



*E2E DATA
STANDARDS,
the need for a new
generation of metadata
repositories
(Paper DH04)*



Dr. Isabelle de Zegher

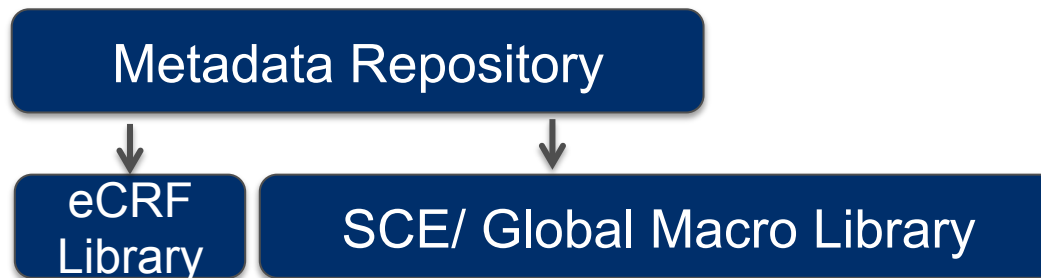
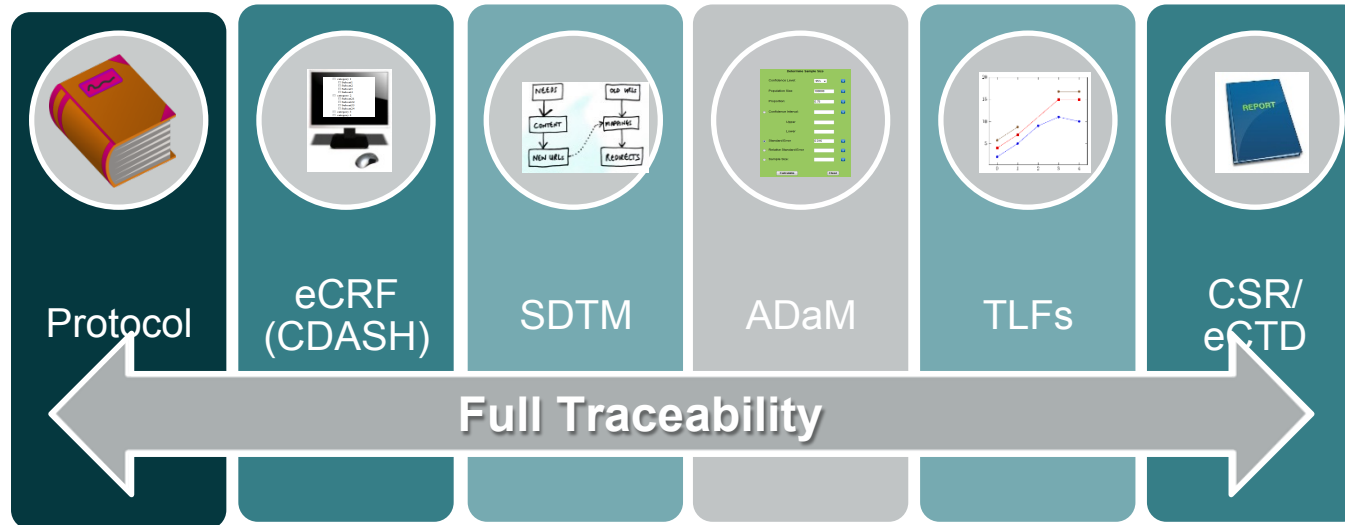
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TABLE OF CONTENT

- **E2E Data standards: rationale & approach**
- **The need for a new generation MDR**
 - Concept layer in “hub & spoke” approach
 - Concept and eCRF library
 - Using standards within operations: Study Instance Metadata (SIM)
- **Deployment challenges of an MDR within a CRO**
- **Conclusion**

ENHANCING GLOBAL DATA OPERATIONS THROUGH E2E DATA STANDARDS



ENFORCING E2E STANDARDS

MDR driven automation of

- data DB builds,
- data retrieval,
- transformation and analysis
- drives process efficiency,
- increases compliance and
- simplifies traceability

