

The use of electronic Health Records in Clinical Research - The value of CDISC Standards

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Who is Jozef Aerts?

- CDISC volunteer since 2001
- Contributed to several CDISC standards
 - ODM, Define-XML, SDM-XML, CTR-XML, ...
- Professor in Medical Informatics since 2012
in Graz, **Austria**



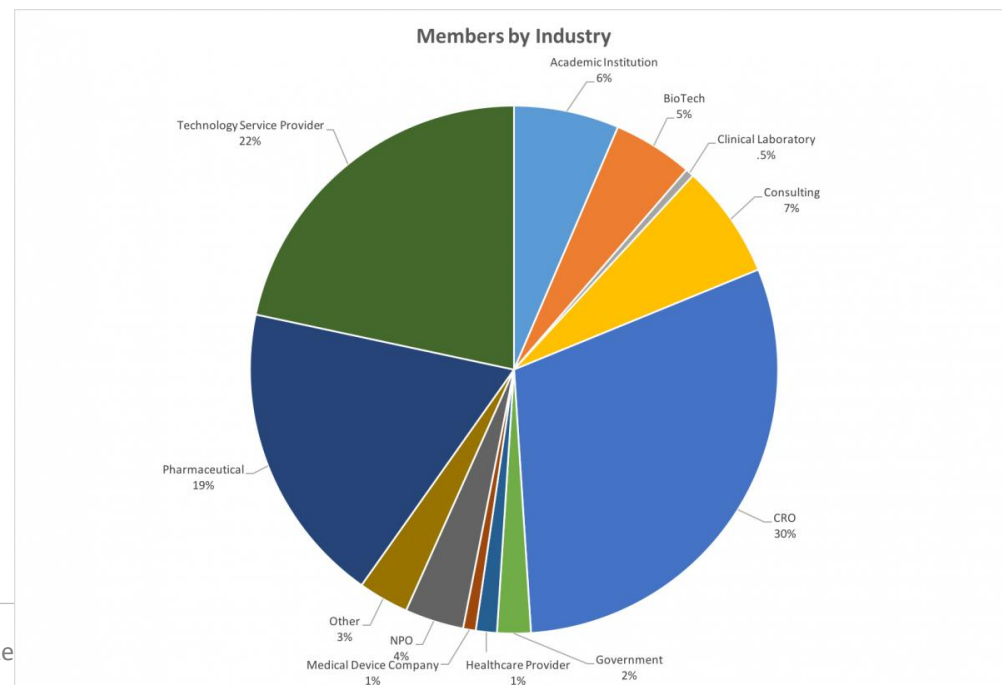
Who is Jozef Aerts?

- Owner and CEO of XML4Pharma
- A consultancy and software company specializing in the implementation of CDISC standards
 - With emphasis on XML technologies



CDISC

- Clinical Data Interchange Standards Consortium
- Consortium structure: >420 members (Japan: >100)
 - Pharma companies
 - CROs
 - Software vendors
 - Academic institutions
 - Consultants
 - Laboratories
 - ...
- Volunteer organization
 - Consensus organization



Jozef Aerts and CDISC

- Just 1 of the several thousand volunteers
 - But a very active and critical one ...
- Started volunteering in 2001
- Member of different CDISC development teams
 - ODM (Operational Data Model)
 - Define-XML (regulatory metadata submission standard)
 - SDM-XML (Study Design in XML)
 - CTR-XML (Clinical Trial Registries standard)
- Integration of healthcare data

CDISC as an SDO

- CDISC is a "standardization organisation" (SDO)
- We create **syntactic** and **semantic** standards for use in clinical research
- These are often different than the standards used in healthcare
 - Healthcare is "event" driven
 - Clinical research is "protocol" driven

Use of healthcare data in clinical research

- Healthcare and clinical research data systems are traditionally different and separated
- Same data needs to be entered twice
- Historical data needs to be copy-paste
 - Medical history
 - Prior medications



Use of healthcare data in clinical research

- Nowadays, much more healthcare data is available in electronic form, and we should use it in clinical research
- So we need to automate the use of healthcare data in clinical research
- There are however obstacles:
 - Technical
 - Different semantics
 - Different regulations

Sources of healthcare data for use in clinical research

- Directly from the (own) Hospital Information System
 - Limited to "hospital owned" data
 - Requires custom programming
- From HL7-v2 messages (within or between hospitals)
- From HL7 CDA documents (Electronic Health Records - EHRs)
- From HL7 FHIR documents / messages

Use of healthcare data in clinical research

- Reduces duplication of work
- Data quality can be a problem
 - But this can also be the case in CRF data
- Possibility of retrieval of historical data
 - Prior diseases (MH)
 - Prior medications, therapies and procedures
- Post-marketing data (ADR) - Mihari project
- Do countries already have a life-long EHR?



Use of EHRs in clinical research - Regulations

- ICH (International Committee of Harmonisation)
 - E.g. audit trails (USA: 21 CFR Part 11)

4.9.3 Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an **audit trail** should be maintained); this applies to both written and electronic changes or corrections (see 5.18.4 (n)). Sponsors should provide guidance to investigators and/or the investigators' designated representatives on making such corrections. Sponsors should have written procedures to assure that changes or corrections in CRFs made by sponsor's designated representatives are documented, are necessary, and are endorsed by the investigator. The investigator should retain records of the changes and corrections.

