Navigating Post-Go-Live Changes in Automated Clinical Study Builds: Optimizing USDM/M11 for EDC and Beyond

Michelle Ajayi - Principal Design Consultant

Joerg Dillert – Consulting Solution Senior Director

Oracle – Health and Life Sciences

14-May 2025

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Meet the Speakers

Joerg Dillert

Title: Consulting Solution Senior Director – Enterprise Architect

Organization: Oracle – Health and Life Sciences

I’m working in the Health and Life Science Industry for more than 33 years with a deep understanding of the domain requirements and combine this with my technical knowledge. Actual I’m responsible as an Enterprise Architect to map business requirements to health and life sciences systems and lead respective implementations.

Michelle Ajayi

Title: Principal Design Consultant

Organization: Oracle – Health and Life Sciences

I've worked in various roles within the industry for over 20 years, currently as a design consultant for the last 13 years. Knowledge in designing trials in several different therapeutic areas from requirements to Go-live and post go-live changes.

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.*

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Assumptions

- No AI in this presentation
- No deep technical discussion on USDM
- Focus on operational “challenges”
- Definition **Beyond**: Any clinical system which is part of the study life cycle

Chuck Cooper

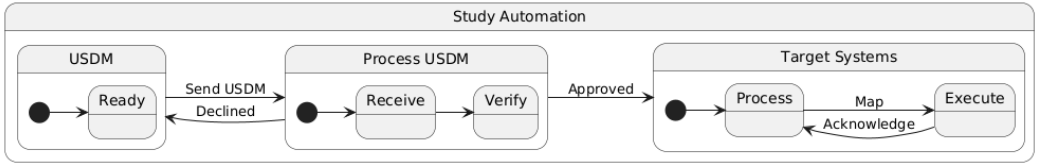
former FDA CDER Deputy Office Director, Office of Computational Sciences

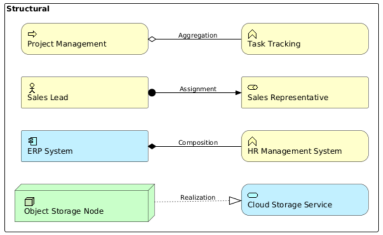
- “Even if we get Clinical Study structures standardized and automated one day, it will be still unbelievable complex!”

