Introduction to CDISC

CDISC®

Setting the
Global Standard
for Clinical Data

CLINICAL DATA INTERCHANGE
STANDARDS CONSORTIUM

1st April 2008

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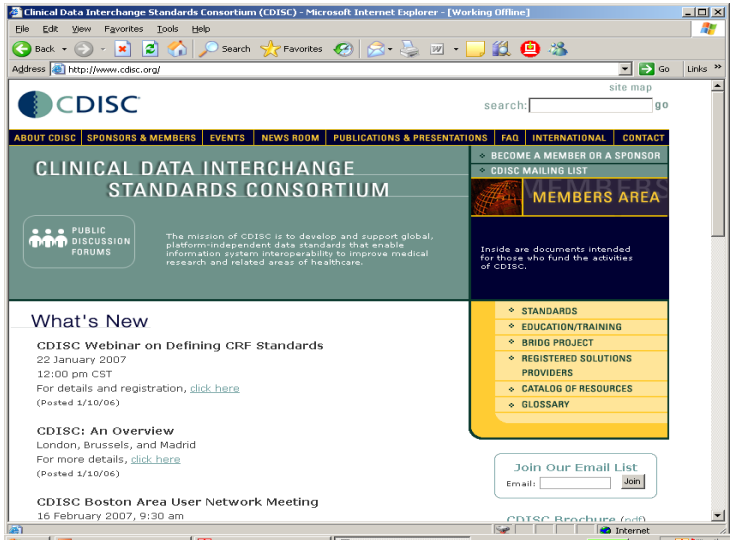
Agenda

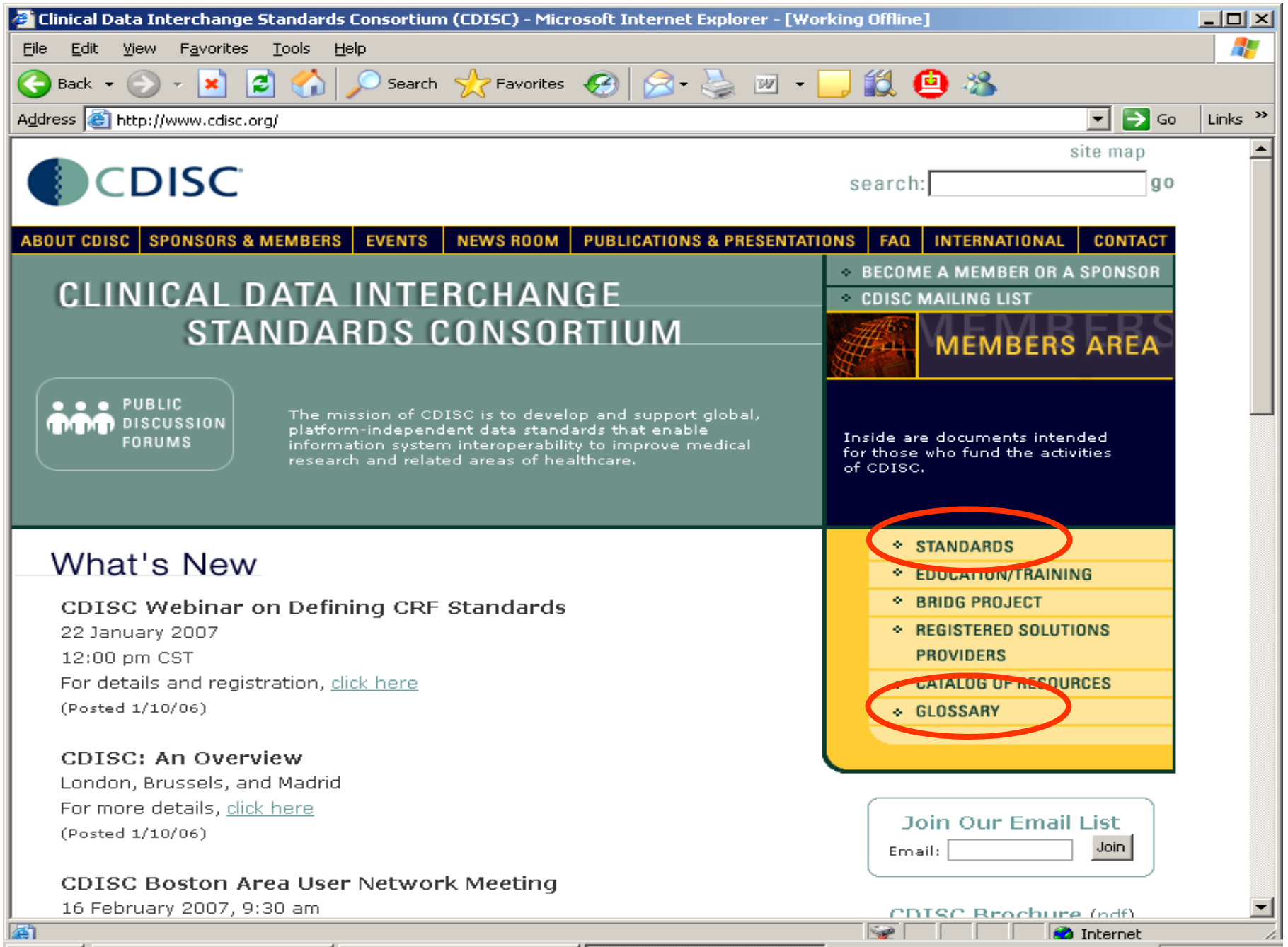
- Introduction générale à CDISC
  - Pierre-Yves Lastic 30 min
- Protocole et recueil des données
  - Nicolas de Saint-Jorre 50 min
  - PGR, ODM, LAB
- Stockage et analyse des données
  - Nathalie Sabin 50 min
  - SDTM, AdAM
- Projet CDASH et Interoperabilité
  - Pierre-Yves Lastic 30 min
  - Terminology & BRIDG
- Conclusion et discussion
  - tous 20 min

CDISC Snapshot

- **Global, open, multi-disciplinary non-profit organization**
  - Founded in 1997; incorporated in 2000
  - Liaison A Status with ISO TC 215
  - Charter agreement with HL7 since 2001
  - Over 200 member organizations
  - Active Coordinating Committees
    - Europe
    - Japan
  - Additional activities
    - Australia
    - India
    - S. America and Africa



- **Established industry standards to support the electronic acquisition, exchange, submission and archiving of data to support regulated clinical research**
  - Freely available on the CDISC website (www.cdisc.org)
  - Developed through open, consensus-based approach


Clinical Data Interchange Standards Consortium (CDISC) - Microsoft Internet Explorer - [Working Offline]
File Edit View Favorites Tools Help
Back Search Favorites
Address http://www.cdisc.org/
Go Links
site map
search: go
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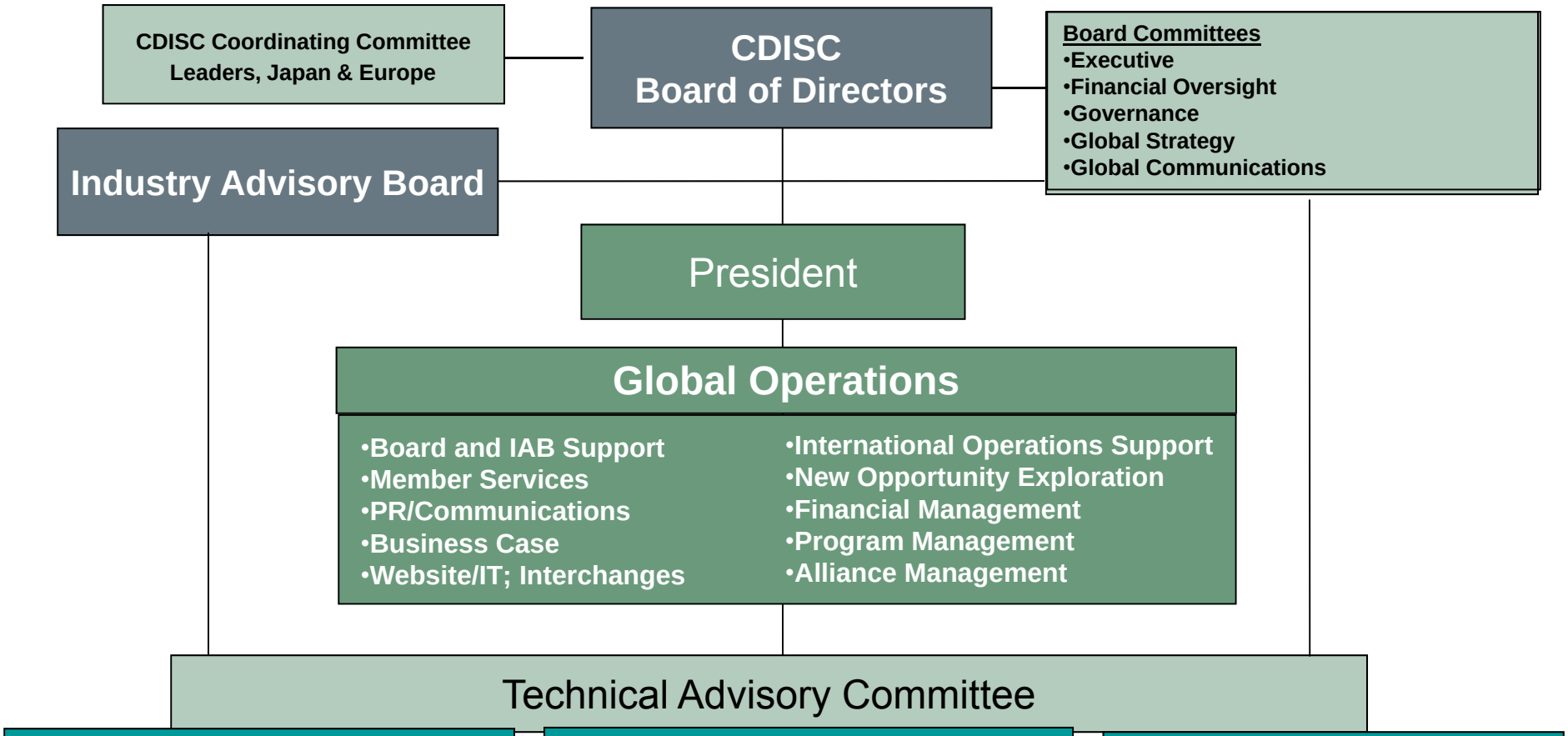
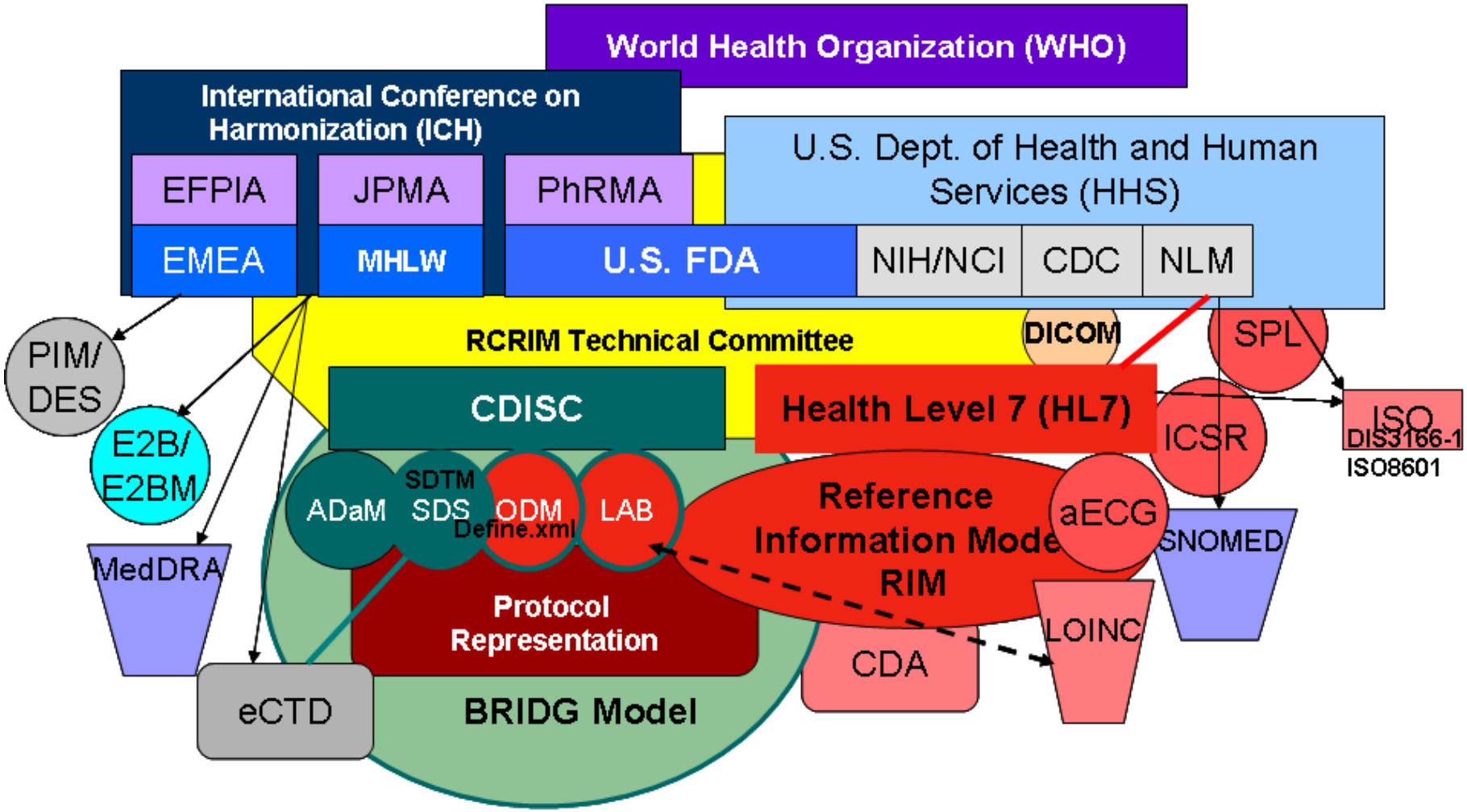
CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM
PUBLIC DISCUSSION FORUMS
The mission of CDISC is to develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare.
BECOME A MEMBER OR A SPONSOR
CDISC MAILING LIST
MEMBERS AREA
Inside are documents intended for those who fund the activities of CDISC.
STANDARDS
EDUCATION/TRAINING
BRIDG PROJECT
REGISTERED SOLUTIONS PROVIDERS
CATALOG OF RESOURCES
GLOSSARY
What's New
CDISC Webinar on Defining CRF Standards
22 January 2007
12:00 pm CST
For details and registration, click here
(Posted 1/10/06)
CDISC: An Overview
London, Brussels, and Madrid
For more details, click here
(Posted 1/10/06)
CDISC Boston Area User Network Meeting
16 February 2007, 9:30 am
Join Our Email List
Email: Join
CDISC Brochure (pdf)
Internet


CDISC Coordinating Committee Leaders, Japan & Europe
CDISC Board of Directors
Board Committees
•Executive
•Financial Oversight
•Governance
•Global Strategy
•Global Communications
Industry Advisory Board
President
Global Operations
•Board and IAB Support
•Member Services
•PR/Communications
•Business Case
•Website/IT; Interchanges
•International Operations Support
•New Opportunity Exploration
•Financial Management
•Program Management
•Alliance Management
Technical Advisory Committee
Production Standards
•Production Standards Updates (SDTM, SEND, define.xml, ODM, LAB, ADaM, Glossary)
•End-to-end Documentation
•Implementation Guide/Std Enhancemnt (e.g. TDM, PK, device, vaccine)
Implementation Services
•Education Courses
•Global User Network Support
•Regional CDISC Coordinating Comm. (Japan, Europe)
•U.S. Networks
•Implementation Enablers ('proto-tools')
•Certification
•Help Desk
Innovation Initiatives
•BRIDG Modeling
•SDTM-ADaM Pilot
•Submission in ODM XML
•eSource Data Interchange
•Terminology and NIH Grants
•Data Collection Standards
•Protocol Representation
•Healthcare Link
•Industry Architecture Proposal Doc

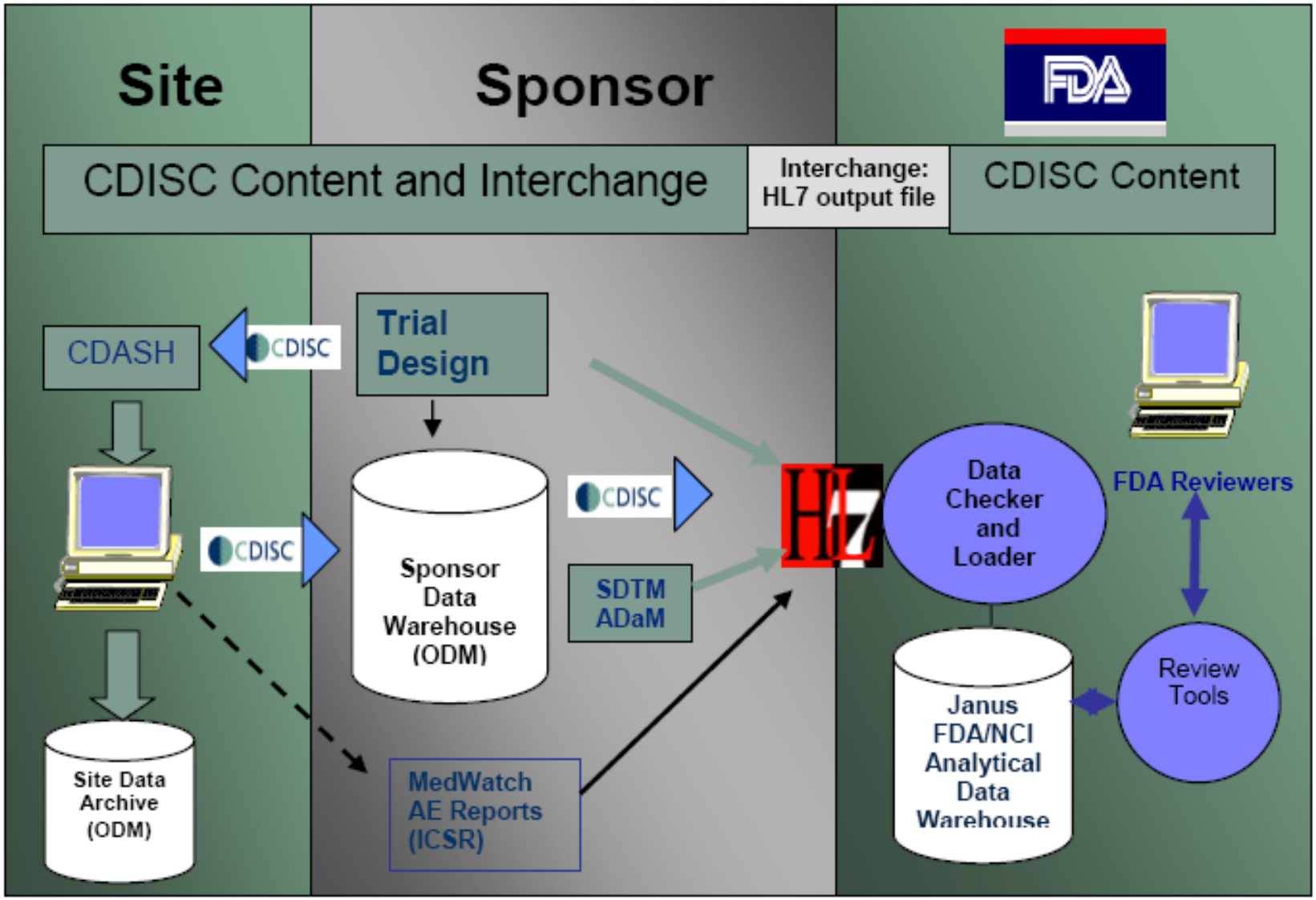
Standard	Description	Implementation Version Release Date
SDTM, SEND	Ready for regulatory submission of CRT 9,600 downloads as of mid-2007	2004*
ODM	CDISC Transport Standard for acquisition, exchange, submission (define.xml) archive	2001*
Define.xml	Case Report Tabulation Data Definition Specification	2005*
LAB	Content standard – available for transfer of clinical lab data to sponsors	2002
ADaM	General Considerations document and examples of datasets for submission	2004
Protocol Representation	Collaborative effort to develop machine-readable standard protocol with data layer	In progress
Terminology Codelists	Developing standard terminology to support all CDISC standards	2006 (Pkg1) Pkg 2 in progress
CDASH	Data acquisition (CRF) standards	In progress