Enforcement / Automation

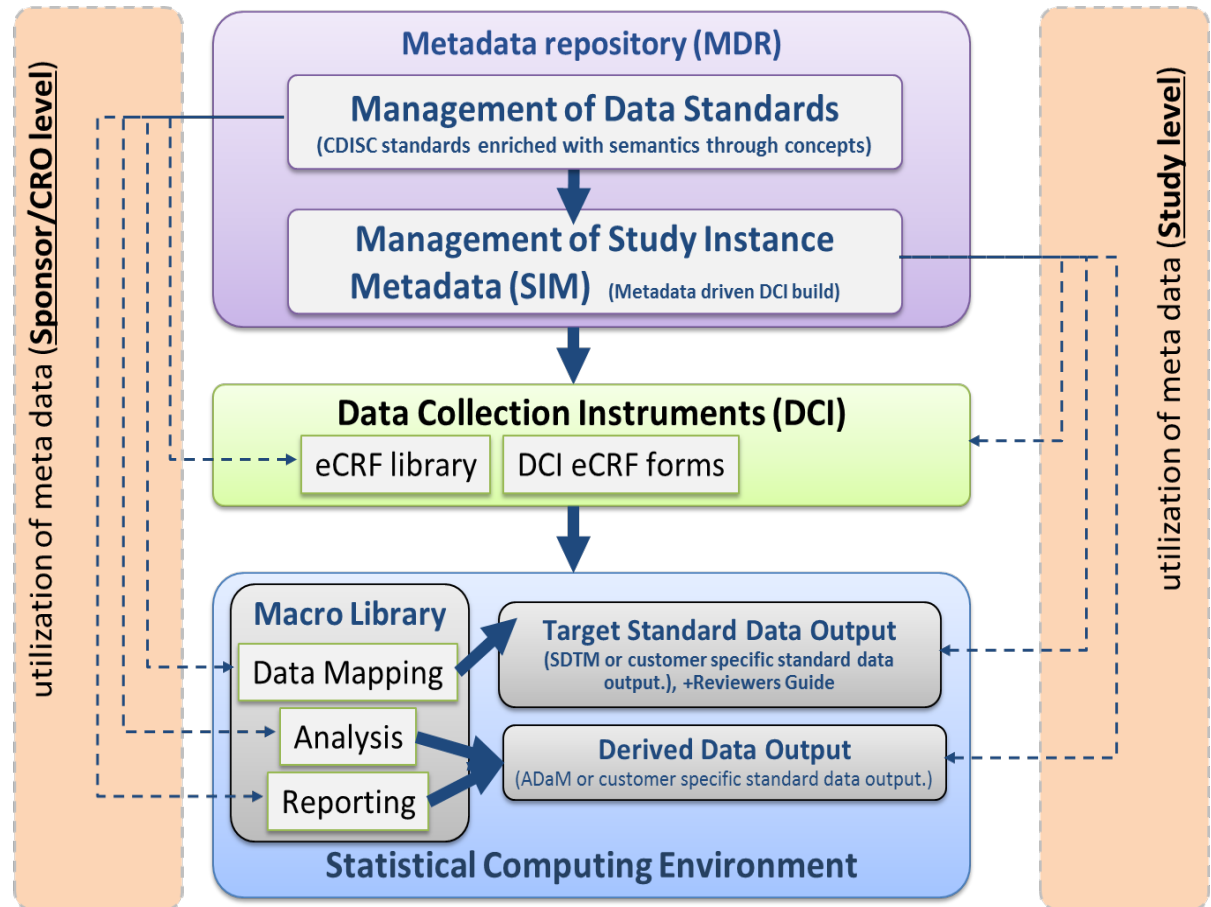
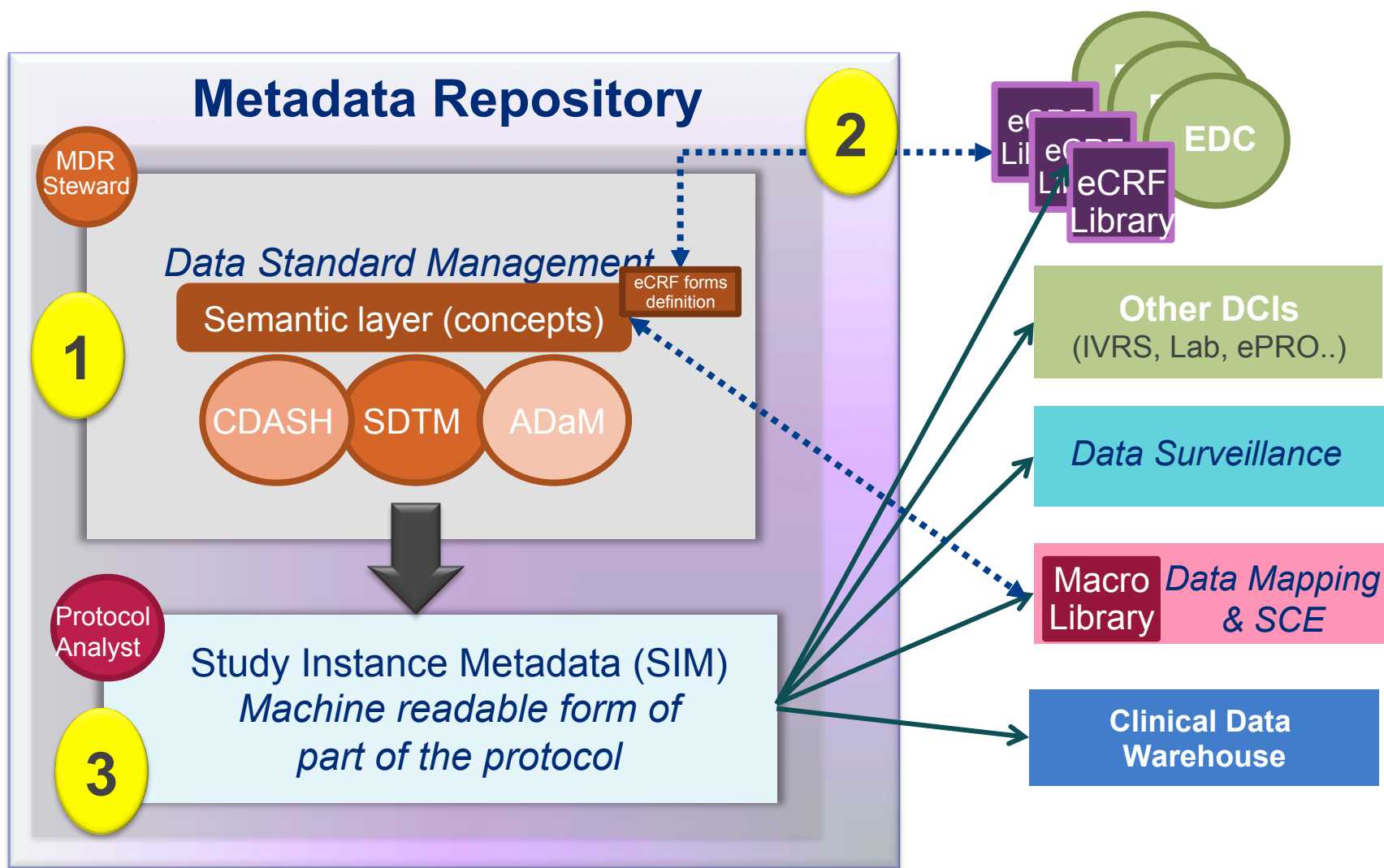


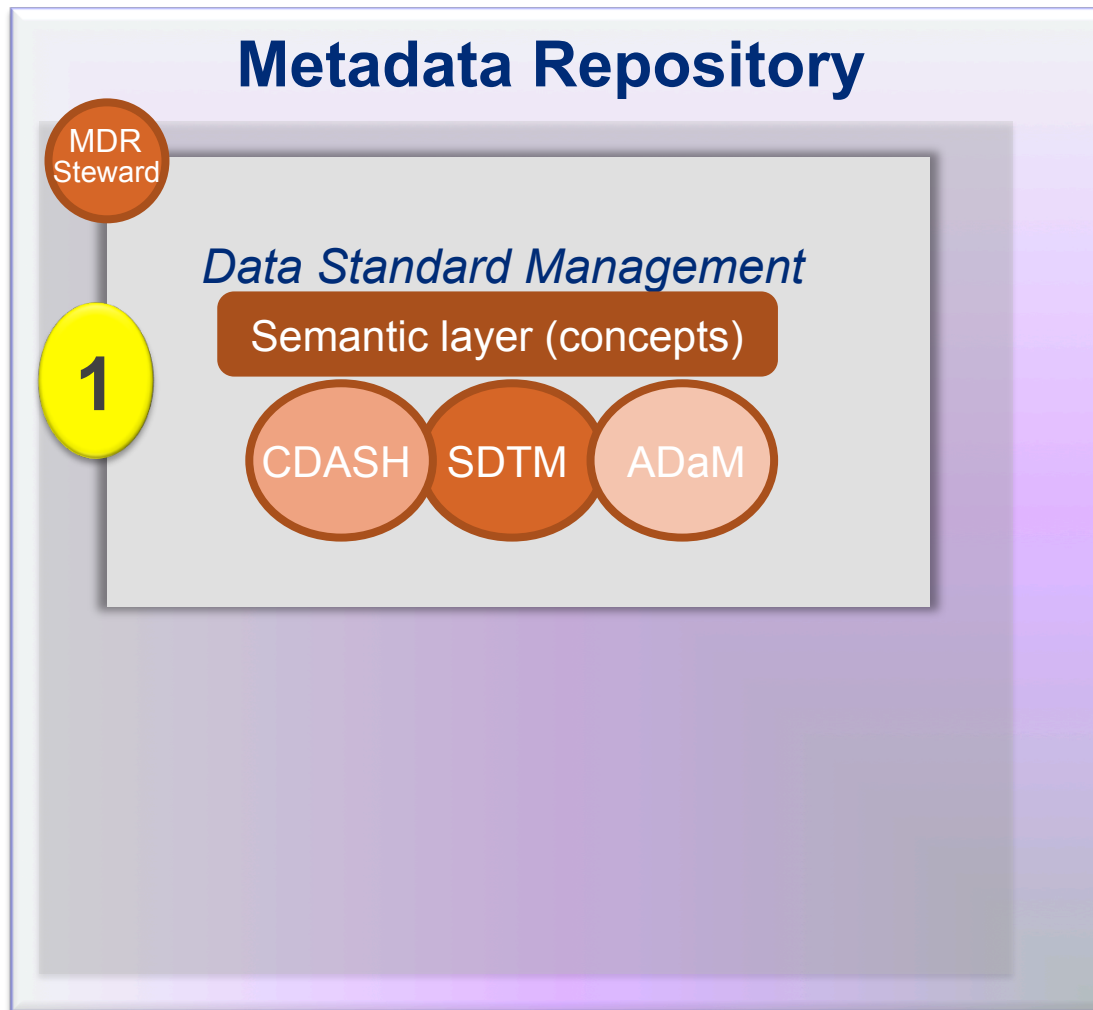
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THE NEED FOR NEW GENERATION METADATA REPOSITORY



