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SDTM Metadata Repositories, Governance, Versioning

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CDISC UG Meeting (@Bayer) Leverkusen

26. Februar 2013

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Agenda

1. Merck Serono SDTM Team
2. Current: (SDTM) Metadata Libraries
3. Current: Standard Maintenance/Governance
4. Current: (SDTM) Standard Versioning
5. Future scope : (SDTM) Metadata Libraries
6. Future scope : Standard Maintenance/Governance
7. Future scope: (SDTM) Standard Versioning

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Merck Serono SDTM Team

SDTM Team constituted in Q3/2009

- Team Tasks while start (3 people, local):
  - review of SDTM annotated Case Report Forms
  - review of SDTM Mapping Specifications (Source data structure > SDTM submission data)
  - review of SDTM datasets (domains) and define.xml file
  - Set up of SDTM guidelines for Merck Global Clinical Data Management (GCDS)

- Team Tasks today (~17 people, global, 3 subgroups)
  - Maintenance of SDTM related standard libraries (aCRF, MS SDTM domains, VLM, CT)
  - Maintenance of SDTM Guidelines and related tools
  - Develop and apply new TA specific Guidelines and Model enhancements
  - Provide guidance on how to integrate SDTM @Merck, interface with internal Partners
  - Set up of training material and organisation of SDTM related Trainings
  - Mentorship of future SDTM experts within Merck Global Clinical Data Management (GCDS)

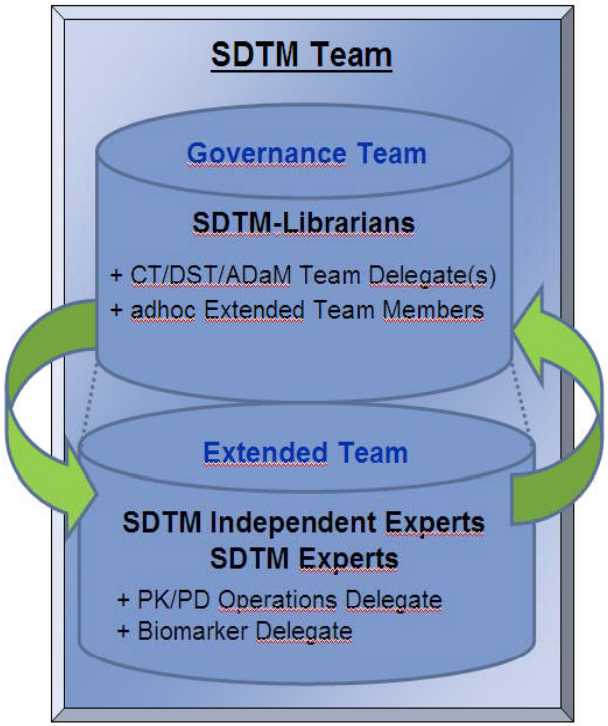
Merck Serono SDTM Team Today

The Merck Serono SDTM Team today has two functional Levels:

- Governance Team
- Extended Team

…and three different SDTM Team roles:

- SDTM Librarian
  - SDTM Librarians constitutes the SDTM Governance Team which manages development, use, maintenance and documentation of the Merck Serono SDTM Standards.
- SDTM Independent (Senior) Expert
  - Local Support and Contact within GCDS
  - Mentor for SDTM Experts
- SDTM Expert
  - Prospective SDTM Independent Expert



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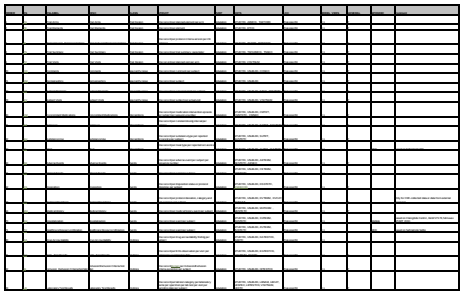
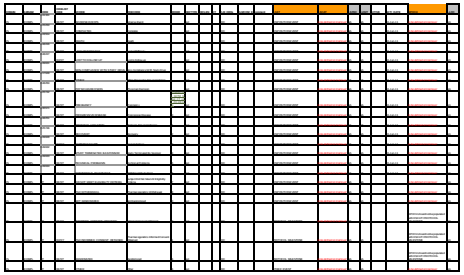
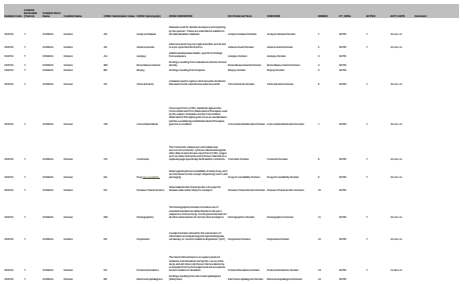
(SDTM) Metadata Libraries Today