<https://www.pmda.go.jp/files/000156725.pdf>

- FDA: "Electronic Source Data in Clinical Investigations"
<https://www.fda.gov/downloads/drugs/guidances/ucm328691.pdf>

The value of CDISC standards

- For new medications or therapies, subject data must be submitted to the PMDA in a standardized way
- The CDISC SDTM (Submission Data Tabulation Model) provides the structure and contents of these data
- The data are not (and cannot) be captured in this way
 - SDTM contains a good number of derived data
 - Data needs to be transformed, categorized
 - Not every data point must be submitted

SDTM Dataset Example: Medical History (MH)

	STUDYID	DOMAIN	USUBJID	MHSEQ	MHSPID	MHTERM	MHLLT	MHDECOD	MHHLT	MH
1	CDISCPIL01	MH	01-701-1015	9		ALZHEIMER'S DISEASE				
2	CDISCPIL01	MH	01-701-1015	1	E01	VERBATIM_0135	PALPITATIONS	PALPITATIONS	HLT_0493	HLG
3	CDISCPIL01	MH	01-701-1015	8		VERBATIM_0140	SUBTOTAL HYS...	HYSTERECTOMY	HLT_0675	HLG
4	CDISCPIL01	MH	01-701-1015	2	E03	VERBATIM_0301	HEADACHE	HEADACHE	HLT_0064	HLG
5	CDISCPIL01	MH	01-701-1015	10		VERBATIM_0539	GALLBLADDER ...	CHOLELITHIASIS	HLT_0084	HLG
6	CDISCPIL01	MH	01-701-1015	3	E05	VERBATIM_0825	TINNITUS	TINNITUS	HLT_0570	HLG
7	CDISCPIL01	MH	01-701-1015	4	E02	VERBATIM_0841	HEARTBURN	DYSPEPSIA	HLT_0244	HLG
8	CDISCPIL01	MH	01-701-1015	6		VERBATIM_1004	THYROIDECTO...	THYROIDECTO...	HLT_0243	HLG
9	CDISCPIL01	MH	01-701-1015	11		VERBATIM_1230	SORE THROAT	PHARYNGOLAR...	HLT_0130	HLG
10	CDISCPIL01	MH	01-701-1015	7		VERBATIM_1716	TONSILLECTOMY	TONSILLECTOMY	HLT_0202	HLG
11	CDISCPIL01	MH	01-701-1015	5	E04	VERBATIM_1779	NUMBNESS IN ...	HYPOAESTHESIA	HLT_0014	HLG
12	CDISCPIL01	MH	01-701-1023	16		ALZHEIMER'S DISEASE				
13	CDISCPIL01	MH	01-701-1023	21		VERBATIM_0073	CELLULITIS OF ...	CELLULITIS	HLT_0613	HLG
14	CDISCPIL01	MH	01-701-1023	1	E02	VERBATIM_0249	GASTROESOPH...	GASTROOESOP...	HLT_0407	HLG
15	CDISCPIL01	MH	01-701-1023	19		VERBATIM_0291	LOW BACK PAIN	BACK PAIN	HLT_0115	HLG
16	CDISCPIL01	MH	01-701-1023	15		VERBATIM_0342	HYPERTENSION	HYPERTENSION	HLT_0228	HLG
17	CDISCPIL01	MH	01-701-1023	17		VERBATIM_0388	PENILE PROST...	PENILE PROST...	HLT_0448	HLG
18	CDISCPIL01	MH	01-701-1023	2	E06	VERBATIM_0461	MUSCULAR PAIN	MYALGIA	HLT_0700	HLG
19	CDISCPIL01	MH	01-701-1023	12		VERBATIM_0596	NUMBNESS OF ...	HYPOAESTHESIA	HLT_0014	HLG
20	CDISCPIL01	MH	01-701-1023	3	E03	VERBATIM_0699	HIATAL HERNIA	HIATUS HERNIA	HLT_0159	HLG
21	CDISCPIL01	MH	01-701-1023	8		VERBATIM_0788	APPENDICITIS	APPENDICITIS	HLT_0703	HLG
22	CDISCPIL01	MH	01-701-1023	4	E04	VERBATIM_0800	INDIGESTION	DYSPEPSIA	HLT_0244	HLG
23	CDISCPIL01	MH	01-701-1023	5	E05	VERBATIM_0929	HEADACHE	HEADACHE	HLT_0064	HLG

A few important questions

- How can clinical research data be captured so that it can easily and smoothly be used for the submission?
- How can healthcare data be used in such a way that it can easily and smoothly be used for the submission?

