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Data Standards and Governance

Industry Standards – what else exists beside CDISC

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ABSTRACT

CDISC is to become the definite standard for data and analysis structures for clinical trial data. But, CDISC standards are not the only ones in our industry. Let's have a look into our biomedical & clinical research domain and see, which other 'standards' or –de-facto standards are existing and should be known. The presentation will give an overview of industry standards beside CDISC. The presentation would start to categorize these standards into three groups:

1. Regulatory standards (ex. CDISC)
2. Industry knowledge / related standards (ex. Coding Dictionaries)
3. Technical Standards (ex. HL7)

For each category several standards will be introduced and explained. The summary will then show, where are they overlapping and can serve as a cheat sheet for starting to dive diving deeper into investigation of the standard. Benefits: This presentation offers an overview about other important Industry Standards beside CDISC in the biomedical and clinical research world, touching healthcare, the interactions and a little bit of future visions

INTRODUCTION

Our industry is widely spread across the globe. Multiple cultures, technology implementation and enablement, regulatory aspects and the related domain knowledge has led to several of different terminologies, technical standards and regulatory requirements. Over the last 10-15 years, our industry began to standardize many areas of our domain knowledge to get drug submissions, adverse event handling and other industry related work better and faster organized, at the end to make our work more efficient on our mission to submit drugs faster to the market and help people to become or stay healthy.

This presentation will introduce industry standards beside CDISC, which are useful to know in daily conversations with everybody working in our domain – Life Sciences and Healthcare.

WHAT IS AN 'INDUSTRY STANDARD'?

First question should be a definition of what is an industry standard. I think, Collins English Dictionary gives the best answer:

"An industry standard is an established standard, norm or requirement in a particular area of business".

With this, we have to investigate the key stakeholders of our industry, which are responsible to drive these standards.

KEY STAKEHOLDERS

DOMAIN & BUSINESS USER

As in every industry, the domain experts are driving the business. In our world, the domain experts are the Clinicians, Investigators, Clinical Protocol Developers, Data Managers, Medical Writer, Statisticians, Ethics Committee member – at the end everybody who brings his/her domain knowledge into the daily work. They define the content and the terminology, which is used for communication. They also think about the business process workflow, how to optimize it and bring a clinical study to a successful end.

IT & TECHNOLOGY USER

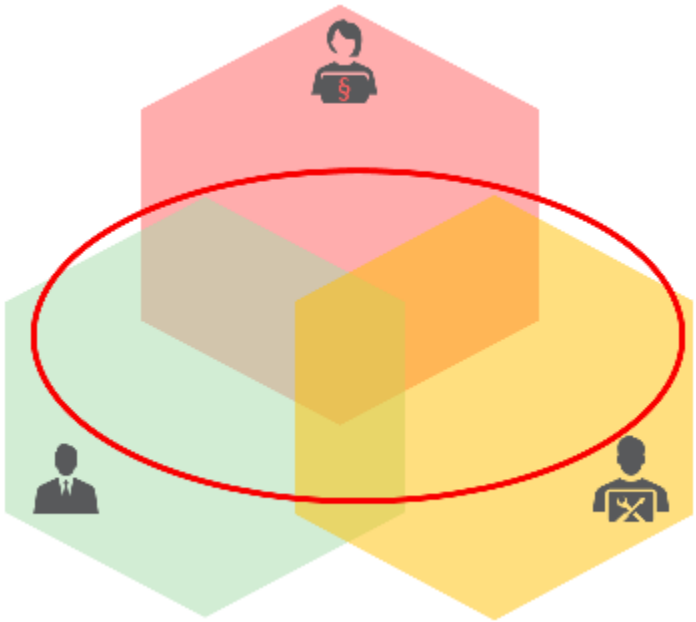
The Life Sciences and Healthcare industry is as of today, enabled through IT. Sure, we still can think of doing everything on paper and fall back in the 70th-ies or 80th-ies. But without IT enablement we can't imagine to run our work anymore. With the acceptance of this we must include IT as a stakeholder when we talk about industry standards. And – more complicated, usually the knowledge background is different between the domain users and IT, therefore the 'language' they speak is often misinterpretation. Everybody thinks he understand the other party, but in reality this leads often to project failures.