* Specification referenced in FDA Final Guidance

CDISC in Context



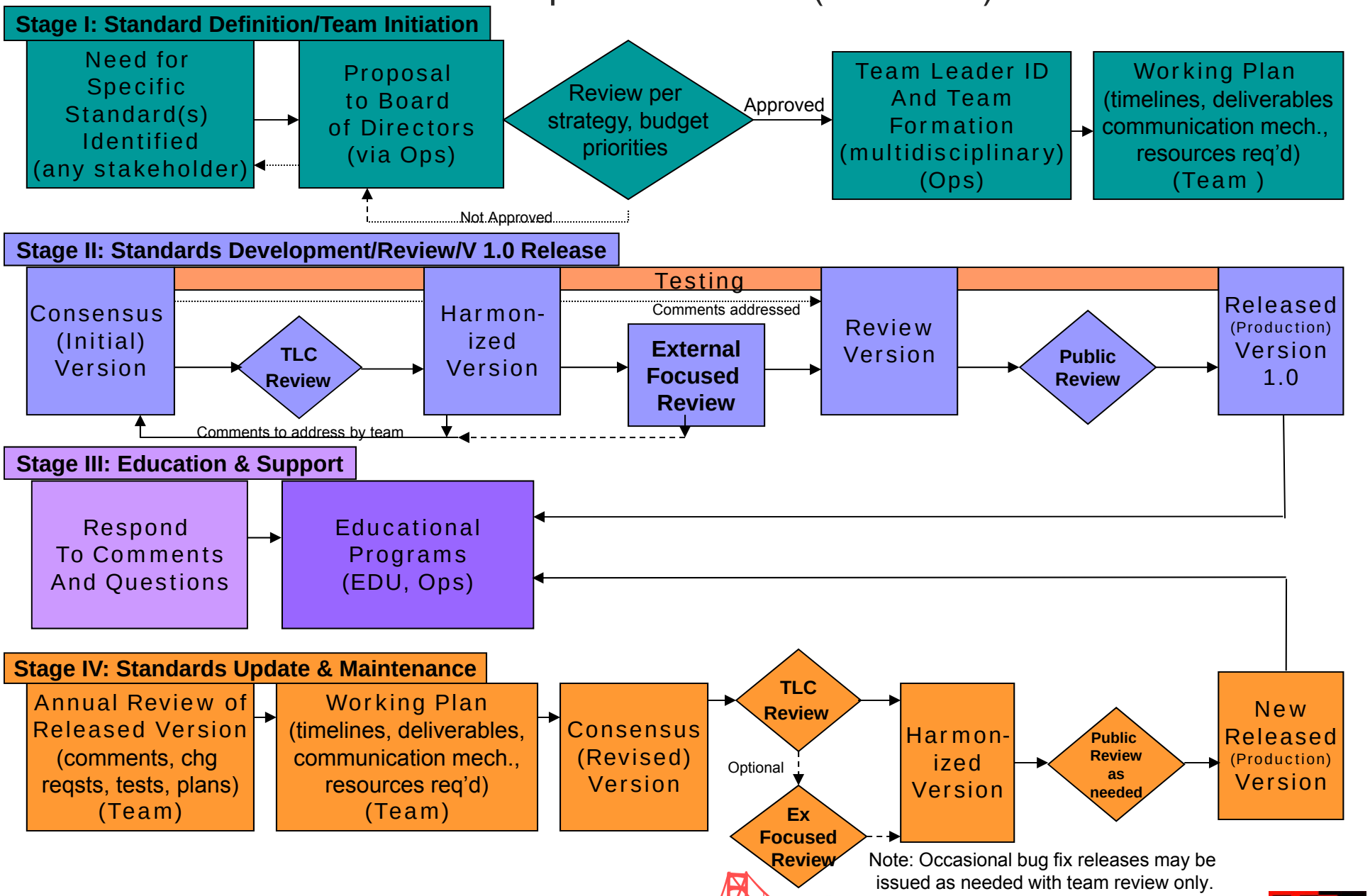
CDISC and FDA



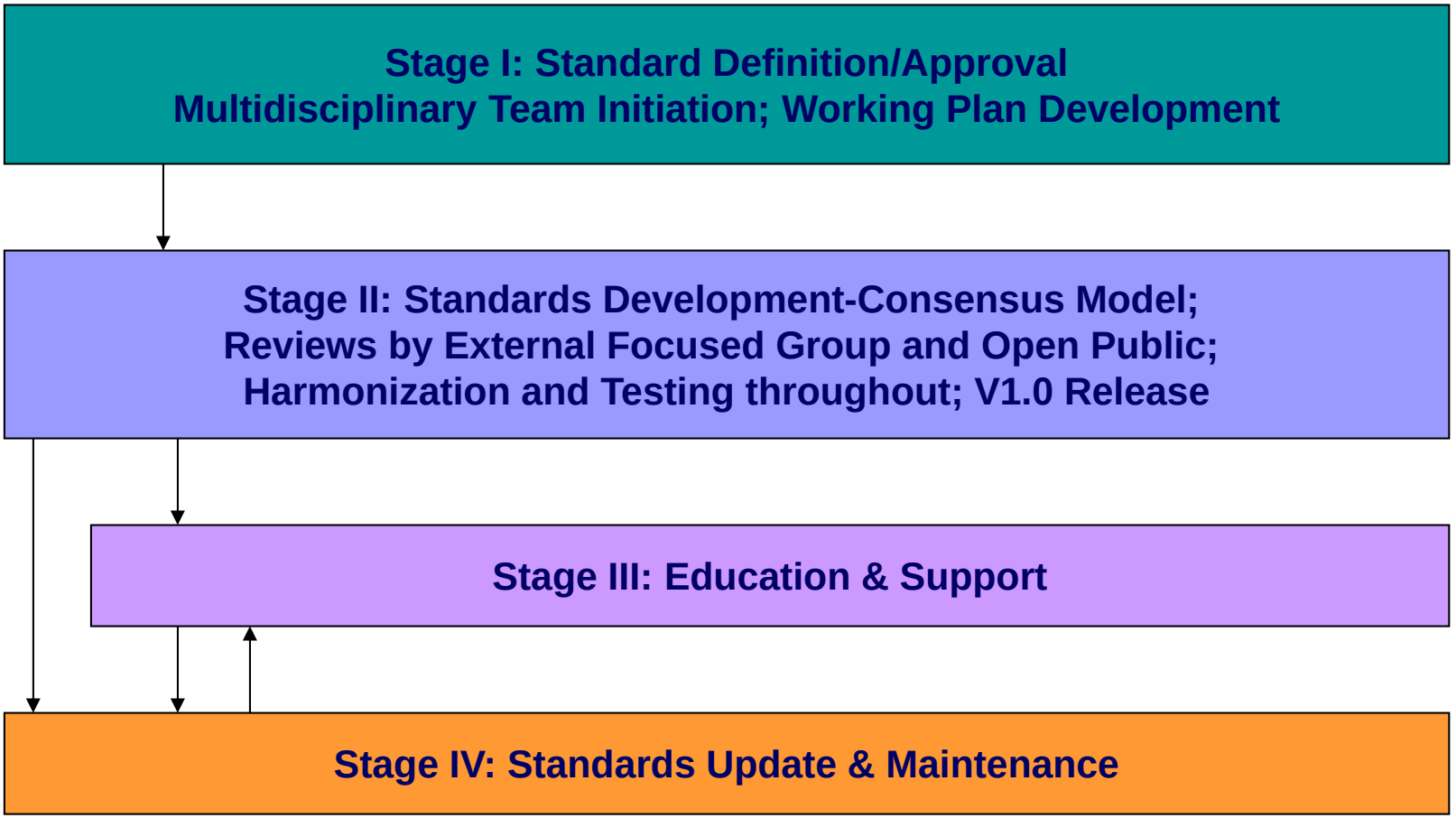
CDISC Approach to Standards

- The CDISC models are the products of contributions from numerous organizations, functional groups, and individuals; they do not have a sole source.
- Consensus building
  - Involves different disciplines within the industry
  - Involves ‘consolidating’ existing models, review comments and testing
  - Takes time, but results in widely accepted models
- Freely available on the CDISC website (www.cdisc.org)

CDISC Standards Development Process (COP-001)



CDISC Standards Development Process (COP-001)
Primary Stages



The mission of CDISC is to…

develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare.

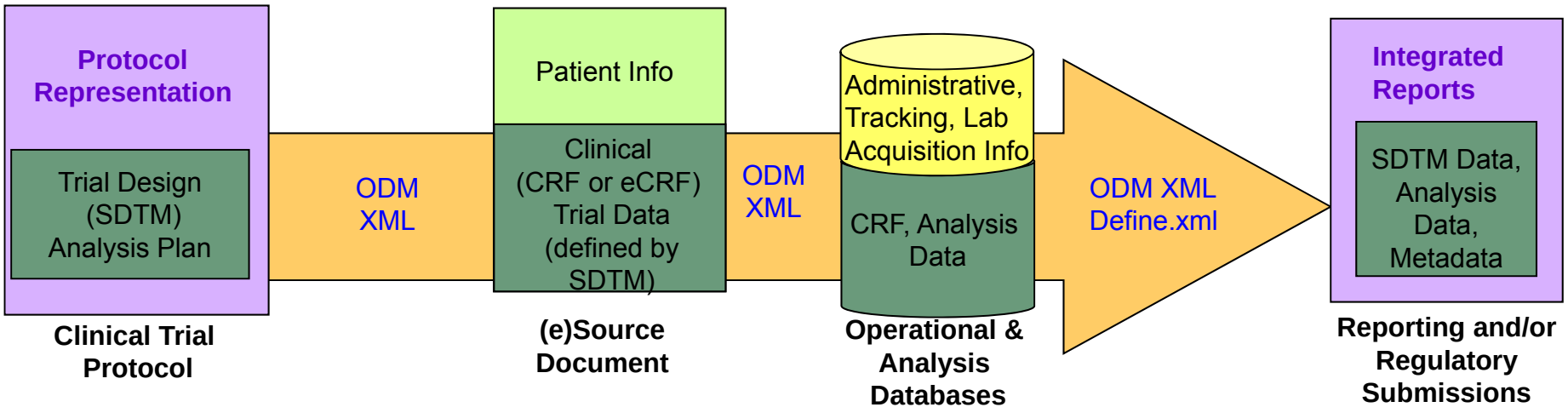
Data Flow Using CDISC

= ODM (transport)

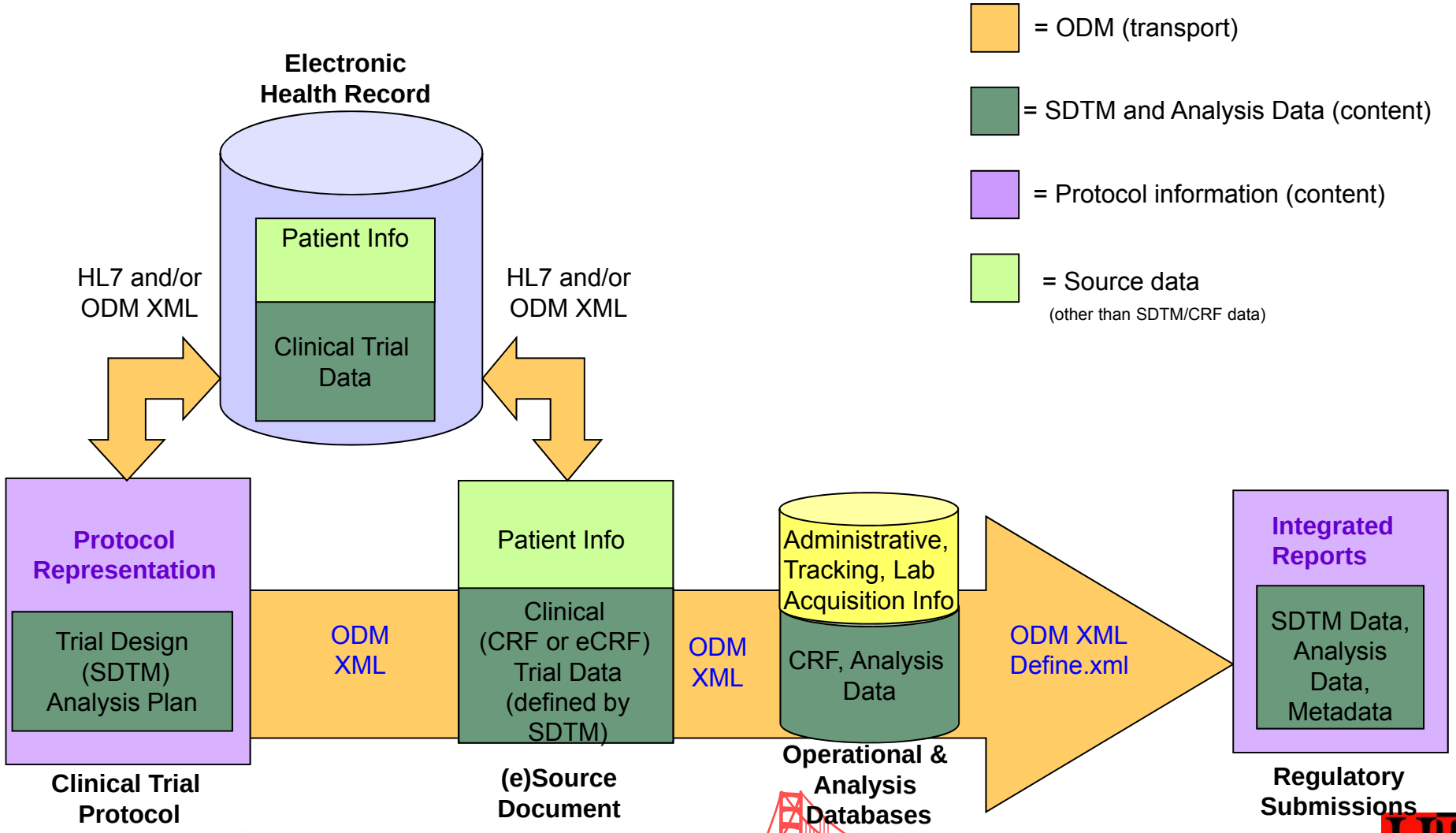
= SDTM and Analysis Data (content)

= Protocol information (content)

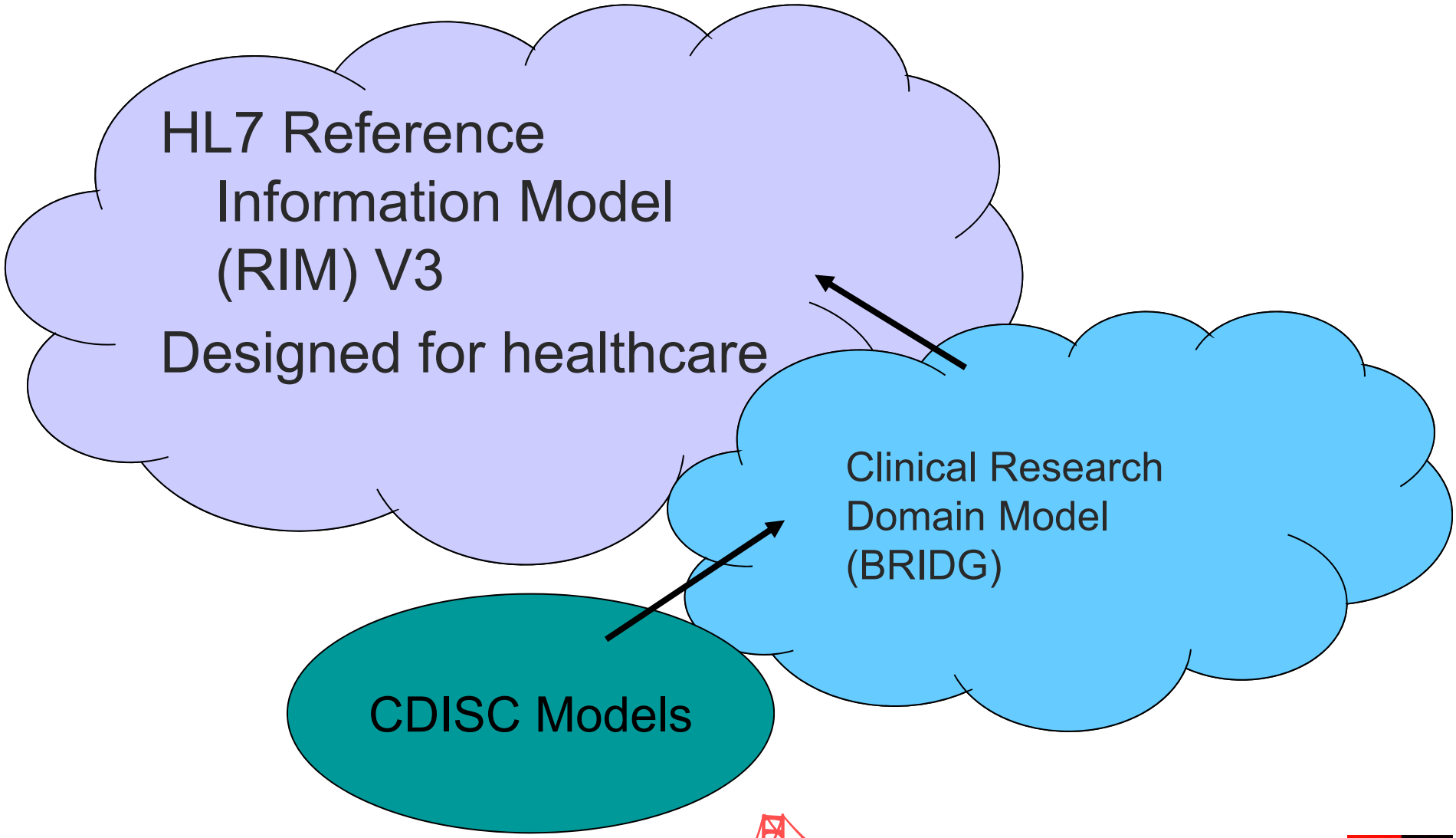
= Source data
(other than SDTM/CRF data)



Data Flow Using CDISC Standard Linking Clinical Research and Healthcare



Towards interoperability…..



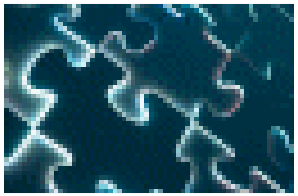
The BRIDG Model*

A clinical research domain analysis model (UML)
initiated by CDISC, BRIDGing
- *Organizations (CDISC, HL7, FDA, NCI)*
- *Standards*
- *Research and Healthcare*

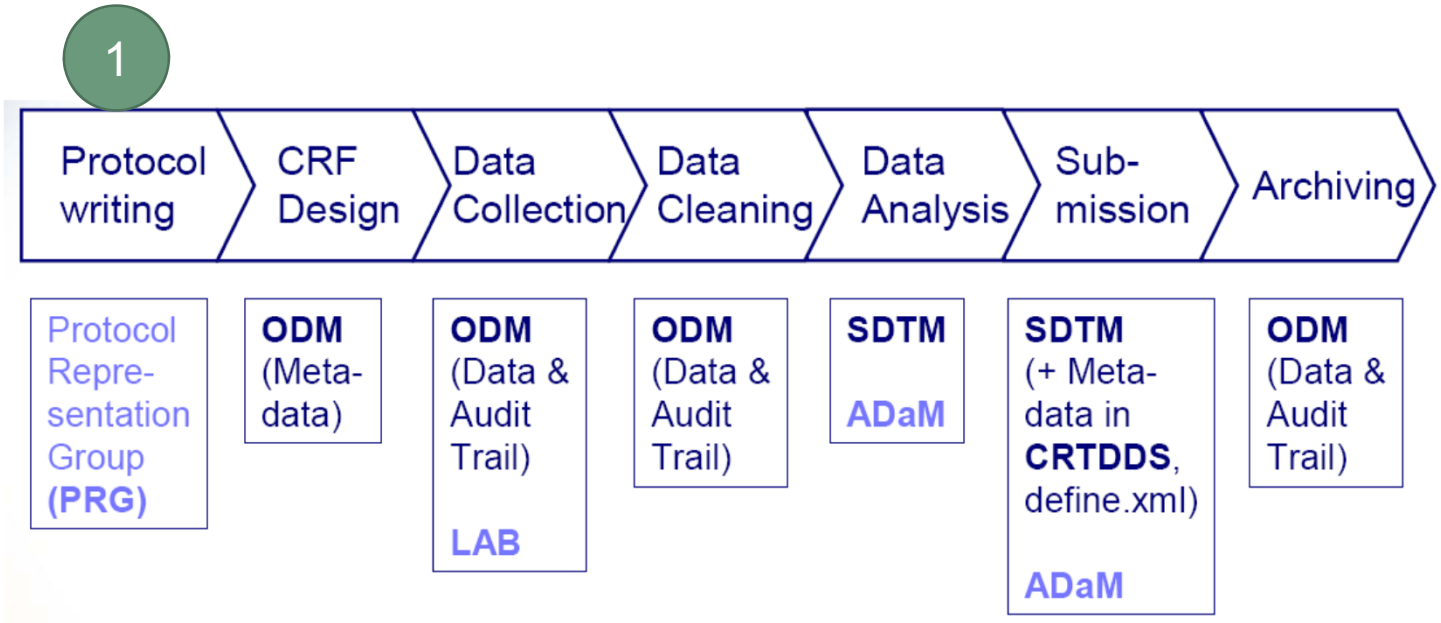
Open Source
- *See BRIDG Project on CDISC website*
  or www.bridgproject.org