Answer:
CDISC standards
from the start

A simple example - Adverse event

■ Adverse event severity (AESEV)

Your protocol / CRF:

- 1 - very mild, unrelated
- 2 - mild
- 3 - mild to severe, no action required
- 4 - severe, apply concomitant medication
- 5 - hospitalization required
- 6 - fatal



PMDA expected categories -
(CDISC AESEV)

- Mild
- Moderate
- Severe

PMDA expected categories -
(CDISC AEOU)

- Recovered/Resolved
- ...
- Fatal

CDISC Controlled Terminology:

<https://www.cdisc.org/standards/semantics/terminology>

PMDA expectation (SDTM-AE)

AEHOSP = Y or AEHOSP= N

Solution: use CDISC Standards from the start

- CDASH: Clinical Data Acquisition Standards Harmonization
- Defines **20 standardized CRFs**
 - Standardized content
 - Standardized (CDISC) controlled terminology
- Makes it very easy to transform captured data to submission data
- Can easily be implemented in any study design tool (XML representation available)

<https://www.cdisc.org/standards/foundational/cdash>

CDASH example: AE form with annotations






Were any adverse events experienced? <input type="checkbox"/> NOT SUBMITTED <input type="checkbox"/> AEYN	<input type="radio"/> Yes <input type="radio"/> No
Adverse Event Category: <i>Defaulted</i> <input type="checkbox"/> AECAT	Sponsor Defined
Adverse Event Subcategory: <i>Defaulted</i> <input type="checkbox"/> AESCAT	Sponsor Defined
What is the adverse event identifier? <input type="checkbox"/> AESPID	_____
What is the adverse event term? <input type="checkbox"/> AETERM	_____
Start Date <input type="checkbox"/> AESTDTC <input type="checkbox"/> AESTDAT	--/--/----
Is the adverse event ongoing? <input type="checkbox"/> AEENRF / <input type="checkbox"/> AEENRPT <input type="checkbox"/> AEENTPT <input type="checkbox"/> AEONGO	<input type="radio"/> Yes <input type="radio"/> No
End Date <input type="checkbox"/> AEENDTC <input type="checkbox"/> AEENDAT	--/--/----
What is the severity of the adverse event? <input type="checkbox"/> AESEV	<input type="radio"/> MILD <input type="radio"/> MODERATE <input type="radio"/> SEVERE
Was the adverse event serious? <input type="checkbox"/> AESER	<input type="radio"/> Yes <input type="radio"/> No

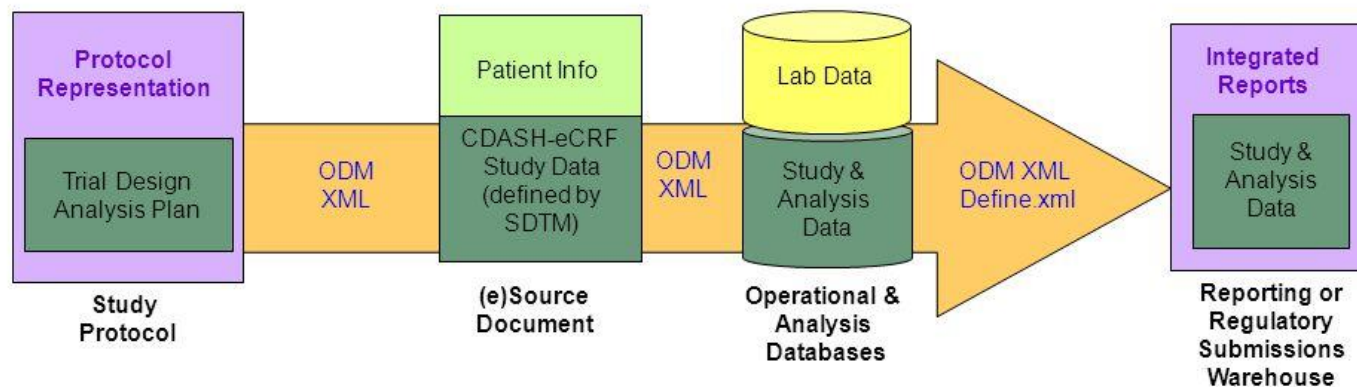
How do we exchange the data between systems?

- CDISC ODM (Operational Data Model) standard
- XML-based standard
- Metadata (study design)
- AdminData
- ReferenceData (non-subject data)
- ClinicalData
 - Possibility for full audit trails