THE NEED FOR NEW GENERATION METADATA REPOSITORY: SEMANTIC LAYER (CONCEPTS)



CONCEPT BASED MDR

WHAT IS A CONCEPT

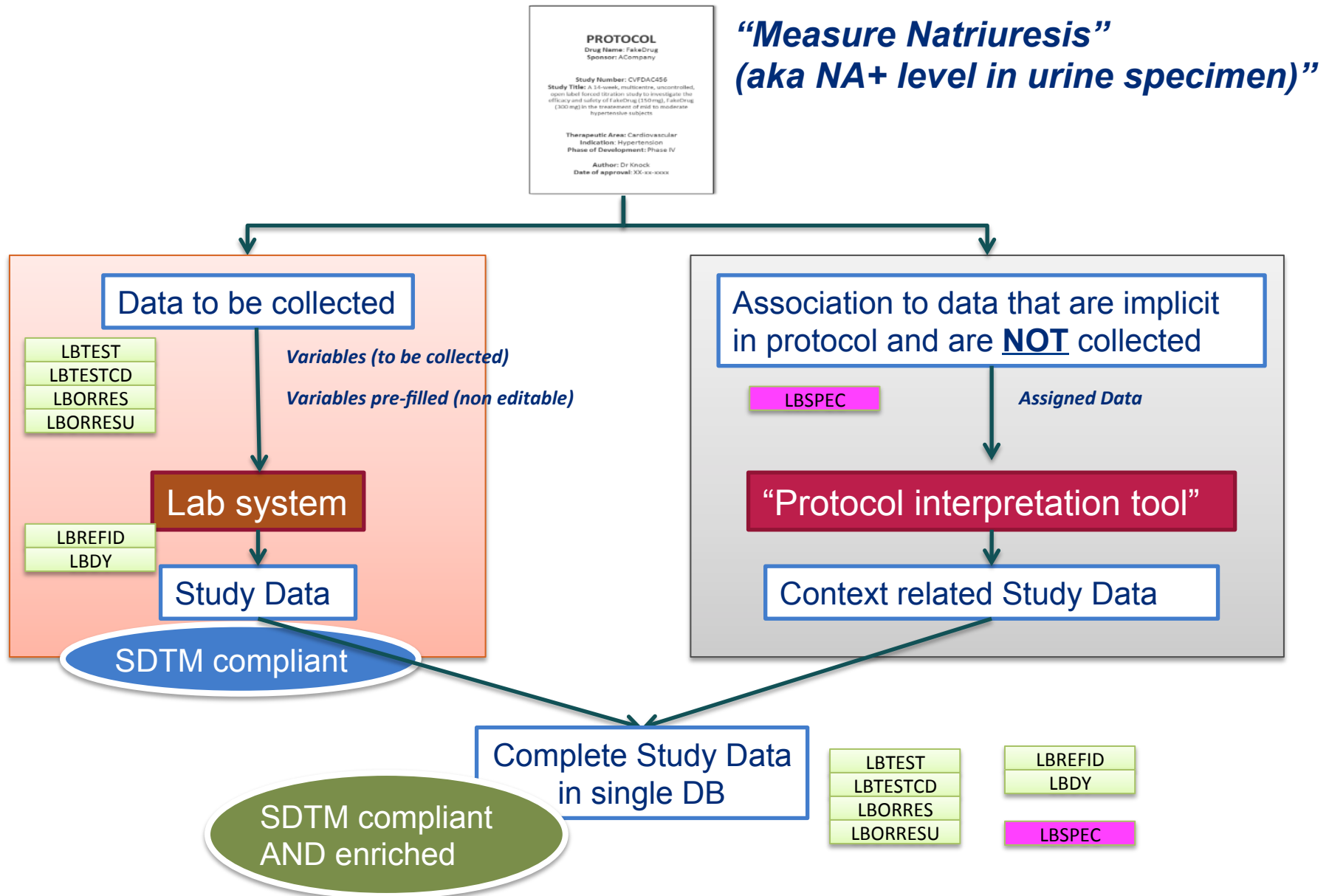
- A concept is a group of variables that must be managed together to provide something meaningful in clinical research

Period	Screening	Study treatment period		Follow-up
Week	-2			
Visit	1			
Type of contact	Vis			
Inclusion and Clinical evaluation:		Concept	CDASH Question	CDASH Variable
Informed Consent	X	Subject	What is the sex of the subject?	SEX
Patient Demographics	X		What is the subject's date of birth?	BIRTHDAT or BRTHYR BRTHMO BRTHDY
Medical and surgical history	X		What is the ethnicity of the subject?	ETHNIC
Physical Examination	X		What is the race of the subject?	RACE
Vital Signs and Body Weight	X		What is the subject's age?	AGE
Previous and Concomitant Medication	X		What are the age	AGEU
Inclusion and Exclusion Criteria	X			
Randomization				
Central Laboratory Testing:				
HbA1c				
Lipid Profile ¹ (in fasting state)				
Biochemistry ²				
Serum Pregnancy Test				
Treatment:				
Dispensation of insulin glargine or premixed insulin and corresponding training				
Dispensation of insulin glulisine if needed (see section 9.1.3) and corresponding training				
Accountability of Investigational Products				
Plasma Glucose Self-Monitoring:				
Dispensation of plasma glucose meter	X			
Dispensation and collection of diaries	X			
Training of the patient (PG meter, diary)	X			
Plasma glucose values of 3 consecutive days in the week before the visit				
7-point plasma glucose profile of 3 consecutive days in the week before the visit				
Insulin dose(s) of the day before the visit				
Efficacy and Safety:				
Treatment Satisfaction Questionnaires	X			
Hypoglycemia				
AE / SAE				

eCRF content description

SDTM mapping

CONCEPTS: INTEGRATING ALL DATA NEEDED FOR ANALYSIS



AE concept template (part 1/2)

Concept:

Adverse event (any)

ADVERSE EVENT CODING

Verbatim

Text

Modified term (for coding)

MedDRA Term (PT)

MedDRA Text

PT MedDRA Code

xxxxxxxx

LLT Term

MedDRA Text

LLT MedDRA Code

xxxxxxxx

HLT MedDRA Term

MedDRA Text

HLT MedDRA Code

xxxxxxxx

HLGT MedDRA Term

MedDRA Text

HLGT MedDRA Code

xxxxxxxx

Body System (SOC) Term

MedDRA Text

Body System (SOC)
Code

xxxxxxxx

Primary SOC Term

MedDRA Text

Primary SOC
Code

xxxxxxxx

Category

xxxxxxxx

Sub-Category

xxxxxxxx

(Anatomic) Location

xxxxxxxx

Pre-specified?