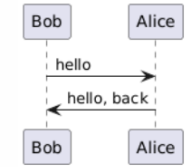
2013 @ CDISC EU Interchange

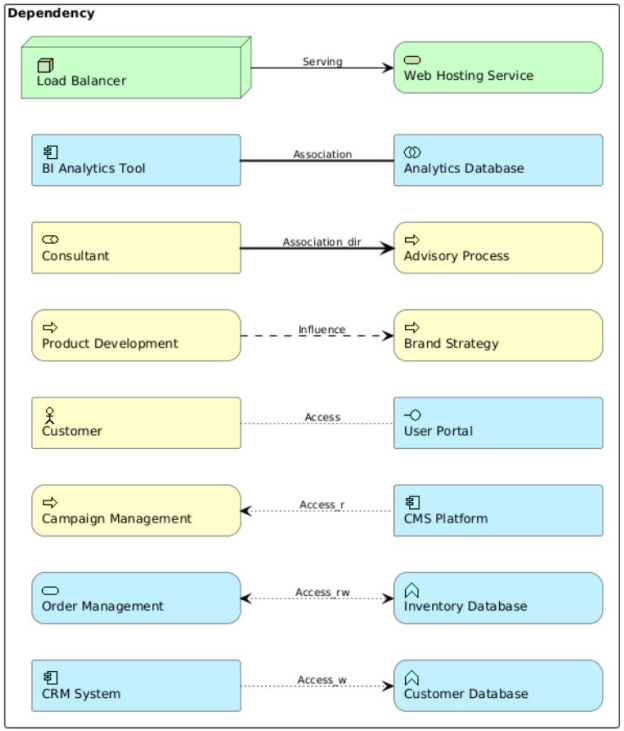
Bad Nauheim

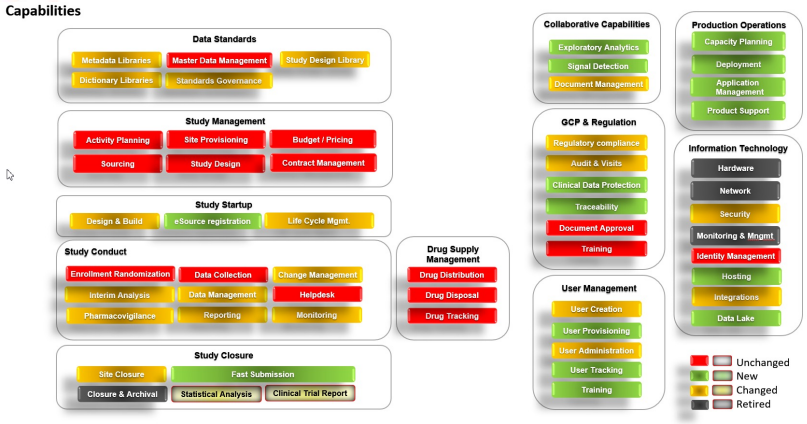
Enterprise Architect's view

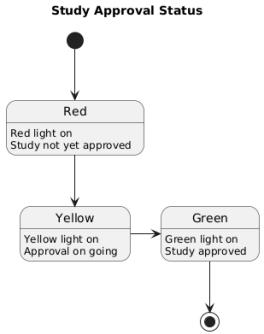


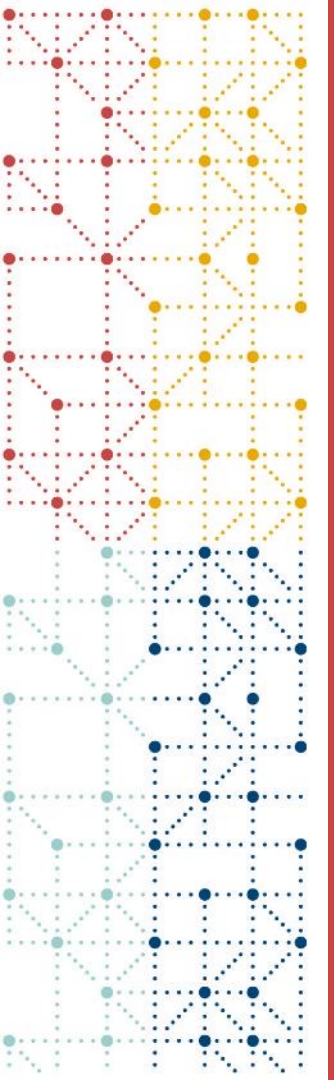






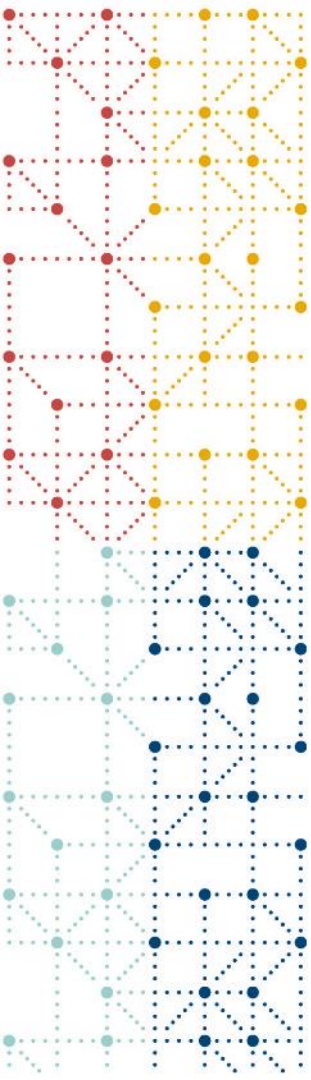






Agenda

1. Problem
2. Investigation
3. Solution
4. Conclusion



Problem

Use Case:

How can we automate the site assignment for a particular study version …

… where not all sites are at the same version in ALL downstream systems combined with a change in drug supply?

What is a study amendment?

DEFINITIONS

"amendment" means an amendment to —

(a) any term of an application for certification to conduct a clinical trial; or

(b) any particulars or documents (including a protocol) accompanying that application;

"substantial amendment", in relation to a clinical trial, means an amendment —

(a) which changes a sponsor or principal investigator of the trial; or

(b) which is likely to **affect to a significant degree** —

(i) the safety, or physical or mental integrity, of any subject of the trial;

(ii) the scientific value of the trial;

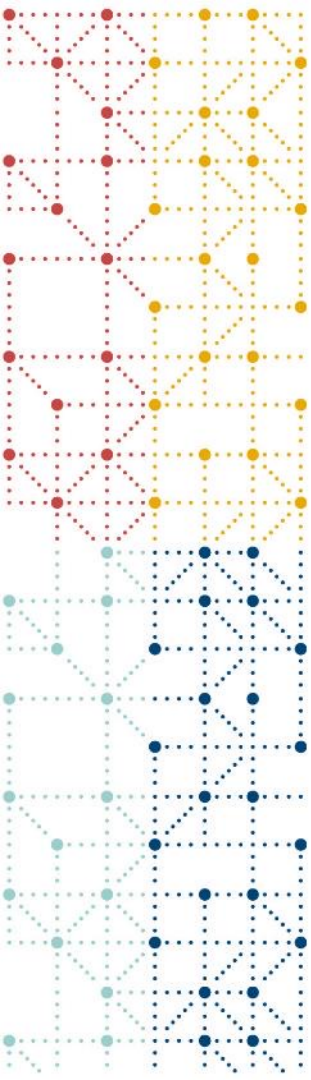
(iii) the conduct or management of the trial; or

(iv) the quality or safety of any investigational therapeutic product used in the trial

https://www.hsa.gov.sg/docs/default-source/hprg-io-ctb/hsa_gn-ioctb-05_substantial_amd.pdf?sfvrsn=67b5b225_4