Clinical Research Data Flow using CDISC-ODM

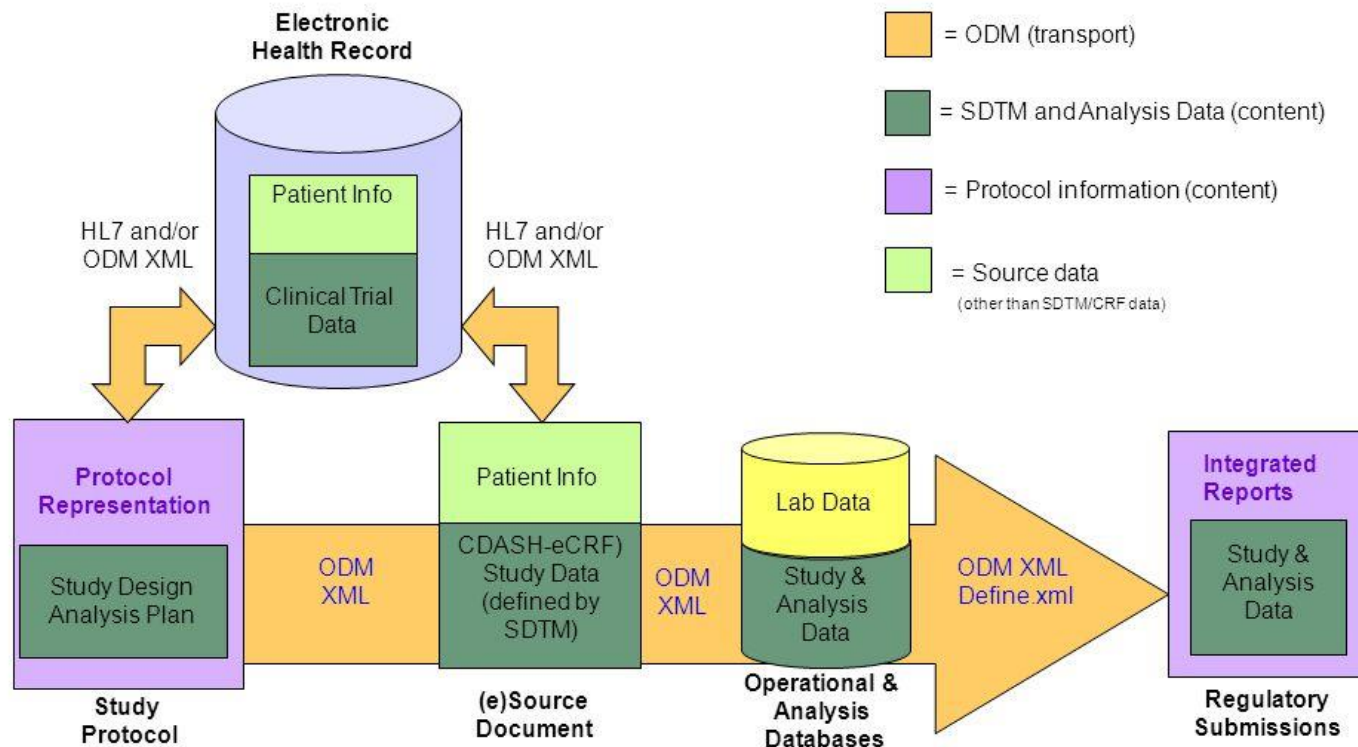
Data Flow Using CDISC Standards

-  = ODM - Operational Data Model (transport of data and metadata... "the message")
-  = SDTM - Study Data Tabulation Model and ADaM - Analysis Dataset Model (content)
SEND for Non-clinical Data
-  = Protocol Representation Standard (content)
-  = LAB - Laboratory Data Standard
-  = Source data
(other than SDTM/CRF data)



Healthcare Data Flow in Clinical Research - CDISC ODM

Data Flow Using CDISC Standards linking clinical research & healthcare



Healthcare data into Clinical Research data Data from Hospital Information Systems

■ Example: Smart Challenge (2010)

The screenshot shows a medical record interface. On the left is a navigation menu with icons for Cardiac Risk, Got Status?, Med Adherence, Med Calendar, Med List, Med Risk Maps, My App, and NLP Meds. The main area displays a table of medications:

rosuvastatin 20 MG Oral Tablet [Crestor]	30	2005-09-10	2007-08-03		2007-09-02	1	tablet	1	/d
Hydrochlorothiazide 12.5 MG / Lisinopril 10 MG Oral Tablet	30	2003-11-18	2007-09-02		2007-10-02	1	tablet	1	/d
rosuvastatin 20 MG Oral Tablet [Crestor]	30	2005-09-10	2007-09-02		2007-10-02	1	tablet	1	/d
Hydrochlorothiazide 12.5 MG / Lisinopril 10 MG Oral Tablet	30	2003-11-18	2007-10-06		2007-11-05	1	tablet	1	/d
rosuvastatin 10 MG Oral Tablet [Crestor]	30	2005-01-24	2007-10-06		2007-11-05	1	tablet	1	/d

Below the table, it says "Patient is involved in Clinical Study # 123" and provides links to transfer medical record data to CDASH Demographics CRF and CDASH Concomitant Medication. A "More information a" link is also present.

The CDASH form is titled "Group: Concomittant medication" and includes fields for:

- Medication No.*: 1
- Drug Name (Brand or Generic)*: Hydrochlorothiazide 12.5 MG / Lisinopril 10 MG Oral Tablet
- Total Dose Per Frequency Checked*: 1
- Unit*: tablet
- Frequency*: 1/d
- Start Date*: 2003-11-18
- Is medication still continuing*: No
- Stop Date*: 2003-12-18

Below this form, another medication entry is partially visible:

- Medication No.*: 2
- Drug Name (Brand or Generic)*: Niacin 500 MG Extended Release Tablet [Niaspan]

