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From Electronic Health Records to Electronic Data Capture systems

PhUSE Beerse Event

EHR2EDC – Exploring a novel approach for automated data transfer

11 September 2019

Presenters

- Marija Todorovic
  - Senior Manager at Janssen R&D (Hospital Engagement Lead – RWD), Janssen Clinical Innovation/IDAR/GCDO

Marija Todorovic

- Massimo Raineri
  - Senior Director, Group Leader Integration, EBIS/GCDO

Massimo Raineri

- David Voets
  - Director Engineering Europe, InSite – a TriNetX Company

David Voets

EHR2EDC

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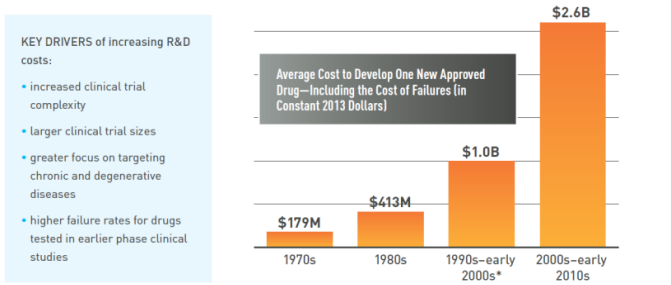
Agenda

- EHR2EDC general overview & objectives: **Marija Todorovic**
- EHR2EDC novel approach – technical solution
- Past, current and future solutions for automated data transfer
- Questions

The problems that we are facing with

Sponsors

FIGURE 15: The Costs of Drug Development Have More Than Doubled Over the Past Decade



*Previous research by same author estimated average R&D costs in the early 2000s at $1.2 billion in constant 2000 dollars [see DiMasi JA, Grabowski HG. The cost of biopharmaceutical R&D: is biotech different? *Managerial and Decision Economics*. 2007;28: 469–479]. That estimate is based on the same underlying survey as the author's estimates for the 1990s to early 2000s reported here [$800 million in constant 2000 dollars], but updated for changes in the cost of capital.

Source: DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. *J Health Economics*. 2016;47:20-33.

TRENDS IN CLINICAL TRIAL PROTOCOL COMPLEXITY	2000–2003	2008–2011	Increase in Complexity
Total procedures per trial protocol (median) (eg, bloodwork, routine exams, x-rays)	105.9	166.6	57%
Total investigative site work burden (median units)	28.9	47.5	64%
Total eligibility criteria	31	46	48%
Clinical trial treatment period (median days)*	140	175	25%
Number of case report form pages per protocol (median)	55	171	211%

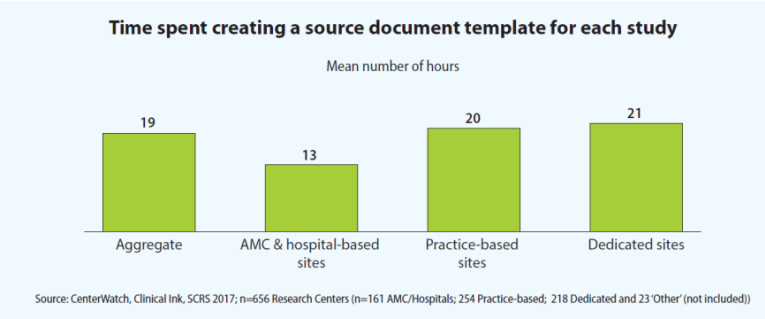
*These numbers reflect the "treatment duration" of the protocol only.

Sources: Getz KA, Campo RA, Kaitin KI. Variability in protocol design complexity by phase and therapeutic area. *Drug Inf J*. 2011;45(4):413-420; updated data provided through correspondence with Tufts Center for the Study of Drug Development.

Hospitals

- Over 40% of clinical trial data is **entered into both** Electronic Health Records (EHR), the clinical trial Electronic Data Capture (EDC) system and possibly a third paper copy
- This cause a significant delay between data availability and the manual data entry

(EDC Site Survey: Investigational Site Perspectives on Clinical Trial Information Systems. eClinical Forum 2009. www.eclinicalforum.org)



Increasing time and cost

EHR2EDC

References slide 34

Back in history ... The EHR4CR project

- Former IMI project 2011-2016 - 35 partners

- Objectives & scope
  - Develop a **trustworthy re-use of EHR data** for clinical research
  - Initiate the **Champion Program**, connecting hospitals to the InSite platform, collaboration between hospitals and sponsors
  - Establish the **European Institute for Innovation through Health Data** – an independent governance body