*Biomedical Research Integrated Domain Group (BRIDG) Model

Fin de la première Partie



CDISC Standards position



PRG 10’

- Standard en développement
- Définition standard d’un protocole: PRElements_FullLists2-0-0.pdf (October 12, 2005)
- Elements:
  - a data item or a block of text representing a unique piece of information
- CDISC Glossary
  - Applied Clinical Trials, Dec 2004

PRG structure

1) General Information
2) Background Info.
3) Trial objectives & purpose
4) Trial Design
5) Subject Selection / Withdrawal
6) Treatment of Subject
7) Assessment
8) Efficacy Assessment
9) Assessment of Safety
10) Statistics
11) Direct access to source data / documents
12) Quality control & quality assurance
13) Ethics
14) Data handling & record keeping
15) Financing & Insurance
16) Publication policy
17) Supplements (+18 pages)

Numéro de l'élément

Nom de l'élément

Définition de l'élément

6. CLINICAL TRIAL PROTOCOL AND PROTOCOL AMENDMENT(S)

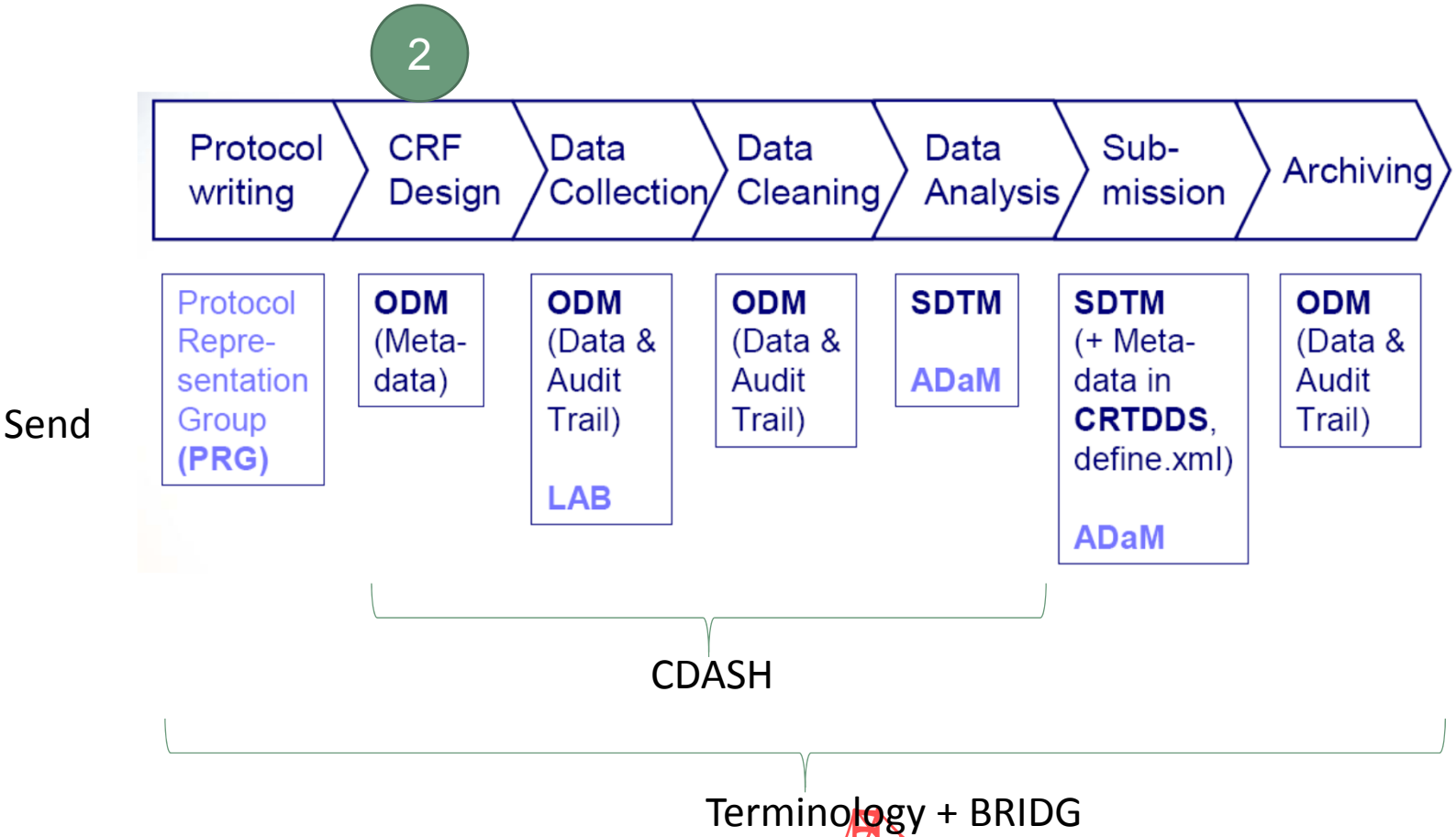
The contents of a trial protocol should generally include the following topics. However, site specific information may be provided on separate protocol page(s), or addressed in a separate agreement, and some of the information listed below may be contained in other protocol referenced documents, such as an Investigator's Brochure.

6.1 General Information

6.1.1 Protocol title, protocol identifying number, and date. Any amendment(s) should also bear the amendment number(s) and date(s).

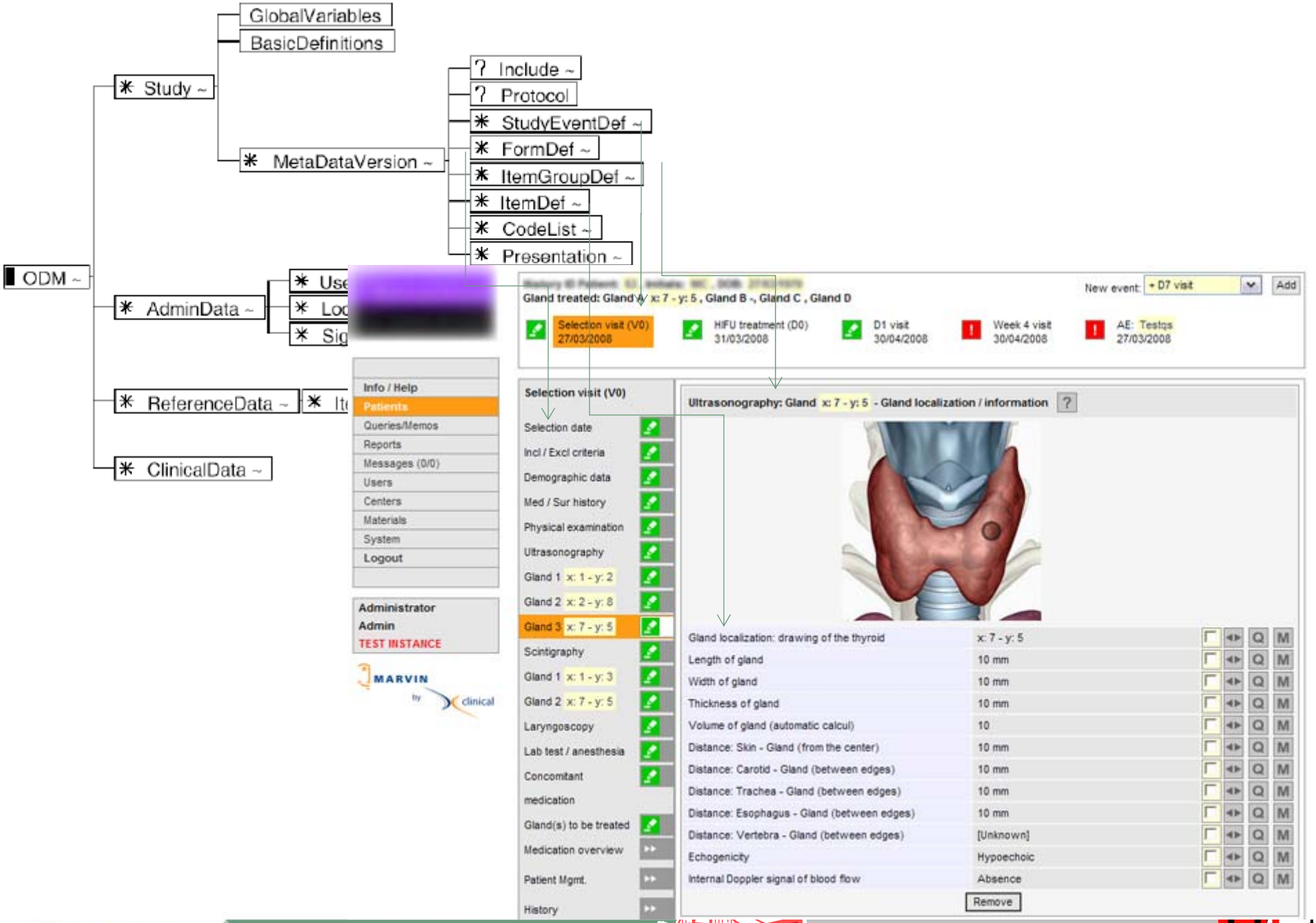
ELEMENT NUM	ELEMENT NAME	ELEMENT DEFINITION (FROM GLOSSARY)	DEFINITION SOURCE	ELEMENT EXPLANATION (recommendations/ examples for usage)	ELEMENT SOURCE	ELEMENT SOURCE CONTENTS	NOTES
Document Type							
GENERAL INFORMATION							
1	Protocol Title			Full text of the protocol/study title	*ICH E6 6.1.1, EUDRACT*	*Appendix I A. Full title of the protocol*	
2	Protocol Short Title			Name or abbreviated title of the trial wherever available	*EUDRACT*	*Appendix I A.Abbreviated title of the trial*	
3	Protocol identifying			Sponsor protocol number;and/or Unique	ICH E6 6.1.1, EUDRACT	*National trial # reference, EUDRACT clinical trial number, Sponsor code = sponsor*	EUDRACT stated that this was a national identificaton
264	Provision of Data to Authors			All authors whether from within a sponsoring company or external, will be given the relevant statistical tables, figures, and reports needed to support the planned publication.	PhRMA Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results (http://www.phrma.org/publications/policy//2002-06-24.430.pdf0)		

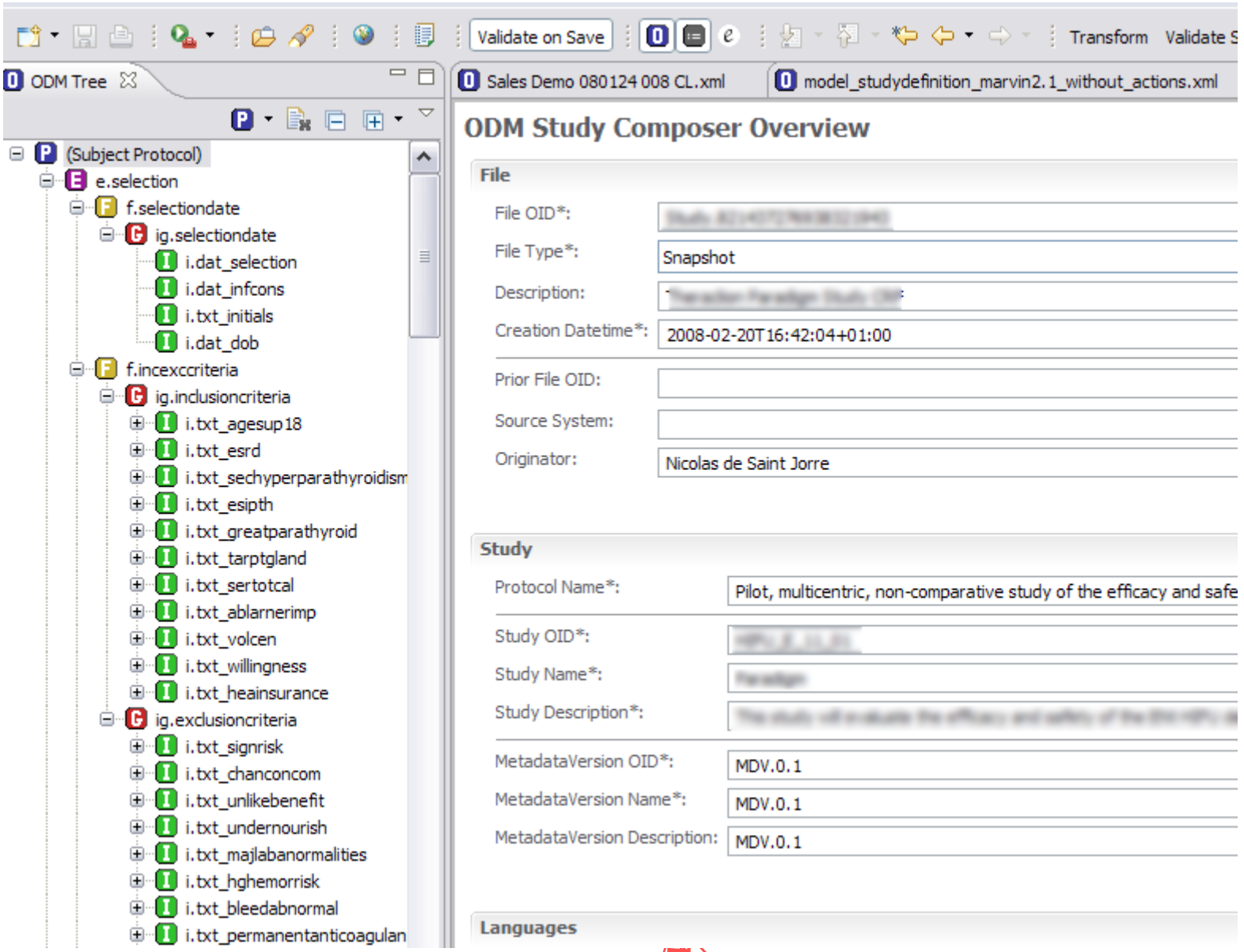
CDISC Standards position



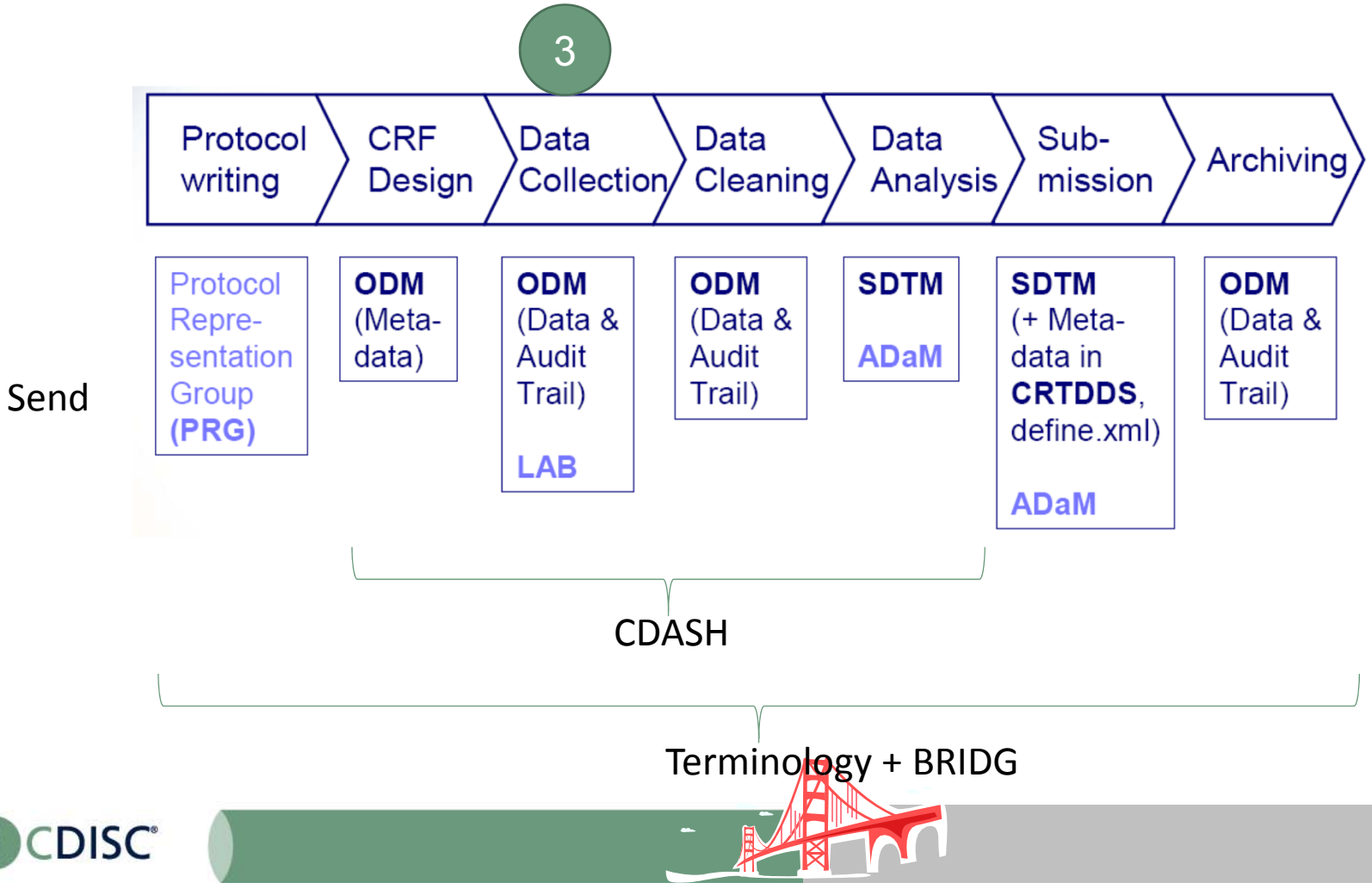
ODM

- ODM: Traduction des objectifs d'un protocole clinique en cahier d'observation (avec une dimension standard électronique)
- Les versions en production :
  - (ODM V1.3)
  - (ODM V1.2.1)


GlobalVariables
BasicDefinitions
Study ~
MetaDataVersion ~
Include ~
Protocol
StudyEventDef ~
FormDef ~
ItemGroupDef ~
ItemDef ~
CodeList ~
Presentation ~
ODM ~
AdminData ~
ReferenceData ~
ClinicalData ~
Info / Help
Patients
Queries/Memos
Reports
Messages (0/0)
Users
Centers
Materials
System
Logout
Administrator
Admin
TEST INSTANCE
MARVIN
by clinical
Gland treated: Gland V, x: 7 - y: 5 , Gland B -, Gland C , Gland D
New event: + D7 visit
Add
Selection visit (V0) 27/03/2008
HIFU treatment (D0) 31/03/2008
D1 visit 30/04/2008
Week 4 visit 30/04/2008
AE: Testqs 27/03/2008
Selection visit (V0)
Selection date
Incl / Excl criteria
Demographic data
Med / Sur history
Physical examination
Ultrasonography
Gland 1 x: 1 - y: 2
Gland 2 x: 2 - y: 8
Gland 3 x: 7 - y: 5
Scintigraphy
Gland 1 x: 1 - y: 3
Gland 2 x: 7 - y: 5
Laryngoscopy
Lab test / anesthesia
Concomitant medication
Gland(s) to be treated
Medication overview
Patient Mgmt.
History
Ultrasonography: Gland x: 7 - y: 5 - Gland localization / information
Gland localization: drawing of the thyroid x: 7 - y: 5
Length of gland 10 mm
Width of gland 10 mm
Thickness of gland 10 mm
Volume of gland (automatic calcul) 10
Distance: Skin - Gland (from the center) 10 mm
Distance: Carotid - Gland (between edges) 10 mm
Distance: Trachea - Gland (between edges) 10 mm
Distance: Esophagus - Gland (between edges) 10 mm
Distance: Vertebra - Gland (between edges) [Unknown]
Echogenicity Hypoechoic
Internal Doppler signal of blood flow Absence
Remove


Validate on Save
Transform
Validate S
ODM Tree
Sales Demo 080124 008 CL.xml
model_studydefinition_marvin2.1_without_actions.xml
(Subject Protocol)
e.selection
f.selectiondate
ig.selectiondate
i.dat_selection
i.dat_infcons
i.txt_initials
i.dat_dob
f.incexccriteria
ig.inclusioncriteria
i.txt_agesup18
i.txt_esrd
i.txt_sechyperparathyroidism
i.txt_esipth
i.txt_greatparathyroid
i.txt_tarptgland
i.txt_sertotcal
i.txt_ablarnerimp
i.txt_volcen
i.txt_willingness
i.txt_heainsurance
ig.exclusioncriteria
i.txt_signrisk
i.txt_chanconcom
i.txt_unlikebenefit
i.txt_undernourish
i.txt_majlabanormalities
i.txt_hghemorrisk
i.txt_bleedabnormal
i.txt_permanentanticoagulan
ODM Study Composer Overview
File
File OID*:
File Type*:
Snapshot
Description:
Creation Datetime*:
2008-02-20T16:42:04+01:00
Prior File OID:
Source System:
Originator:
Nicolas de Saint Jorre
Study
Protocol Name*:
Pilot, multicentric, non-comparative study of the efficacy and safe
Study OID*:
Study Name*:
Study Description*:
MetadataVersion OID*:
MDV.0.1
MetadataVersion Name*:
MDV.0.1
MetadataVersion Description:
MDV.0.1
Languages

