocor
Frederik Malfait, SVP Information Architecture, Nurocor

Meet the Speakers

Bob Brindle

Title: VP Product Management

Organization: Nurocor



Frederik Malfait

Title: SVP Information Architecture

Organization: Nurocor





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(s) have no real or apparent conflicts of interest to report.*



Agenda

1. The road to digitalization
2. Upstream and downstream
3. Breaking down the document barrier
4. Clinical document authoring

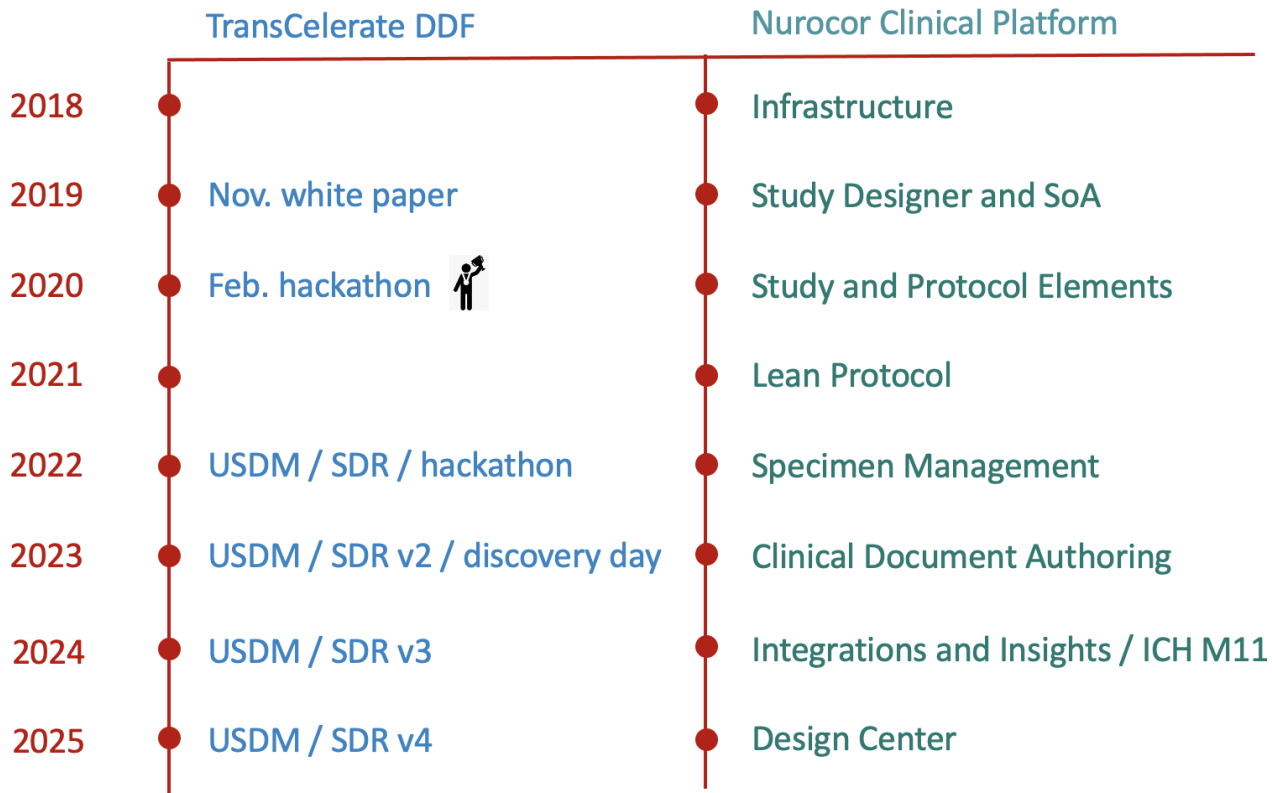


The road to digitalization

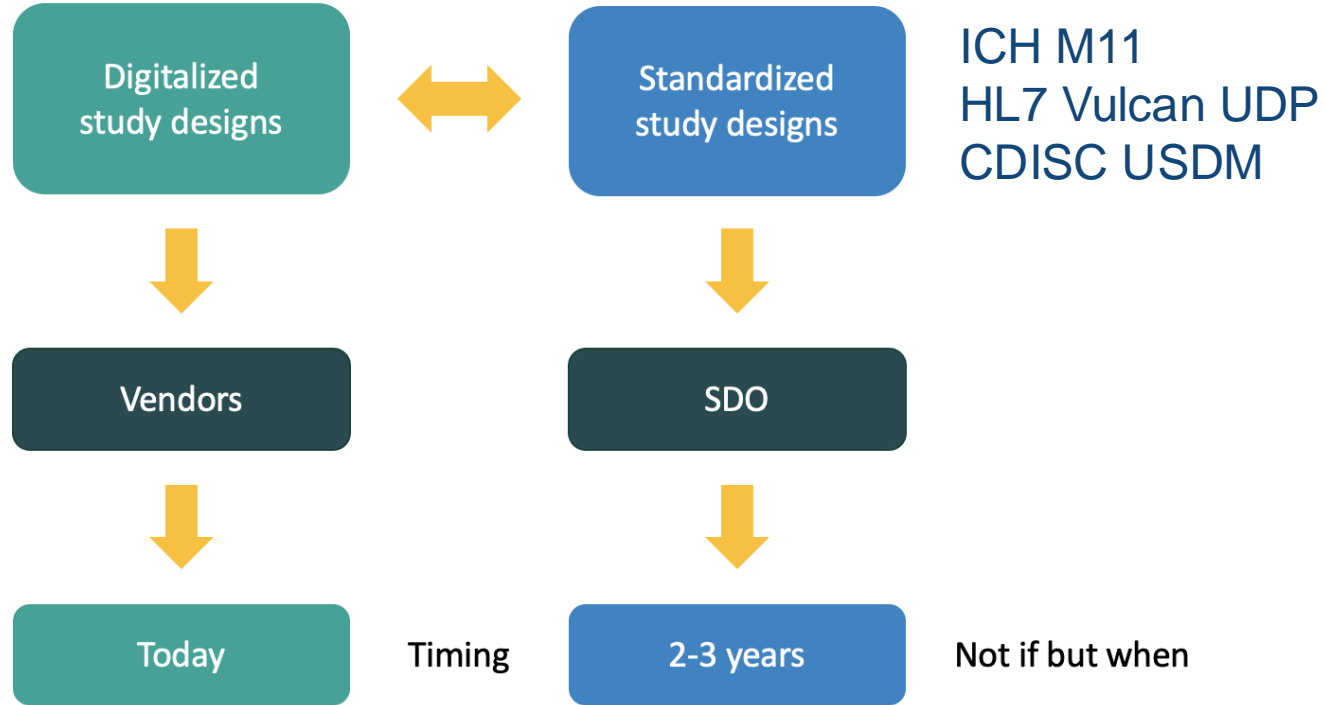
It's a dangerous business, Frodo, going out your door. You step onto the road, and if you don't keep your feet, there's no knowing where you'll be swept off to.

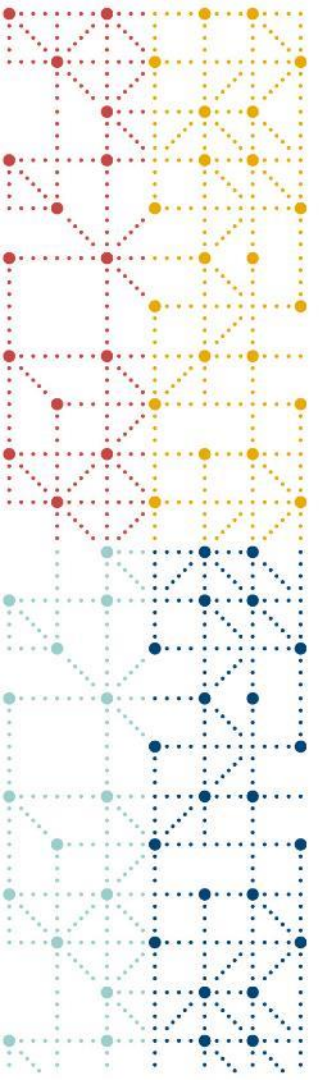
J.R.R. Tolkien

The Journey (so far)