Source: Slide courtesy of Dipak Kalra, i-HD – info slide 35

Background summary

Research Project
S1S2
Developement

2011

Champion Program
S1S2
Evaluation

2016

Market Access
S1S2
commercialization

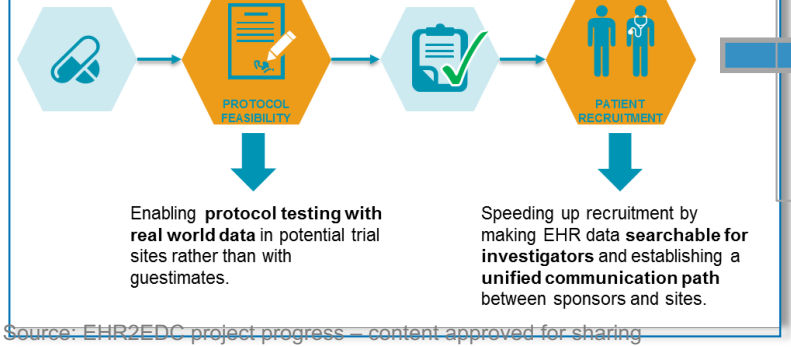
2017

S3
Development
& Evaluation

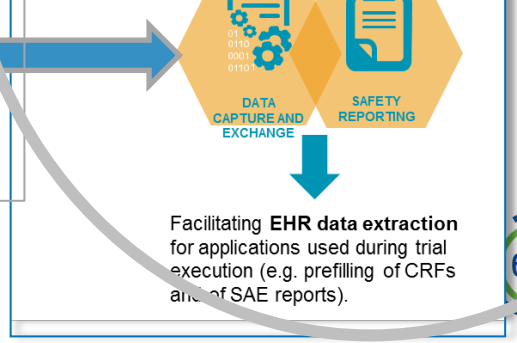
2018

2019

Champion Program

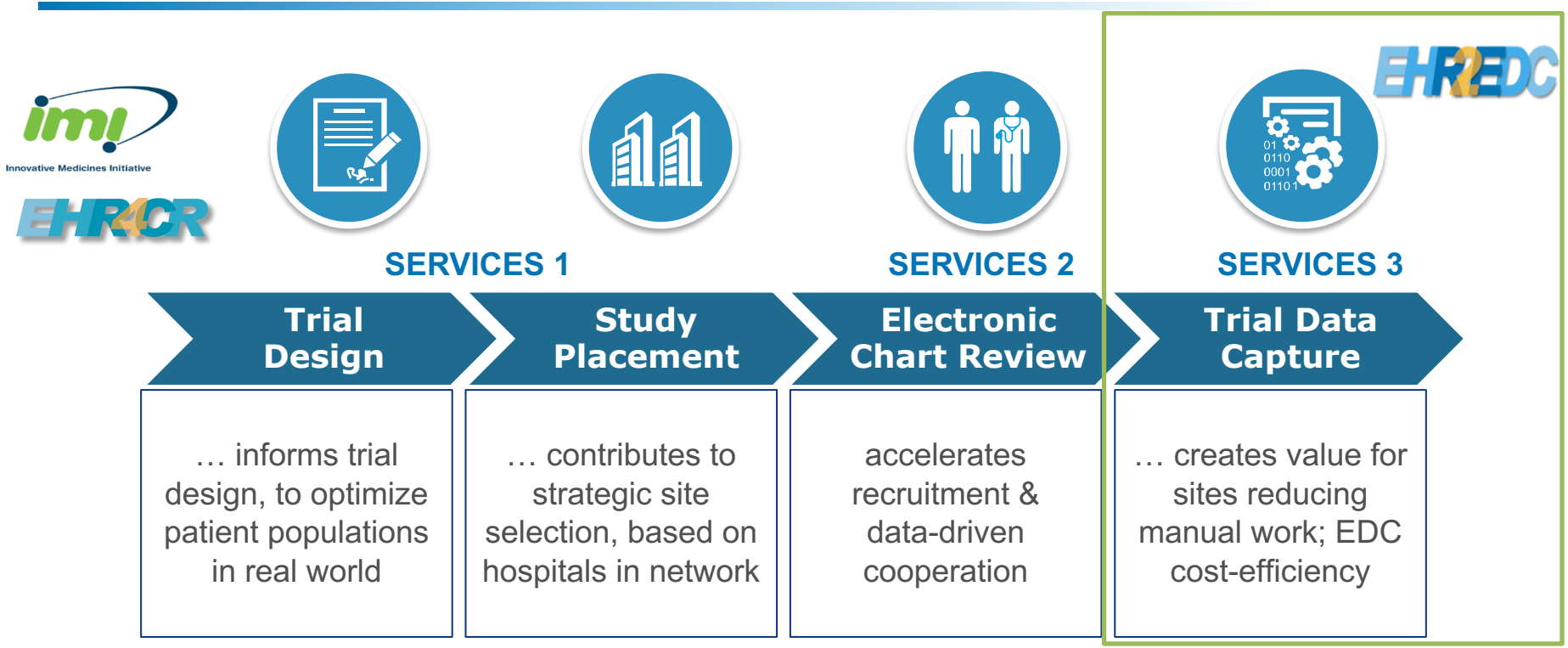


Automatic transfer of **15%** of manually entered protocol data



Source: EHR2EDC project progress – content approved for sharing

Leverage EHR data across the clinical research cycle to optimize research



Source: Lewi & Ammour, *SCOPE Barcelona (2018)*

EHR2EDC …The Foundation

Problem

Manual data entry and required SDVs costs M€ and is prone to errors

How

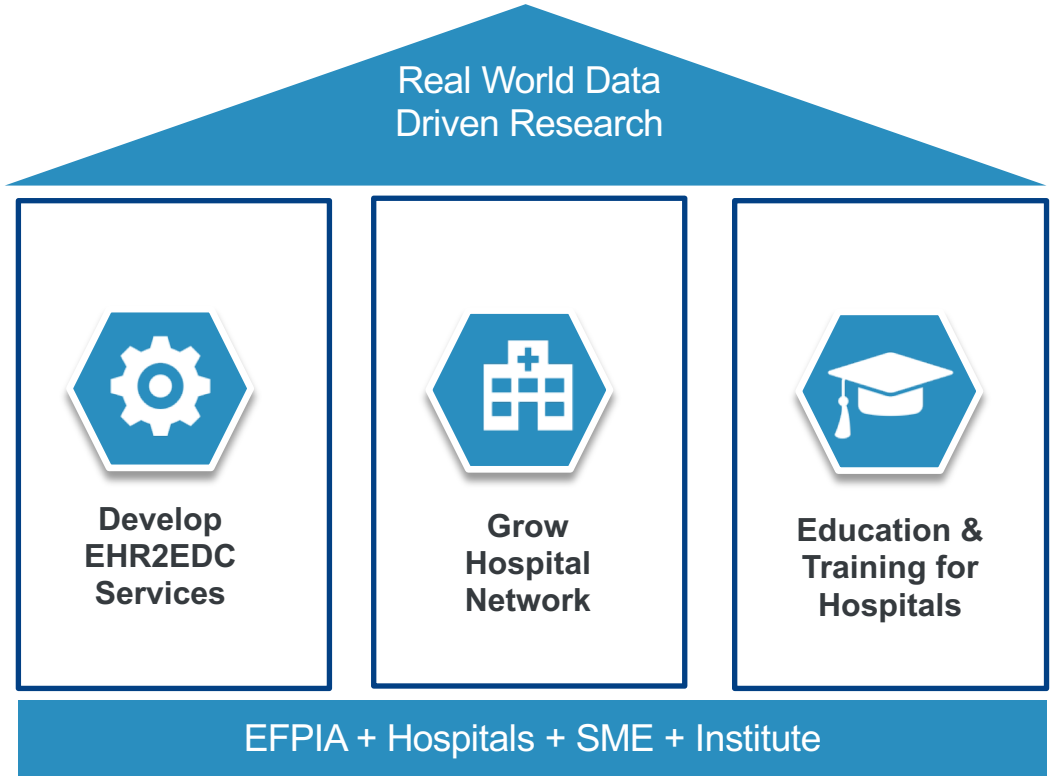
Enable use of Electronic Health Records as a source for Clinical Trials