Let’s focus on

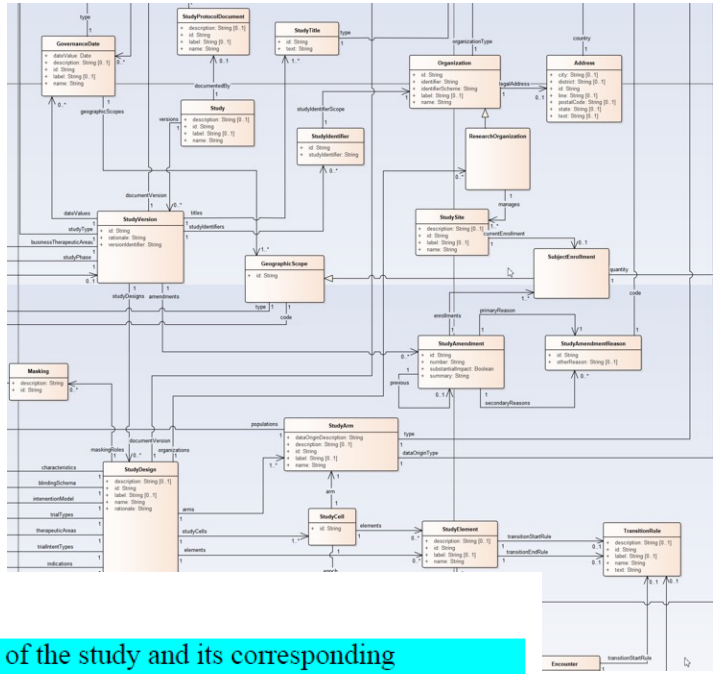
- CTMS
- RTSM
- EDC
- Safety



Investigation

USDM

- Attached entities



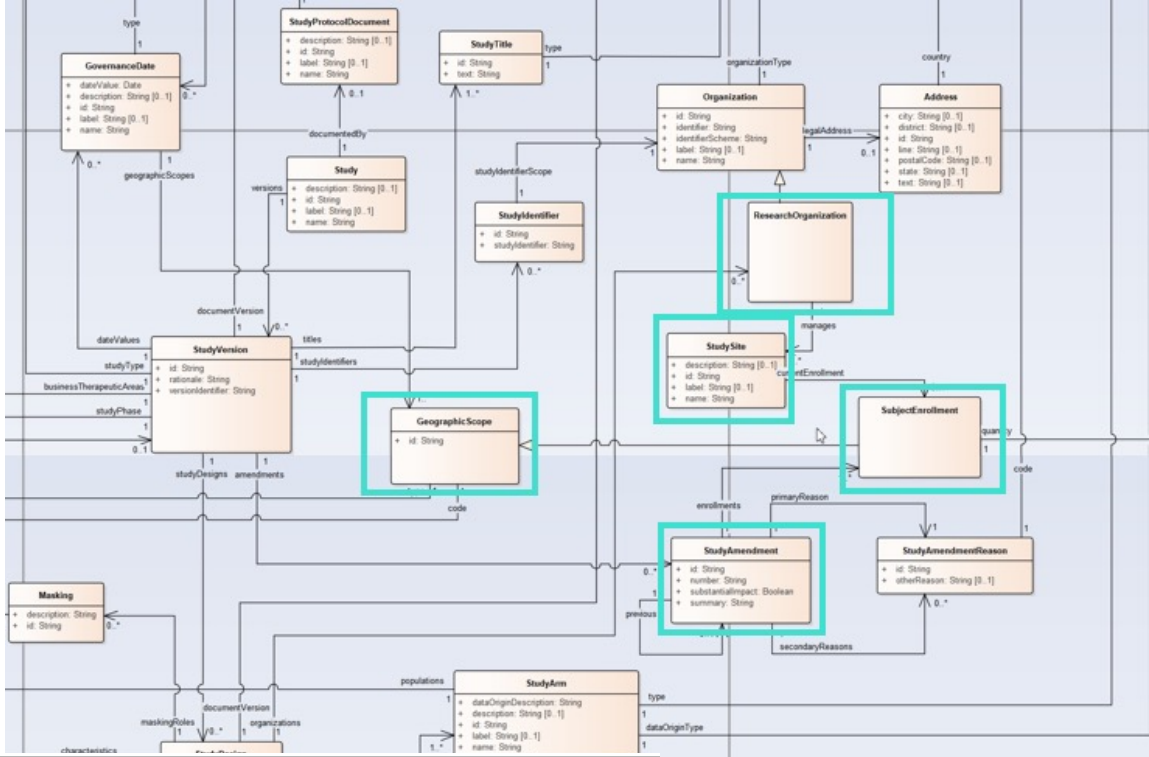
4.6 Study, Protocols, and Amendments

The Study class is the root of the USDM, collecting together the definition of the study and its corresponding versions as a whole. A study is documented by a study protocol document. The overarching study and the study protocol document each have their versioning with corresponding governance dates. These dates are to be focused to a specific geographic scope (e.g. global, regional, country).

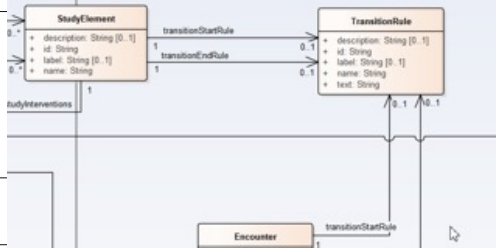
Because the traditional paper/PDF protocol document has been split into 2 parts (i.e., the document and an electronic design using the USDM), there is a need to link which electronic definition is valid with which version of the document. The Study Version class links to the StudyProtocolVersion class to define to which versions of an external protocol document the study definition relates. The study version provides a few basic study details (e.g., type, phase, rationale) and links the study with its constituent parts that include 1 or more study designs (see Section 4.8), identifiers, and titles (last 2 not shown in the following diagram) for the study.

Entities

- StudyAmendment
- GeographicScope
- SubjectEnrollment
- StudySite
- ResearchOrganzation (hmm?)