NO

Attribute that
is also an
SDTM
variable

Fixed value

Value set
("code
list")

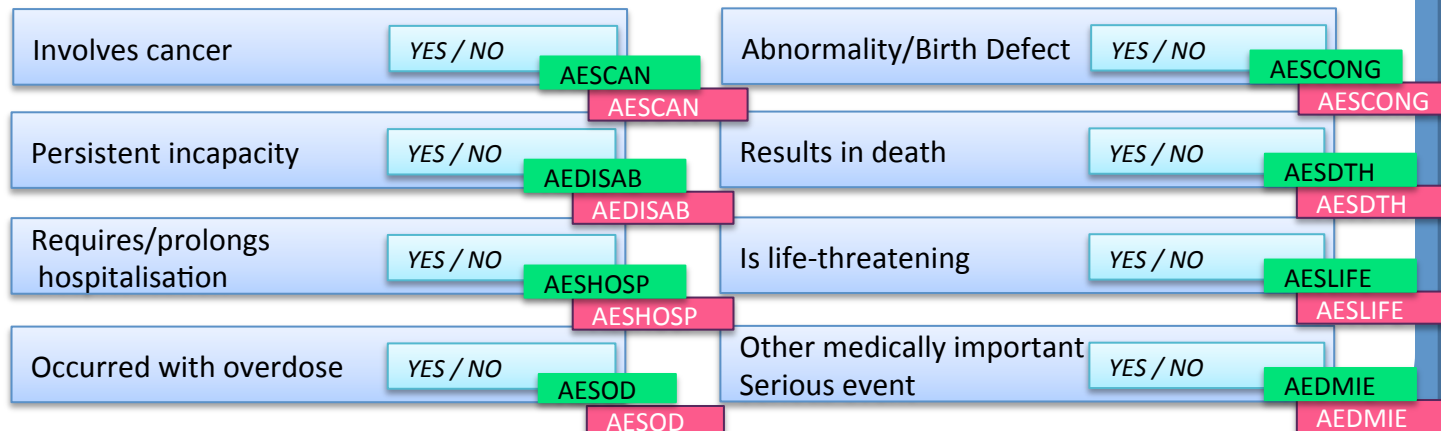
Additional
concept
grouping
information

AE concept template (part 1/2)

Concept:

Adverse event (any)

SEVERITY FLAGS

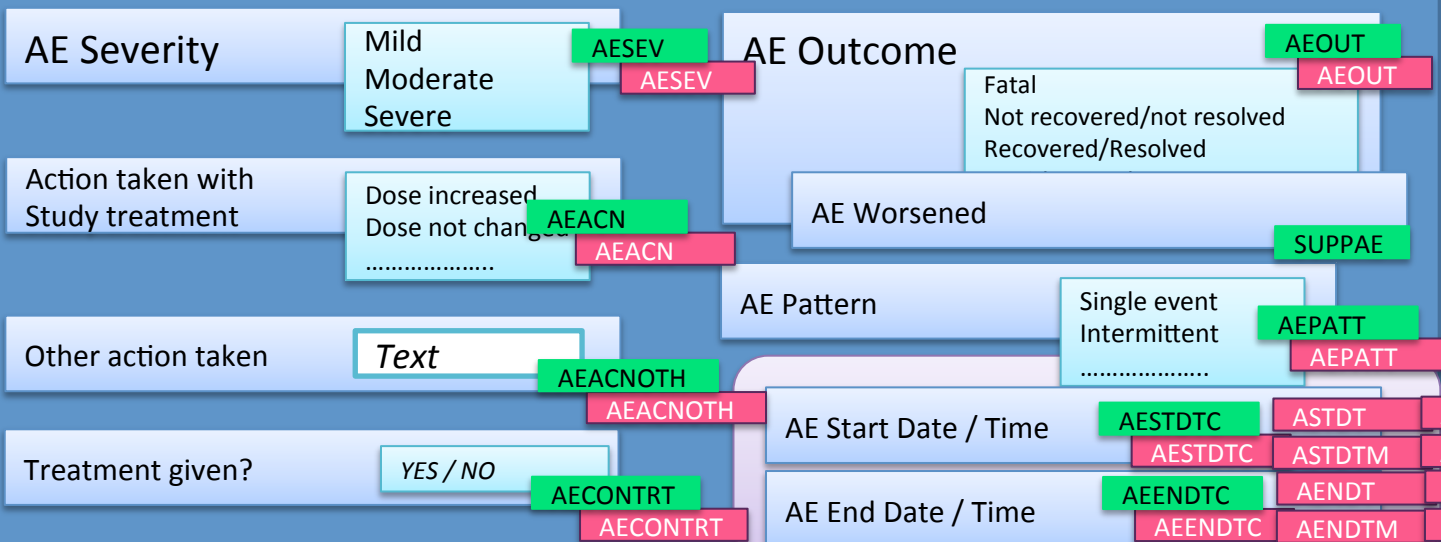


Attribute that is also an SDTM variable

Fixed value

Value set ("code list")

Additional concept grouping information



SDTM Variable

ADaM Variable

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URTI in Asthma TA , based on AE template.

Concept:

Upper Respiratory Tract Infection (as AE)

AETERM

AELLT

AEDECOD

FAOBJ

SEVERITY FLAGS

Involves cancer

YES / NO

AESCAN

Abnormality/Birth Defect

YES / NO

AESCONG

Persistent incapacity

YES / NO

AEDISAB

Results in death

YES / NO

AESDTH

Requires/prolongs
hospitalisation

YES / NO

AESHOSP

Is life-threatening

YES / NO

AESLIFE

Occurred with overdose

YES / NO

AESOD

Other medically important
Serious event

YES / NO

AEDMIE

Severity flags that are inappropriate to the particular AE would not be enabled

AE Severity

Mild
Moderate
Severe

AEEV

AE Outcome

AEOUT

Fatal
Not recovered/not resolved
Recovered/Resolved
.....

Action taken with
Study treatment

Dose increased
Dose not changed
.....

AEACN

Other action taken

Text

AEACNOTH

AE Pattern

Single event
Intermittent
.....

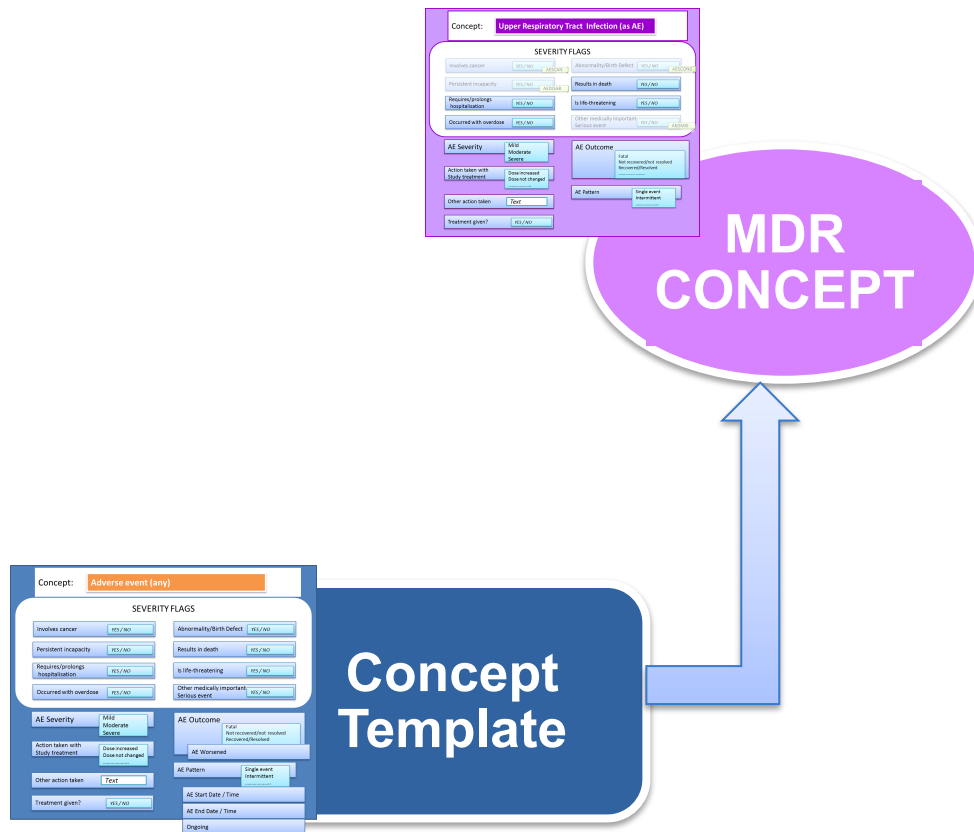
AEPATT

Treatment given?