Adoption versus Standardization



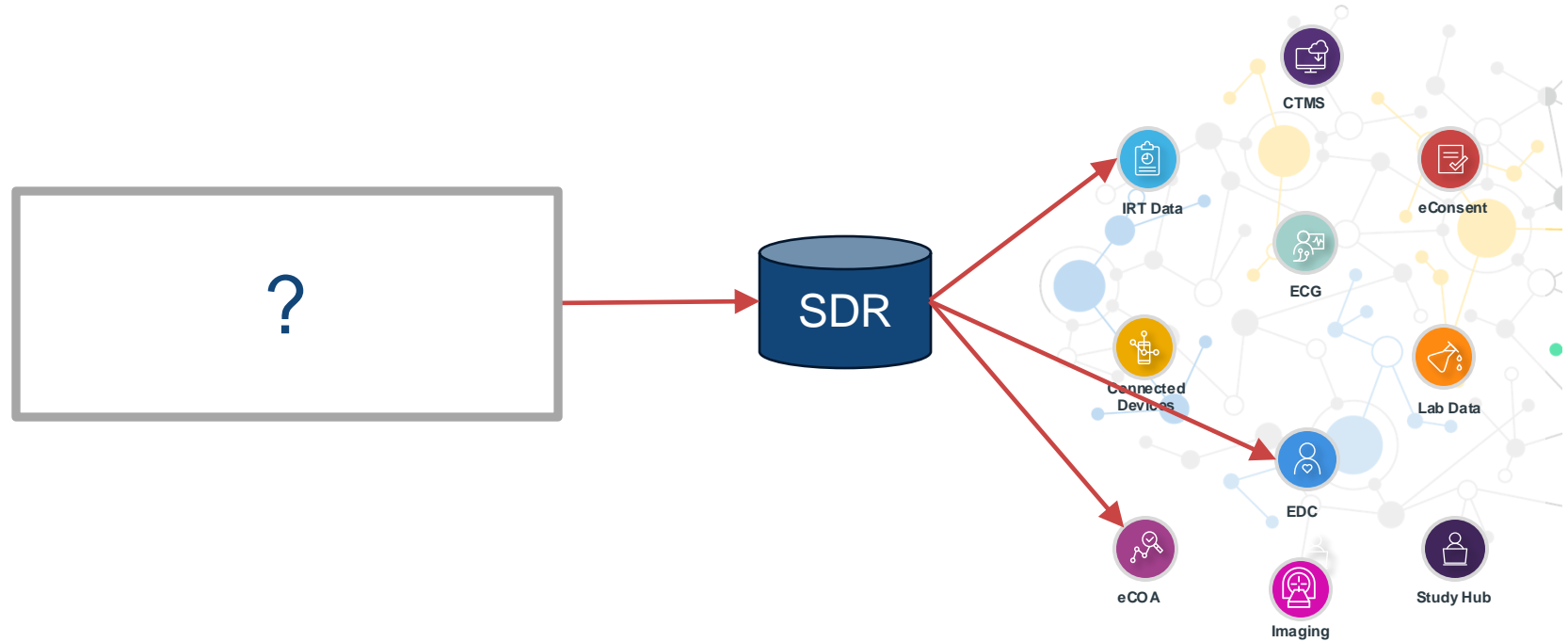


Upstream and downstream

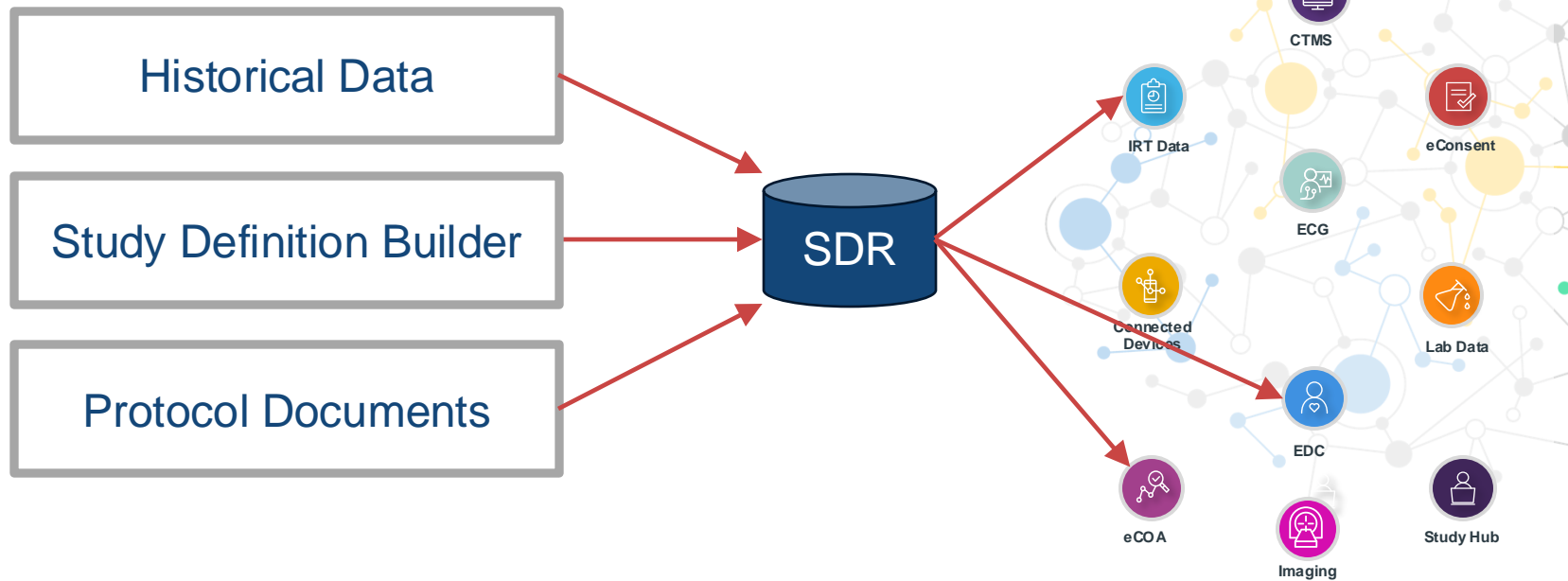
There comes a point where we need to stop just pulling people out of the river. We need to go upstream and find out why they're falling in.