What

Build First generation *EHR2EDC* technology to reduce double data entry

Source: Lewi & Ammour, *SCOPE Barcelona (2018)*

Objectives & partners



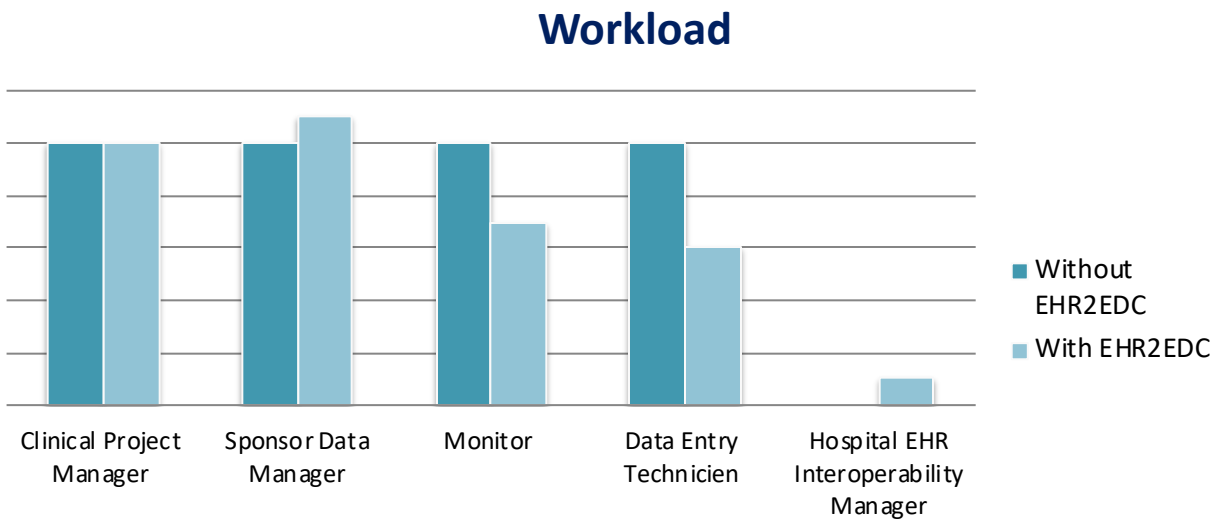
Hospital partners

Source: EHR2EDC Project charter; EIT website

Expected benefits for the clinical trials

↓ Data entry
↓ Monitoring
↓ Data cleaning
↑ Quality
↑ Safety

time & cost savings



Source: EHR2EDC project progress – content approved for sharing

How are we dealing with major challenges using EHRs?

Ensuring compliance with regulatory requirements:

- ✓ Conducted a Data Protection Impact Assessment (DPIA)
- ✓ Ensured that EHR2EDC data flows meet GDPR & GCP requirements
- ✓ Defining a code of conduct for EHR2EDC partners to safeguard data protection
- ✓ Ensuring compliance with new FDA guidance on the use of EHR data in studies

Stringency and uncertainties in new regulatory requirements

Heterogeneity in data standards, difficulty to interoperate

Data element repository:

- ✓ Identified data elements commonly used in clinical trials and routinely collected in EHRs
- ✓ Developing CIM (Common Information Model)
- ✓ Developed Initial Inventory of EHR2EDC data items (50 data items & > 60000 concepts

Free text extraction and conversion to structured data will be explored as a Proof of Concept during the project

Large portion of data captured as free text

EHR data quality below clinical trial standards

Data Quality Assessment (DQA) will be developed by the i-HD to help HCOs increase the value of EHR data for research. Will be offered as a service – including DQA and Remediation Services

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Source: EHR2EDC project progress – content approved for sharing & reference slide 34

Pilot studies selection

Janssen

- 2 studies – Oncology indications
- 3 different hospitals

Sanofi

- 2 studies – Oncology & Diabetes/CVS indications
- 2 different hospitals

AstraZeneca

- 2 studies – Oncology & CVS indications
- 2 different hospitals

No impact on the study team
No impact on the quality, timelines and budget of the clinical trial

Selection criteria for the pilots:

- Conducted in **at least one** of the EHR2EDC hospital partners (12deOct, IRST, AP-HP)
- Planned to **include patients during evaluation period** (July-Nov 2019)
- The study has **high amount of local lab data**
- **PIs** of the selected studies **are well-known** to our hospital partners

Source: EHR2EDC project progress – content approved for sharing

What is the expected impact?