THE REGULATORY ASPECTS

Beside, our industry is heavily regulated, mainly to save the life of patients and people - during clinical investigations but also to regulate the daily usage of drugs through a standardized adverse event reporting. Means we have to bring in the regulatory user as well as a stakeholder, when we talk about standardization in our industry.

OVERLAPPING INTERESTS

All of these stakeholders can define their standards by themselves. But in practice, it makes more sense to work together as early as possible and identify the overlapping interests. A practical example (even if CDISC is out of scope for this presentation) – the definition of the CDISC BRIDG model has key stakeholders from all 3 parties: HL7 (Health Level 7) for the technology part, NCI (National Cancer Institute) and CDISC for the domain expertise and the FDA (US Food and Drug Administration) for the regulatory aspects. Now, in the IT world we have technical standards without the need as they may define core technologies. We shouldn't forget them in this presentation, even if we feel they are 'there anyway – as everybody is working with computers every day". Also, the domain can define controlled terminology independent from the other stakeholders, but may come quick to the view, that regulatory should be at least informed.



STANDARDS DEVELOPMENT ORGANIZATIONS (SDO)

KEY STANDARDS DEVELOPMENT ORGANIZATIONS

Before we look into the standards itself we have to identify the key standard development organizations. Groups and Organizations, which feel responsible to own the development of certain standards. There are SDOs for all 3 key stakeholder groups (a final list of abbreviations are at the end of this document):

Domain	Regulatory	Technology
CDISC	ISO	W3C
HL7	US Federal Register	OASIS
	<- ICH* ->	OMG
WHO		ANSI
MSSO		
NCI		
OBO foundry		

** Regulatory Authorities are included in ICH!*

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REGULATORY STANDARDS

ICH

ICH – the International Council of Harmonization – is, in my opinion, the key industry standard platform, which everybody should know. Mainly the industry comes together with Regulatory and also Technical Standards are included.

ICH has 4 major areas for Standards:

Q: Quality (ex. GMP)
S: Safety (pre-clinical!)
E: Efficacy (ex. Clinical Study Reports)
M: Multidisciplinary (includes technical agreements, ex. eCTD)

Even if all standards touch our Life Sciences and Healthcare industry, the focus for 'Clinical Research' are the E and M standards.

List of E standards:

E1 Clinical Safety for Drugs used in Long-Term Treatment	E10 Choice of Control Group in Clinical Trials
E2A - E2F Pharmacovigilance	E11 Clinical Trials in Pediatric Population
E3 Clinical Study Reports	E12 Clinical Evaluation by Therapeutic Category
E4 Dose-Response Studies	E14 Clinical Evaluation of QT
E5 Ethnic Factors	E15 Definitions in Pharmacogenetics / Pharmacogenomics
E6 Good Clinical Practice	E16 Qualification of Genomic Biomarkers
E7 Clinical Trials in Geriatric Population	E17 Multi-Regional Clinical Trials
E8 General Considerations for Clinical Trials	E18 Genomic Sampling
E9 Statistical Principles for Clinical Trials	Cross-cutting Topics

List of M standards:

M1 MedDRA Terminology
M2 Electronic Standards
M3 Nonclinical Safety Studies
M4 Common Technical Document
M5 Data Elements and Standards for Drug Dictionaries
M6 Gene Therapy
M7 Genotoxic Impurities
M8 Electronic Common Technical Document (eCTD)
M9 Biopharmaceutics Classification System-based Biowaivers
M10 Bioanalytical Method Validation

There is one good example for overlapping standards: E2B – Clinical Safety Data Management: Originally agreed in ICH, version 2, E2B was a pure ICH standards. The new, actual version R3 is now HL7 structured and the core definition is an ISO standard. Which brings us to the next SDO: ISO

ISO – INTERNATIONAL ORGANIZATION FOR STANDARDIZATION

ISO is a pure global standards organization. Standards defined here should be standards in all countries, where the particular standard has been accepted.

Where ISO standardize anything and everything also for and from other industries, for us and our industry, the ISO/TC 215 (Technical Committee) is the first entry point.