Desmond Tutu

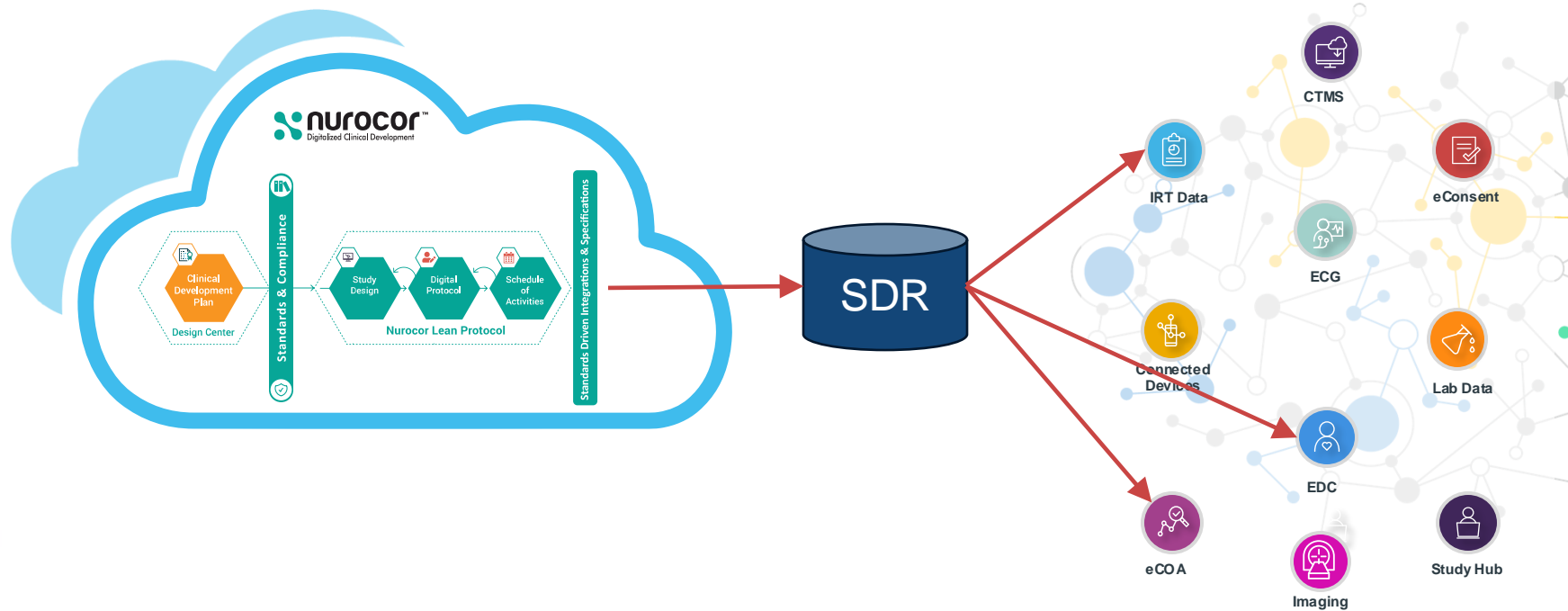
Driving digitalization – Hub Architecture



Upstream possibilities



Upstream study definition builder





Breaking down the document barrier

Disrupt yourself before someone else does.

Jay Samit



Codify the study design into components

- Components are well defined entities
- Components have well defined relationships
- Components can be templated
- Components can receive, carry, and send information
- Components can have many representations
- Components can be tracked
- Components can be reused (write once, read many)
- Components are actionable
- Components can be assembled

Study dashboards

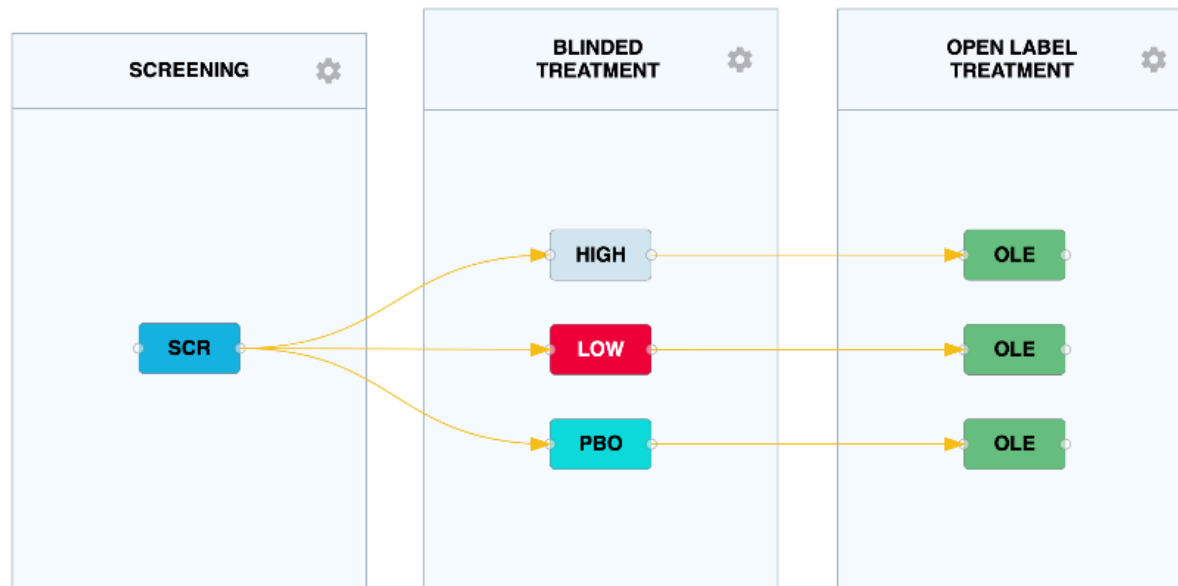
The screenshot displays the NCP Dashboard Enterprise interface. At the top, there is a navigation bar with the NCP logo, the text "NCP Dashboard Enterprise", a notification bell icon with a "4" badge, and a user profile icon labeled "FM". Below the navigation bar are three tabs: "STUDIES" (selected), "DOCUMENTS", and "CHANGE REQUESTS".