YES / NO

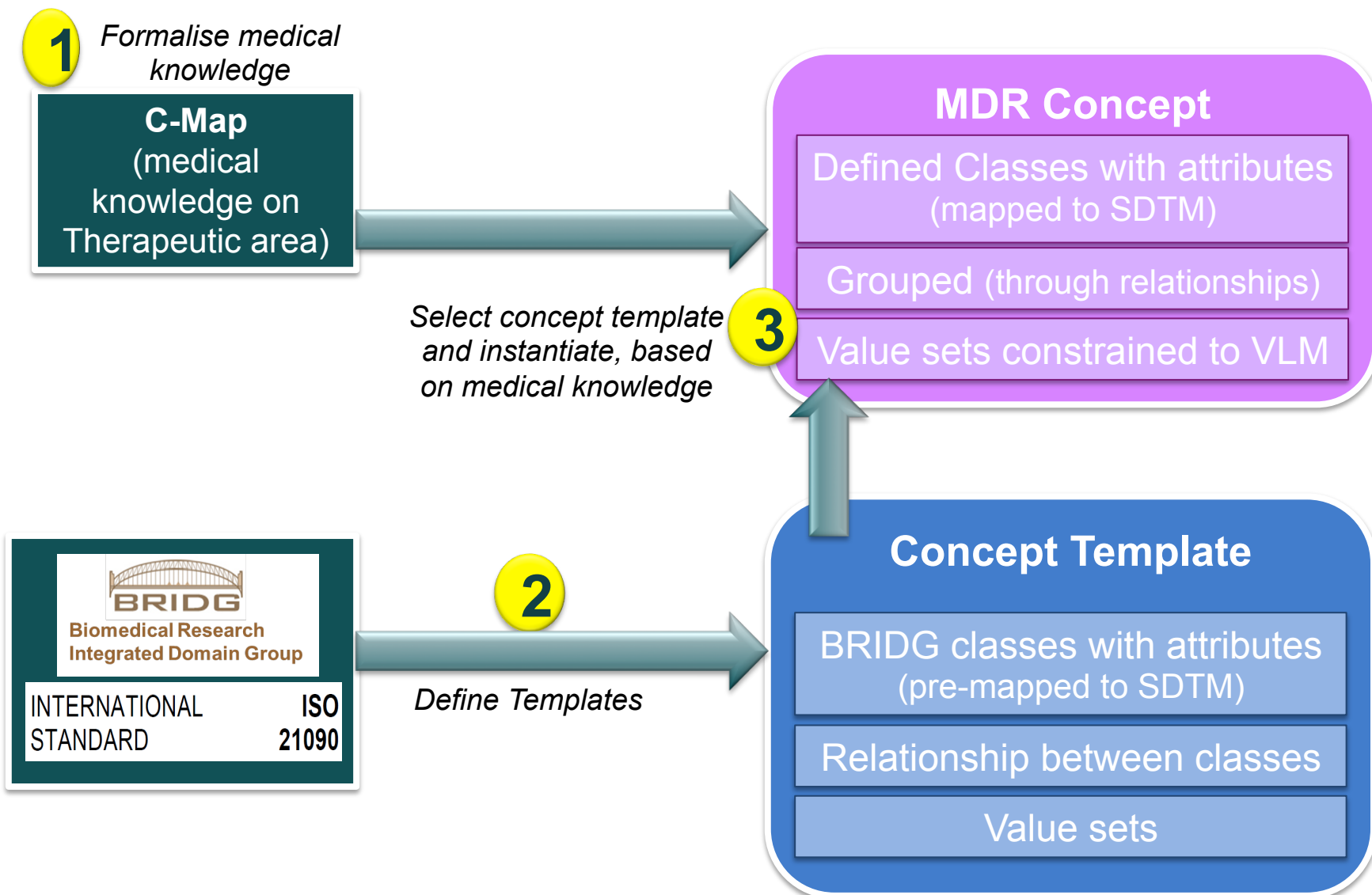
AECONTRT

CONCEPT – GENERATED FROM A CONCEPT TEMPLATE

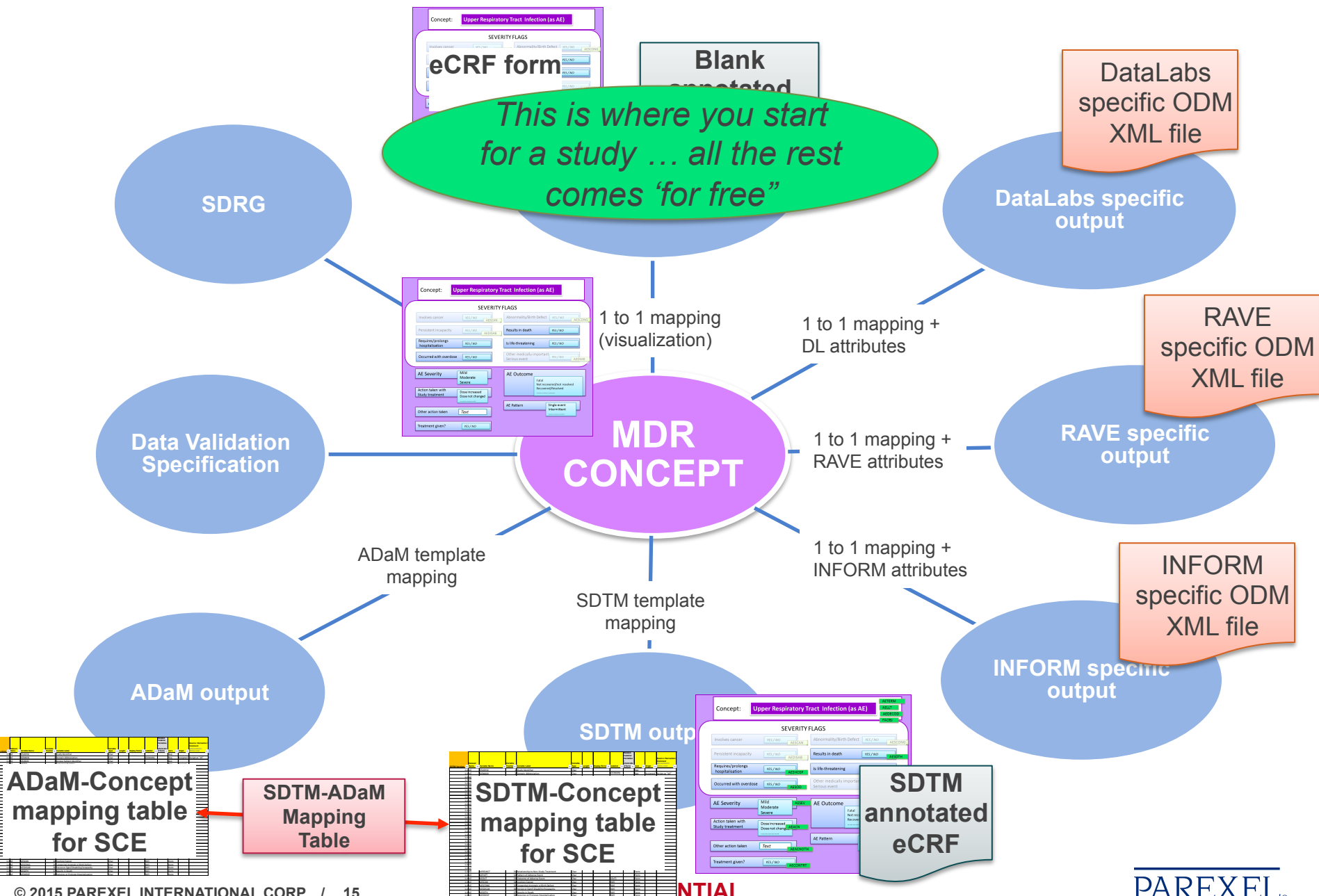


CONCEPT – GENERATED FROM A CONCEPT TEMPLATE

CONTENT FROM BUSINESS & COMPUTATIONAL SEMANTIC



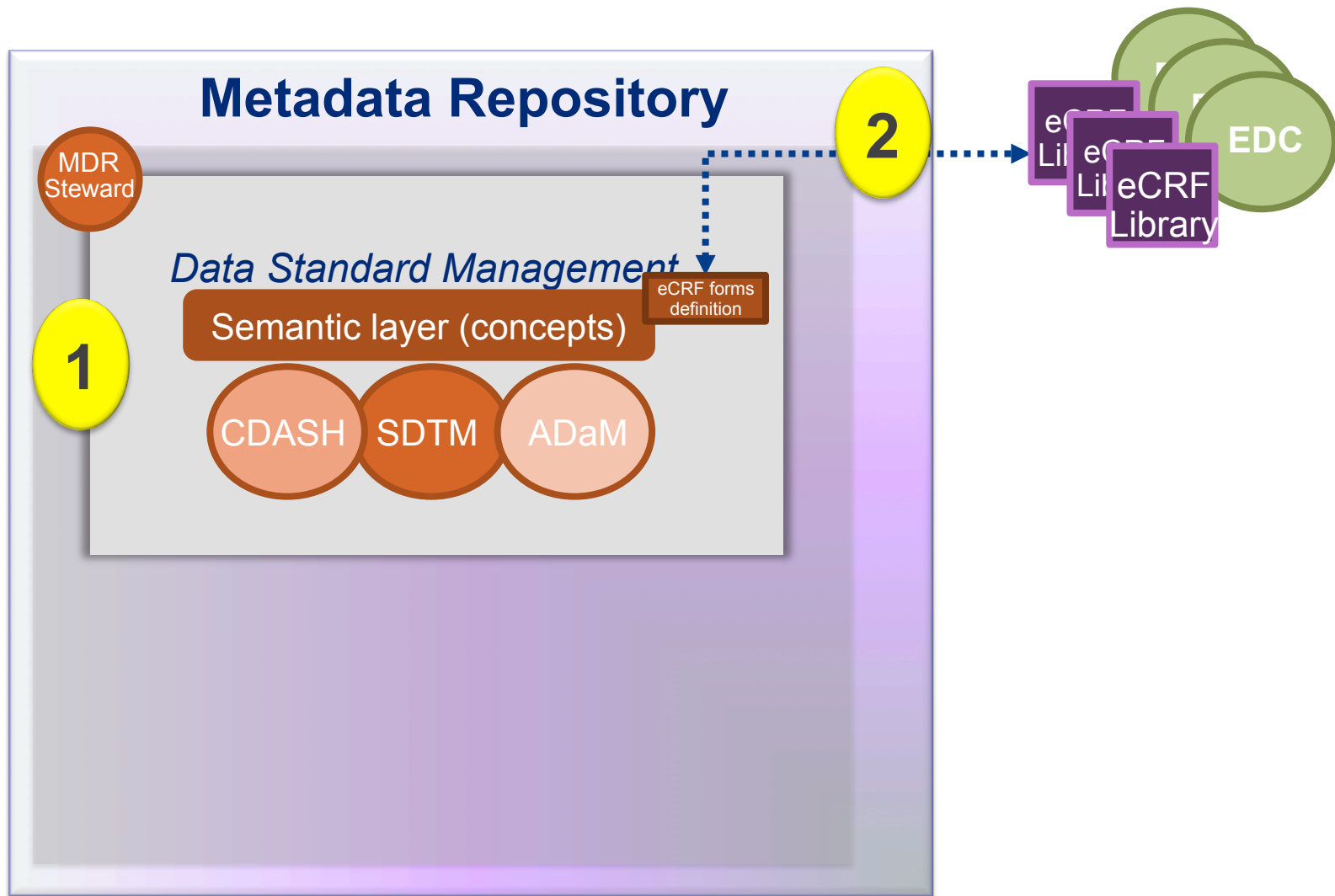
CONCEPT: AT THE CORE OF A HUB AND SPOKE



BENEFITS OF A SEMANTIC – CONCEPT BASED MDR

- **More intuitive and easier to manage concepts than variables.**
 - Protocol authors speak about concept, programmer speak about variables
 - ~ 200.000 variables needed to cover TAs=> not manageable without additional construct.
- **Used to generate semantically sound TA standards**