Class Name	Attribute Name	Data Type	NCI C-Code	Cardinality	Preferred Term	Definition	Codelist Ref	Inherited From
GeographicScope			CNEW		Geographic Scope	The extent or range related to the physical location of an entity.		
	id	string						
	code	AliasCode	CNEW	0..1	Geographic Scope Code|	A symbol or combination of symbols which is assigned to the geographic scope.	(Point out to external dictionaries: Standard code is ISO-3166; Alias codes drawn from GENC, UN Region Codes, etc.)	
	type	Code	CNEW	1	Geographic Scope Type	A characterization or classification of the geographic scope.	CNEW - Geographic Scope Type Response	



Geographic Scope


```
"id": "SubjectEnrollment_3",
"type": {
  "id": "Code_44",
  "code": "C25464",
  "codeSystem": "http://www.cdisc.org",
  "codeSystemVersion": "2023-12-15",
  "decode": "Country",
  "instanceType": "Code"
},
"code": {
  "id": "AliasCode_9",
  "standardCode": {
    "id": "Code_43",
    "code": "DNK",
    "codeSystem": "ISO 3166 1 alpha3",
    "codeSystemVersion": "2020-08",
    "decode": "Denmark",
    "instanceType": "Code"
  },
  "standardCodeAliases": [],
  "instanceType": "AliasCode"
```


Class Name	Attribute Name	Data Type	NCI C-Code	Cardinality	Preferred Term	Definition	Codelist Ref	Inherited From
GeographicScope			CNEW		Geographic Scope	The extent or range related to the physical location of an entity.		
	id	string						
	code	AliasCode	CNEW	0..1	Geographic Scope Code	A symbol or combination of symbols which is assigned to the geographic scope.	(Point out to external dictionaries: Standard code is ISO-3166; Alias codes drawn from GENC, UN Region Codes, etc.)	
	type	Code	CNEW	1	Geographic Scope Type	A characterization or classification of the geographic scope.	CNEW - Geographic Scope Type Response	

Code lists [edit]

M.49 area codes (as of December 2021)

Geographical supranational regions
(See also BCP 47 where these were imported as region subtags)

Code	Area	Subregions
001	World	249 002, 009, 010, 019, 142, 150
002	Africa	60 015, 202
015	Northern Africa	7 012, 434, 504, 729, 732, 788, 818
202	Sub-Saharan Africa	53 011, 014, 017, 018
011	Western Africa	17 132, 204, 270, 288, 324, 384, 430, 466, 478, 562, 566, 624, 654, 686, 694, 768, 854
014	Eastern Africa	22 086, 108, 174, 175, 231, 232, 260, 262, 404, 450, 454, 480, 508, 638, 646, 690, 706, 716, 728, 800, 834, 894
017	Middle Africa	9 024, 120, 140, 148, 178, 180, 226, 266, 678
018	Southern Africa	5 072, 426, 516, 710, 748
010	Antarctica	1 010
019	Americas	57 (021, 419) or (003, 005)
003	North America[5]	41 013, 021, 029
021	Northern America	5 060, 124, 304, 666, 840
419	Latin America and the Caribbean	52 005, 013, 029
005	South America	16 032, 068, 074, 076, 152, 170, 218, 238, 239, 254, 328, 600, 604, 740, 858, 862
013	Central America	8 084, 188, 222, 320, 340, 484, 558, 591
029	Caribbean	28 028, 044, 052, 092, 136, 192, 212, 214, 308, 312, 332, 388, 474, 500, 531, 533, 534, 535, 630, 652, 659, 660, 662, 663, 670, 780, 796, 850
142	Asia	50 030, 034, 035, 143, 145
030	Eastern Asia	7 156, 344, 392, 408, 410, 446, 496
034	Southern Asia	9 004, 050, 064, 144, 356, 364, 462, 524, 586
035	South-eastern Asia	11 096, 104, 116, 360, 418, 458, 608, 626, 702, 704, 764
143	Central Asia	5 398, 417, 762, 795, 860
145	Western Asia	18 031, 051, 048, 196, 268, 275, 368, 376, 400, 414, 422, 512, 634, 682, 760, 792, 784, 887
150	Europe	52 039, 151, 154, 155
039	Southern Europe	16 008, 020, 070, 191, 292, 300, 336, 380, 470, 499, 620, 674, 688, 705, 724, 807
151	Eastern Europe (including Northern Asia)	10 100, 112, 203, 348, 498, 616, 642, 643, 703, 804
154	Northern Europe	17 208, 233, 234, 246, 248, 352, 372, 428, 440, 578, 744, 752, 826, 833, 830
830	Channel Islands	3 831, 832
155	Western Europe	9 040, 056, 250, 276, 438, 442, 492, 528, 756
009	Oceania	29 053, 054, 057, 061
053	Australia and New Zealand	6 036, 162, 166, 334, 554, 574
054	Melanesia	5 090, 242, 540, 548, 598
057	Micronesia	8 296, 316, 520, 580, 581, 583, 584, 585
061	Polynesia	10 016, 184, 258, 570, 612, 772, 776, 798, 876, 882

Let’s get focused!

CTMS

- USDM feeds into EDC and CTMS
- Protocol / Study Setup as such straight forward (TA, blinded type) etc
  - Using “Templates” (SoA / Visits)
  - Sites and Regions are set
  - “Finding”: on amendments/updates created in EDC should return to CTMS via “templates” - better than direct (site in a region assigned to a new / separate version) – utilizing existing integrations
- Drug Supply strategies are not the highest priority in CTMS

RTSM

?