Reduce trial complexity, enable near real-time patient safety monitoring and reduce research costs

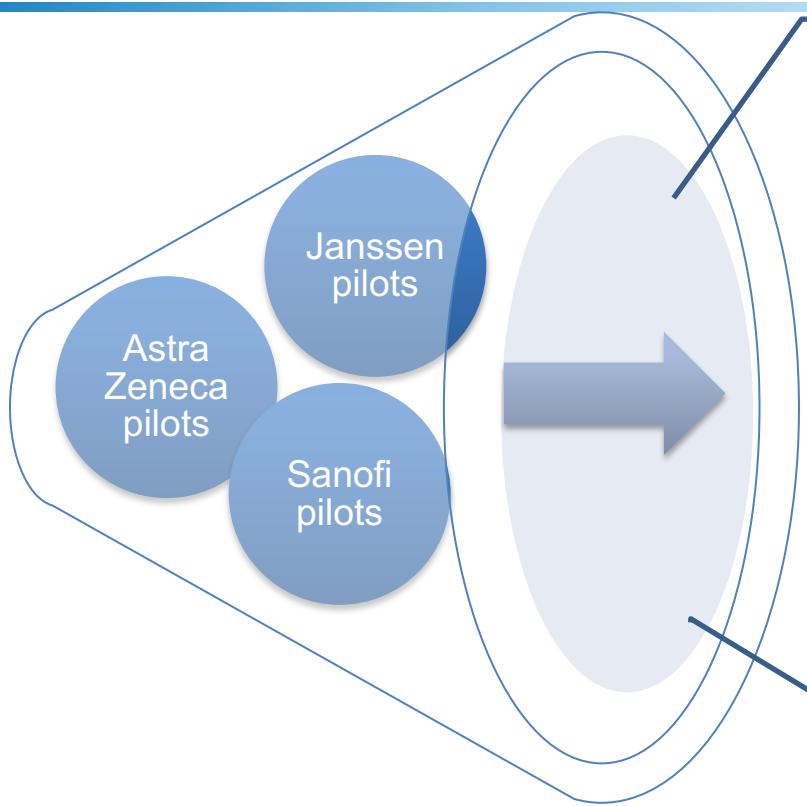
Provide access to patient data in Europe, through a GDPR-compliant data network

Enabling health learning systems to improve patient care and quality / speed of research

EHR2EDC public/ private project is open to new partners for future development

Source: EHR2EDC Project charter; EIT website

Next steps : Project Extension



Moving from pilot phase to project extension:

- 3-year plan (2020-2022)
- Oncology and Cardiovascular
- Public-private Consortium with industry funding
- Two additional key objectives
  1. increase data quality
  2. establish data linkage

Source: EHR2EDC project progress – content approved for sharing

Agenda

- EHR2EDC general overview & objectives
- EHR2EDC novel approach – technical solution: **David Voets**
- Past, current and future solutions for automated data transfer
- Questions

Goals

Hospital clinical data mappings should **work with different studies**

Core of the solution should be EHR and EDC **vendor agnostic**

EHR2EDC

Source: Courtesy from and presented by David Voets/Custodix

eit Health

Goals

Setup of a study at a site should be **a question of minutes**

Must be able to deal with study protocol and mapping **changes transparently**

Must be able to deal with data **corrections**, data coding **changes** & terminology **updates**

Source: Courtesy from and presented by David Voets/Custodix

Goals

Transferred data should be **100% accurate**

Data extractions & transformations applied to meet sponsor's format requirements must be **fully auditable**

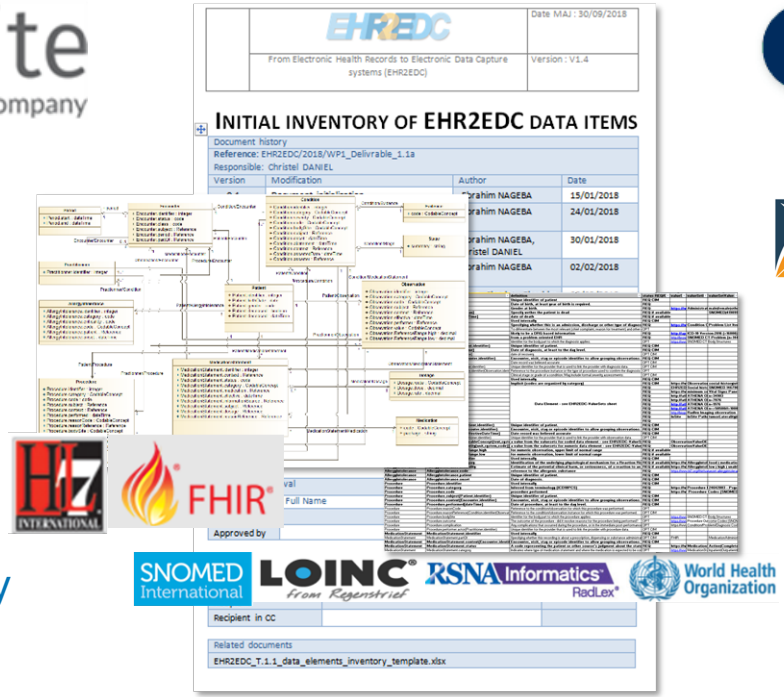
Provenance of data must be **traceable**

Source: Courtesy from and presented by David Voets/Custodix

Semantic Interoperability

InSite
A TriNetX Company

- ✓ Identified data elements commonly used in clinical trials
- ✓ Common information model
- ✓ Alignment with InSite/FHIR and standard clinical terminologies
- ✓ Alignment with CDISC
- ✓ Alignment with sponsor/study eCRF models