Merck Serono specific implementation of SDTM-IG and SDTM Metadata defined in excel spreadsheets

- Merck Serono specific domain implementation
  - List of all domains used @Merck including sponsor defined extensions and domain specific metadata (labels, descriptions, key structures etc.)
  - Separate sheets with detailed domain level metadata specifications for all domains (one sheet / domain)
- Merck Serono SDTM Controlled Terminology
  - CDISC CT plus sponsor specific extensions and codes
  - Excluding all terminology which is defined as VLM
- Merck Serono Value Level Metadata (VLM) library
  - Facilitates define.xml creation and VLM nesting







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Working Instruction on Clinical Data Standards Management

- Effective since 31st July 2012
- The objective of the WI is to describe the management of the general and therapeutic area data standards, Study Data Tabulation Model (SDTM) and Analysis Data Model (ADaM) in relation to the creation, use, maintenance and documentation of the standards to ensure data consistency and to facilitate regulatory submissions
- The new governance requires if the current clinical data standards do not cover all the requirements for setting up any of the trial specifications (e.g. eCRF, SDTM, ADaM) or anything which does not comply with an existing standard a New, Change or Exemption Request Form is completed and approved prior to implementation.
- Associated Tools/Forms
  - Clinical Data Standards New, Change or Exemption Request Form
  - Clinical Data Standards Approval Form

Standard Governance Process

Standard Types
General and Therapeutic Area Data Standards Collection Modules (*)
EMD Serono/Merck Serono SDTM Standards (*)
EMD Serono/Merck Serono ADaM Standards (*)
Controlled Terminology (*)
Value Level Metadata (*)
GBS Output Standards
Standard algorithms
The official CDISC Standards
Standard validated programs and tools