There is a long list of standards, for this presentation I just name two of them: ISO 14199:2015 – Information models – Biomedical Research Integrated Domain Group (BRIDG) Model and ISO/HL7 27953-1 2011 and ISO/HL7 27953-2 2011, which handles the framework for adverse event handling and human pharmaceutical reporting requirements for Individual case safety reports (ICSRs).

GLOBAL, REGION OR LOCAL REGULATORY STANDARDS

When we look into standards, we should differentiate between global, region and local requirements. Global standards are standards agreed on the ICH level for example. By regional standards we define standards for example on the European Union Level and the leading authority here – the EMA. Local standards are standards coming from local member states – example rules defined in Germany.
If we see the United States as a 'local' member, the US CFR had a huge impact into our industry – everybody is aware of the "CFR 21 Part 11", which is a local definition of the United States, but accepted as standard across the industry and therefore referenced everywhere.

PROCESS STANDARDS

Finally, beside CFR21 Part11, HIPAA and ICH GCP, there are some more 'process standards'. Process standards describe the request from the Regulatory view the process which has to be followed. They should be included, as they have an impact for the industry work.

DOMAIN STANDARDS

The presentation will introduce the following domain standards. The color code at the end of the table will define the impact on the overlapping interests: D= Domain, T=Technology, R=Regulatory

CODING DCITIONARIES

Organization	Standard		D	T	R
MSSO	MedDRA	Medical Dictionary for Regulatory Activities	✔	✘	✔
WHO	WHO DD	WHO Drug Dictionary	✔	✘	✔
WHO	WHO ATC	Anatomical Therapeutic Chemical Classification System	✔	✘	!
WHO	WHO ICD	International Statistical Classification of Diseases	✔	✘	!
IHTSDO*	Snomed CT	Systematized Nomenclature of Medicine - Clinical Terms	✔	✘	!
Regenstrief Institute	LOINC	Logical Observation Identifiers Names and Codes	✔	✘	!
CDISC	*CT*	*Out of scope*	✔	✘	✔

*IHTSDO has transferred its business, including the intellectual property rights in SNOMED CT, to a newly-incorporated company based in England. With effect from 31 December 2016, the new company will assume responsibility for maintaining SNOMED CT. The new company will trade under the name of SNOMED International (Company Registration Number 9915820).
IHTSDO and SNOMED International are the same entity. International Health Terminology Standards Organisation (IHTSDO) is the legal name of the new English company, while SNOMED International is its trading name.

VOKABULARY, ONTOLOGY, DATA MODELS

Organzation	Standard		D	T	R
ISA Working Group	ISA	ISA data model - **I**nvestigation' (the project context), '**S**tudy' (a unit of research) and '**A**ssay' (analytical measurement) – isa-tools.org	✔	!!	✘
National Cancer Institute	EVS, caBIG	NCI Enterprise Vocabulary Services, Cancer Biomedical Informatics Grid	✔	!	!
University of Washington	FMA	Foundational Model of Anatomy, also map with SNOMED	✔	!	✘
Gene Ontology Consortium	Gene Ontology	consistent descriptions of gene products across databases	✔	!	✘
Open Biomedical Ontologies consortium	OBO foundry	Multiple Ontologies, serve as core for the industry	✔	!	✘
National Center for Biomedical Ontology	Bioportal	Lookup ontologies (incl. OBO)	✔	!	✘
	Ontology Lookup Service	Lookup ontologies (incl. OBO)	✔	!	✘
?	LOV	Linked Open Vocabularies over the Web	✔	!	✘
ISO	*CDISC BRIDG*	*Out of scope*	✔	!	✔

OTHER, INDUSTRY RELATED STANDARDS

Organization	Standard		D	T	R
ISPE	GAMP	Good automated manufacturing practice	✓	✗	✓
HL7	Multiple	Health Level 7, based on HL7-RIM	✓!	✓	✓
ISO	DICOM	Digital Imaging and Communications in Medicine	✓	✓	!
IHE	IHE	Integrating the Healthcare Enterprise	✓	✓	✗

TECHNOLOGY STANDARDS

CORE TECHNOLOGY STANDARDS WORTH TO BE MENTIONED

Organization	Standard		T	D	R
W3C	XML	XML as foundation for other standards like ODM(++)	✓	!	!
W3C	OWL (RDF)	Web Ontology Language (RDF)	✓	✓	✗
OASIS	SAML, EDXL	Organization for the Advancement of Structured Information Standards (Security Assertion Markup Language, Emergency Data Exchange Language)	✓	✗	!
OMG	FHIR	See HL7	✓	!	!
OMG	BPM(N)	Business Process Modelling	✓	✗	✗
ANSI	ANSI X.12	inter-industry electronic exchange of business transactions	✓	✗	!