CDISC

OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

- ✓ Scope: DM | VS | LB | CM
- ✓ 3 sites
- ✓ 6 clinical trials
- ✓ 360 eCRF variable mappings
- ✓ > 3000 eCRF code mappings

EHR2EDC

Source: Courtesy from and presented by David Voets/Custodix

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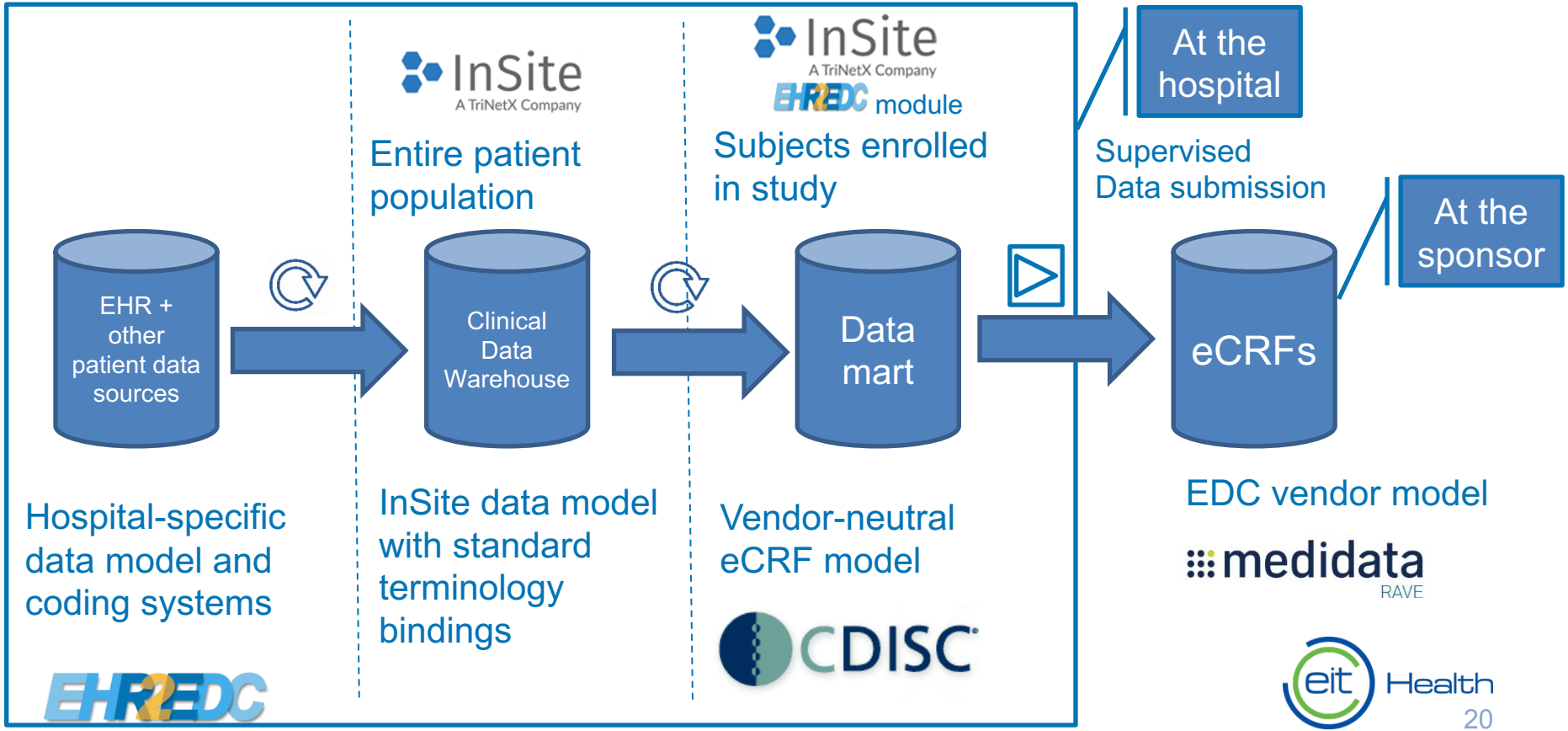
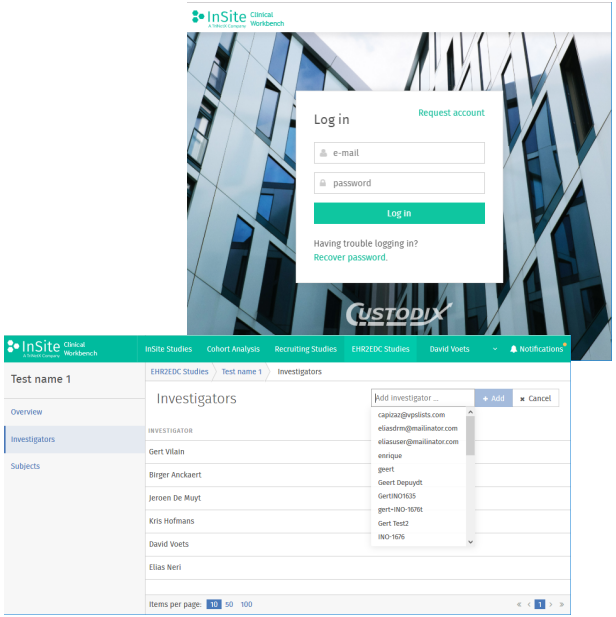
EHR2EDC Leverages InSite's Harmonization Process