Randomization is not (yet) covered in USDM

EDC

- Designer analyzes the protocol amendment to understand the design changes needed in EDC. The impact on study design for visits, forms and rules needs to be assessed and is usually documented in a specification
- This impact analysis will also assess the effect of the EDC changes on integrated services:
  - Downstream Data Management (incl push back queries to EDC)
  - Drug Supply
  - Safety
  - Coding
- After specification approval, Design/Development team make the updates in EDC
- Verification/QA team test the updates
- UAT is conducted by stakeholders in EDC
- Go Live

USDM EDC “Missing features”?

- EDC is still more complex than USDM covers at this time
- I can't find anything related to:
  - Different item properties such as completion requirements (mandatory, optional), visability (read only, hidden) and many more
  - Rules
  - RTSM, Drug Supply, Dispensation visits

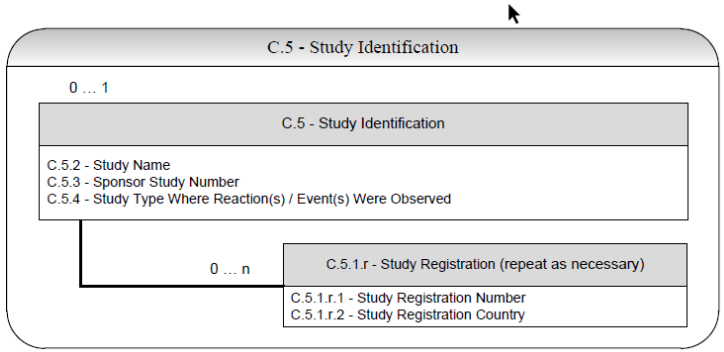
And then there's the change process:

- These changes need to be verified in USDM BEFORE going to downstream systems
- How would that approval process flow?
- Who would validate this and maintain the documentation?

Safety

- ICH E2B defines the interaction
- Usually, regions are covered as part of safety workflow
- Safety system may have additional attributes (study version)

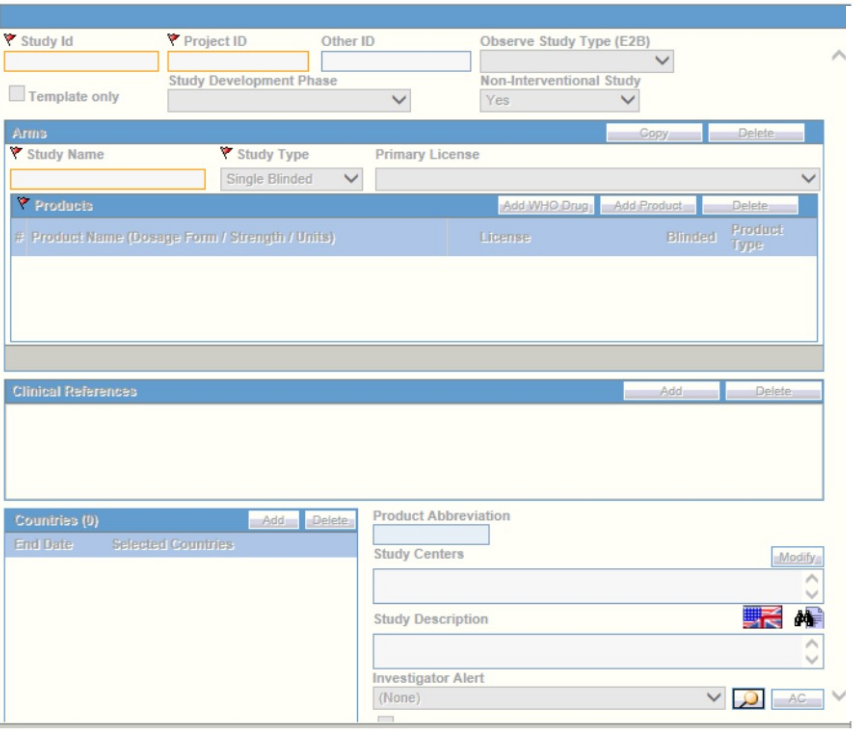
C.5 Study Identification



C.5.1.r Study Registration (repeat as necessary)

C.5.1.r.1 Study Registration Number

User Guidance	This repeatable data element should be populated with the study registration number as assigned in a reporting region, e.g. EudraCT number for reporting in the *European Economic Area* (EEA). Refer to regional implementation guides for details.
Conformance	Optional
Data Type	50AN
OID	2.16.840.1.113883.3.989.2.1.3.6
Value Allowed	Free text nullFlavor: ASKU, NASK
Business Rule(s)	
	Please see Section 3.3.6 for further guidance on the use of nullFlavor to describe missing or non-transmitted information. The following notation will be used to represent C.5.1.r.1: <id extension="study registration number" root="2.16.840.1.113883.3.989.2.1.3.6"/> The root indicates the namespace of C.5.1.r.1, the actual study registration number is populated at id extension.