The main content area features a filter section with "Filter By: None Applied" and a "Creation Date" dropdown menu. A prominent blue button labeled "CREATE NEW STUDY" is located in the top right of the main area.

The dashboard displays a grid of six study cards, each with a status indicator (AMENDIT, 202301WF2SDR, SDR Integration Test, 202301E2E, SPECMCOHORT, SPECMPARTIAL) and a progress status (Original, In Progress). Each card includes the study title, creation date, and a set of action icons (share, print, calendar, trash, refresh, and menu).

Study ID	Status	Progress	Title	Created On
AMENDIT	Original	In Progress	Studying the process of protocol amendments	September 14, 2023
202301WF2SDR	Original	In Progress	2023-01 WF to SDR Test	August 24, 2023
SDR Integration Test	Original	In Progress	SDR-T1	August 24, 2023
202301E2E	Original	In Progress	2023-01 End to End Test	August 15, 2023
SPECMCOHORT	Original	In Progress	Specimen Management Cohorts Setup	July 19, 2023
SPECMPARTIAL	Original	In Progress	Specimen Management Demo - Partial Study Setup	July 19, 2023

Trial design schematic



Interventions and products

Study Interventions and Products

Interventions

▼ **Xanomeline high dose**

1 Arm 2 Administered Products

Intervention Details

Intervention Name: **Xanomeline high dose**

Intervention Type: **Drug**

Description:
81mg xanomeline, given by daily application of 2 patches, 1x50cm² 54mg xanomeline and 1x25cm² 25mg xanomeline. Patches to be worn continuously throughout the day for 12-14 hours and removed in the evening

Intervention Alias:
LY246708

Related Items:

Arms:

- **High dose**

Administered Products:

- **Xanomeline 25cm 27mg patch**
- **Xanomeline 50cm 54mg patch**

Eligibility criteria

Eligibility Criteria	
Inclusion Criteria	
Protocol Text	Submission Text
Participant must be male or a postmenopausal female	Males and postmenopausal females
Aged \geq 50 year(s), at the time of signing the informed consent	At least 50 years of age
Meets the Diagnostic and Statistical Manual of Mental Disorders Version 5 (DSM-5) criteria and/or National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorder Association's (NINCDS-ADRDA) criteria for probable AD	Diagnosis of probable Alzheimer's Disease

Objectives and endpoints

The screenshot displays the 'STUDY AND PROTOCOL ELEMENTS' section of a CDISC software interface. The left sidebar lists various study elements, with 'Objectives and Endpoints Elements' selected. The main content area is titled 'Primary Objectives and Endpoints / Estimands' and is divided into two columns: 'OBJECTIVES' and 'ENDPOINTS'. The 'OBJECTIVES' column contains two entries, each with a vertical ellipsis icon to its right. The 'ENDPOINTS' column contains two entries, each with a vertical ellipsis icon to its right. Below the 'OBJECTIVES' column is a '+ ADD OBJECTIVE' button. Below the 'ENDPOINTS' column are two 'Add Endpoint' links. At the bottom of the main content area, there are three sections: 'Secondary Objectives and Endpoints / Estimands' with a 'Display Table' toggle switch, 'Tertiary/Exploratory Objectives and Endpoints / Estimands' with a 'Display Table' toggle switch, and 'Schedule of Activities' with an edit icon.

OBJECTIVES	ENDPOINTS
To evaluate the efficacy of DS-8500a compared with Insulin treatment administered in individuals with Type 2 Diabetes Mellitus (T2DM)	The percentage change in HbA1c from Baseline to Week 4, Week 8 and Week 12
To document the safety profile of Xanomeline TTS	The change from Baseline to Week 4, Week 8, Week 12 and Week 24 in continuous laboratory tests: Hepatic Function Panel



+ ADD OBJECTIVE




Secondary Objectives and Endpoints / Estimands Display Table

Tertiary/Exploratory Objectives and Endpoints / Estimands Display Table

Schedule of Activities

Schedule of Activities

DEFINED ACTIVITIES STUDY ACTIVITIES **PLANNED ACTIVITIES** RELATED REQUESTS (0)  