Source: Courtesy from and presented by David Voets/Custodix

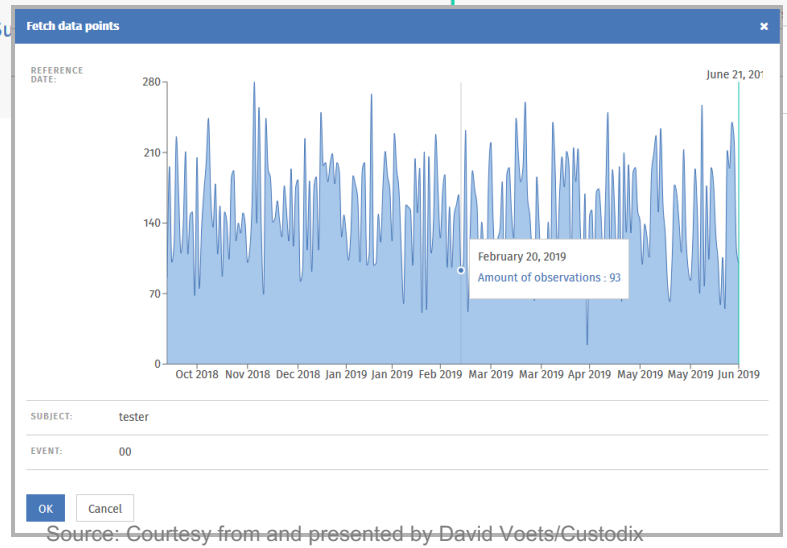
Setup

- **Sponsor (EDC)**
  - Provisioning of test & live environments & accounts
  - Validate new EDC mappings (if any)
- **InSite virtual appliance**
  - Install EHR2EDC module
  - Register study with metadata, queries & EDC connection configuration
- **Site**
  - Firewall update to allow InSite EHR2EDC module to push data to EDC
  - Validate new mappings for study (if any)
  - Staff access and training



Source: Courtesy from and presented by David Voets/Custodix

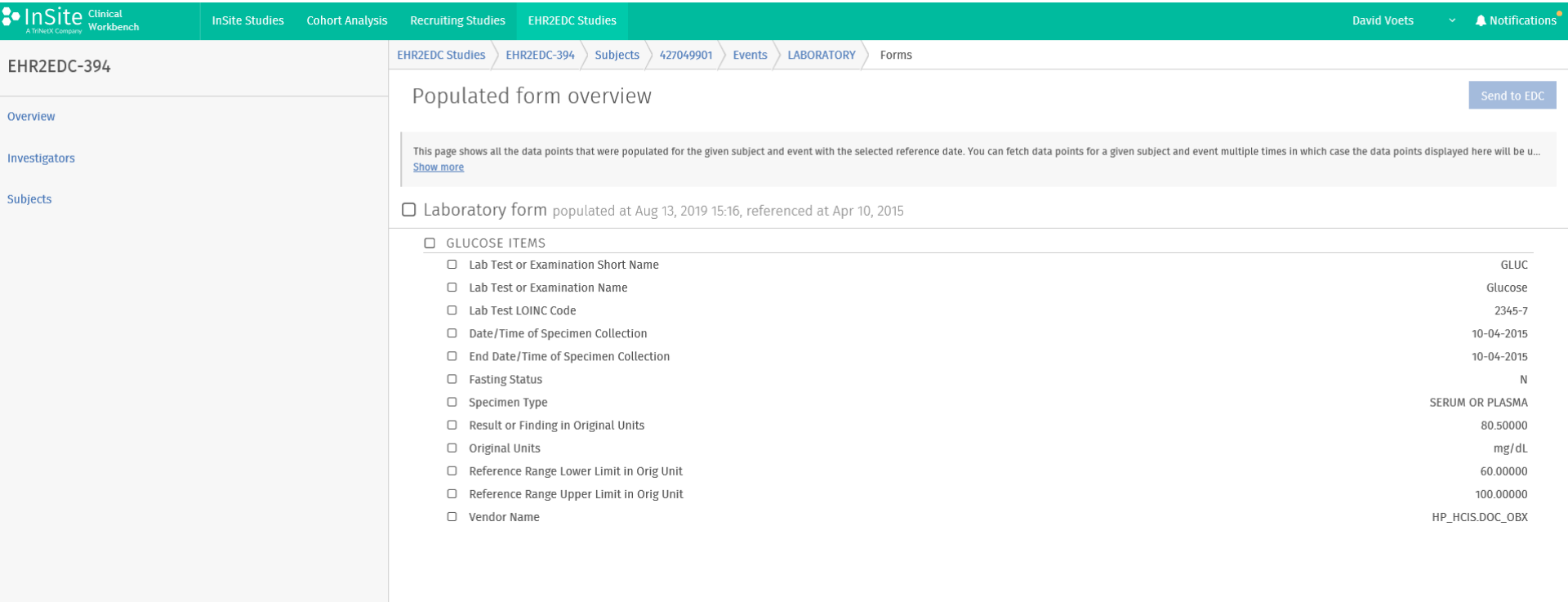
Populate Forms



Source: Courtesy from and presented by David Voets/Custodix

Clinical patient visits & data recordings do typically not correspond 1:1 with study calendar. Interface allows to pick the right reference date for extracting data points.

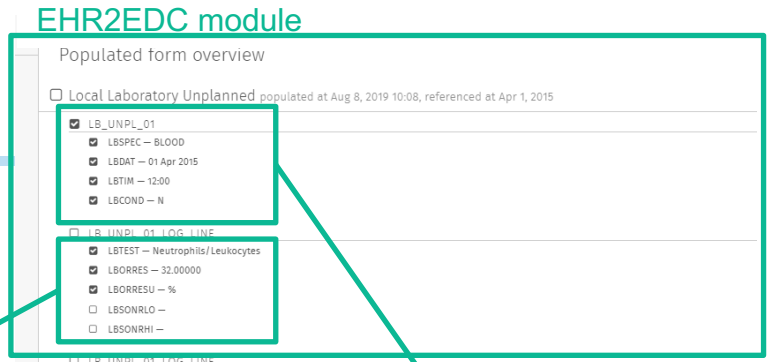
Populated Form Review



User can unselect items that should not be transferred to the EDC

Source: Courtesy from and presented by David Voets/Custodix

EDC integration



Medidata Rave

Subject: **E2v2**
Page: **Local Laboratory Unplanned - Unscheduled Lab Sampling**