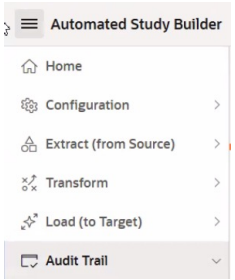
Clinical References Field or Control Name	Description
Reference Type	Shows the various reference types that can be setup for this study.
Country	Enables you to select a country for the clinical reference type.
Reference Number	Captures the reference number that will be reflected on the regulatory reports.
Add	Enables you to add another clinical reference.
Delete	Enables you to delete the selected clinical reference.
Countries	Enables you to select a country for the clinical reference type.
License	This is the license of the primary (company) product participating in the study.
Product Abbreviation	This enables you to enter an up to 5 character abbreviation of the study name which would be used in Case numbering when Product' is selected in the system numbering configuration in case of study cases.
Centers	The system displays the selected study centers for the study.
Study Description	Enables you to enter a brief description of the study. Opens the study description in zoom mode and provides a spell check dialog. Opens the multi lingual dialog allowing you to choose the language from the list. The global language icon is displayed if the study description data is entered in a language different than English or Japanese.
Investigator Alert	Enables you to select an existing Advanced Condition. Under Investigator alert, an advanced condition can be created / selected. When this condition is satisfied, the system automatically sends an e-mail to the investigator group associated with this study.
Investigator Alert - select	Opens up the Advance Condition browser.
Study is eligible for Unblinding	Check this box if the study can be unblinded. If the Study Type selected is Not Blinded", this field is disabled. This check box is enabled when a study has at least one Arm with Study type as Blinded (Single/Double).
Enable Study Specific Encoding	User checks this box if Study specific Auto encoding has to be enabled.
Autoencoding: Drugs(dict)	If unchecked (default state) the study will use the dictionaries configured using the Case form Configuration options. If checked, the Auto encoding button is activated.
Autoencoding: Events & Indications	Select this field to enable the system to encode Events & Indications using the dictionary you selects from the list.

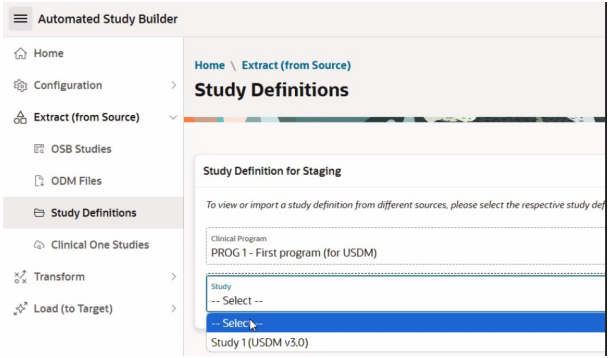
Solution

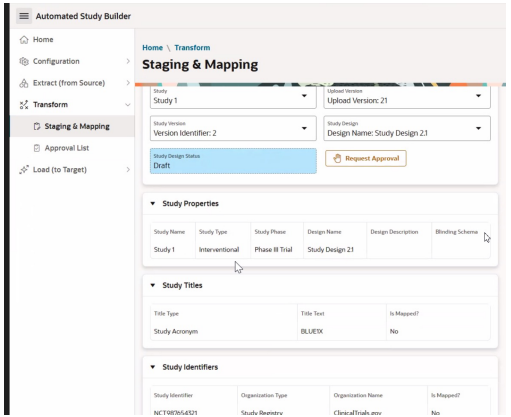
Solving the problem

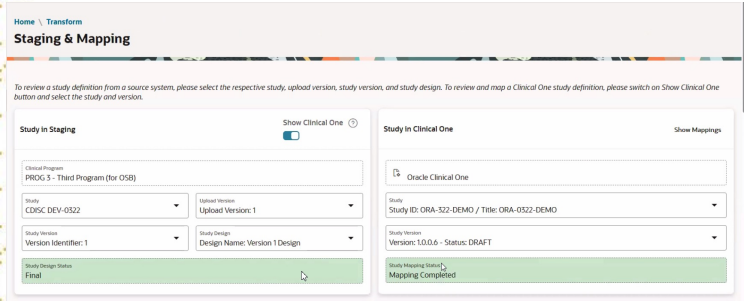
- Business end-user friendly “ETL” on top of SDR
  - Extract controlled from any source (USDM, ODM, OSB)
  - Transform where you can automatic, BUT cover manual interventions
    - for impact analysis, approval process, validation aspects
  - Load into ANY target system, even support cross service flows
  - In case of amendments be able to read “back” already implemented “structures” from the targets systems (for impact analysis)