 - Concept templates (BRIDG, ISO21090) used to define new concepts
- **Used to support mapping between each “spike”**
 - Different view in the E2E data standard chain
 - Any new standards – and new standard version – is mapped through the hub
- **Used to specify data collection (eCRF) forms**
 - EDC agnostic specification linked with EDC specific implementation
 - Re-usable for Data collection instrument

THE NEED FOR NEW GENERATION METADATA REPOSITORY: SEMANTIC LAYER (CONCEPTS)



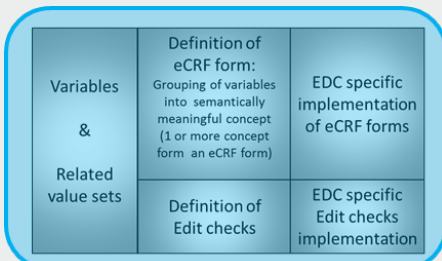
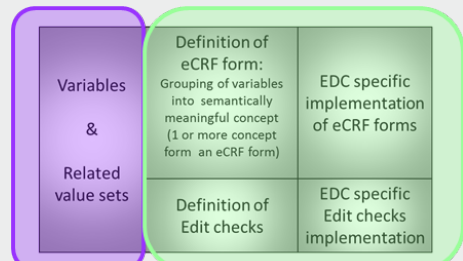
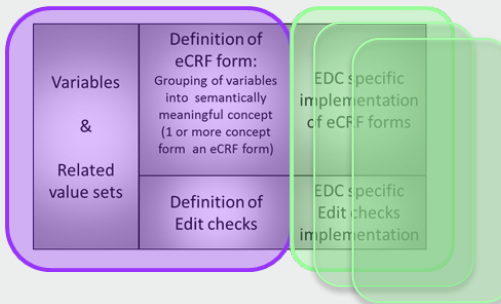
CONCEPT BASED MDR AND eCRF LIBRARY