CHANGING ROLE OF CERTAIN 'TECHNOLOGY SDO'S

Some core Technology SDO's started to move into the development and support of domain standards as well. A good example is the OMG, which is now supporting the Healthcare world and especially focused on the EHR (Electronic Health Record) and integration and usage of EHRs in Life Sciences.

RFC STANDARDS

Finally, we should look into RFC standards – "Request for Comments" – a way of define technical standards in a 'relaxed' way. Everybody can publish and open a (technology / IT related) standard and ask for comments. After an agreement, the RFC become 'de-facto' a standard. Standards like SMTP (Simple Mail Transfer Protocol – "How an email server receives emails") are defined here. This may be not direct related to the Life Sciences world as is, but a lot of these elements are also used in the 'normal' daily business process workflow. For example - the AS/2 standard is used to send Drug Safety "E2B cases" from a sender to a receiver.

CONCLUSION - "CHEAT SHEET" – OR BETTER "CHEAT DIAGRAM"

With all this in mind - the key stakeholders, their independent standards but also the overlapping interests - a diagram can developed and used to categorize the different standards.
The diagram use the three colors defined at the beginning of the presentation – red for Regulatory aspects, green for the Domain experts and yellow for the IT 'geeks'.
Not all standards, which has been introduced in this presentation are listed in this diagram. But with this knowledge, it should be easy for everyone to categorize this now.

Looking forward to which standards comes next in our 'industry' – Life Sciences and Healthcare.

ACKNOWLEDGMENTS

My acknowledgments are going to all people and organizations, which spend and spent their energies to create these standards, fight for them to be a standard and maintain these standards where necessary.

LIST OF ABBREVIATIONS AND FURTHER LINKS, GLOSSARY

Abbreviation	Description	Link to:
CDISC	Clinical Data Interchange Standards Consortium	www.cdisc.org
EA	Enterprise Architecture	
HL7	Health Level 7	www.hl7.org
WHO	World Health Organization	www.who.int
MSSO	MedDRA Maintenance and Support Services Organization	www.meddra.org
NCI	National Cancer Institute	www.cancer.gov
ISO	International Organization for Standards	www.iso.org
CFR	US Federal Register	www.federalregister.gov
ICH	International Council of Harmonization	www.ich.org
W3C	World Wide Web Consortium	www.w3.org
OASIS	Organization for the Advancement of Structured Information Standards	www.oasis-open.org

OMG	Object Management Group	www.omg.org
ANSI	American National Standards Institute	www.ansi.org
OBO	Open Biomedical Ontologies	www.obofoundry.org
IHTSDO	International Health Terminology Standards Organisation	www.snomed.org
SNOMED International	Tradename of International Health Terminology Standards Organisation	www.snomed.org
LOINC	Logical Observation Identifiers Names and Codes	www.loinc.org
ATC	Anatomical Therapeutic Chemical Classification System	www.whocc.no/atc_ddd_index
ICD	International Statistical Classification of Diseases	www.who.int/classifications/icd/en
DD	(WHO) Drug Dictionary	www.who-umc.org/whodrug/whodrug-portfolio
MedDRA	Medical Dictionary for Regulatory Activities	www.meddra.org
ISA	**I**nvestigation' (the project context), '**S**tudy' (a unit of research) and '**A**ssay' (analytical measurement)	isa-tools.org
NCI EVS	NCI Enterprise Vocabulary Services	evs.nci.nih.gov
caBIG	Cancer Biomedical Informatics Grid	cagrid.org
FMA	Foundational Model of Anatomy	si.washington.edu/projects/fma
LOV	Linked Open Vocabularies	lov.okfn.org/dataset/lov/

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