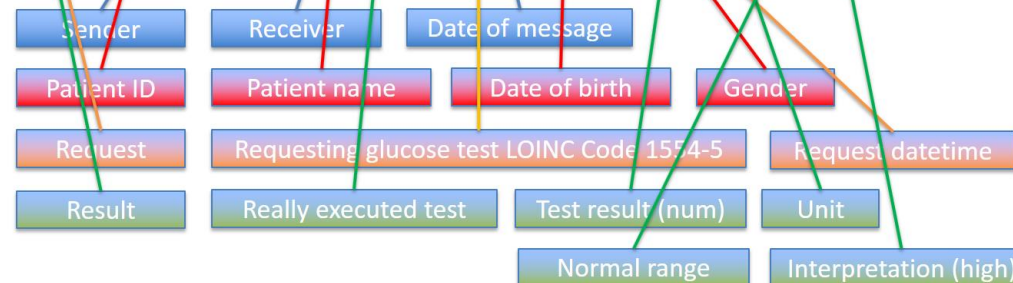
http://www.xml4pharma.com/Smart_Challenge/

Requires custom programming
versus HIS-API

Healthcare data to research data from HL7-v2 messages

- Is very well feasible
- Not often done, as:
 - Messages are usually not kept in the HIS (not persistent) - they flow into the core HIS (extract)
 - Exception:** SS-MIX HL7-v2.5 (Japan)
 - Most of the data from messages never appears in the discharge documents or transfer-of-care document

```
1 MSH|^~\&GHH LAB|ELAB-3^GHH OE|BLDG4^200202150930||ORU^R01|CNTRL-3456|P|2.4
2 PID||555-44-4444^EVERYWOMAN/EVE^E^^^^^JONES^19620320^F||153 FERNWOOD DR.^STATESVILLE^OH
3 OBR|1|84543^GHH OE|1045813^GHH LAB|1554-5^GLUCOSE|||200202150730|||||555-55-5555^PRIMAR
4 OBX|1|SN|1554-5^GLUCOSE^POST/12H CFST:MCNC:Pt:SER/ELAS:QNT|182 mg/dl|70 105|H||F
```



Clinical Research Data from HL7-CDA documents

- HL7-CDA (XML) is in more and more countries used for:
 - Discharge documents
 - Transfer-of-care documents
 - Laboratory and radiology reports
 - E-Medication
- However:
 - CDAs usually contain an extract of the collected data (incomplete information)
 - Use of the information for clinical research heavily depends on which (semantic) coding systems are used



Clinical Research Data from HL7-CDA documents

Some history

- 2006: CDISC starts "Healthcare Link"
(Landen Bain)

"CDISC, which is spearheading the demonstration project, views data capture as a 'single-source encounter between an investigator/physician and subject/patient,' says Landen Bain, CDISC liaison to healthcare. The 'key idea' is to have a data-capture form appear on the computer screen in an EHR session. 'If you have an EHR, it's contorted to go to a different computer and a different application to enter data for a clinical trial when the data originates inside the EHR and that's where you do [most of] your work.' "

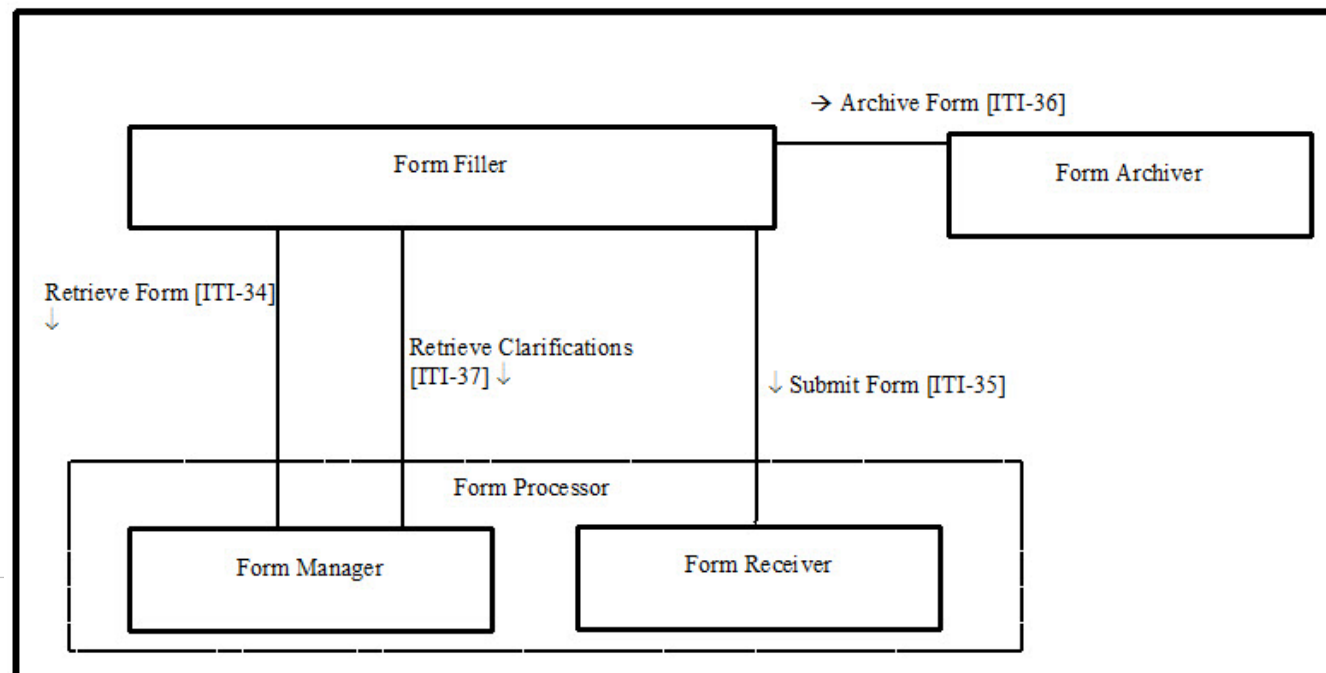
Clinical Research Data from HL7-CDA documents