DEFINITION OF AN eCRF LIBRARY

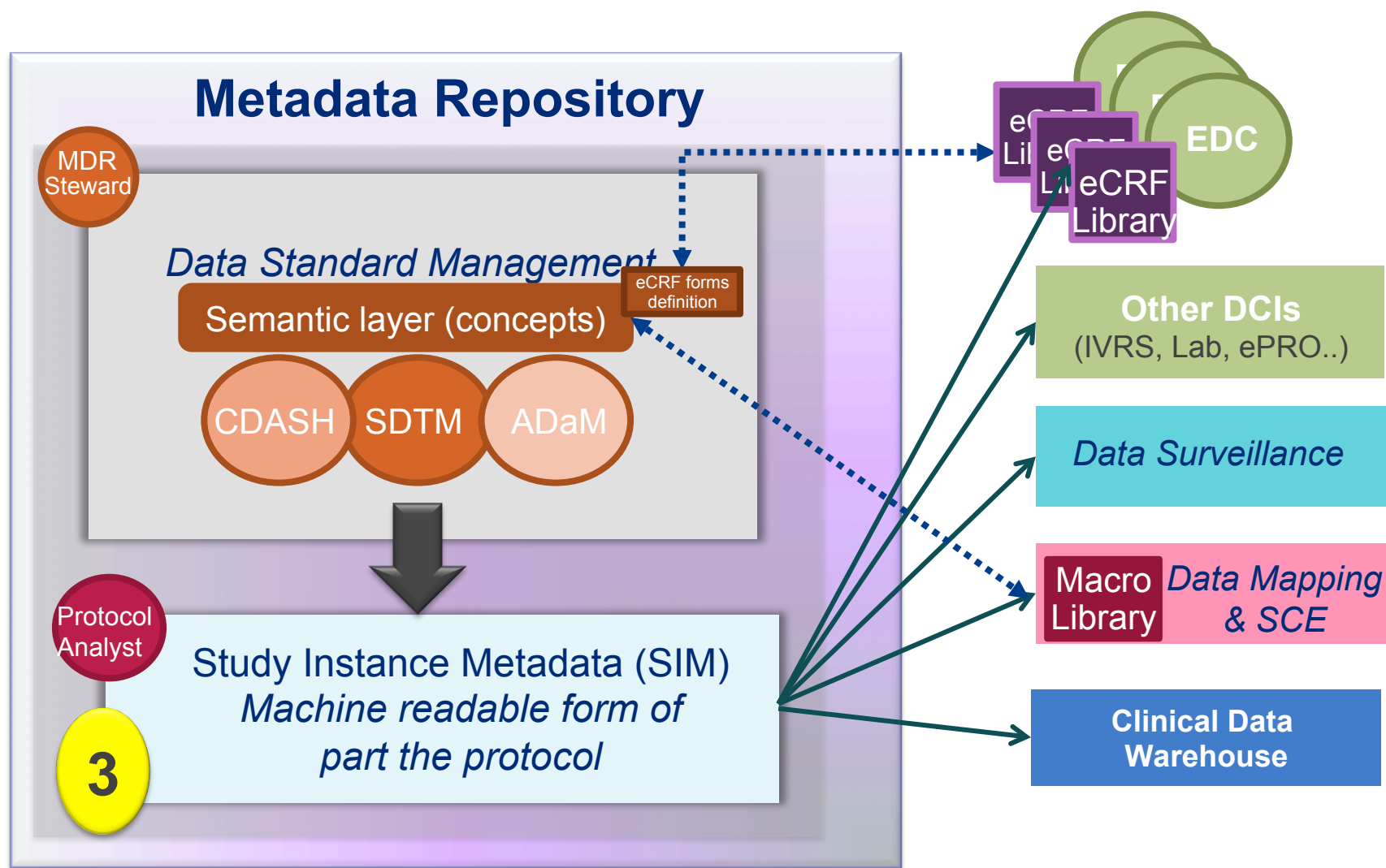
Variables & Related value sets (or code lists)	Definition of eCRF form: Grouping of variables into semantically meaningful concept (1 or more concept form an eCRF form)	EDC specific implementation of eCRF forms
	Definition of Edit checks	EDC specific Edit checks implementation

CONCEPT BASED MDR AND eCRF LIBRARY

3 APPROACHES FOR AN eCRF LIBRARY

	Monolithic EDC Global library 	Variable based MDR with FAT eCRF library 	Concept based MDR with LEAN eCRF library 
Description	“eCRF library” contains - Variables, - Related value sets - Definition & Implementation of forms & edit checks Combination of MDR and eCRF library for 1 specific EDC	- MDR contains only variables and value sets - eCRF library contains forms definition related to variables from MDR, and EDC implementation specific components	- MDR contains variables and value sets + logical definition of forms (i.e. concepts) organized by TA, drug, ... - eCRF library contains EDC specific implementation
Overview	Global eCRF lib 	MDR eCRF lib 	MDR eCRF libs 
Approach	- Proprietary to one EDC - No flexibility – reuse across EDC - No connection with other DCIs	Requires 2 separate governance process ⇒ heavy	- One governance process (maintenance and during for study set-up & amendments) - Consistency across ALL EDC (in case of outsourcing)