(*) Subject to Clinical Data Standards Working Instruction

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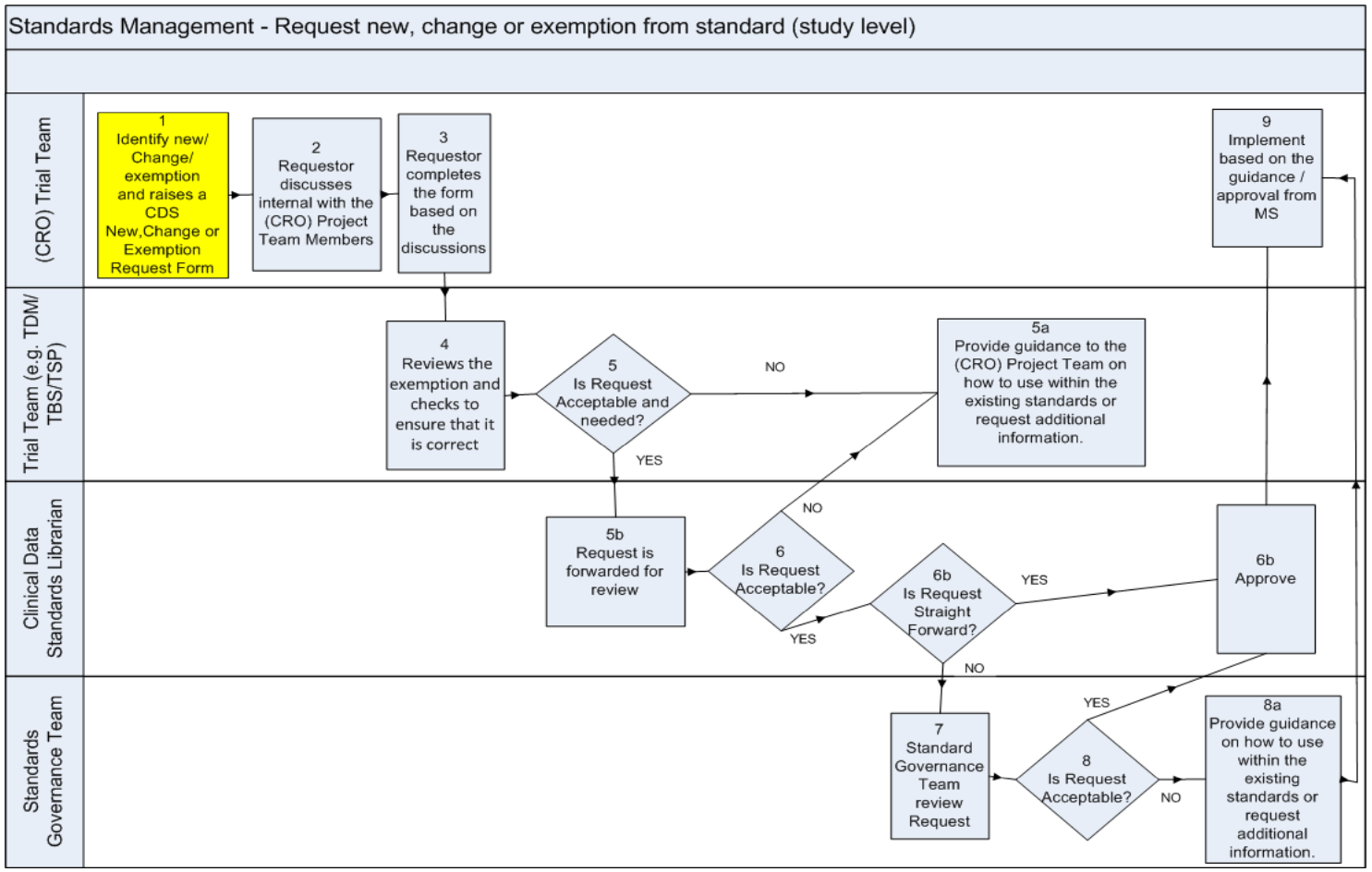
Standard Governance Teams

Governance Teams	Membership
General Data Standards (DS) Team	DS Team Lead General Data Standards Librarian(s) Controlled Terminology Librarian
Therapeutic Area Data Standards (TA DS) (One for each of the main Therapeutic Areas)	TA DS Team Lead Controlled Terminology Librarian(s)
Merck Serono (MS) SDTM Team	SDTM Team Lead SDTM Standard Librarian(s) Controlled Terminology Librarian(s) MS ADaM Team Representative
Merck Serono (MS) ADaM Team	MS ADaM Team Lead Statistical Standards Librarian(s) (ADaM) Statistical Programmer(s) Biostatistician(s)

Standard Governance Process



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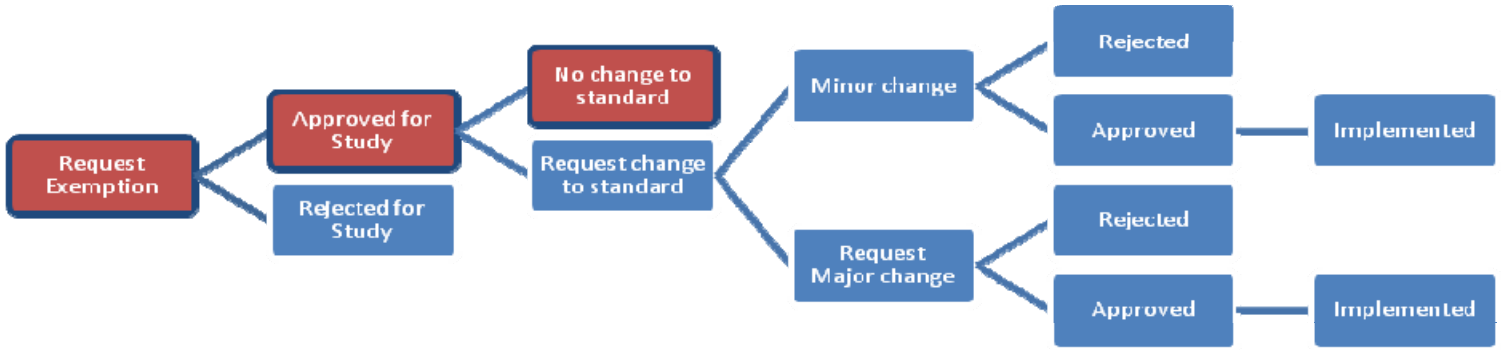
Versioning of Standards