CDISC Standards position



LAB

- Standard qui permet de capturer les données de laboratoire (complet et répondant aux attentes des labo centraux et des sponsors)
- Base Model Version 1.0.1
- 12 niveaux hiérarchiques (calqués sur la hiérarchie des données de laboratoire)
- Structure dé-normalisée : 1 résultat de test ⇔ 1 record
- 92 items (obligatoires ou non):
  Tous présents mais vides autorisés
- Code-lists: suggérées mais pas obligatoires

Les 12 niveaux du Lab…

- 01. Good Transmission Practice
- 02. Study
- 03. Site
- 04. Investigator
- 05. Subject
- 06. Visit
- 07. Accession
- 08. Record Extension Type
- 09. Base Specimen
- 10. Base Battery
- 11. Base Test
- 12. Base Result

- Niv 12. Base Result: 3 niveaux Reporté / Conventionnel / SI

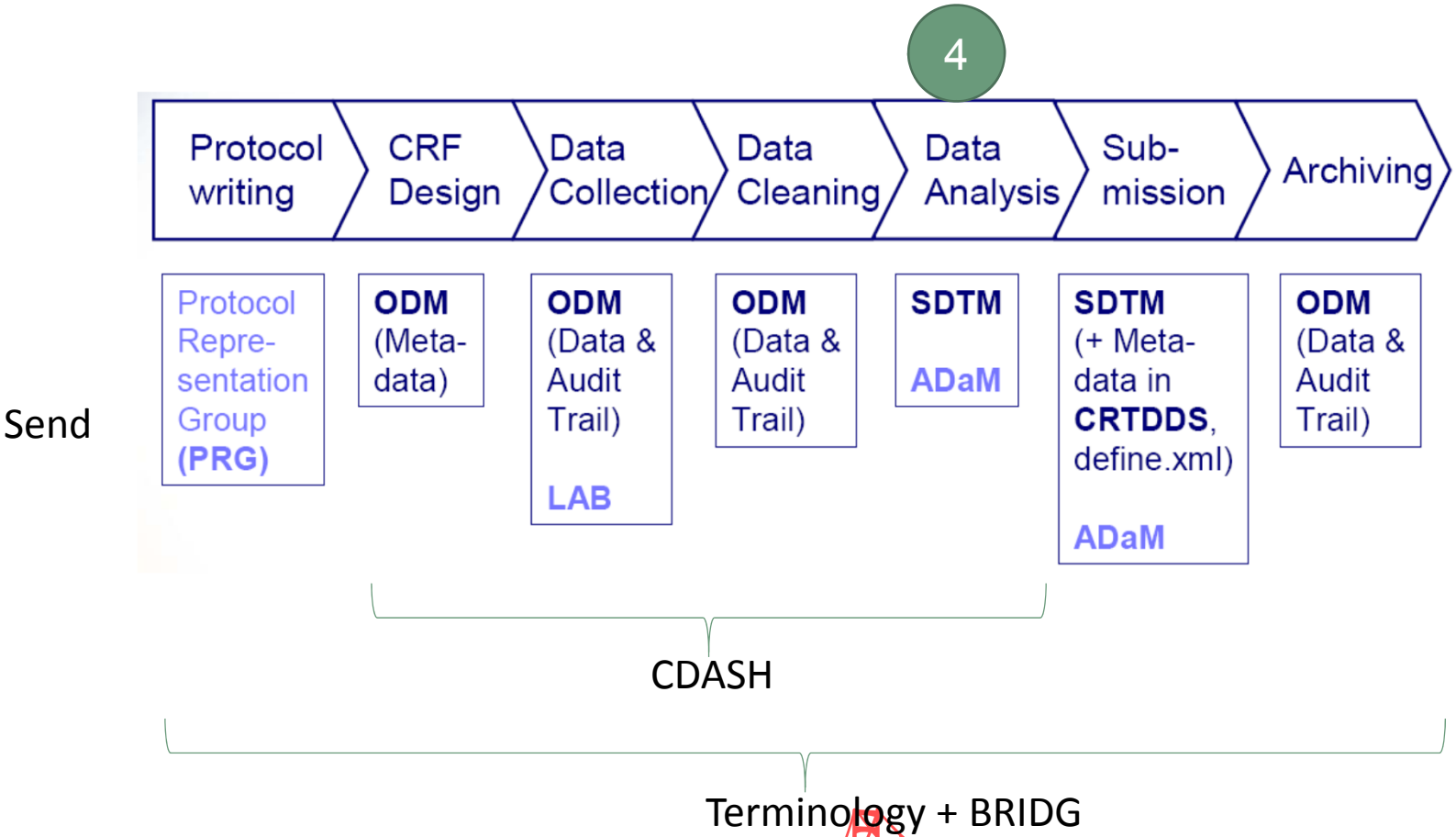
Reported Text Result	Résultat au format texte émis par le laboratoire
Reported Text Result Code List ID	Si applicable, code et version du résultat
Reported Numeric Result	Résultat numérique émis par le laboratoire
Reported Numeric Result Precision	Précision sur le résultat (5,3: champs sur 5 digits et 3 décimales)
Reported Reference Range Low	Valeur inférieure de référence
Reported Reference Range High	Valeur supérieure de référence
Reported Units	Unités utilisées par le laboratoire
Reported Units Code List ID	Si applicable, code et version des unités

- Niv 12. Base Result (suite):

Conventional Text Result	Résultat conventionnel sous forme de texte au niveau du laboratoire
Conventional Text Result Code List ID	Si applicable, code et version du résultat conventionnel
Conventional Numeric Result	Résultat conventionnel numérique émis par le laboratoire
Conventional Numeric Result Precision	Précision sur le résultat conventionnel (5,3: champs sur 5 digits et 3 décimales)
Conventional Reference Range Low	Valeur conventionnelle inférieure de référence
Conventional Reference Range High	Valeur conventionnelle supérieure de référence
Conventional Units	Unités conventionnelle utilisées par le laboratoire
Conventional Units Code List	Si applicable, code et version des unités conventionnelle

SI Text Result	Résultat standard international sous forme de texte au niveau du laboratoire
SI Text Result Code List ID	Si applicable, code et version du résultat standard international
SI Numeric Result	Résultat standard international numérique émis par le laboratoire
SI Numeric Result Precision	Précision sur le résultat standard international (5,3: champs sur 5 digits et 3 décimales)
SI Reference Range Low	Valeur standard international inférieure de référence
SI Reference Range High	Valeur standard international supérieure de référence
SI Units	Unités standard international utilisées par le laboratoire
SI Units Code List	Si applicable, code et version des unités standard international

CDISC Standards position



SDTM

- Standard décrivant la structure d'une base de données tabulées pour une exploitation statistique (Tabulation datasets, which are electronic listings of individual observations for a subject that comprise the essential data collected in a clinical trial)
- Base Model Version
  - (SDTM IG V3.1.1)
  - (SDTM V1.1)

- Avantages:
  - Pour les reviewers réglementaires,
  - Facilité pour développer / utiliser des logiciels standards
  - Travail plus efficace avec les Autorités
  - Echanges plus faciles entres partenaires
  - Partage des données facilité lors des fusions

SDTM par domain

Special-Purpose Domains:

- Demographics - DM
- Comments - CO

Interventions:

- Concomitant Medications - CM
- Substance Use - SU
- Exposure - EX

Events:

- Adverse Events - AE
- Medical History - MH
- Disposition - DS
- *Protocol Deviations - DV

Findings:

- *Drug Accountability - DA
- Inclusion/Exclusion Exceptions - IE
- *Microbiology Specimens - MB
- *Microbiology Susceptibility - MS
- *Pharmacokinetics Concentrations - PC
- *Pharmacokinetics Parameters - PP
- ECG Tests - EG
- Laboratory Tests - LB
- Questionnaires - QS
- Physical Examinations - PE
- Subject Characteristics - SC
- Vital Signs - VS

Trial Design Domains:

- Trial Elements - TE
- Trial Arms - TA
- Trial Visits - TV
- Subject Elements - SE
- Subject Visits - SV
- Trial Inclusion/Exclusion Criteria – TI
- Trial Summary - TS

Dataset	Description	Location	Structure	Purpose	Key Variables
DM	Demographics	dm.xpt	One record per subject	Tabulation	STUDYID, USUBJID
CO	Comments	co.xpt	One record per comment per subject	Tabulation	STUDYID, USUBJID, COSEQ
CM	Concomitant Medications	cm.xpt	One record per medication intervention episode per subject	Tabulation	STUDYID, USUBJID, CMTRT, CMSTDTC

Special-Purpose Relationship Datasets (defined in Section 8):

- Supplemental Qualifiers - SUPPQUAL
- Relate Records - RELREC

Pour chaque domain
3 types de variables:

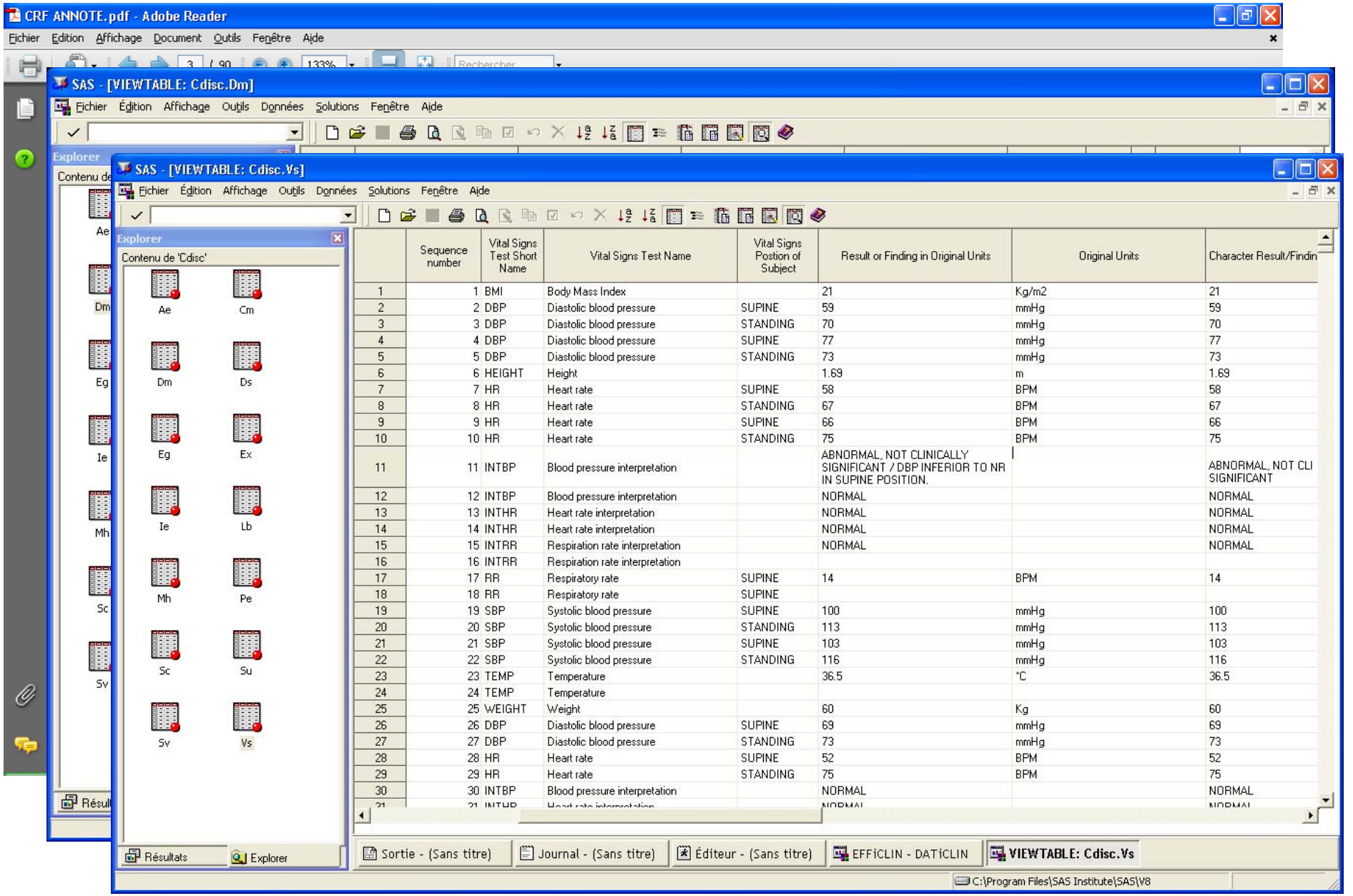
- A **Required variable** is any variable that is basic to the identification and meaning of a data record (i.e., essential key Identifiers and a Topic variable). Values cannot be null.
- An **Expected variable** is any variable necessary to make a record meaningful in the context of a specific domain. In most cases, some but not all values for expected variables may be null in a domain if unknown or not done. But when an expected variable has not been collected, a null column should still be included and a comment should be included in the define data definition document to state it was not collected.
- A **Permissible variable** may be used as appropriate, when collected or derived.
  - All timing variables are considered permissible.
  - Any qualifier variables from the same general class are permissible for that domain.

Exemple : domain DM

5.1.1 Demographics Domain Model — DM

dm.xpt, Demographics — Version 3.1.1, August 26, 2005. One record per subject, Tabulation

Variable Name	Variable Label	Type	Controlled Terms or Format	Origin	Role	CDISC Notes	Core	References
STUDYID	Study Identifier	Char		CRF	Identifier	Unique identifier for a study within the submission.	Req	SDTM 2.2.4
DOMAIN	Domain Abbreviation	Char	**DM	Derived	Identifier	Two-character abbreviation for the domain most relevant to the observation.	Req	SDTM 2.2.4
USUBJID	Unique Subject Identifier	Char		Sponsor Defined	Identifier	Unique subject identifier within the submission. This can be a unique number or a compound identifier formed by concatenating STUDYID-SITEID-SUBJID. Since a subject may participate in more than one study (as in a follow-on), the USUBJID may differ from the SUBJID in some cases.	Req	SDTM 2.2.4
SUBJID	Subject Identifier for the Study	Char		CRF	Topic	Subject identifier used within the study. Often the ID of the subject as recorded on a CRF.	Req	
RFSTDTC	Subject Reference Start Date/Time	Char	ISO 8601	Sponsor Defined	Timing	Reference Start Date/time for the subject in ISO 8601 character format. Usually equivalent to date/time of first intake of drug. Required for all randomized subjects; null for screen failures (if screen failures are submitted).	Exp	SDTMIG 4.1.4.1
RFENDTC	Subject Reference End Date/Time	Char	ISO 8601	Sponsor Defined	Timing	Reference End Date/time for the subject in ISO 8601 character format. Usually equivalent to the date/time when subject was determined to have ended the trial, and often equivalent to date/time of last intake of drug. Required for all randomized subjects; null for screen failures (if screen failures are submitted).	Exp	SDTMIG 4.1.4.1
SITEID	Study Site Identifier	Char		CRF or Derived	Record Qualifier	Unique identifier for a study site within a submission.	Req	
INVID	Investigator Identifier	Char	*	CRF or Derived	Record Qualifier	An identifier to describe the Investigator for the study. May be used in addition to the SITEID. Not needed if SITEID is equivalent to INVID.	Perm	
INVNAM	Investigator Name	Char		CRF or Derived	Synonym Qualifier	Name of the investigator for a site.	Perm	
BRTHDTC	Date/Time of Birth	Char	ISO 8601	CRF or Derived	Result Qualifier	Date/time of birth of the subject.	Perm	SDTMIG 4.1.4.1



	Sequence number	Vital Signs Test Short Name	Vital Signs Test Name	Vital Signs Postion of Subject	Result or Finding in Original Units	Original Units	Character Result/Findin
1	1	BMI	Body Mass Index		21	Kg/m2	21
2	2	DBP	Diastolic blood pressure	SUPINE	59	mmHg	59
3	3	DBP	Diastolic blood pressure	STANDING	70	mmHg	70
4	4	DBP	Diastolic blood pressure	SUPINE	77	mmHg	77
5	5	DBP	Diastolic blood pressure	STANDING	73	mmHg	73
6	6	HEIGHT	Height		1.69	m	1.69
7	7	HR	Heart rate	SUPINE	58	BPM	58
8	8	HR	Heart rate	STANDING	67	BPM	67
9	9	HR	Heart rate	SUPINE	66	BPM	66
10	10	HR	Heart rate	STANDING	75	BPM	75
11	11	INTBP	Blood pressure interpretation		ABNORMAL, NOT CLINICALLY SIGNIFICANT / DBP INFERIOR TO NR IN SUPINE POSITION.		ABNORMAL, NOT CLI SIGNIFICANT
12	12	INTBP	Blood pressure interpretation		NORMAL		NORMAL
13	13	INTHR	Heart rate interpretation		NORMAL		NORMAL
14	14	INTHR	Heart rate interpretation		NORMAL		NORMAL
15	15	INTRR	Respiration rate interpretation		NORMAL		NORMAL
16	16	INTRR	Respiration rate interpretation				
17	17	RR	Respiratory rate	SUPINE	14	BPM	14
18	18	RR	Respiratory rate	SUPINE			
19	19	SBP	Systolic blood pressure	SUPINE	100	mmHg	100
20	20	SBP	Systolic blood pressure	STANDING	113	mmHg	113
21	21	SBP	Systolic blood pressure	SUPINE	103	mmHg	103
22	22	SBP	Systolic blood pressure	STANDING	116	mmHg	116
23	23	TEMP	Temperature		36.5	°C	36.5
24	24	TEMP	Temperature				
25	25	WEIGHT	Weight		60	Kg	60
26	26	DBP	Diastolic blood pressure	SUPINE	69	mmHg	69
27	27	DBP	Diastolic blood pressure	STANDING	73	mmHg	73
28	28	HR	Heart rate	SUPINE	52	BPM	52
29	29	HR	Heart rate	STANDING	75	BPM	75
30	30	INTBP	Blood pressure interpretation		NORMAL		NORMAL

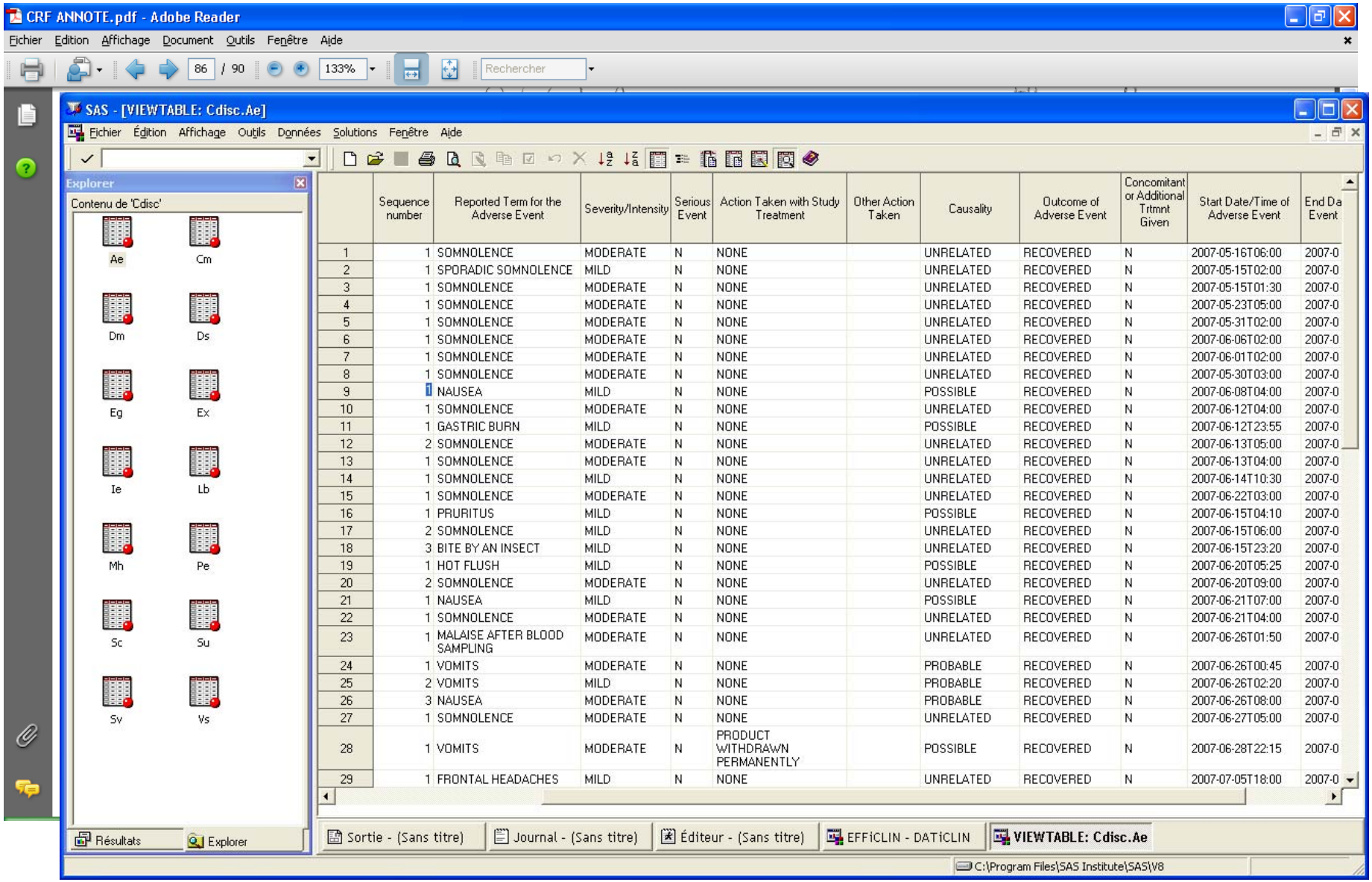
Exemple domain AE

Sample data that illustrates the above:

	STUDYID	DOMAIN	USUBJID	AESEQ	AETERM	AESTDTC	AEENDTC	AEMODIFY	AEDECOD
Row 1	ABC123	AE	123101	1	POUNDING HEADACHE	2003-10-12	2003-10-12	HEADACHE	HEADACHE
Row 2	ABC123	AE	123101	2	BACK PAIN FOR 6 HOURS	2003-10-13T13:05	2003-10-13T19:00	BACK PAIN	BACK PAIN
Row 3	ABC123	AE	123101	3	PULMONARY EMBOLISM	2003-10-21			PULMONARY EMBOLISM

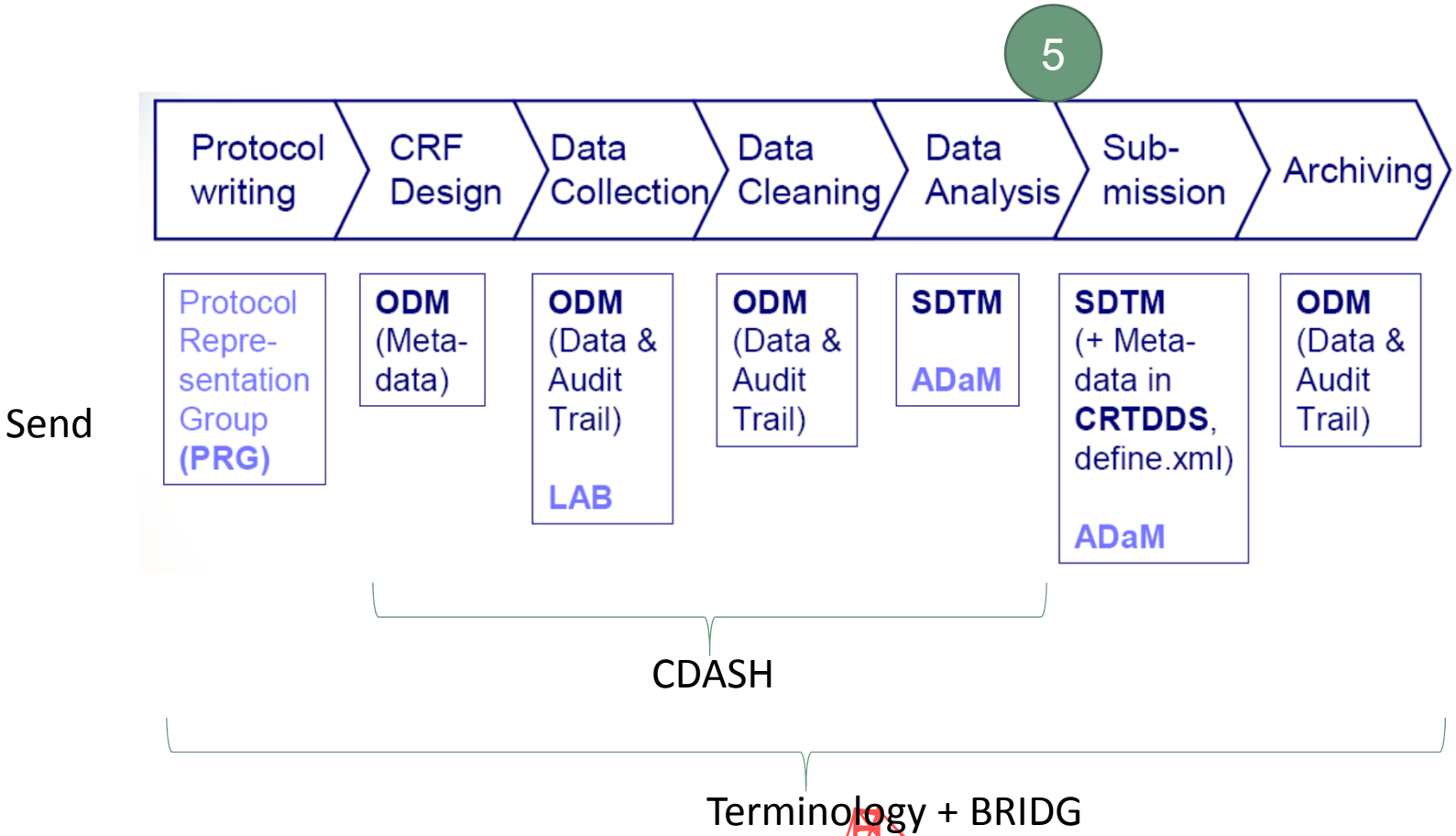
	AEBODSYS	AESEV	AESER	AEACN	AEREL
Row 1 (cont)	NERVOUS SYSTEM DISORDERS	SEVERE	N	NOT APPLICABLE	DEFINITELY NOT RELATED
Row 2 (cont)	MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	MODERATE	N	DOSE REDUCED	PROBABLY RELATED
Row 3 (cont)	VASCULAR DISORDERS	MODERATE	Y	DOSE REDUCED	PROBABLY NOT RELATED

	AEOUT	AESCONG	AESDISAB	AESDTH	AESHOSP	AESLIFE	AESMIE	AESTDY	AEENDY	AEENRF
Row 1 (cont)	RECOVERED/RESOLVED							-1	-1	
Row 2 (cont)	RECOVERED/RESOLVED							1	1	
Row 3 (cont)	RECOVERING/RESOLVING				Y	Y		9	.	AFTER



	Sequence number	Reported Term for the Adverse Event	Severity/Intensity	Serious Event	Action Taken with Study Treatment	Other Action Taken	Causality	Outcome of Adverse Event	Concomitant or Additional Trtmnt Given	Start Date/Time of Adverse Event	End Da Event
1	1	SOMNOLENCE	MODERATE	N	NONE		UNRELATED	RECOVERED	N	2007-05-16T06:00	2007-0
2	1	SPORADIC SOMNOLENCE	MILD	N	NONE		UNRELATED	RECOVERED	N	2007-05-15T02:00	2007-0
3	1	SOMNOLENCE	MODERATE	N	NONE		UNRELATED	RECOVERED	N	2007-05-15T01:30	2007-0
4	1	SOMNOLENCE	MODERATE	N	NONE		UNRELATED	RECOVERED	N	2007-05-23T05:00	2007-0
5	1	SOMNOLENCE	MODERATE	N	NONE		UNRELATED	RECOVERED	N	2007-05-31T02:00	2007-0
6	1	SOMNOLENCE	MODERATE	N	NONE		UNRELATED	RECOVERED	N	2007-06-06T02:00	2007-0
7	1	SOMNOLENCE	MODERATE	N	NONE		UNRELATED	RECOVERED	N	2007-06-01T02:00	2007-0
8	1	SOMNOLENCE	MODERATE	N	NONE		UNRELATED	RECOVERED	N	2007-05-30T03:00	2007-0
9	1	NAUSEA	MILD	N	NONE		POSSIBLE	RECOVERED	N	2007-06-08T04:00	2007-0
10	1	SOMNOLENCE	MODERATE	N	NONE		UNRELATED	RECOVERED	N	2007-06-12T04:00	2007-0
11	1	GASTRIC BURN	MILD	N	NONE		POSSIBLE	RECOVERED	N	2007-06-12T23:55	2007-0
12	2	SOMNOLENCE	MODERATE	N	NONE		UNRELATED	RECOVERED	N	2007-06-13T05:00	2007-0
13	1	SOMNOLENCE	MODERATE	N	NONE		UNRELATED	RECOVERED	N	2007-06-13T04:00	2007-0
14	1	SOMNOLENCE	MILD	N	NONE		UNRELATED	RECOVERED	N	2007-06-14T10:30	2007-0
15	1	SOMNOLENCE	MODERATE	N	NONE		UNRELATED	RECOVERED	N	2007-06-22T03:00	2007-0
16	1	PRURITUS	MILD	N	NONE		POSSIBLE	RECOVERED	N	2007-06-15T04:10	2007-0
17	2	SOMNOLENCE	MILD	N	NONE		UNRELATED	RECOVERED	N	2007-06-15T06:00	2007-0
18	3	BITE BY AN INSECT	MILD	N	NONE		UNRELATED	RECOVERED	N	2007-06-15T23:20	2007-0
19	1	HOT FLUSH	MILD	N	NONE		POSSIBLE	RECOVERED	N	2007-06-20T05:25	2007-0
20	2	SOMNOLENCE	MODERATE	N	NONE		UNRELATED	RECOVERED	N	2007-06-20T09:00	2007-0
21	1	NAUSEA	MILD	N	NONE		POSSIBLE	RECOVERED	N	2007-06-21T07:00	2007-0
22	1	SOMNOLENCE	MODERATE	N	NONE		UNRELATED	RECOVERED	N	2007-06-21T04:00	2007-0
23	1	MALAISE AFTER BLOOD SAMPLING	MODERATE	N	NONE		UNRELATED	RECOVERED	N	2007-06-26T01:50	2007-0
24	1	VOMITS	MODERATE	N	NONE		PROBABLE	RECOVERED	N	2007-06-26T00:45	2007-0
25	2	VOMITS	MILD	N	NONE		PROBABLE	RECOVERED	N	2007-06-26T02:20	2007-0
26	3	NAUSEA	MODERATE	N	NONE		PROBABLE	RECOVERED	N	2007-06-26T08:00	2007-0
27	1	SOMNOLENCE	MODERATE	N	NONE		UNRELATED	RECOVERED	N	2007-06-27T05:00	2007-0
28	1	VOMITS	MODERATE	N	PRODUCT WITHDRAWN PERMANENTLY		POSSIBLE	RECOVERED	N	2007-06-28T22:15	2007-0
29	1	FRONTAL HEADACHES	MILD	N	NONE		UNRELATED	RECOVERED	N	2007-07-05T18:00	2007-0

CDISC Standards position - ADaM



ADaM - Analysis Dataset Model

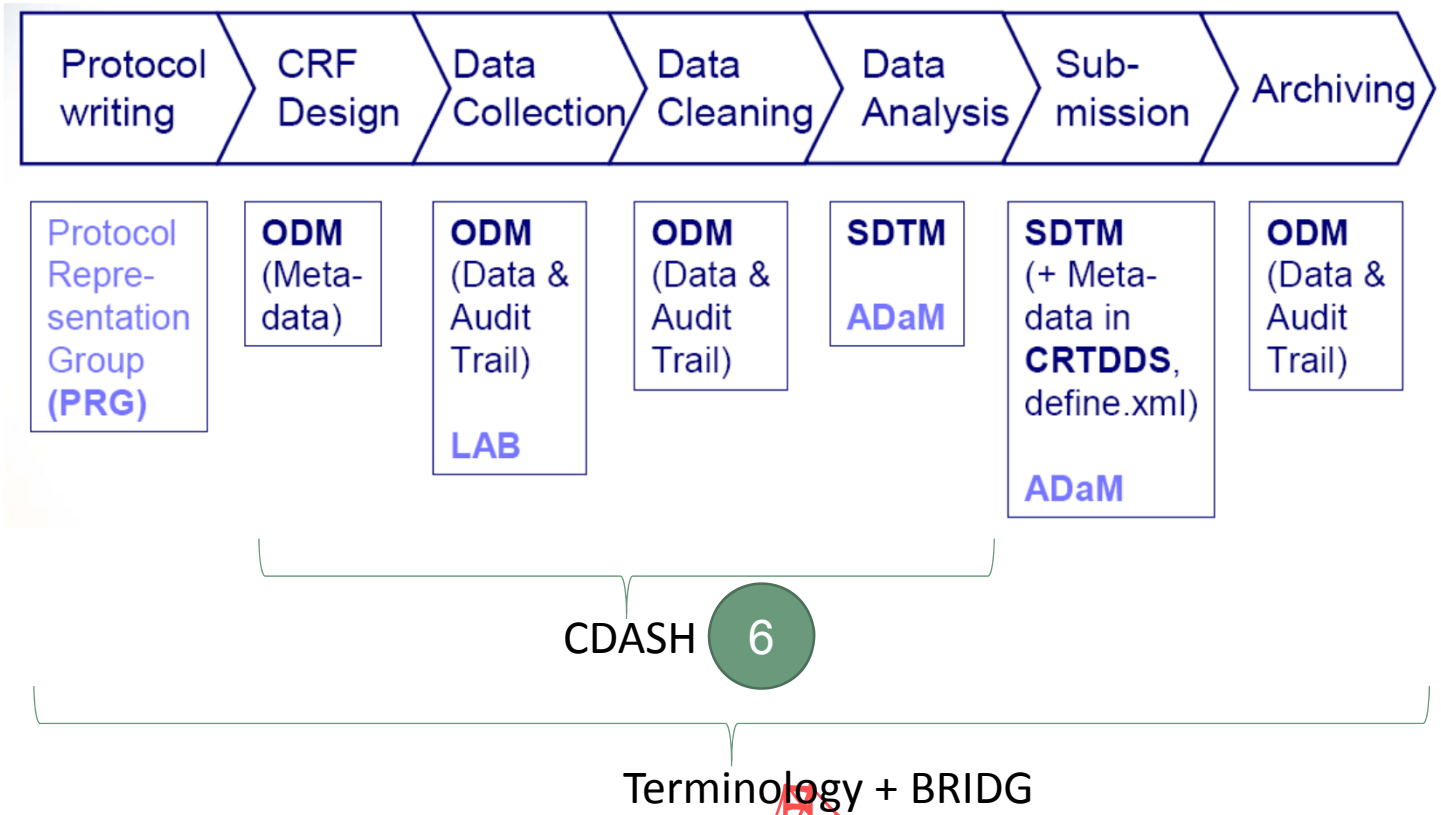
- Fournir des modèles de métadonnées et des exemples d'analyse de données utilisée pour produire les résultats statistiques d'une soumission réglementaire (Provide metadata models and examples of analysis datasets used to generate the statistical results for a regulatory submission)
- Analysis Data Model Version 2.0 (production)
- 3 niveaux d'analyse:
  - analysis dataset metadata,
  - analysis variable metadata,
  - and analysis results metadata

Juste une approche

ADaM

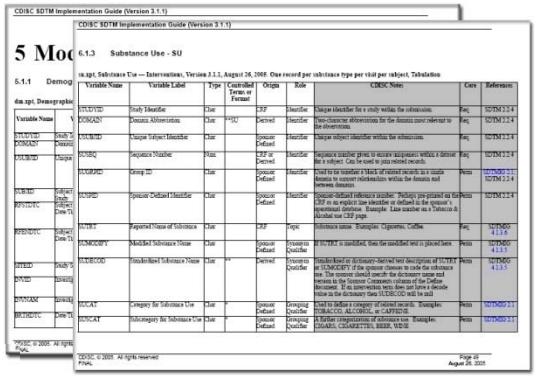
- Construction du modèle à partir de la version SDTM 3.1.1
- La présentation des résultats statistiques au format ADaM est en adéquation avec la structure du eCTD (electronic Common Technical Document)

CDISC Standards position - CDASH



CDASH
Clinical Data Aquisition Standard Harmonization

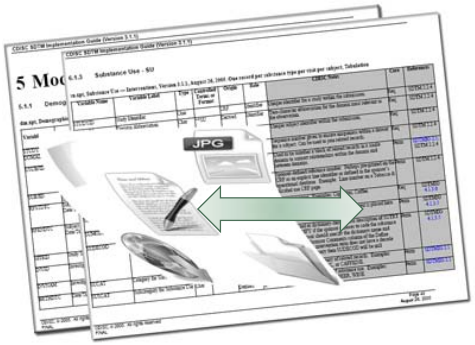
⑤
Mise au point des Packages CDASH



①
SDTM

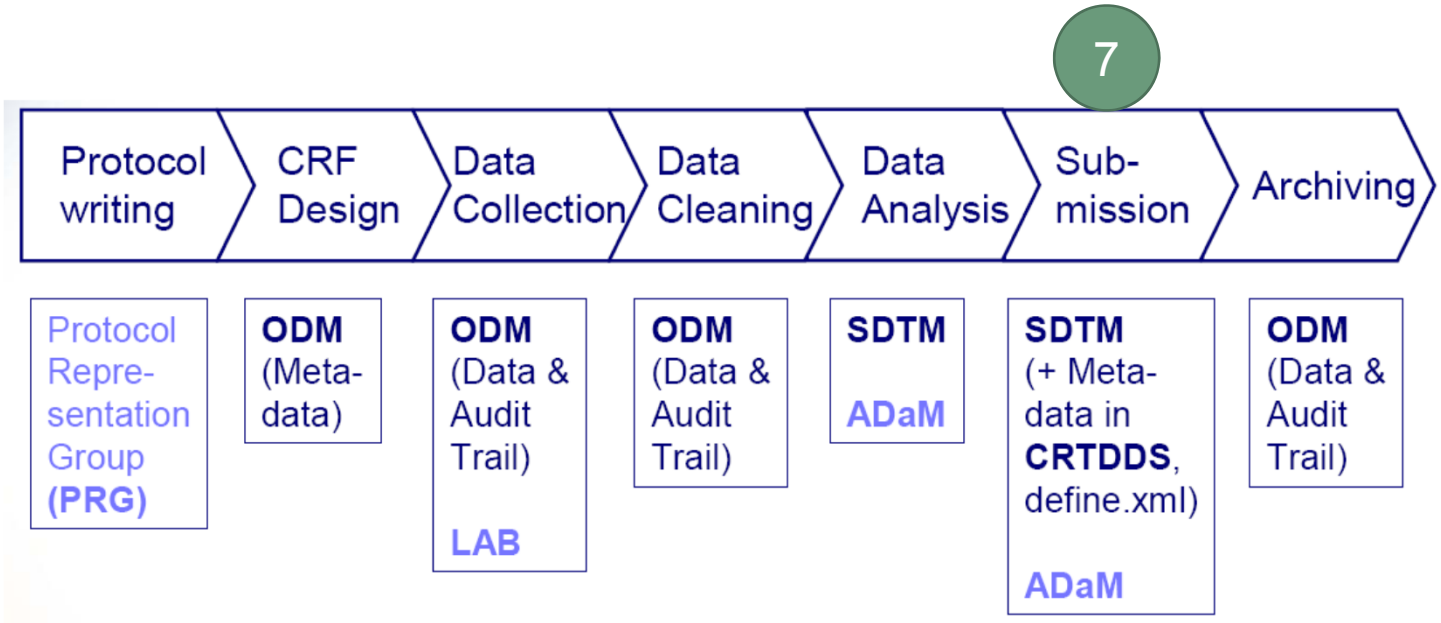
②
CRF samples

③
Analyse du contenu
≠
présentation



④
Evaluation des similitudes / différences

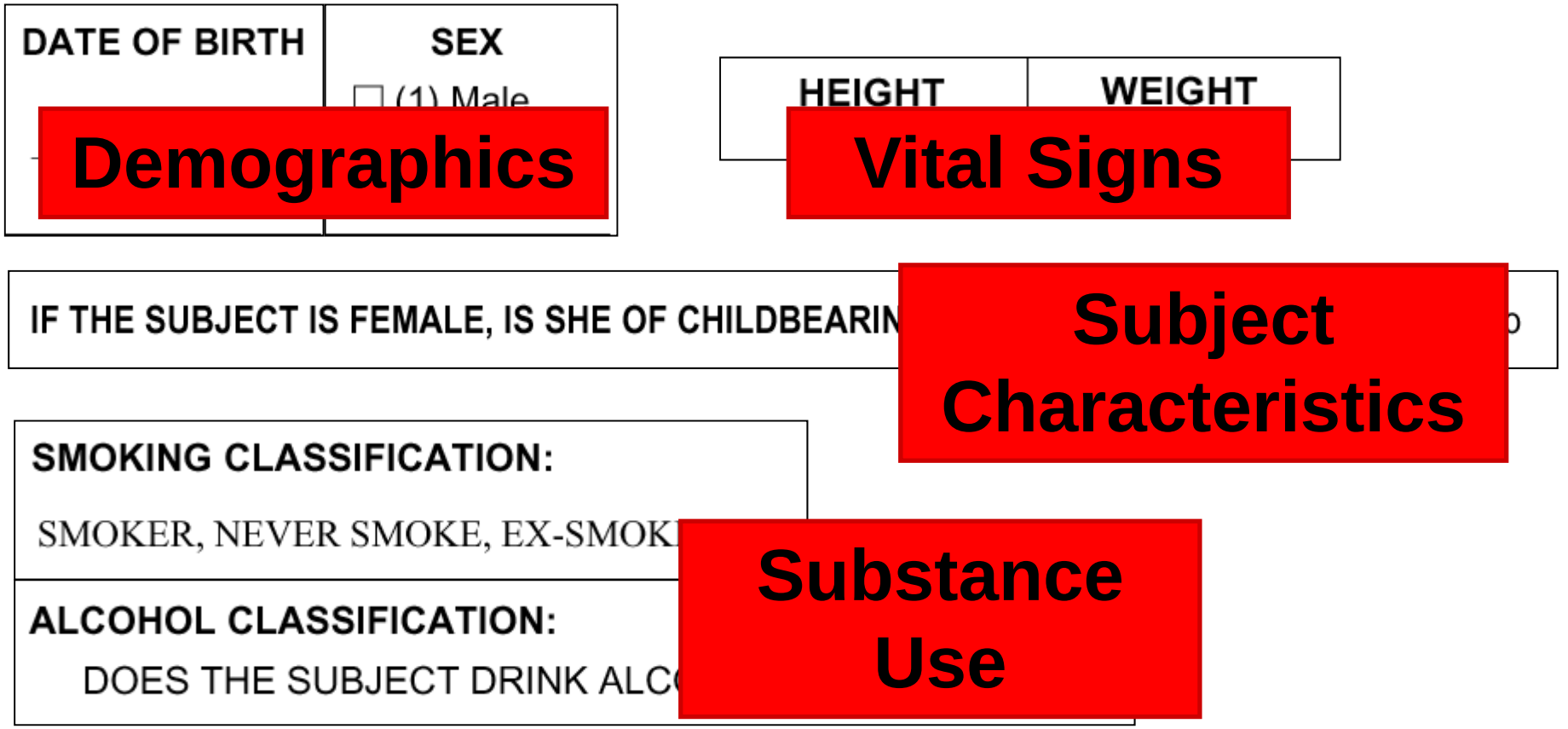
CDISC Standards position - CRTDDS



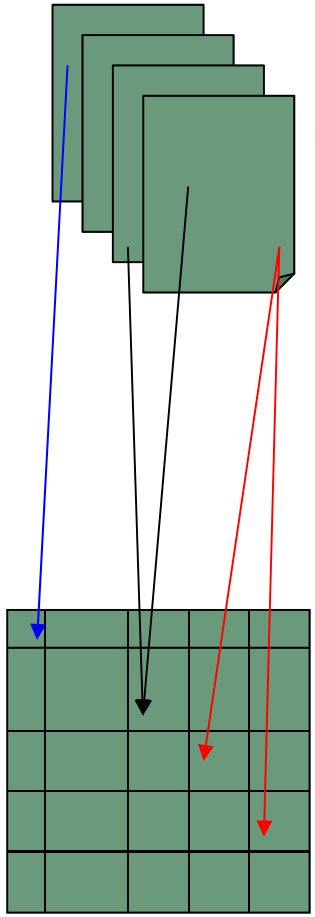
CRTDDS - Case Report Tabulation Data Definition Specification