Technical framework

- Another healthcare consortium, IHE (Integrating the Healthcare Enterprise) defines (vendor-neutral) **standardized process flows** for use in healthcare
- Provides the technical framework for such exchanges
- These are named "IHE Profiles"
"Retrieve Form for Data Capture" (RFD)

IHE Profiles for use of healthcare data in clinical research

- RFD: Retrieve Form for Data Capture
- CRD: Clinical Research Document
- Both use existing standards and technologies (XML, SOAP, ...)



Implementations of RFD and CRD

- Concentrating on HL7-CDA on the healthcare data side
 - Especially CCD (Continuity of Care Document - USA)
- Works very well with CDASH forms
- Flow to EDC works best with CDISC ODM

Own work in the field (2005-2010)

- Demonstrate feasibility of the concept
- Using following technologies & standards:
 - CDISC CDASH
 - W3C XForms
 - CDISC ODM
- Currently being used by several vendors (OpenClinica, ClinPal, ...)

Weight

Gender Female Male

Date of Birth

Ethnic Group

May 1957						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
28	29	30	1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30	31	1
2	3	4	5	6	7	8

Today: 3/9/2004

Problems with RFD / CRD

- **Semantic** mapping is the problem
- Works well for US CCD standard
- Must be adapted when other codes / coding systems are used
- CDISC controlled terminology is often not granular enough

Problems with RFD / CRD

- CCD ("Continuity of Care Document") is a "transfer of care" document
- Such documents usually only contain a limited amount of (the most relevant) information
- Much information that is in the Hospital Information System never appears in the CCD

Europe: The EHR4CR Project



- EU-funded programm 2011-2015
- 16 Million € (>2 Billion ¥)
- 35 academic and private partners (10 pharmaceutical companies)
- Goal: to build a platform to use de-identified data from hospital EHR systems
- Result: real life implementation: InSite platform
 - Used by several sponsors and (university) hospitals

EHR4CR: Participants



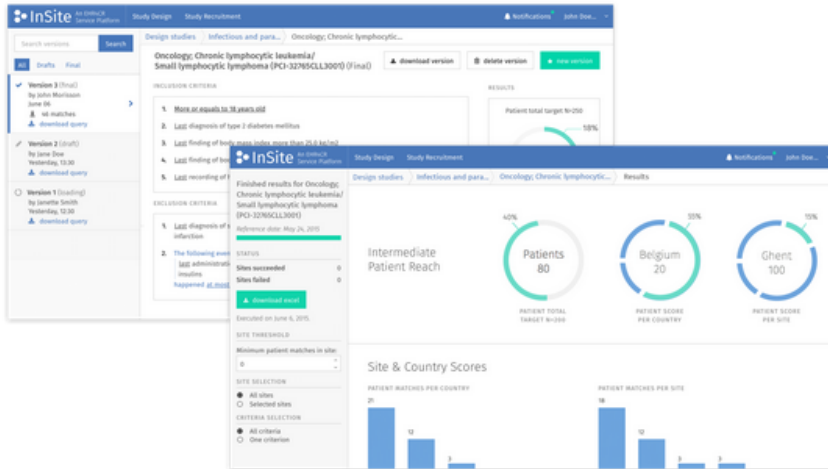
<http://www.ehr4cr.eu/9april2014/presentations/EHR4CR%20-%20April%2009%20-%20Sundgren.pdf>

EHR4CR: main topics

- Protocol feasibility platform
 - Will it be hard to find subjects for this study?

- Patient recruitment
 - Site tools to:
 - Identify potential candidates (based on IE criteria)
 - Contact treating physicians
 - Evaluate and recruit patients

EHR4CR: The InSite platform



Deploying All Over Europe in 2016-2017

InSite is a private initiative determined to define and realise a **sustainable eco-system for Real World Data driven clinical trial design and execution**. We build upon the outcome of several international research projects aimed at accelerating research through re-use of care data (EHR, primary care, Personal Health Records, ...) and the collaboration with pharmaceutical industry through the **EHR4CR - Electronic Health Records for Clinical Research project**.

Supported by a number of pharmaceutical companies, CROs and hospitals we are shaping a trustworthy environment for clinical data re-use from which all stakeholders — industry, care providers, patients — benefit.