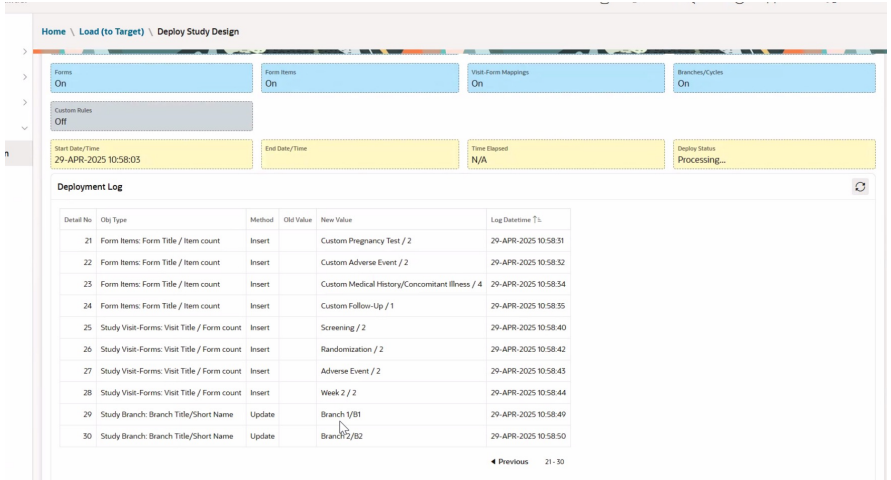
End user in mind



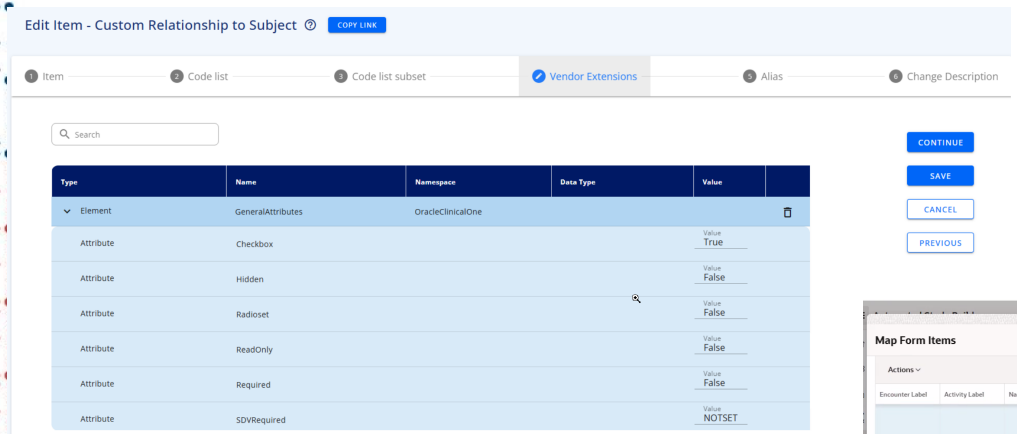


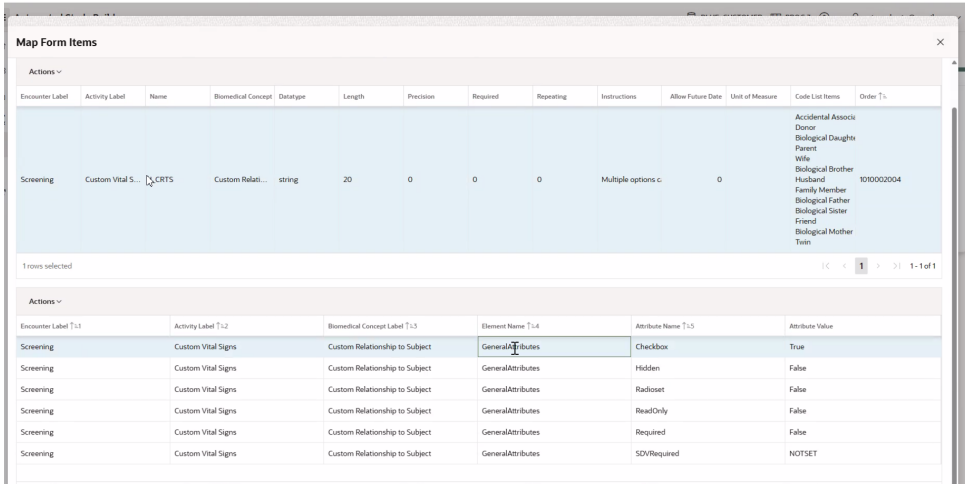






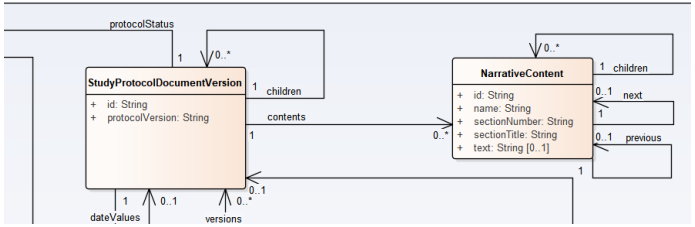
OSB (vendor) extensions

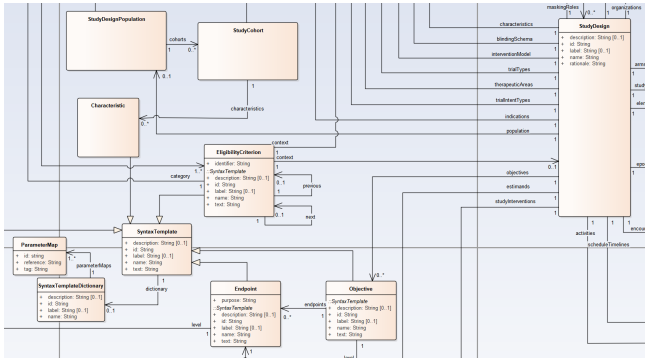


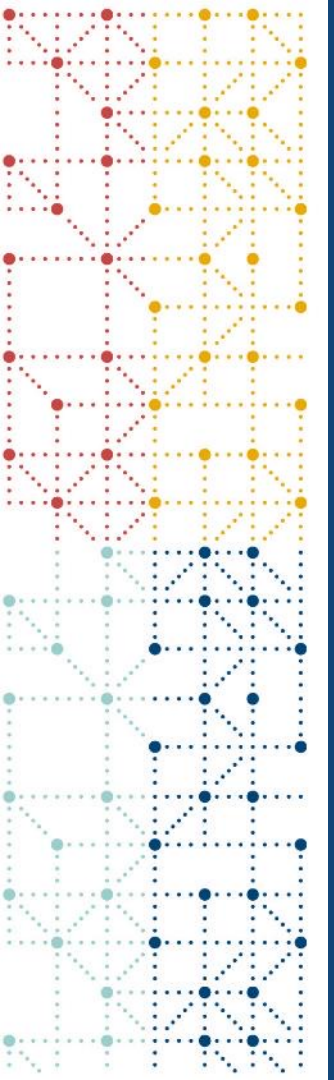


Solving the problem

- Where does the “++” goes in?
  - USDM IG 4.20 Unstructured content
    - Any (X)HTML format
  - NarrativeContent
    - StudyProtocolDocument level
  - USDM IG 4.21 Syntax Templates
    - StudyDesign level
  - Technical Parallels
    - Use of ODM inside USDM
    - trigger direct integration to sender systems aka API to pull more data (OSB?)