ODM	CRTDDS	SDTM
Screening Demography Date of birth	Dérivation →	DM (Demographics) AGE
Sex (M/F)	Direct →	SEX

Transformation ODM vers SDTM via CRTDDS



Transformation ODM vers SDTM via CRTDDS



Cahier d'observation

1:1

ODM = CRF avec métadata + clinical data

- StudyEvents, Forms, ItemGroups, Items

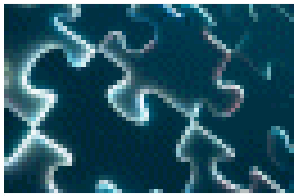
N:M => CRTDDS

Domain SDTM

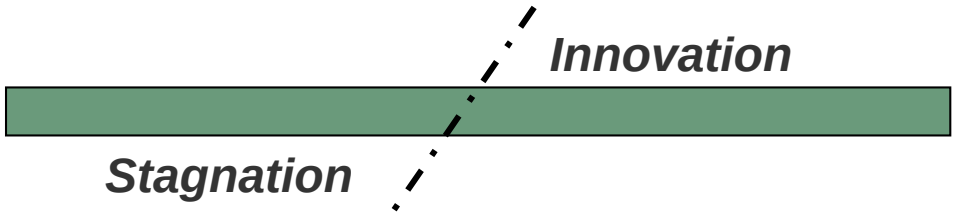
SDTM = Case Report Tabulations

- « ItemGroups », Items

CDASH
Clinical Data Acquisition Standards Harmonization



FDA's Critical Path Initiative



A serious attempt to bring attention and focus to the need for targeted scientific efforts to modernize the techniques and methods used to evaluate the safety, efficacy and quality of medical products as they move from product selection and design to mass manufacture.

J. Woodcock, FDA

Challenge and Opportunity on the Critical Path to New Medical Products
FDA, March 2004

FDA Critical Path Opportunities and CDISC

#44. Development of Data Standards.

"Currently, clinical investigators, clinical study personnel, data managers, and FDA reviewers must cope with a plethora of data formats and conventions. Some clinical investigators report the presence of many different computer systems for data entry at their sites (for various trials), each of which uses different data conventions. Lack of standardization is not only inefficient, it multiplies the potential for error…."

CDISC and HL7 are noted in the Opportunity List as currently working on this Opportunity.

#45. Consensus on Standards for Case Report Forms

"*Clinical trial data collection, analysis, and submission can be inefficient and unnecessarily expensive. A wide array of different forms and formats are used to collect clinical trial information, and most data are submitted to the FDA on paper. Differences in case report forms across sponsors and trials creates opportunities for confusion and error."*

ACRO initiated, but CDISC Requested to lead this Opportunity.

CDASH Initiative

CDASH = Clinical Data Acquisition Standards Harmonization

Project Charter

- To develop a set of 'content standards' (element name, definition, metadata) for a basic set of global industry-wide data collection fields that will support clinical research. The initial scope will be the 'safety data/domains'.
- These safety domains cut across all therapeutic areas, beginning with approximately 12-14 domains.
- Follow CDISC Operating Procedure (COP) for Standards Development.

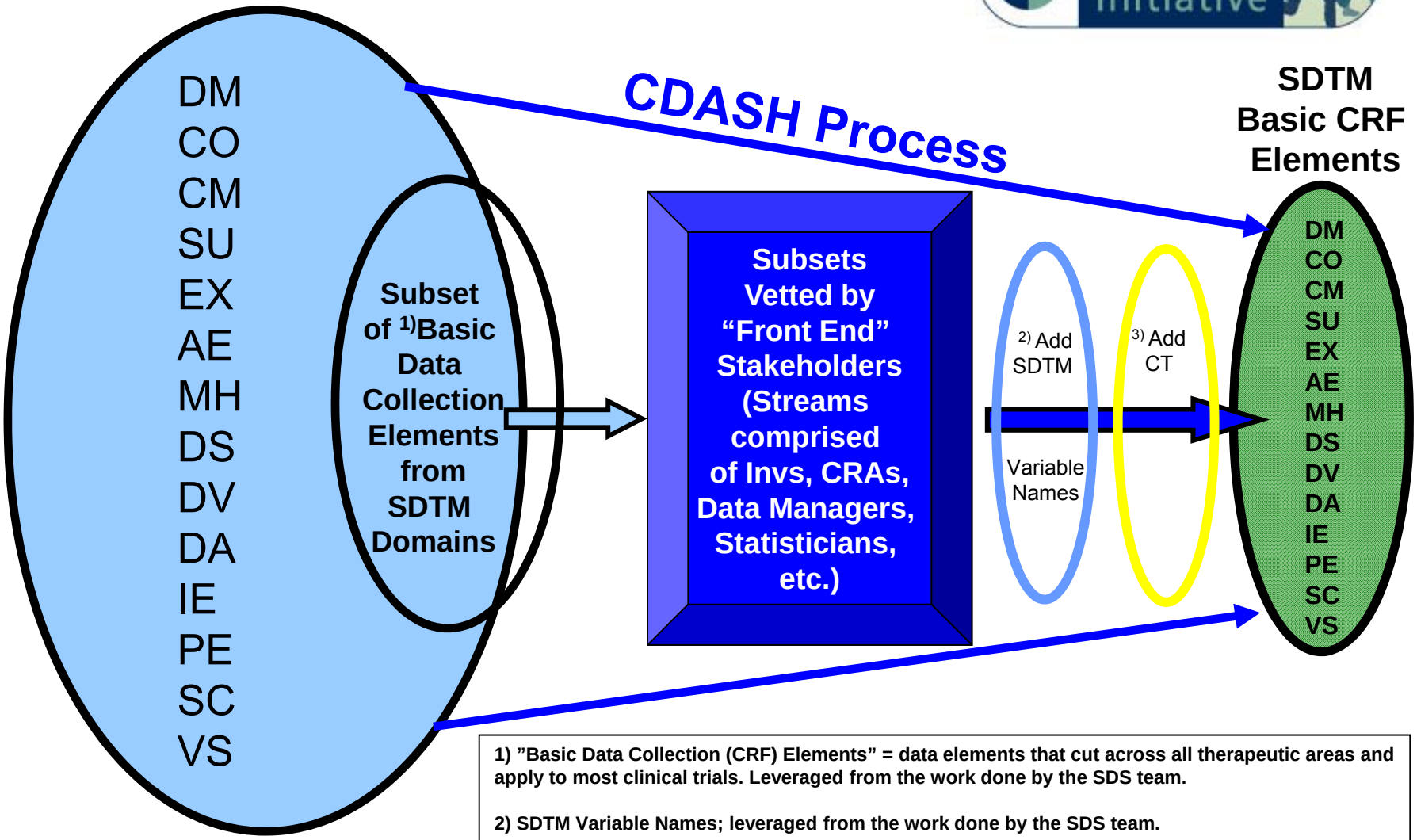
CDASH Project Update

Collaborative Group = Provides expertise and strategic input into the CDASH Initiative

Collaborative Group Members

- American Medical Informatics Association (AMIA)
- Association of Clinical Research Organizations (ACRO)
- Association of Clinical Research Professionals (ACRP)
- Baylor College of Medicine
- Biotechnology Industry Organization (BIO)
- Clinical Data Interchange Standards Consortium (CDISC)
- Clinical Research Forum
- Critical Path Institute (C-Path)
- Duke Clinical Research Institute (DCRI)
- Food and Drug Administration (FDA)
- National Institutes of Health (NIH) – Office of Policy, NCI, NCRR, NICHD
- Pharmaceutical Research and Manufacturers Association (PhRMA)
- Society for Clinical Data Management (SCDM).

Relationship of CDASH and SDTM



1) "Basic Data Collection (CRF) Elements" = data elements that cut across all therapeutic areas and apply to most clinical trials. Leveraged from the work done by the SDS team.

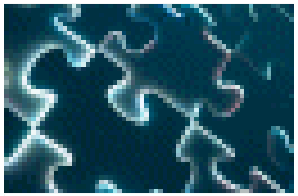
2) SDTM Variable Names; leveraged from the work done by the SDS team.

3) CT = Controlled Terminology; leveraged from the work done by the Terminology Team.

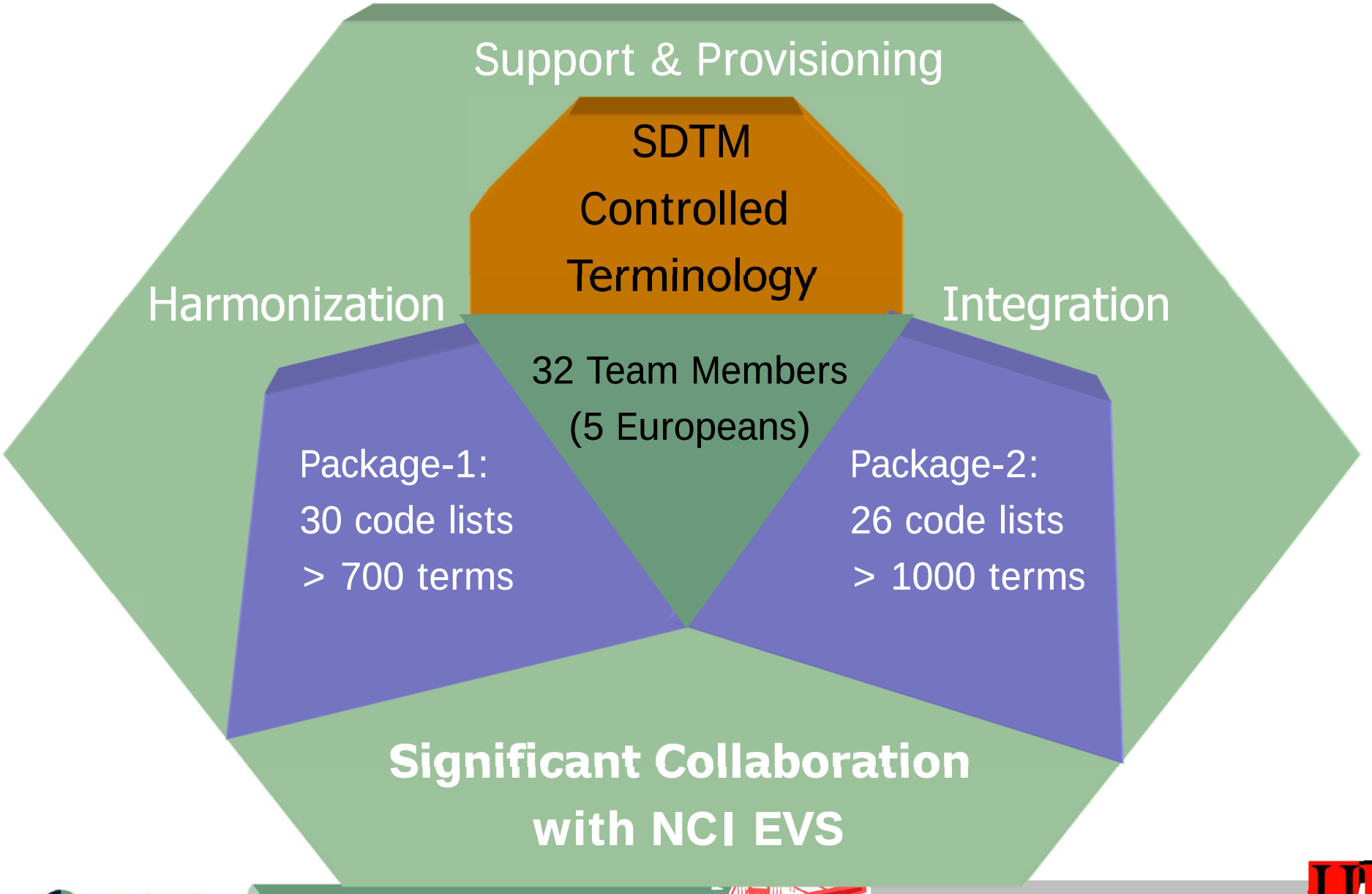
CDASH Project Update

	Initial Consensus Version	TLC Review	Harmonized Version	Collaborative Group Review	Reviewed Version	Public Review	Released Version 1.0
Adverse Events	Dec. 2006	March 2007	May 2007	June-July 2007	Oct 2007	Q108	Q2 2008
Prior & Concomitant Medication	Jan 2007	April 2007	May 2007	June –July 2007	Oct 2007	Q108	Q2 2008
Demographics & Subject Characteristics	Jan. 2007	April 2007	May 2007	June –July 2007	Oct 2007	Q108	Q2 2008
Inclusion/Exclusion Criteria	February 2007	May 2007	August 2007	Sept 2007	Oct 2007	Q108	Q2 2008
Medical History and Substance Use	February 2007	May 2007	August 2007	Sept 2007	Oct 2007	Q108	Q2 2008
Physical Exam & Vital Signs	February 2007	May 2007	August 2007	Sept 2007	Oct 2007	Q108	Q2 2008
End of Study/ Disposition	June 2007	Aug 2007	Sept 2007	Oct 2007	Nov 2007	Q108	Q2 2008
Drug Accountability/ Exposure	June 2007	Aug 2007	Sept 2007	Oct 2007	Nov 2007	Q108	Q2 2008
Protocol Deviations/ Comments	June 2007	Aug 2007	Sept 2007	Oct 2007	Nov 2007	Q108	Q2 2008
Lab & ECG	Sept 2007	Oct. 2007	October 2007	Nov.- Dec. 2007	Jan 2008	Q108	Q2 2008

Terminology



CDISC Terminology Overview



CDISC

Source: Andreas Gromen

HL7

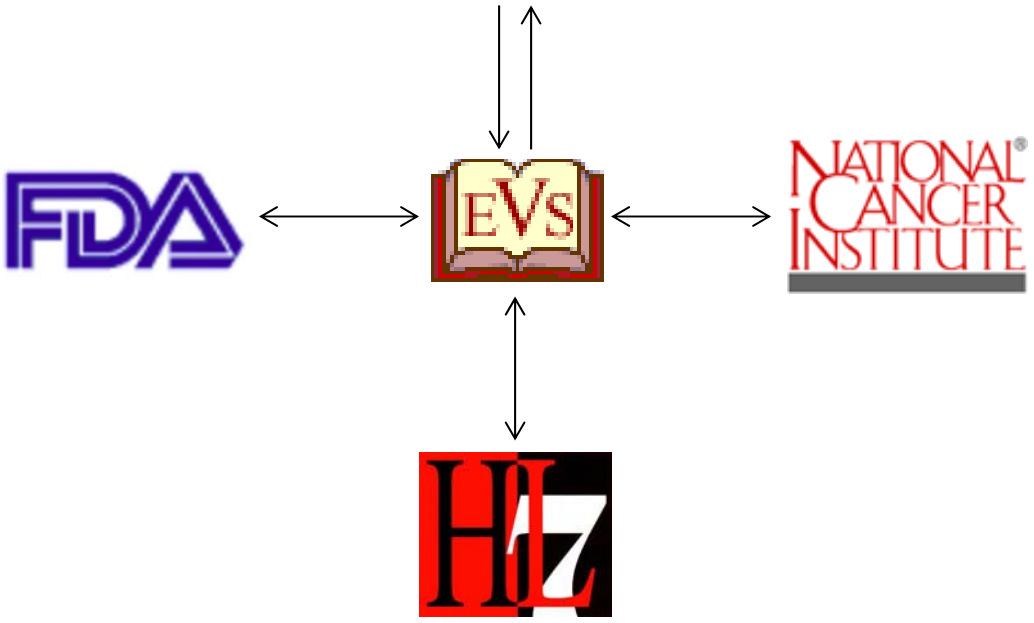
Terminology Collaboration - Harmonization

Terminology Tutorials

Please see:

Bron Kisler (CDISC)

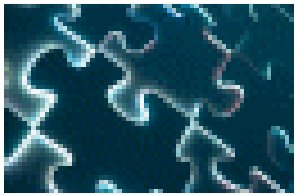
Margaret Haber (NCI)



EVS = NCI Enterprise Vocabulary Services

Source: Andreas Gromen

The BRIDG Model



What is BRIDG?

Biomedical **R**esearch **I**ntegrated **D**omain **G**roup

- A formal model
- A communication bridge
- An open community of stakeholders
- The semantic foundation for application and message development

So how did BRIDG get started?

- Three important streams of development came together
  - **CDISC**: In early 2004, CDISC started constructing a Domain Analysis Model to support harmonization of their standards for clinical research as well as with the Health Level Seven (HL7) healthcare standard.
  - **NCI**: In late 2004, NCI's Cancer Biomedical Informatics Grid (caBIG™) initiative joined the CDISC BRIDG efforts to construct a structured protocol representation for its Clinical Trials Management Systems (CTMS) Workspace, in order to further interoperability among clinical trials research in cancer.
  - **HL7**: In 2005, the BRIDG model was adopted by the HL7 Regulated Clinical Research Information Management (RCRIM) Technical Committee as the RCRIM Domain Analysis Model.