Treatment 2 arms   Events & Timepoints  Export Schedule

	Screening	Baseline	Week 4	Week 8	Week 12	Week 24
	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
∨ Disposition - Randomization	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
∨ Prior and Concomitant Medications	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
∨ Exposure	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
∧ Vital Signs	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
∨ Vital Signs - General	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
∨ Vital Signs - Systolic Blood Pressure	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
∨ Vital Signs - Diastolic Blood Pressure	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
∨ Vital Signs - Height	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
∨ Vital Signs - Weight	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
∨ Vital Signs - BMI	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
∨ Adverse Events	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

Specimen Management Plans

Specimen Management

Subject groups 0 Biospecimens 0 Plans 0

Manage collection groups

Search Filter

State	Name	Description	Collection matrix	Assay count	
Valid	Laboratory Panels 1	A sample description for Specimen A.	1 Matrix 1	3	
Invalid	Laboratory Panels 2	A sample description for Specimen B.	Matrix 2	4	
Valid	Laboratory Panels 3	A sample description for Specimen C.	XMatrix 3	5	
Invalid	Laboratory Panels 4	A sample description for Specimen D.	Y Matrix 4	6	
Valid	Laboratory Panels 5	A sample description for Specimen E.	Matrix 5	7	

Items per page: 10 1-10 of 5 results < >

Lean Protocol™

The screenshot displays the Lean Protocol software interface. At the top, the header includes a logo, the study identifier '202301E2E', a dropdown menu set to 'ORIGINAL', another dropdown menu set to 'LEAN PROTOCOL', and a button labeled 'Enterprise'. On the right side of the header, there are notification icons and a user profile icon labeled 'FM'.

The main interface is divided into two panels. The left panel, titled 'All Processes', contains a list of process levels:

- LEVEL 1
 - Level 1: (F) Early Indication Feas... (Yellow dot)
 - Level 1: (DM) Draft** (Yellow dot, highlighted)
 - Level 1: (M) Draft (Yellow dot)
 - Level 1: (SAP) Draft (Yellow dot)
 - Level 1: (SM) Draft (Yellow dot)
- LEVEL 2
 - Level 2: (F) Protocol Feasibility (Yellow dot)
- LEVEL 3
 - Level 3: (F) Site Feasibility (Yellow dot)
 - Level 3: (DM) Final (Yellow dot)
 - Level 3: (M) Final (Yellow dot)
 - Level 3: (SAP) Final (Yellow dot)
 - Level 3: (SM) Final (Yellow dot)

The right panel, titled 'Level 1: (DM) Draft', shows a table of conditions with their status and actions:

Level 1: (DM) Draft			
Conditions			
Schedule of Activities	Completed	🔒	📄
Study Model Elements	Completed	🔒	📄
Trial Arms	Completed	🔒	📄
Study Planning	Completed	🔒	📄
Study Extensions	Completed	🔒	📄
Study Interventions and Products	Completed	🔒	📄
Objectives and Endpoints	In Progress		📄

Workflow driven system integrations (SDR)

Lean Protocol Gate Approval Request

Protocol Lead	Frederik
Attachments (0)	
Disposition	Approving will submit the study from NCP to SDR.

CANCEL **CHOOSE AN ACTION** ▾

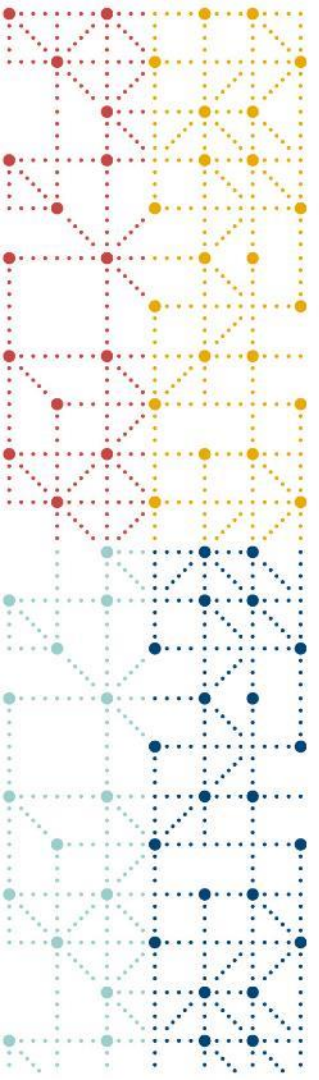
- Request SME feedback
- Approve
- Reject
- Save

Comments and discussions (1 Comment) ⓘ ⋮

Frederik Malfait ⋮
Posted 1 minute ago
General discussion

[0 REPLIES](#)

NEW COMMENT



Clinical document authoring

Every writer I know has trouble writing.