Conclusion

Ok, a little bit AI … ;-)

- **Amendments are Inevitable - Be Ready**
  - true value comes when they can handle the full lifecycle, not just study startup
- **Current Standards: A Work in Progress**
  - not complete, will be complex, will create “friction” in practice
- **Holistic Change Management is Key**
  - Need strong governance, “automating a bad process just makes bad outcomes faster”
- **Impact on Stakeholders**
  - Reduce burdon on stakeholders
- **Looking Ahead**
  - position your organization to “navigate post-go-live”

Conclusion

- Randomization is not given (yet) in USDM

- Global new version of USDM should be no-brainer
- If local amendments happen
  - EDC / CTMS
    - Use UN world region instead of ISO-3166 code list to define region
    - CTMS can translate and automate the assignment of a version for/from EDC
  - Safety: Focus on AE
    - USDM load into safety can setup Study versioning
    - Date when AE happen should be the differentiator on which version to use in the Safety system

- Sponsor internally defined templates or USDM ++?
  - NarrativeContext vs SyntaxTemplate
  - Standard in a standard? How to avoid industry separation?

- Reduce training efforts (remove barrier between end user UI vs technical ETL)

Next steps

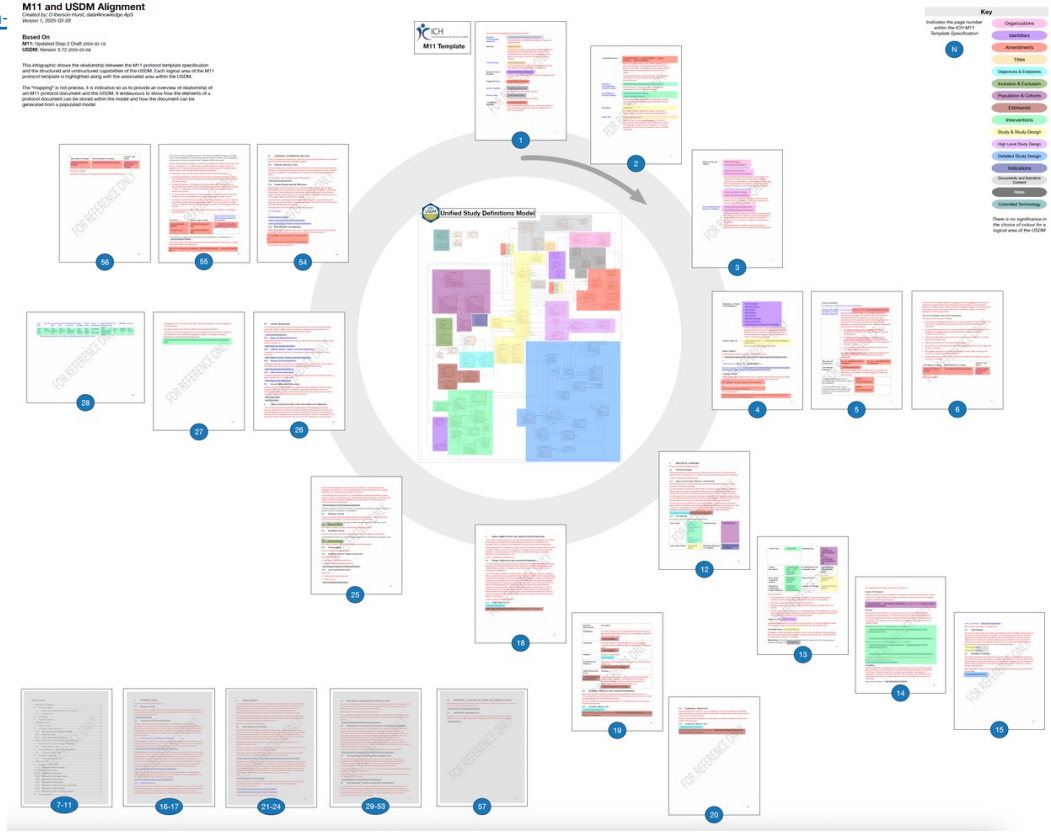
- After understanding USDM, it’s capabilities and missing's from a full end to end flow …
  - Re-thinking SDR
    - “++” vs multiple standards in one SDR
  - If USDM - define required “++” elements as a structure / model
    - “technical documents” (unstructured content, syntax templates, footnotes) as attachment and mix and match multiple formats together (OSB, ODM, USDM)
  - identify further automation options (existing standards and AI), where human interaction is required

Dave Iberson-Hurst

https://www.linkedin.com/pulse/document-model-dichotomy-dave-iberson-

The USDM manages to blend the desire for machine readable structure while allowing for a protocol document to be created.

I will predict that, over the coming years, **we will see a move to more tables within the document** and less text while preserving those sections of the protocol where the text needs to be precise and carefully controlled. I also would suggest we start thinking about presenting the content currently seen in the classic Schedule of Activities in better and more varied ways to better accommodate the direct needs of the range of users (roles) that make use of the protocol today.



Thank You!