NCI's caBIG Project and BRIDG

- BRIDG used for Application Development
- CTMSi Project: Proof of Concept
- BRIDG is fundamental part of the CTMS WS software development process

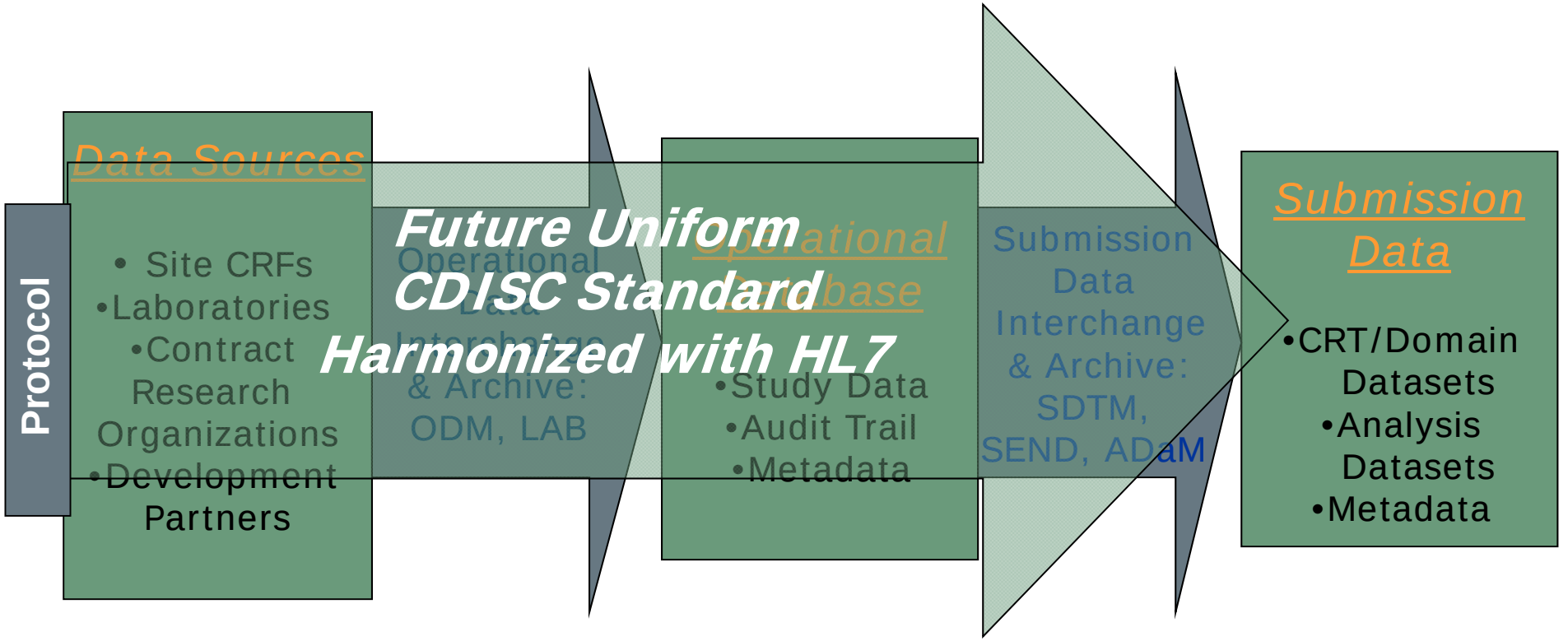
CDISC Mission

The mission of CDISC is to develop and support global, platform-independent data standards that

enable information system interoperability

to improve medical research and related areas of healthcare.

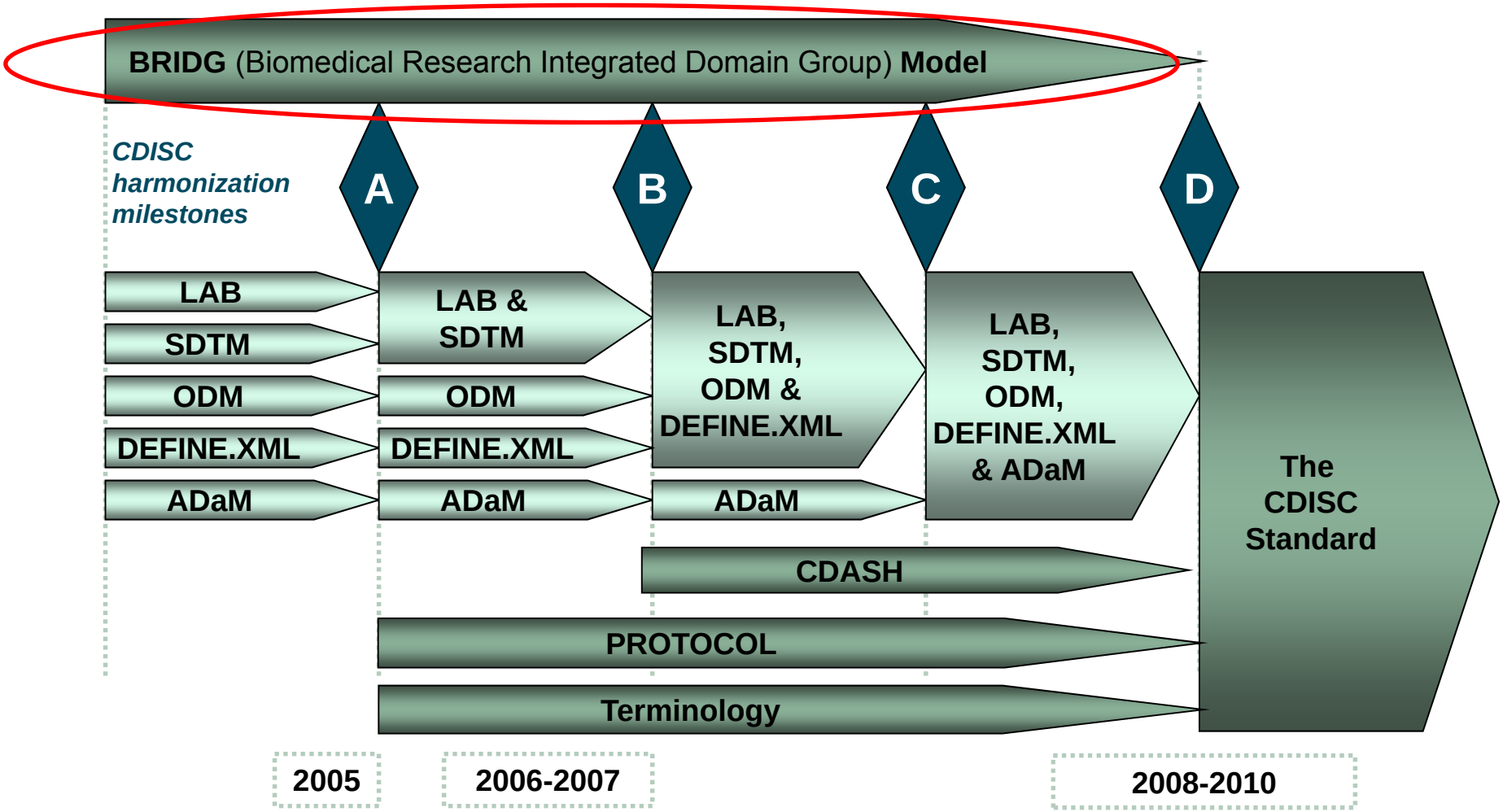
Future of CDISC Models



ODM = Operational Data Model
LAB = Laboratory Data Model
SDS = Submission Domain Standards
ADaM = Analysis Dataset Models
SEND = Std. Exchg. Non-clinical Data

Standard Protocol Representation and Terminology

CDISC Technical Roadmap



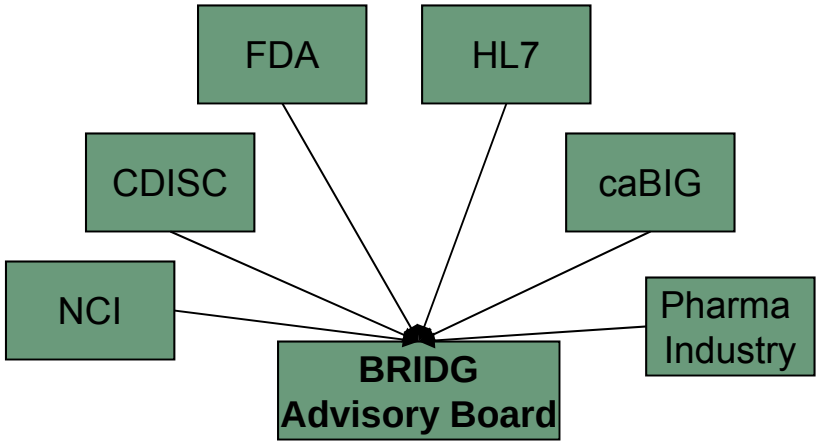
BRIDG Scope

Protocol-driven research and its associated regulatory artifacts,

i.e. the data, organization, resources, rules, and processes involved in the formal assessment of the utility, impact, or other pharmacological, physiological, or psychological effects of a drug, procedure, process, or device on a human, animal, or other biologic subject or substance plus all associated regulatory artifacts required for or derived from this effort.

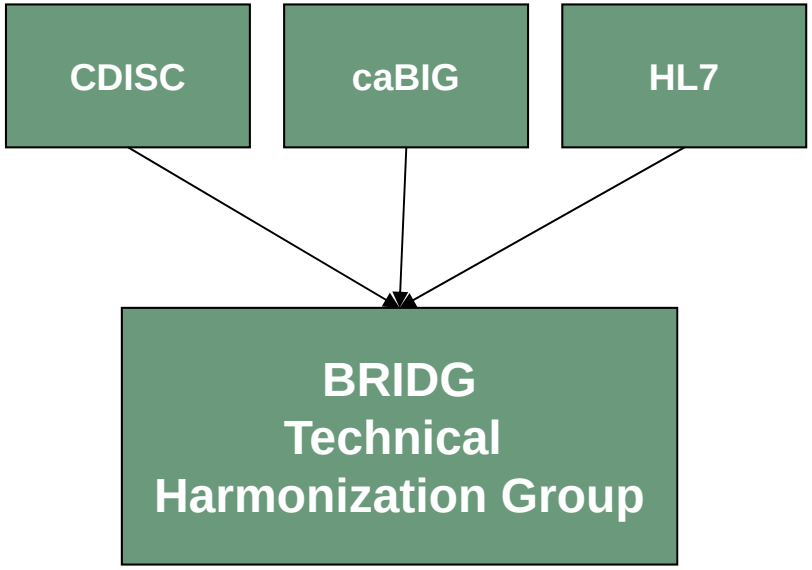
BRIDG Organization

Current Organization of the BRIDG project – BRIDG Advisory Board



- **BRIDG Advisory Board**
  - Representation from the current stakeholders
  - Helps to allocate priorities and identify resources
  - Assists with vetting the model in the various constituents

Current Organization of the BRIDG Project – Technical Harmonization Committee



- **Technical Harmonization Committee**
  - Responsible for ongoing model maintenance
  - Harmonizes subdomain projects into the main model

Current Organization of the BRIDG Project – Multiple Projects Being Developed

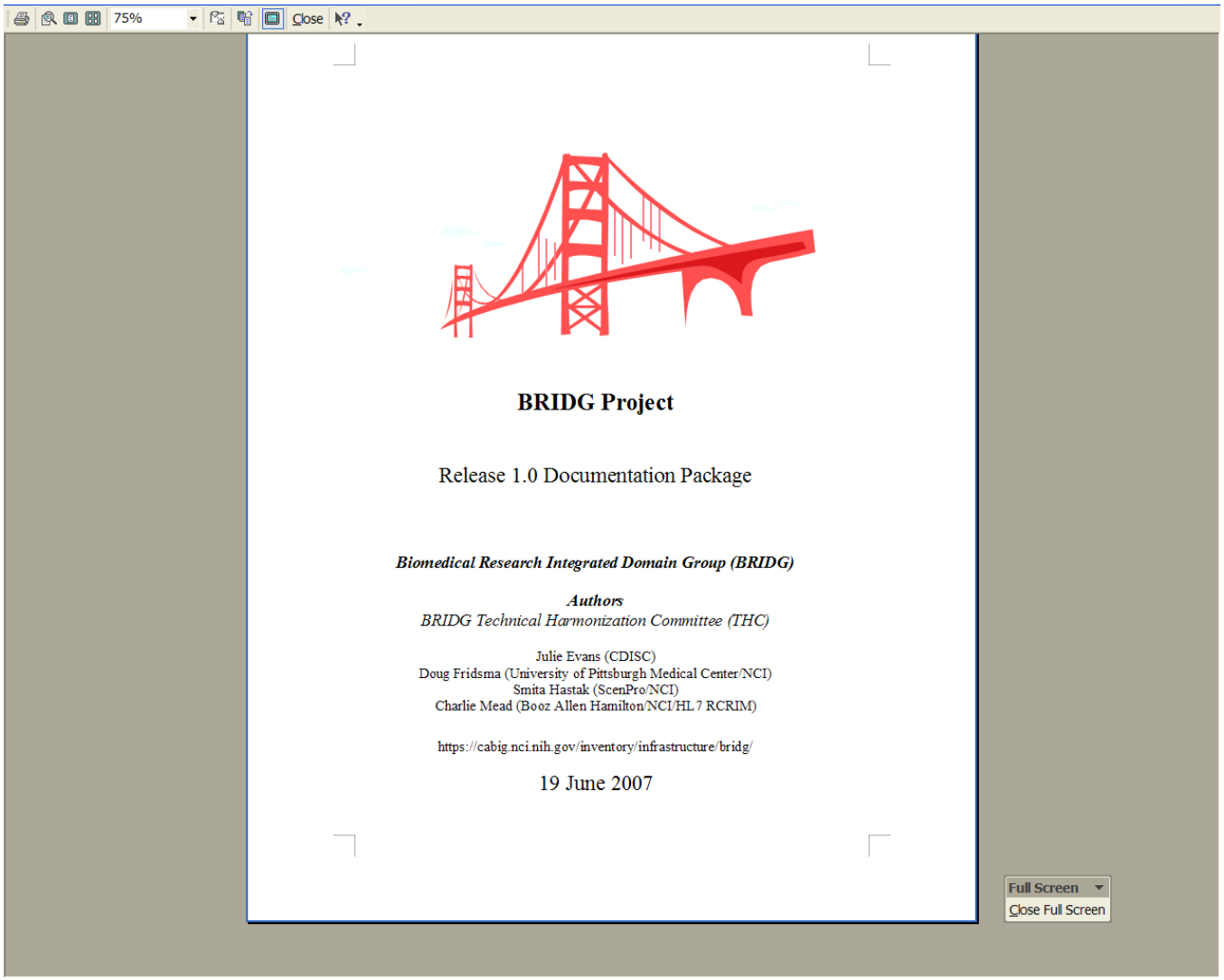
- **CDISC:** Trial Design, Clinical Trial Registry, SAP
- **NCI:** C3PR, caAERS
- **HL7 RCRIM:** Structured Product Label, Regulated Product Submission, eDCI

The BRIDG Model

Release 1 Important Components

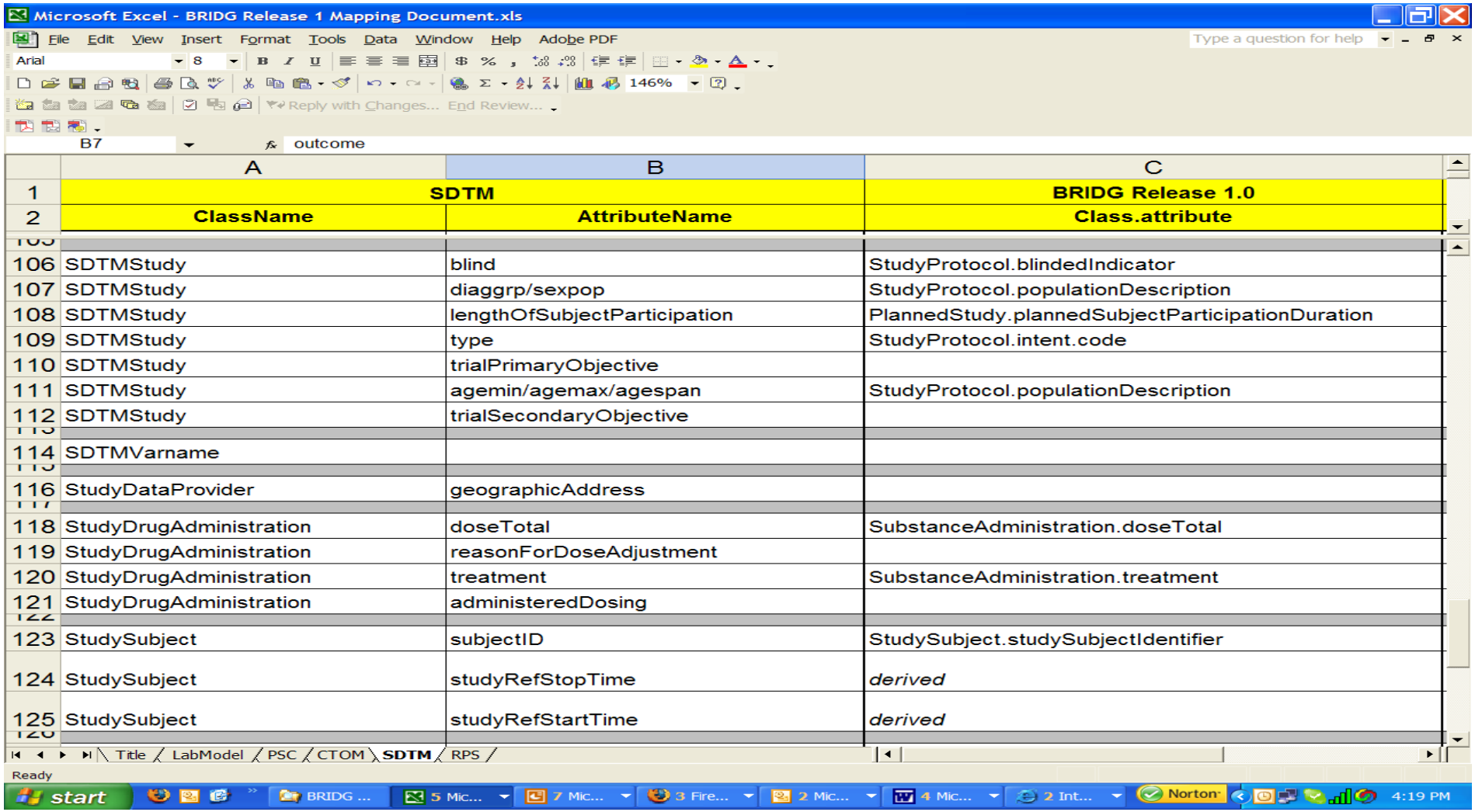
- Project Documentation and Release Notes
- Mapping Spreadsheet
- Model
  - Backbone
  - Views

Project Documentation & Release Notes



https://cabig.nci.nih.gov/inventory/infrastructure/bridg/

Release 1.0 Mapping Spreadsheet



Microsoft Excel - BRIDG Release 1 Mapping Document.xls

File Edit View Insert Format Tools Data Window Help Adobe PDF

Type a question for help

Arial 8 146%

Reply with Changes... End Review...