- Manual versioning of updated Standard Specifications in excel spreadsheets based on major/minor classification:
  - A change will be considered major if the change has an (suspected) impact on the costs and/or timelines of a trial/project, impact on other departments, impact on data pooling capabilities or whenever the respective Standards Governance Team(s) decides that an approval on a higher level is required
  - A change will be considered minor if it does not satisfy any of the major criteria (e.g. the change is only impacting a single domain, correcting typos, adding clarification and/or correcting technical issues)



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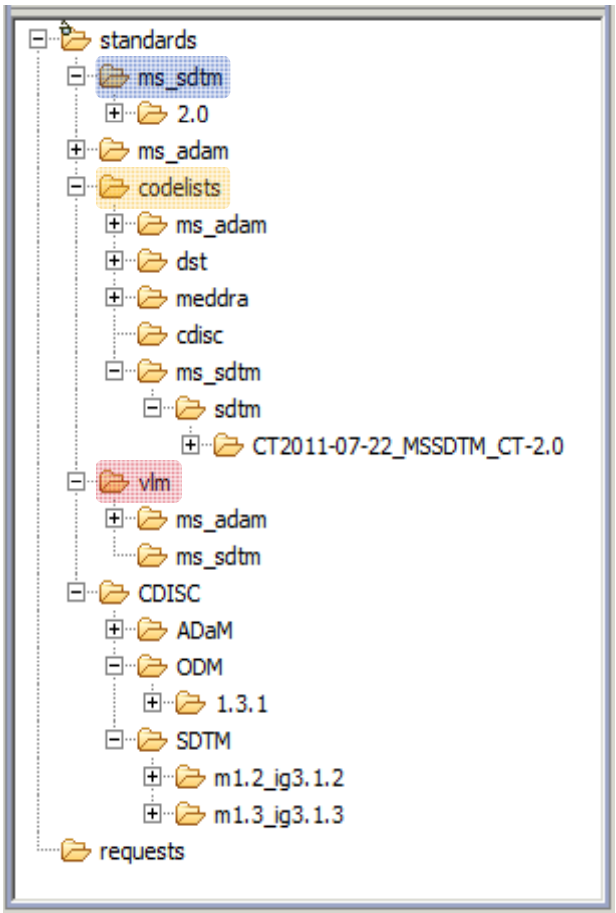
Metadata Libraries Tomorrow

Standard Metadata defined in new metadata repository (entimICE® Software Implementation)

- Standard (domain) Library
  - One metadata object per domain
- Controlled Terminology Library
  - Either as catalogue or single codelists
  - Library Level: All CDISC CT plus sponsor specific extensions and codes, except VLM (e.g. TESTCD/TEST)
  - Trial Level: All CDISC CT plus sponsor specific extensions and codes, except VLM (e.g. Testcodes)
- Value Level Metadata (VLM) Library
  - On library level as single table/dataset containing all VLM specifications (generic as in excel spreadsheet)
  - On trial level as subset in system specific VLM structure to facilitate define.xml creation



Domain Metadata Structure excerpt...