<https://www.insiteplatform.com/>

- Although (partially) paid by tax money, not open

Use of EHRs for clinical research in Europe

- Healthcare in Europe is hopelessly divided
- Each country has its own healthcare system, laws, ...
 - Sometimes even huge differences between provinces
- The only common denominator is the EU data protection regulation

Use of EHRs for clinical research in Austria

- Austria has a national EHR exchange system (ELGA)
- ELGA system manages interoperable health documents (CDA) between healthcare providers / patients
 - Discharge letters
 - Laboratory / radiology reports
 - E-Medication
- Use of ELGA documents for clinical research is **NOT** allowed



The ELGA-EHR System in Austria

- Technically, based on HL7-CDA documents
- Exchange over IHE-XDS profile
(Cross-Enterprise Document Sharing)
- Used for "continuity of care"
- E-Medication currently rolled out

The ELGA-EHR System in Austria - Patient Portal

- Login through "e-card" or mobile phone TAN

The screenshot displays the ELGA patient portal interface. At the top, the browser address bar shows the URL <https://www.test.elga-online.gv.at/web-gui/protected/start.xhtml>. The page header includes the ELGA logo with the text "Meine elektronische Gesundheitsakte. Meine Entscheidung!" and the user's name "Peter Mustermann" with options for "Auftragsliste" and "Logout". A navigation menu contains tabs for "Startseite", "e-Befunde", "e-Medikation", "GDA", "Protokoll", and "Teilnahme". The main content area is titled "Willkommen in Ihrer ELGA!" and features six service cards:

- e-Befunde:** "Hier finden Sie eine Liste Ihrer e-Befunde." It shows "10 Befunde vorhanden" and "aktueller Befund vom 14.02.2016". A note states "Seit dem letzten Login keine neuen Befunde".
- e-Medikation:** "Hier sehen Sie eine Liste Ihrer verordneten und in der Apotheke abgegebenen Medikamente." It displays "Keine Medikation gefunden."
- GDA:** "Hier finden Sie Ihre Gesundheitsdiensteanbieter (GDA) - Ihre behandelnden oder betreuenden Ärzte, Spitäler, Apotheken und Pflegeeinrichtungen." It shows "7 GDA sind derzeit zugriffsberechtigt" and "Individuelle Einstellung Keine Zugriffsdauer geändert".
- Protokoll:** "Hier sind die von Ihnen und Ihren GDA durchgeführten Aktionen aufgelistet, etwa Ihre eigenen Änderungen oder wer wann auf Ihre ELGA zugegriffen hat."
- Teilnahme:** "Hier können Sie Ihren aktuellen ELGA-Teilnahmestatus ansehen und gegebenenfalls ändern." It lists "ELGA", "e-Befunde", and "e-Medikation" with checkmarks.
- Hilfe:** "Hier finden Sie Antworten zu den wichtigsten Fragen, Erläuterungen zu den verwendeten Symbolen sowie weiterführende Informationen zur Bedienung des ELGA-Portals."

The footer contains the text "Um PDF-Dokumente betrachten zu können, benötigen Sie einen [PDF-Reader](#)." and navigation links for "Hilfe", "Impressum", "Kontakt", and "Sitemap". A small logo for "W3C MAI-AA WCAG 2.0" is also present.

The ELGA-EHR System in Austria - Patient Rights

- Patient can "opt-out" completely
- Patient can do partial opt-outs
- Patient can make individual documents invisible for specific healthcare providers

- Patient can view all generated documents
 - But currently now download the CDA-XML document
- Patient can see which healthcare providers have inspected each document and when (logging)

The ELGA-EHR System in Austria - Document View

The screenshot shows a web-based interface for viewing a laboratory report. The main content area is titled "Allgemeiner Laborbefund" and is marked as "gesperrt am 23.02.2012 um 16:30".

Header Information:

- Autor:** Dr. Karin Gundelar, Gruppenpraxis Mehl-Eiser Labordiagnostik OEG, Labor
- Unterzeichner:** Prim. Dr. Weiss
- Gesundheitsdienstleistung:** Laborbefund
- Beginn:** 20. Jan 2012, 09:20
- Ende:** 20. Jan 2012, 11:34
- Blutbild groß**
- Gerinnungsstatus**

Zugriffsstatistik: [Anzeigen](#)
Ältere Versionen: [Version 1 - 15.03.2011](#)

Main Content:

- Allgemeiner Laborbefund** (Erzeugt am 20. Jänner 2012 um 11:34 | Version: 2)
- [+] Patient:** Dipl.Ing. Hofrat Herbert Hannes Mustermann, BSc, MBA
Geschlecht: männlich | geboren am: 24. Dezember 1949 | SVN: nicht angegeben
- [+] Auftraggeber(in):** Ordination Dr. Empfänger
- [+] Erstellt von:** Gp. Mehl-Eiser Labdg. OEG **An:** Ordination Dr. Empfänger
- [?] Keine automatischen Warnungen enthalten, bitte manuell überprüfen!**

Probeninformation

Spezimen	Materialart	Abnahme	Ort Gewinnung	Person	Annahme	Bemerkung Labor
BL-081201-02	BLUT	01.12.2008 06:34		Dr. Humpel	01.12.2008 08:15	leicht hämolytisch
PL-081201-01	PLASMA	01.12.2008 06:34		Dr. Humpel	01.12.2008 08:15	