Joseph Heller

Documents in a Digital Data Flow

- Documents in traditional published formats (pdf, docx) are still required as part of many regulatory processes
- Content of documents **MUST** be consistent with the digital study definition
- Current document authoring processes and tools will need to adapt
- ICH M11 is leading us in the right direction



Final Concept Paper

ICH M11: Clinical electronic Structured Harmonised Protocol (CeSHaP)
dated 14 November 2018

Endorsed by the Management Committee on 15 November 2018

Type of Harmonisation Action Proposed

This Concept Paper supports a proposal for a new harmonised guideline that specifies comprehensive clinical protocol organization with standardized content with both required and optional components. The working group will deliver the following:

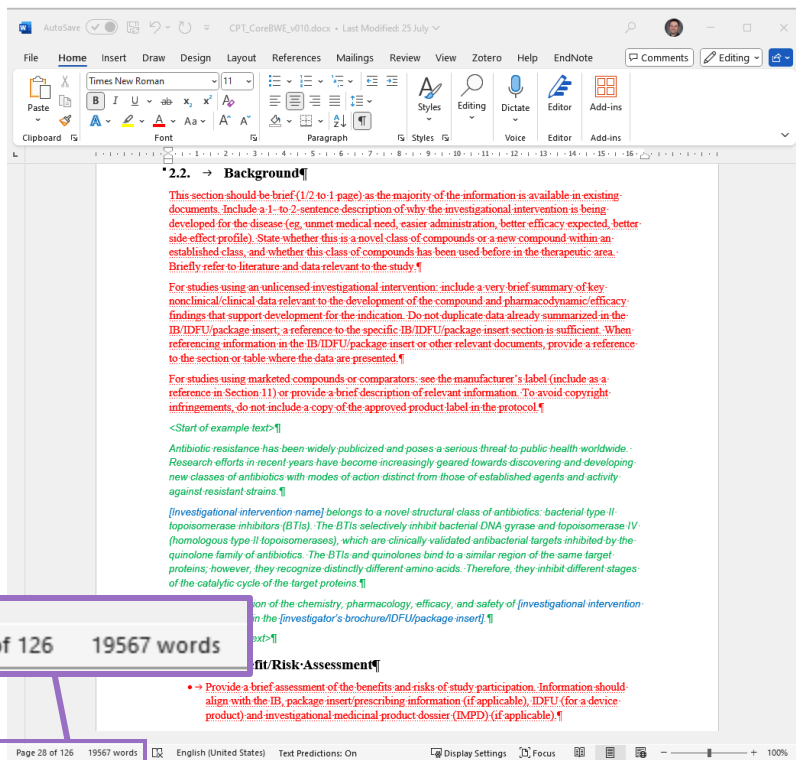
- Guideline outlining two main sets of harmonised approaches
 - a template to include identification of headers, common text and a set of data fields and terminologies which will be the basis for efficiencies in data exchange
 - a technical specification that uses an open, nonproprietary standard to enable electronic exchange of clinical protocol information

Statement of the Perceived Problem

The clinical protocol describes the processes and procedures directing the conduct and analysis of a clinical study. Currently there is no internationally harmonised standard template for the format and content of the clinical protocol document to support consistency across sponsors and exchange of protocol information. This lack of harmonization contributes to inefficiencies and difficulties in reviewing and assessing clinical protocols by regulators, sponsors, ethical oversight bodies, investigators, and other stakeholders. An international guideline and template would support consistency in the development of structured and unstructured protocol content, and a technical specification will facilitate its electronic exchange.

Issues to be Resolved

Templates in a document-based process



- Pushing content into a traditional Word-based document template risks breaking the digital data flow
 - Hard to maintain template structure
 - Hard to control access
 - Hard to control edits
 - Copy/paste culture
 - Versions can proliferate and diverge
- Document preparation overheads
 - Review cycles and comment resolution
 - Formatting and styling
 - Links and cross-references
 - Consistency checking
 - Bibliography

Templates in a digital data flow



- Components are well defined entities
- Components have well defined relationships
- Components can be templated
- Components can receive, carry, and send information
- Components can have many representations
- Components can be tracked
- Components can be reused (write once, read many)
- Components are actionable
- Components can be assembled

Examples

DEFINED ACTIVITIES STUDY ACTIVITIES PLANNED ACTIVITIES RELATED REQUESTS (0)

Treatment 2 arms Events & Timepoints Export Schedule

	Screening	Baseline	Week 4	Week 8	Week 12	Week 24
Disposition - Randomization	●	●				
Prior and Concomitant Medications	●	●	●	●	●	●
Exposure	○	●	○	○	○	○
Vital Signs	●	●	●	●	●	●
Vital Signs - General	●	●	●	●	●	●
Vital Signs - Systolic Blood Pressure	●	●	●	●	●	●
Vital Signs - Diastolic Blood Pressure	●	●	●	●	●	●
Vital Signs - Height	○	○	○	○	○	○
Vital Signs - Weight	●	●	●	●	●	●
Vital Signs - BMI	○	○	○	○	○	○
Adverse Events	○	●	●	●	●	●

Enterprise In Progress Protocol document New review cycle Editing

Styles A | T | A | B | I | U | X₂ | X² | List Styles

Save

1.3 Schedule of Activities (SoA)

Configure View

Activities	Screening			Treatment						
	Visit 1 Week -2	Visit 2 Day -2 ^a	Visit 3 Week 0	Visit 4 Week 4	Visit 5 Week 8	Visit 6 Week 12	Visit 7 Week 16	Visit 8 Week 20	Visit 9 Week 24	Visit 10 Week 26
Study Day	-14 (+2/-0)	-2 (+1/-1)	1 (+3/-3)	29 (+3/-3)	57 (+3/-3)	85 (+4/-4)	113 (+4/-4)	141 (+4/-4)	169 (+4/-4)	183 (+3/-3)
Disposition - Informed Consent	✓									
Patient Information	✓									
Demographics	✓									
Medical History	✓									