B7 outcome

	A	B	C
1	SDTM		BRIDG Release 1.0
2	ClassName	AttributeName	Class.attribute
106	SDTMStudy	blind	StudyProtocol.blindedIndicator
107	SDTMStudy	diaggrp/sexpop	StudyProtocol.populationDescription
108	SDTMStudy	lengthOfSubjectParticipation	PlannedStudy.plannedSubjectParticipationDuration
109	SDTMStudy	type	StudyProtocol.intent.code
110	SDTMStudy	trialPrimaryObjective	
111	SDTMStudy	agemin/agemax/agespan	StudyProtocol.populationDescription
112	SDTMStudy	trialSecondaryObjective	
114	SDTMVarname		
116	StudyDataProvider	geographicAddress	
118	StudyDrugAdministration	doseTotal	SubstanceAdministration.doseTotal
119	StudyDrugAdministration	reasonForDoseAdjustment	
120	StudyDrugAdministration	treatment	SubstanceAdministration.treatment
121	StudyDrugAdministration	administeredDosing	
123	StudySubject	subjectID	StudySubject.studySubjectIdentifier
124	StudySubject	studyRefStopTime	*derived*
125	StudySubject	studyRefStartTime	*derived*

Title / LabModel / PSC / CTOM / SDTM / RPS

Ready

start BRIDG ... 5 Mic... 7 Mic... 3 Fire... 2 Mic... 4 Mic... 2 Int... Norton 4:19 PM

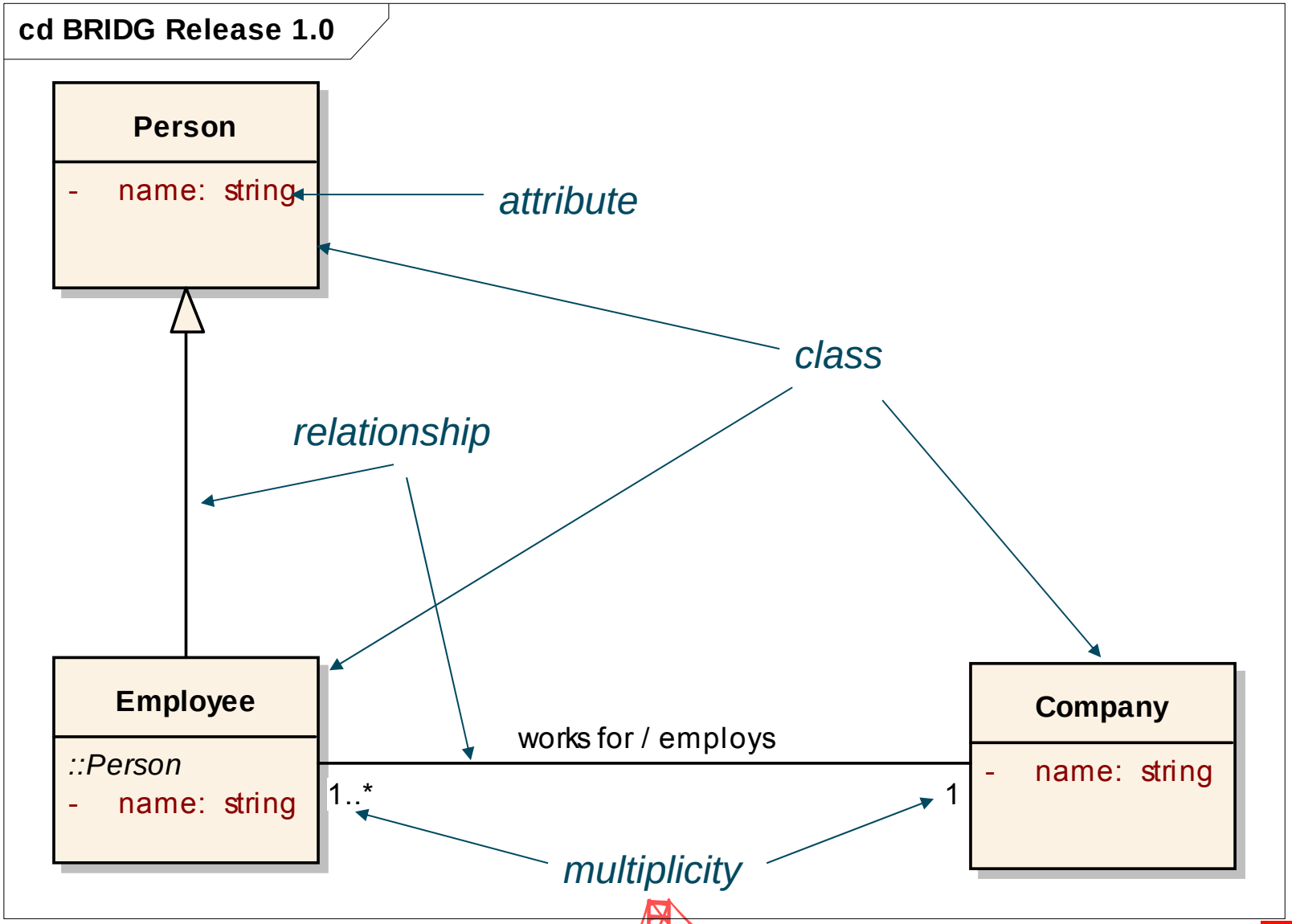
Unified Modeling Language

- Used in the BRIDG model
- The industry-standard language for specifying, visualizing, constructing, and documenting the requirements of software systems
- The BRIDG model uses these UML diagrams:
  - Class diagrams
  - Activity diagrams
  - Instance diagrams

UML Class Diagrams

- **class** – a concept of primary importance the domain-of-interest, depicted as a rectangle labeled with the concept's name
- **attribute** (including datatype specification) – a descriptive feature of a class, depicted as being contained within the class
- **relationship** – one of several types of "lines" between classes

Class diagram example



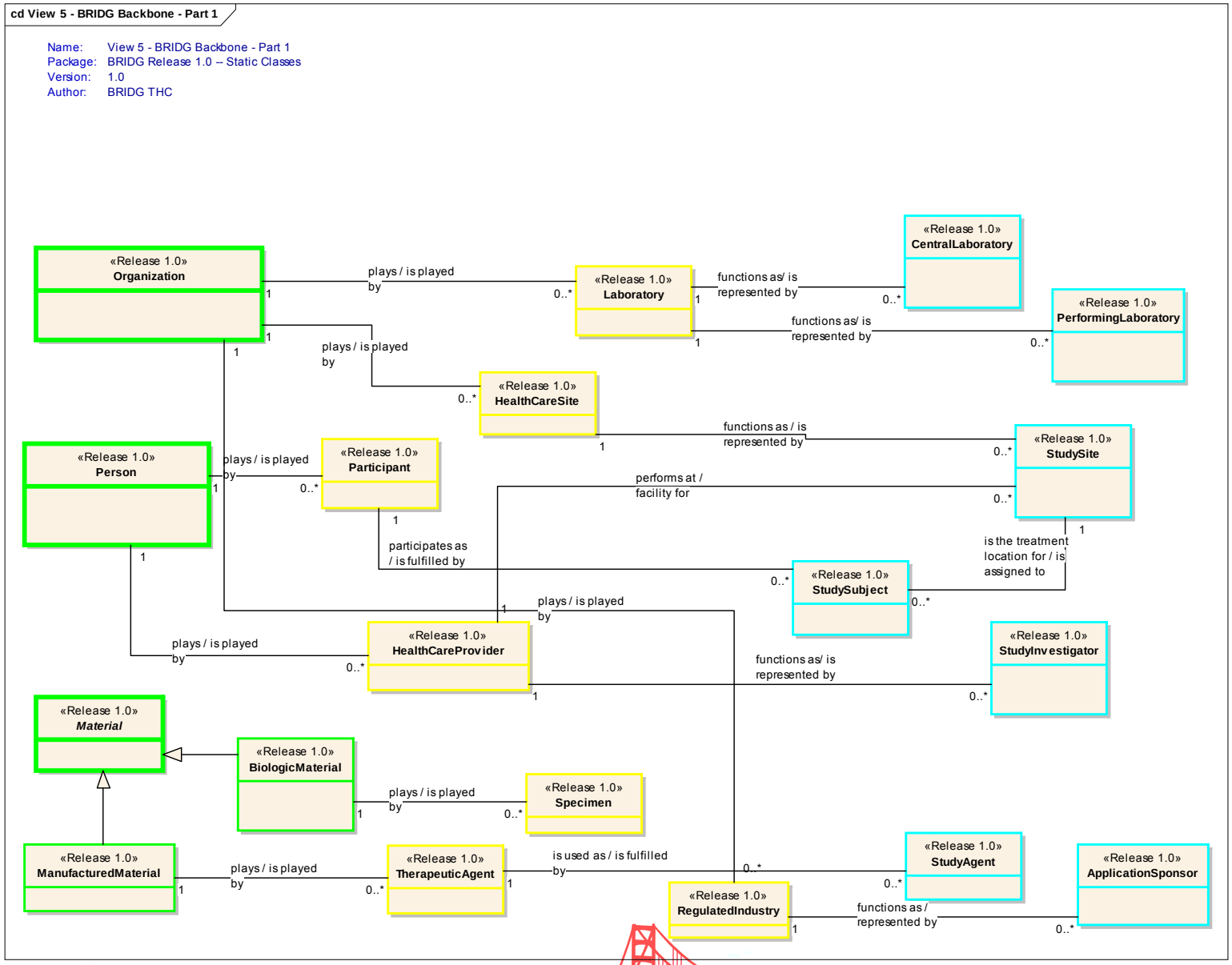
R1 Important Content Concepts

- Planned, Scheduled, Performed Study
- ObservationResult vs. Assessment
- Analysis and Reporting

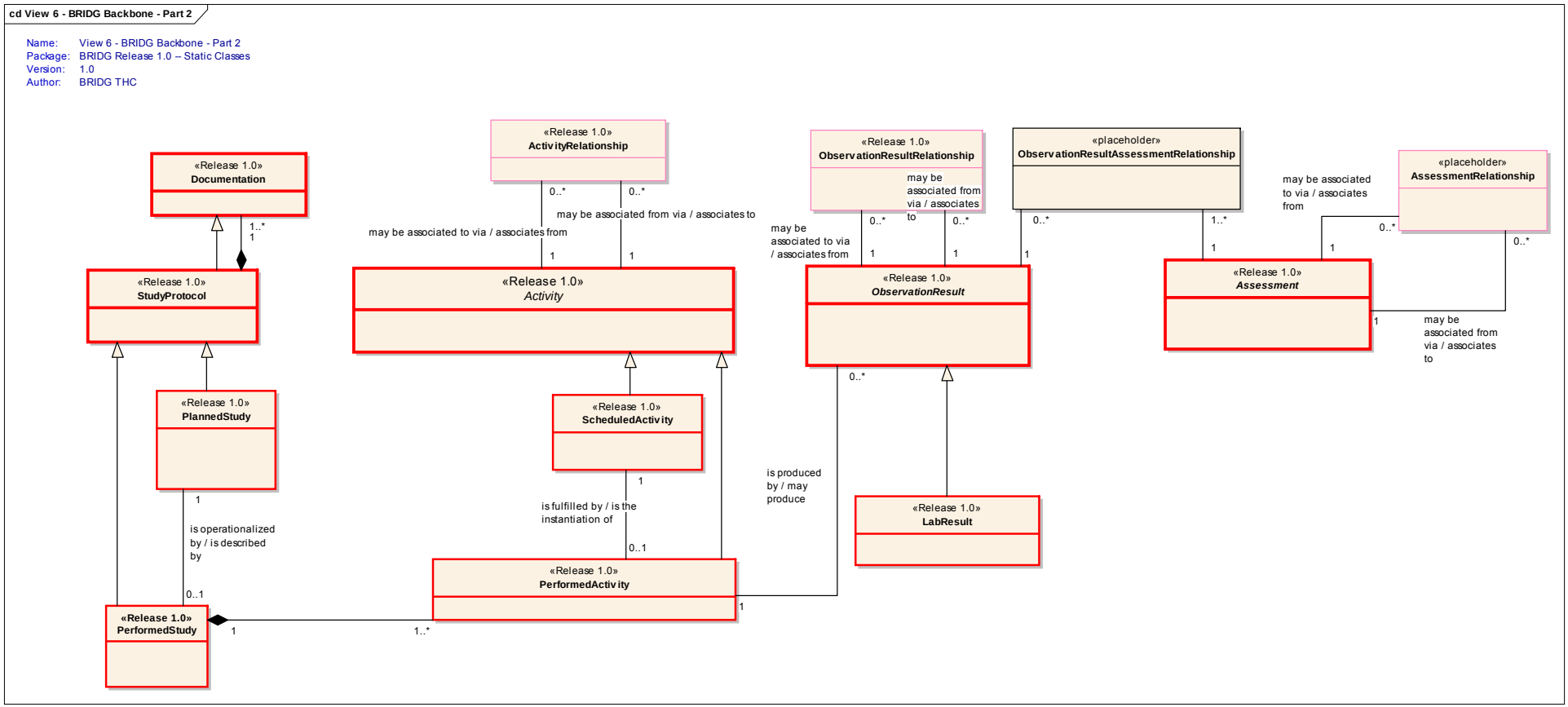
The BRIDG Backbone Classes

- Person
- Organization
- Material
- StudyProtocol
- Documentation
- Activity
- ActivityRelationship
- ObservationResult
- ObservationResultRelationship
- Assessment

The BRIDG Backbone – Part 1



The BRIDG Backbone – Part 2



The Pillars of Interoperability

Necessary but not necessarily sufficient

- Common model across all domains of interest
- Foundation of rigorously defined data types
- Methodology for interfacing with controlled vocabularies
- Formal process and tools for defining interchange structures

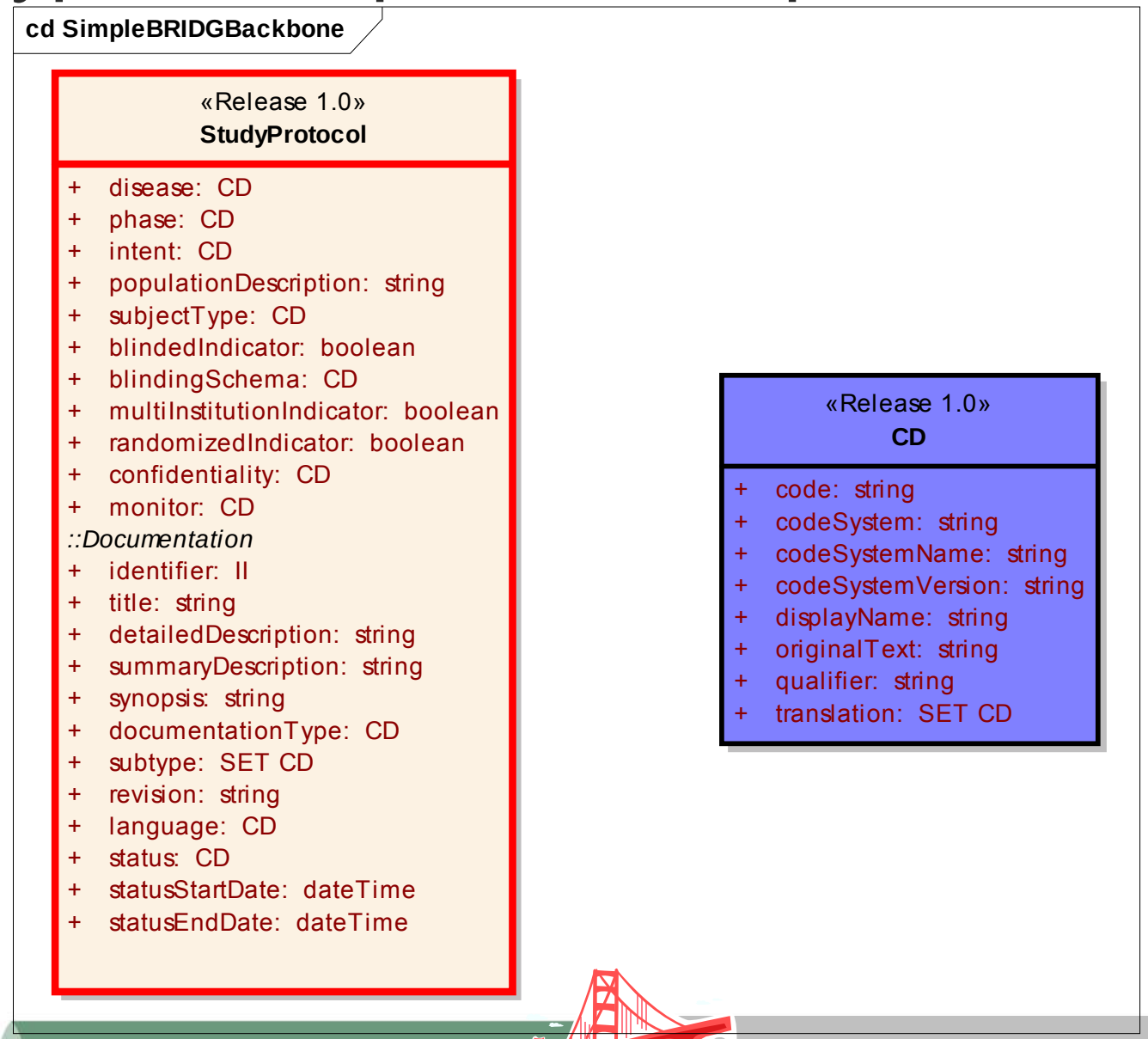
Source: Charlie Mead, MD, HL7

Foundation of rigorously defined data types

- Simple vs Complex
- Simple: Character, String, Text, Numeric

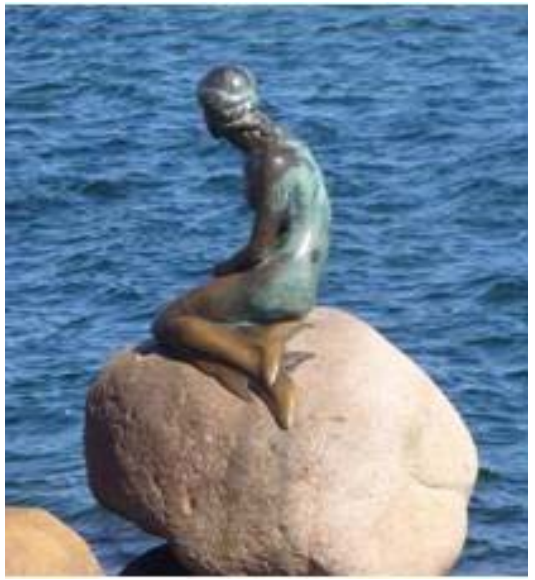
- Plans to use HL7 Datatype specification

Datatypes: Simple vs Complex



5th CDISC European Interchange

Location

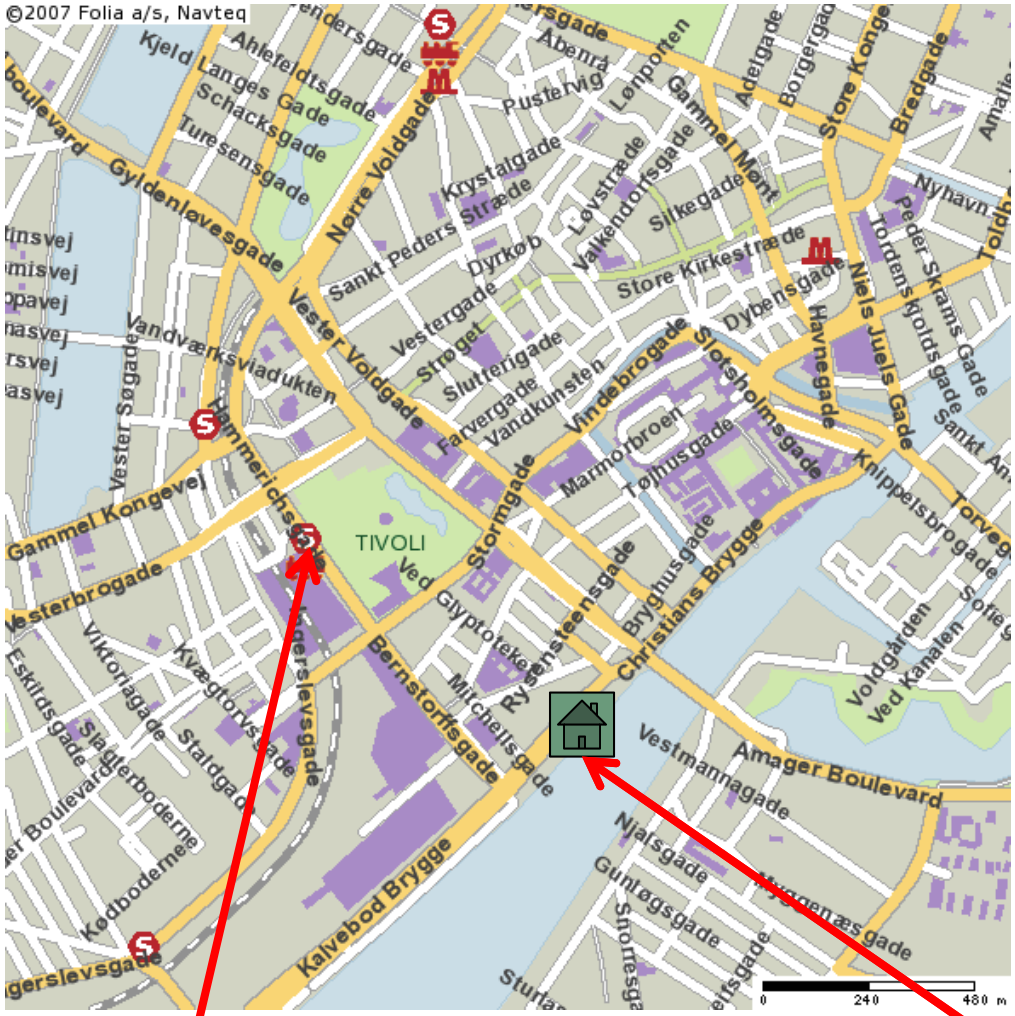


Copenhagen Marriott Hotel

Programme

Monday & Tuesday (21st & 22nd April)	**Workshops & Training**
Wednesday & Thursday (23rd & 24th April)	**Main Conference**
Friday (25th April)	**Workshops & Training**

Travel



Station

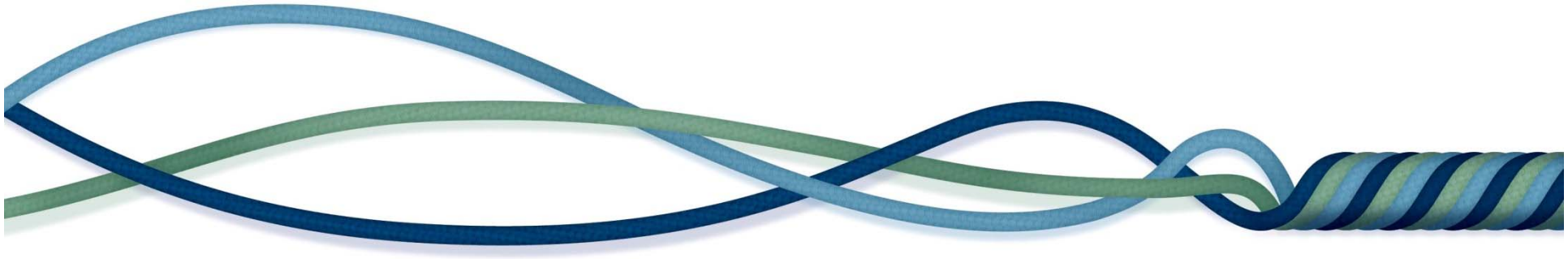
Marriott Hotel

Direct rail link from Copenhagen Airport to the city (15 minutes). Hotel 10 minute walk or 3 minute taxi ride from the station.

Dates

To register or for further information

www.cdisc.org



Strength *through collaboration.*