Planned Time Point	UNPLANNED
Normal Range Type	LOCAL REFERENCE RANGES
Was there any unplanned lab test result to report?	Yes
Specimen Type	Blood
Collection Date	01 APR 2015
Collection Time	12:00
In case of blood sampling, specify if fasting	No

Log lines

	Test Name	Result	Units	What was the lower limit of the reference range for this test?	What was the upper limit of the reference range for this test?	Reference Range Lower Limit - Standard Units	Reference Range Upper Limit - Standard Units	Sta Unit
1	Neutrophils/Leukocytes	32.00000	%					
2	MCHC	26.00000	g/dL	25.00000	29.00000			
3	Monocytes	1.10000		0.00000	1.00000			
4	Lymphocytes	7.30000		3.00000	11.00000			
5	Basophils/Leukocytes	0.30000	%					

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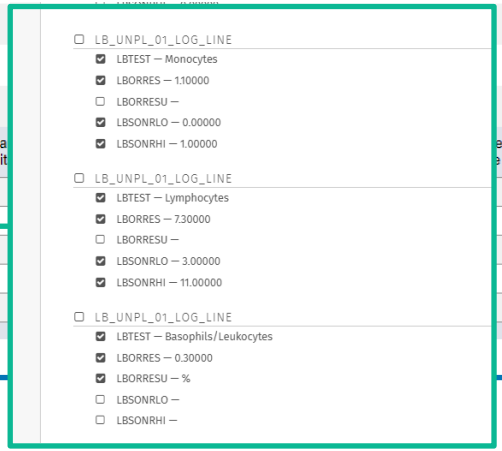
Save Cancel

Log lines



Source: Courtesy from and presented by David Voets/Custodix

Agenda

- EHR2EDC general overview & objectives
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- Past, current and future solutions for automated data transfer: **Massimo Raineri**
- Questions

2006: Issues related to EHR to EDC integration

eClinical forum
March 16, 2006
Brussels

P.B., PHASE FORWARD Chairman and Founder

Fundamental Issues

- General
  - EHR systems data entry components are designed to accept structured and unstructured data gathered about a patient, at any time they are evaluated
  - EDC systems are required to gather highly structured data at specific time points, as quickly and efficiently as possible
  - The process of clinical trial data management is an orchestrated, highly controlled interactive process of data review, revision, and signoff that is highly specific for clinical trials and is virtually absent from most EHR systems
  - There are dozens, if not hundreds of EHR systems in widespread use
  - There are a number of EDC systems in use for 20% -25% of clinical trials

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2006: Predicting the future

eClinical forum
March 16, 2006
Brussels

P.B., PHASE FORWARD Chairman and Founder

Opinion

- The collection of routine clinical trial data should (MUST!) be collected and recorded directly AND electronically into both the medical record and the clinical research databases through a single process
- The path to achieving this is over-simplified by sponsors, healthcare providers, EDC vendors, EHR vendors, standards organizations, governmental agencies, consultants
- This cannot be done alone by either EDC or EHR vendors
- The solution requires the specific collaboration of EHR and CDMS/EDC vendors to develop a robust, commercially-viable solution – with the support and input from all of the above
- **Without this**, we are at least 10-15 years from a solution

EHR2EDC

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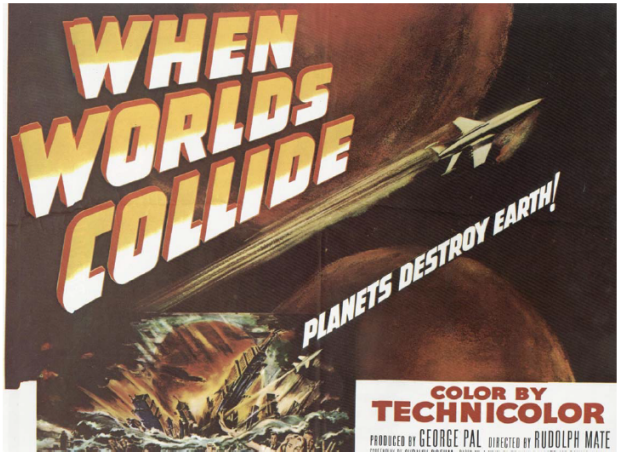
2006: Uncertainty

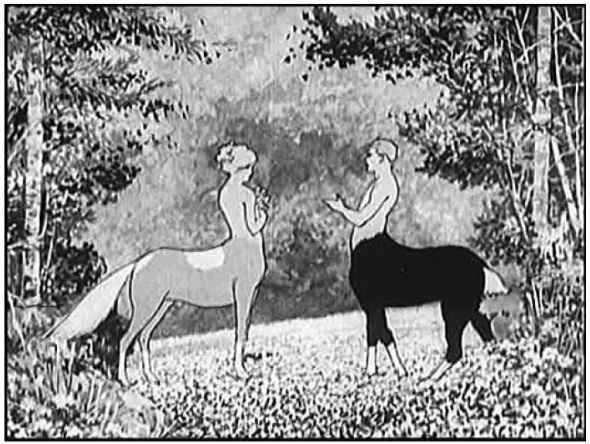
eClinical forum
March 16, 2006
Brussels

P.B., PHASE FORWARD Chairman and Founder

EHR/EDC: Disaster in the making?



Or an idylllic future?