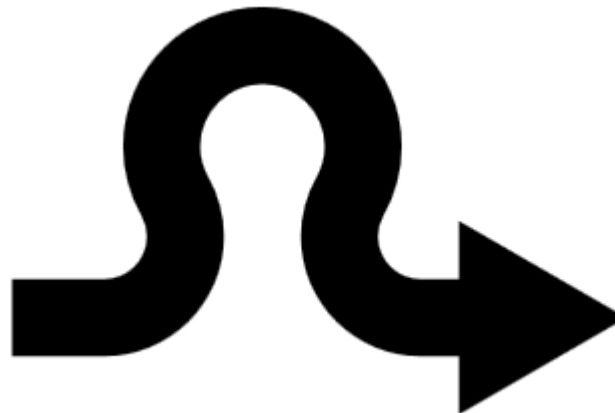
Hämatologie

Blutbild

Analyse	Ergebnis	Einheit	Referenzbereiche	Interpretation	Delta
Leukozyten	26	10 ³ /mm ³	4-10	+	d+
Thrombozyten	165	10 ³ /mm ³	150-360		d-

Use of EHRs for clinical research in Austria

- Essentially not allowed
- Workaround:
 - Investigator must have a "treatment relationship" with patient
 - After informed consent, investigator loads ELGA documents and extracts the information into his own HIS
 - Investigator uses information from the own HIS in the CRF



Use of EHR data for clinical research in other European countries

- Very limited based on EU privacy protection rules
- In some countries (e.g. Germany) EHR data may not be used even when the patient agrees
- Initiatives from different organizations to change (local) regulations
 - Use of anonymized data for research

Opportunities for use of EHRs in clinical research

- Searching for eligible subjects
 - Usually still blocked by legislation
 - Social media are of very good help
- Use of life-long EHRs
 - Detection of long-term effects of medications and treatments (post-marketing surveillance - MIHARI project)
 - Austria: medication data are destroyed after 1 year
 - Usually, hospitals must keep medical records 10-30 years
- Data quality
 - EHR information on "the past" is usually of higher quality (than the patient's memory)

Future developments

- For exchange (and even storage) of healthcare data, the HL7-FHIR standard is coming up
 - XML, JSON, RDF
 - RESTful web services
 - Well-defined basic building bricks: resources
 - Messages and Documents
 - Mappings between HL7-v2 and FHIR exist (see e.g. <https://fhirblog.com/2014/10/05/mapping-hl7-version-2-to-fhir-messages/>)
- "Networks" of data



FHIR and CDISC

- CDISC is currently working on ODMv2
- Will use many of the ideas of FHIR
- ODMv2 will have a RESTful Web Service API
- Unlike what is currently done, data can lie anywhere (cloud ...), one only needs to know the address
 - Distributed data
 - Moving away from "files"

Current gaps

- CDISC really wants to have one transport format from study design to submission: ODM-XML
- Regulatory authorities (including PMDA) still require SAS-XPT (30 years old) for submissions
 - 8-, 40-, 200-character limitations
 - Only for 2D (tabular data)
 - No possibility e.g. to add an EHR data point to the submission data point
 - No support for the Japanese language
 - Some workarounds exist
 - Not well usable with modern technologies such as RESTful web services

Closing the gap

- CDISC developed an ODM-based standard for exchange of submission data: [Dataset-XML](#)
- FDA/PMDA is still reluctant to use Dataset-XML
- PMDA could make a great step forward by accepting submissions in Dataset-XML
 - Japanese language
 - Easy integration of EHR into submissions
 - Allowing for modern IT methodologies like Web Services & Artificial Intelligence

What we even did not talk about ...

- Use of genomic data
- Use of telemonitoring data
- Use of lifestyle data

Obstacles to the use of EHRs in clinical research

- Legislation
- Technical issues are the minor problems
- Major problem are the **semantics**
 - Different coding systems
 - Over-simple CDISC Controlled Terminology
 - Required to be used in PMDA & FDA submissions
 - Many codes for same CDISC controlled term
 - Example: "ALB" (Albumin measurement) in CDISC
 - LOINC: >50 albumin test codes

Conclusions

- EHR information can be used (and is used) in clinical research
- Technical issues are the minor ones
- Distinction between local EHRs and interoperable EHRs
- Legal aspects can be obstacles
- Long-life EHR ideal, but not often there yet

Where to find more information?

- CDISC: www.cdisc.org
- CDISC CDASH:
<https://www.cdisc.org/standards/foundational/cdash>
- CDISC ODM:
<https://www.cdisc.org/standards/transport/odm>
- IHE profiles for clinical research
 - RFD: [https://wiki.ihe.net/index.php/Retrieve Form for Data Capture](https://wiki.ihe.net/index.php/Retrieve_Form_for_Data_Capture)
 - CRD: [http://wiki.ihe.net/index.php/Clinical Research Document](http://wiki.ihe.net/index.php/Clinical_Research_Document)