METADATA REPOSITORY AND STUDY INSTANCE METADATA



STUDY INSTANCE METADATA

DIFFERENT OUTPUT FOR DIFFERENT SYSTEMS

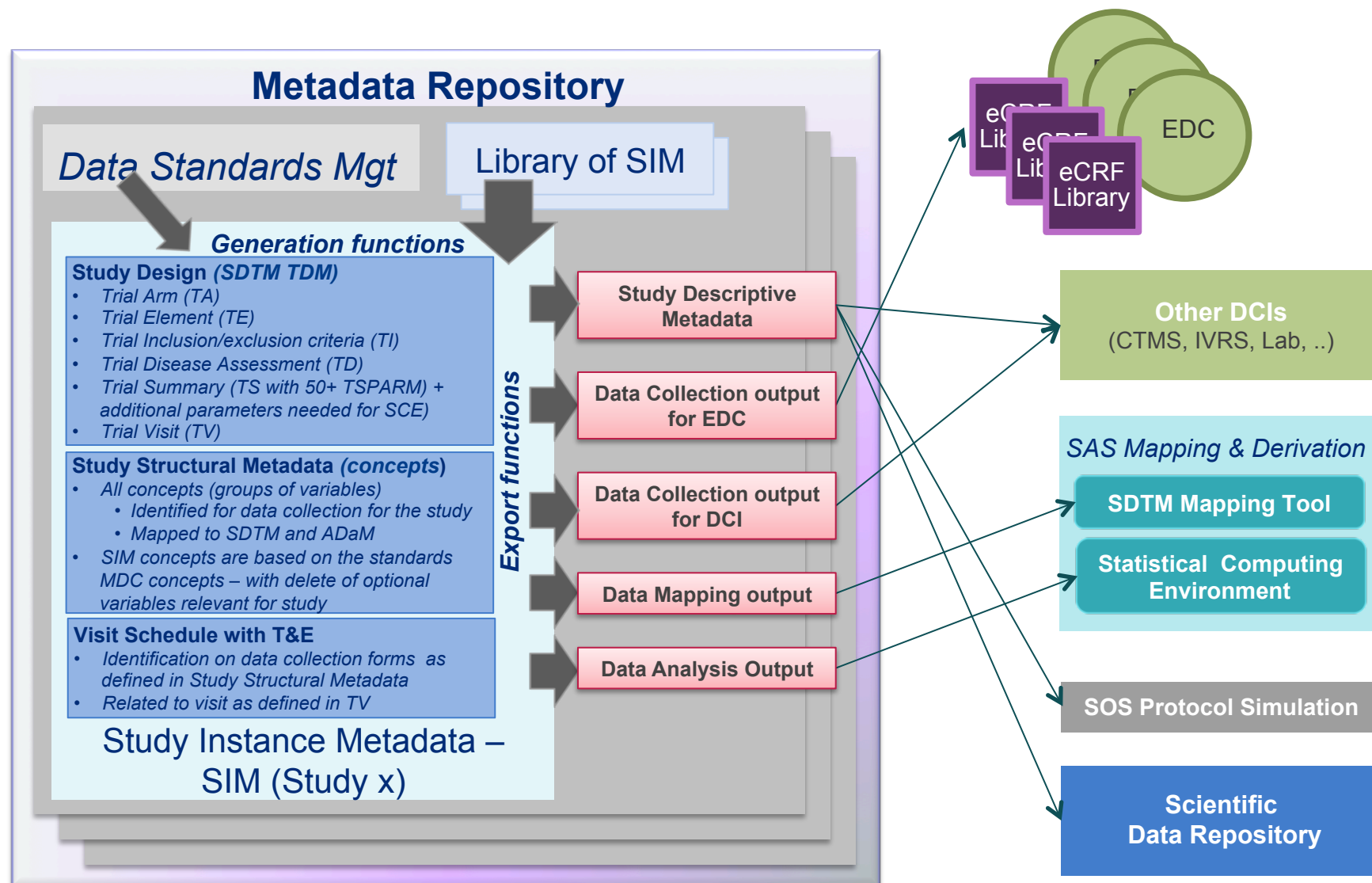


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DEPLOYMENT CHALLENGES

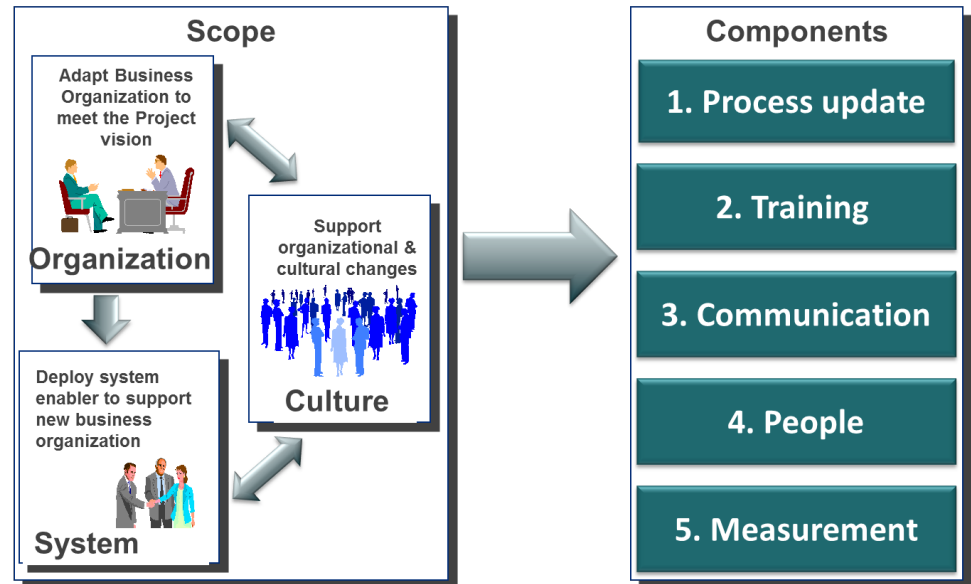
1. CHANGE MANAGEMENT

- **Process redesign/ optimisation in E2E spirit**
- Maintaining data standards centrally
=> BREAK the silos
- Consistent study set-up across different data collection instruments
=> This is not just about EDC
- How can I define what I have never seen
=> AGILE development

• Organizational changes

- Data steward group
- New skill sets

- **CROs need to take into account internal and SPONSOR standards.**



DEPLOYMENT CHALLENGES

2. DATA STANDARD CURATION FOR E2E ENABLEMENT

- **Available**

- CDISC Data standards (CDASH, SDTM, AdaM) with mapping
- CFAST TA standards

- **Issues: incomplete, difference across sponsors**

- no underlying formal concepts based on proven semantic
- do not cover all therapeutic areas..

- **Approach**

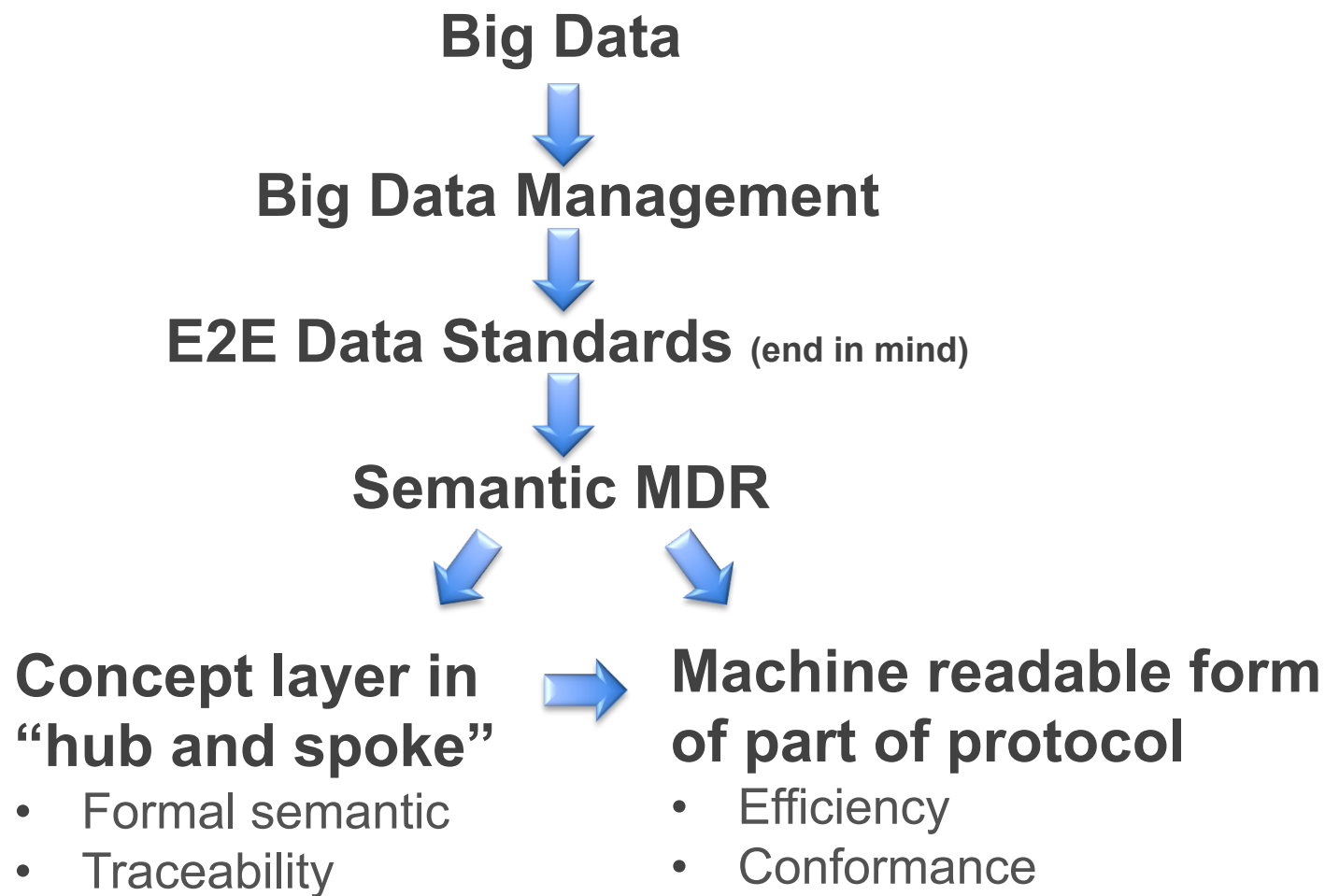
- Define **concept template** – as the basis of a hub – from BRIDG and ISO20190 (e.g. AE)
- Use template to define **concept hub** derived from existing CDISC standards and emerging CFAST c-MAP (e.g. URTI)
- Map CDISC standards and emerging CFAST and/or sponsor standards to the concept hub

We need more people working on enhanced semantic and on concepts !

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CONCLUSION: STOP CREATING THE LEGACY DATA OF TOMORROW => HAVE THE END IN MIND



**We plan to use MDR for new studies
starting early May 2016,
in a stepped approach.**

THANK YOU

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