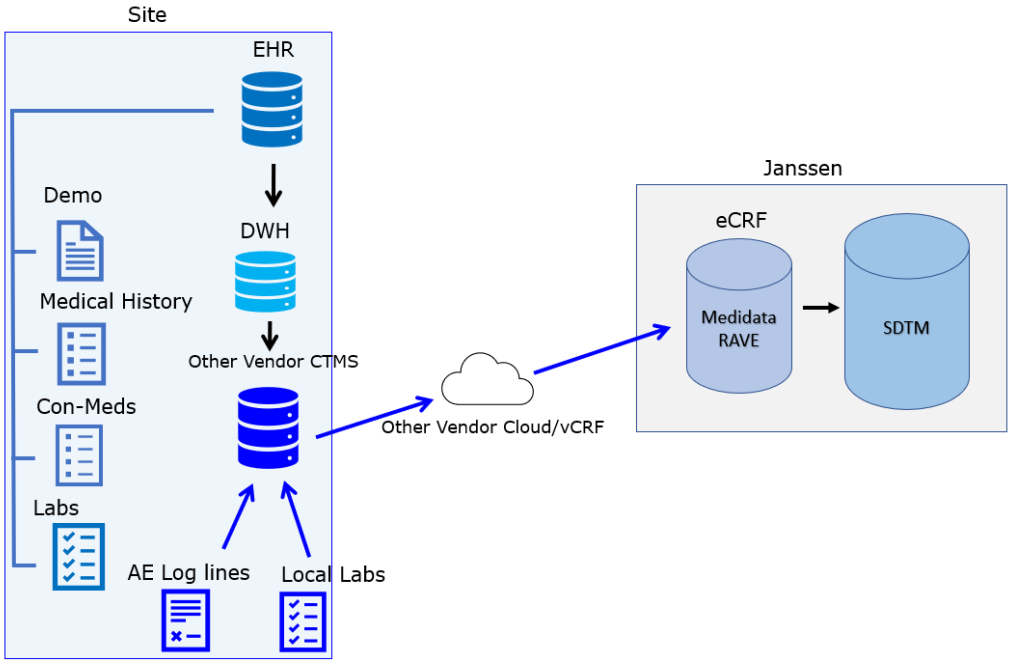


2019 - EUROPE: EHR2EDC PROJECT

- Real project, executing pilots and collecting real data!
- Solid consortium and partnership of Hospitals, Sponsors, Institutions and Technical Partners, with proven results (EHR4CR)
- The idea is simple, the implementation is complex
  - Maintenance of mapping tables
  - Governance of standards (central and local)
  - GCP compliance and Computer System Validation
  - Diversity in EHR systems at sites
  - Diversity in RAVE usage at Sponsors

2019 – US: EHR2CRF Project

EHR2CRF Project
Gurparkash Singh
July, 2019 -
Janssen



- Janssen project
- 1 Site
- 2 trials (Phase II and III)
- Target: 95% of fields
- Implementation started ~ 1.5 years ago

US:
- EPIC controls 70% of the market

EU:
- Many home-grown EHR systems
- Language differences
- GDPR

2019 – US: EHR2CRF Project

EHR2CRF Project
Gurparkash Singh
July, 2019 - **Janssen**

- Preliminary numbers are promising and in line with what others are reporting independently
- We need to gather more information on the data fields in context of different EHRs/sites.
- Scalability: Need to expand to additional sites; validate results
- Possible Sites: some sites better prepared for the EHR2CRF work
- Data Fields: selected forms and fields have been tested
- TA: Oncology

Nicely complementing the EU work

2020 AND BEYOND: STEPS

- Identify most suitable:
  - Forms (e.g. Local Labs, Vital Signs, Demographic, Con Meds)
  - Sites (may not necessary be prominent or high enrollers)
  - Trials (e.g.: Early Dev, Platform Trials, Pragmatic Trials)
  - Therapeutic Areas
- Extend:
  - Beyond RAVE
  - Beyond EDC
- Quantify:
  - Measure costs, benefits, impact on quality
  - Assess scalability of forms and sites
- Validate and Release

Questions?

References and links

References to publications and prior presentations

Slide 3:

- EDC Site Survey: Investigational Site Perspectives on Clinical Trial Information Systems. eClinical Forum 2009. www.eclinicalforum.org
- A CenterWatch Publication, February 2017, Volume 24, Issue 02
- DiMasi JA, Grabowski HG, Hansen RW, Innovation in the pharmaceutical industry: New estimates of R&D costs, J Health Econ. 2016 May;47:20-33. doi: 10.1016/j.jhealeco.2016.01.012.
- KA Getz, RA Campo, KI Kaitin - Variability in protocol design complexity by phase and therapeutic area, Drug Information Journal, 2011 - journals.sagepub.com

Slides 7, 8: Martine Lewi, Nadir Ammour : "*Joining Forces to Enter the Digital Age for Clinical Research Data Capture", SCOPE Barcelona, October 2018*

Slide 11: Kellar E, Bornstein S, Caban A et al. (2016) Optimizing the Use of Electronic Data Sources in Clinical Trials: The Landscape, Part 1. Therapeutic Innovation & Regulatory Science 50(6):682-96

Slide 11: Kellar E, Bornstein S, Caban A et al. (2017) Optimizing the Use of Electronic Data Sources in Clinical Trials: The Technology Landscape. Therapeutic Innovation & Regulatory Science 51(5):551-67.

References and links

Links to more information about EIT Health/EHR2EDC, The European Institute for Innovation Through Health Data (i-HD) and the former IMI project EHR4CR

- **EIT Health Information on EHR2EDC:**
  - https://www.eithealth.eu/ehr2edc
  - https://www.eithealth.eu/-/ehr2edc-a-revolution-in-collecting-and-using-health-data-in-clinical-research
- **i-HD website:** https://www.i-hd.eu/
- **EHR4CR website:** http://www.ehr4cr.eu/

Statement

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