+ Citation + Component + Element

Examples

Study Interventions and Products

Interventions

▼ **Xanomeline high dose**

1 Arm 2 Administered Products

Intervention Details

Intervention Name: Xanomeline high dose

Intervention Type: Drug

Description:

81mg xanomeline, given by daily application of 2 patches, 1x50cm² 54mg xanomeline and 1x25cm² 25mg xanomeline. Patches to be worn continuously throughout the day for 12-14 hours and removed in the evening

Intervention Alias:
LY246708

Related Items:

Arms:

- High dose 1

Administered Products:

- Xanomeline 25cm 27mg patch 1
- Xanomeline 50cm 54mg patch 1

Enterprise

In Progress Protocol document

Styles | In Progress | Protocol document | New review cycle | Editing | 430 | SS

6 Study Intervention(s) and Concomitant Therapy

Study interventions are all pre-specified, investigational and non-investigational medicinal products, medical devices and other interventions (eg, surgical and behavioral) intended to be administered to the study participants during the study conduct.

Save

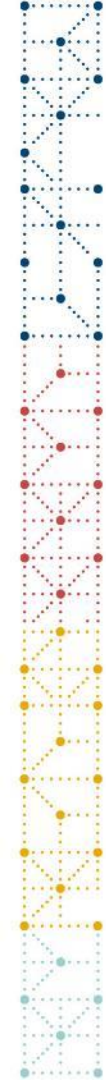
6.1 Study Intervention(s) Administered

Arm Title	A: High dose	B: Low dose	C: Placebo
Arm Type	Experimental	Experimental	Placebo
Arm Description	High dose xanomeline TTS for 26 weeks	Low dose xanomeline TTS for 26 weeks	Placebo patches for 26 weeks
Associated Intervention Labels (with associated administered products)	Xanomeline high dose (Xanomeline 25cm 27mg patch, Xanomeline 50cm 54 mg patch)	Xanomeline low dose (Xanomeline 50cm 54 mg patch, Placebo 25cm patch)	Placebo (Placebo 50cm patch, Placebo 25cm patch)

+ Citation + Component + Element

A complete digital authoring solution

- To achieve success, we need more than templates and standards
- Authors must be supported in developing content that does not flow from components and in producing a polished document as an end product
- A digital authoring solution should focus on improving user experience compared to current processes and tools
 - Collaborative authoring – with guard rails to prevent loss of content
 - Review functionality – structured reviews, traceability of outcome
 - Automatic formatting / styling – use output templates to create final documents
 - Automatic generation of structural items – title page, table of contents, bibliography etc.
 - Opportunities to embed AI for “assisted authoring”
 - Seamless integration into existing approval workflows and document repositories
- Technology is not a problem, change management is key to success



SCIENTIFIC AMERICAN.

SHARE LATEST

SPACE

Fact or Fiction?: NASA Spent Millions to Develop a Pen that Would Write in Space, whereas the Soviet Cosmonauts Used a Pencil

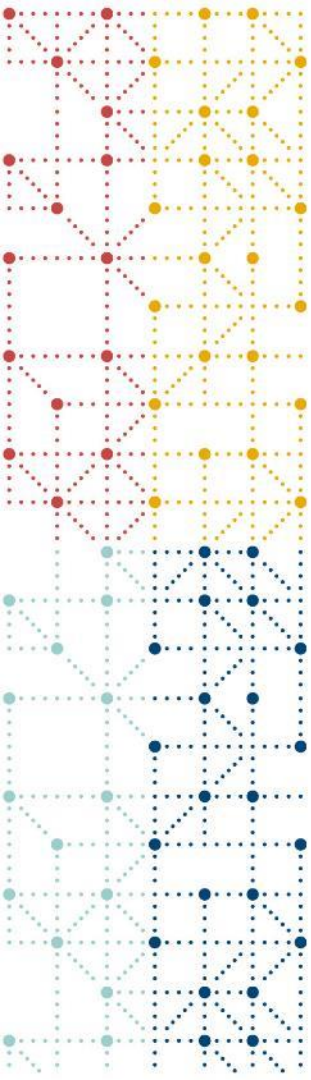
The problem of weightless writing was not solved by either Soviet central planning or good old American sub-contracting, but by a private investor and a good idea

Source: [Scientific American](#)



Conclusion

- DDF has been long in the making
- Standards organizations and regulators are embracing the concepts and developing standards, templates and specifications (e.g. USDM and M11)
- Vendors are increasingly developing technology
- Production grade software is available today – it's time to get started
- Change management and willingness to standardize are the remaining challenges
- Adoption of the tools drives further improvement
- An adoption case study is coming up!



Thank You!

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Frederik Malfait
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