Data set: root/standards/ms_sdtm/2.0/ae.sas7bdat

Row number: 01 to 44 of 44

	LABEL	TYPE	TYPE (formatted)	LENGTH	SEQ	KEY	FORMAT	FORMATL	formatd	MAND	MAND (formatted)	NULL
1	Study Identifier	C	Character	10	1	1				Y	Yes	N
2	Domain Abbreviation	C	Character	2	2	2	DOMAIN			Y	Yes	N
3	Unique Subject Identifier	C	Character	17	3	3				Y	Yes	N
4	Sequence Number	N	Numeric	8	4	4				Y	Yes	N
5	Group ID	C	Character	40	5	5				Y	Yes	N
6	Reference ID	C	Character	40	6	6				Y	Yes	N
7	Sponsor-Defined Identifier	C	Character	40	7	7				Y	Yes	N
8	Reported Term for the Adverse Event	C	Character	200	8					Y	Yes	Y
9	Modified Reported Term	C	Character	200	9					Y	Yes	Y
10	Dictionary-Derived Term	C	Character	200	10		AEDICT_F			Y	Yes	Y
11	Category for Adverse Event	C	Character	100	11		AECAT			Y	Yes	Y
12	Subcategory for Adverse Event	C	Character	100	12					Y	Yes	Y
13	Pre-Specified Adverse Event	C	Character	2	13		NY			Y	Yes	Y
14	Body System or Organ Class	C	Character	200	14		AEDICT_F			N	No	Y
15	Location of Event	C	Character	40	15		LOC			Y	Yes	Y
16	Severity/Intensity	C	Character	40	16		AESEV			Y	Yes	Y
17	Serious Event	C	Character	2	17		NY			N	No	Y
18	Action Taken with Study Treatment	C	Character	40	18		ACN			N	No	Y
19	Other Action Taken	C	Character	40	19		ACNOTH			Y	Yes	Y
20	Causality	C	Character	40	20		AEREL			N	No	Y
21	Relationship to Non-Study Treatment	C	Character	40	21		AERELNS			Y	Yes	Y
22	Pattern of Adverse Event	C	Character	40	22					Y	Yes	Y
23	Outcome of Adverse Event	C	Character	40	23		OUT			Y	Yes	Y
24	Involves Cancer	C	Character	2	24		NY			Y	Yes	Y
25	Congenital Anomaly or Birth Defect	C	Character	2	25		NY			Y	Yes	Y
26	Persist or Signif Disability/Incapacity	C	Character	2	26		NY			Y	Yes	Y

Use of future electronic Metadata Libraries

- Standard (metadata) superset is available in Standard Library
- Required standard objects to be copied for use and refinement on trial level, e.g.
  - delete not used (permissible) variable definitions
  - add additional variables if required, based on existing Merck guidelines and SDTM-IG
  - create trial specific subsets of Controlled Terminology metadata
  - create trial specific subset of Value Level Metadata
- Use of trial specific metadata objects for...
  - creation of define.xml for submission
  - Programming (ADaM)
  - Data pooling
- Origin of changed metadata object always traceable via object history
  - Entry in Version 1.0 „Object copied from root/standards/ms_sdtm/...“

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Standard Governance

- Top-Down Process:
  - System built-in functionality supports compliance check for metadata objects
    -> Trial level versus objects in library (High level Results Report)
  - Customised QC programs for more comprehensive compliance checks
    -> CT subsets, VLM subsets, variable length versus Global Standards or Trial/Project specific metadata (Detailed Results Report)
  - Unexpected deviations to be justified by responsible Data Manager

- Proactive Process:
  - Data Manager uses built-in functions and/or customised QC tools to check for any deviations to standards
  - Any deviations in report are reviewed and discussed within trial team. For required exemptions an approval request is sent to the respective Standard Team (role based workflow supported in system)

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System Supported Versioning

- System supports life-cycle status and versioning of metadata objects
- Life-cycle status of standard objects:
  - Draft (not visible to normal user)
  - Review (not visible to normal user)
  - Pre-production (not visible to normal user)
  - Production (visible for all users, object can be copied)
  - Frozen (visible for all users, but can not be copied for use)
- For all life-cycle statuses the object versioning is enabled
  - Change life-cycle status or edit&save object will create a new version of the object. The objects version index is increased
  - separate Versioning for development and production
    - Keeping retrievable versions of objects in development requires user action „Commit“
    - Versions of objects in production are always kept and retrievable.
  - For each version the status, time of creation, user, etc. is captured in the objects history

Versioning of Standards

- Minor changes/updates to standards will use versioning of standard objects
  - Existing object in production will be checked out to apply changes
  - Edited object will run through life-cycle be applied and old object will be replaced by updated
  - old versions of all objects in production still available via Object/Version history

- Major changes (e.g. new SDTM Model, new CT)
  - new Standard folder will be created

  - new set of standard objects will be created either by
    - copying of old versions and editing
    - import of new object(s) from metadata definition file(s)
  - „Old“ standard remains active for transition period or is set to Frozen with publishing the new version

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