Standard-based integration profiles for clinical research and patient safety
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Abstract

EHRs can now be adapted to integrate seamlessly with existing research platforms. However, key challenges need to be overcome in order to provide a platform that functions across many EHR systems.

The IHE Quality, Research and Public Health (QRPH) domain addresses the information exchange standards necessary to share information relevant to quality improvement in patient care and clinical research. In collaboration with CDISC’s Healthcare Link initiative, IHE QRPH has developed a set of integration profiles that specifically address EHR-enabled research.

The panel participants from three European projects will present how subsets of existing IHE QRPH profiles can be pulled together (and extended when necessary) to form a super profile which will standardize and automate the clinical trial process flow.

The EHR4CR project is providing adaptable, reusable and scalable tools and services for reusing data from hospital EHRs for Clinical Research. TRANSFoRm is developing an informatics infrastructure to support the learning healthcare system in European Primary Care. SALUS project is providing scalable, standard based interoperability framework for sustainable proactive post market safety studies. Overall, the panel will discuss the key steps towards realizing a joint EHR4CR/TRANSFoRm/SALUS European projectathon demonstrating EHR-enabled clinical research across Europe using standard-based integration and content profiles.

General description of the panel and issue(s) that will be examined

- EHRs can now be adapted to integrate seamlessly with existing research platforms thus creating a unique opportunity for many stakeholders, including hospitals, clinical research promoters, pharmaceutical industry and policy makers. However, key challenges, including security and semantic interoperability issues, need to be overcome in order to provide a platform that functions across many EHR systems.

- A set of 9 IHE QRPH profiles and standards that can be pulled together to form a super profile which will standardize and automate the clinical trial process flow of the EHR4CR platform from the patient recruitment to the submission of the clinical trial data to the sponsors will be presented. These profiles address the aspects of
  - i) representing and sharing a clinical research protocol for its execution (CRPC(Clinical Research Process Content), RPE(Retrieve Process for Execution)),
  - ii) representing and sharing clinical research documentation (eCRF, adverse event reporting form) to be pre-populated by existing clinical data in EHRs (RFD(Retrieve Form for Data Capture), CRD(Clinical Research Document), DSC(Drug Safety Content), RSP(Relegation Service Profile)),
  - iii) addressing confidentiality and security aspects (CT(Consistent Time), XUA(Cross-Enterprise User Assertion), ATNA(Audit Trail Node Authentication))
  - iv) additional profiles, currently in the proposal stage, will further refine and extend these capabilities.

- The panel participants will present their technical implementation approaches for integrating EHRs to clinical research and compare it to the specification of the IHE QRPH integration profiles.

- The panel participants will propose a global use case for a projectathon that leverages the use cases of each of the profiles involved (from the ITI technical framework (CT, XUA, ATNA, RFD) and the QRPH technical framework (CRD, DSC, CRPC, RPE)). This global use case reproducing a clinical trial timeline will be a first step towards global interoperability between EHR4CR, TRANSFoRM and SALUS platforms and towards a pan-EU capability for clinical research and patient safety.

- The panel participants will especially focus on semantic interoperability issues. Integrated interoperability for clinics across countries in Europe, requires widespread access to published and maintained collections of coherent and quality-assured semantic resources, including models such as archetypes and templates (providing clinical context) that are based on reference information models (e.g HL7 RIM, openEHR),
standardized data elements based on ISO data types and linked to well specified multi-lingual terminology value sets derived from high quality ontologies. The panel will discuss the specific role of the CDISC SHARE initiative and how semantic resources should be defined, validated, and disseminated. The panel will also discuss how users should be educated to improve the quality and consistency of EHR documentation and the re-use of primary health data.

IHE Quality Research and Public Health, CDISC’s Healthcare Link

*Landen Bain* - CDISC USA

The IHE Quality, Research and Public Health (QRPH) domain, in collaboration with CDISC’s Healthcare Link initiative, addresses the information exchange and electronic health record content standards necessary to share information relevant to quality improvement in patient care and clinical research. Research and clinical trials require identification of patterns of clinical presentation to select patients for inclusion (with consent) in research protocols. Subsequent management, follow up and clinical information requirements require infrastructure and high-level content gathering capabilities similar to those required by quality initiatives and public health. The QRPH domain addresses specifications for patient selection, individual and aggregate data reporting, and privacy and security constraints for re-use of patient information, enabling experts in health quality, research and public health to collaborate and coordinate their activities.

EHR4CR

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The EHR4CR project (http://www.ehr4cr.eu/) is one of the largest public-private partnerships aiming at providing adaptable, reusable and scalable solutions (tools and services) for reusing data from hospital Electronic Health Record systems for Clinical Research. The project is building a platform (systems, organizational structure, data interoperability, governance model, etc.) to demonstrate the viability and scalability of the EHR4CR business model through pilots. The EHR4CR platform aims to implement four use cases from clinical research lifecycle – clinical protocol feasibility, patient identification and recruitment, clinical trial execution and adverse event reporting – to be demonstrated by 10 pilots throughout 5 European countries. Implementing the first use case - use of EHRs or CDWs for eligibility determination - requires: (i) the definition of a formal representation of eligibility rules, and (ii) a semantic mediation between clinical constraints expressed in the eligibility criteria and patient data routinely collected in heterogeneous clinical systems. The EHR4CR Semantic Interoperability Framework provides a template-based query interface at the User Workbench, which allows practitioners to define eligibility criteria based on the standardize terminologies, data elements and value sets using the EHR4CR Terminology. Standard-based computable eligibility criteria are represented as formal queries. Based on the defined formal queries and pre-defined terminology mappings in the terminology server, we apply terminology-based query expansion techniques to obtain an extended query, which can then be transformed and distributed across different clinical data warehouses to obtain more comprehensive query results.

TRANSFoRm

*Brendan Delanay, MD, PhD – King’s College of London, Vasa Curcin PhD - Imperial College London*

TRANSFoRm (www.transformproject.eu) project aims to enhance the safety and evidence base of clinical practice in European Primary Care by developing a modular informatics infrastructure, including provenance, security, and data integration framework, to support a learning healthcare system in the EU. The concept is demonstrated through three use cases covering the requirements of phenotype-genotype studies, randomized controlled trials and knowledge translation in the form of decision support for diagnosis. TRANSFoRm takes a model-based approach, defining models to express both primary care research data and workflow, including computable expressions of eligibility criteria for clinical studies. The clinical data model (CDIM) is maintained as an ontology within LexEVS terminology server, with local data mappings to source data created dynamically when required. The research data model is brought together with the clinical data model through user tools in each of the use cases that utilize computable CDIM expressions for concepts such as demographics, diagnoses, vital signs, medication, or lab results. Upper-level CDIM classes have been defined in accordance with BFO principles. Temporal characteristics can be expressed as absolute and/or relative to a specific occurrence or a range (e.g. dates of encounter or diagnosis). A reference terminology is using the NLM provided mappings via UMLS, extended with the addition of mappings to ICPC2 and Read codes v 2 and 3. The business processes defined in the Clinical Research Information Model (CRIM) are implemented in concrete software tools, which use the provenance framework to capture the execution details in a unified provenance representation across the entire research workflow. This allows the full execution
history of the TRANSFoRm system to be queried, verified, and audited in a consistent manner, irrespectively of the heterogeneity of software tools used.

**SALUS**
*Gokce Banu Laleci Erturkmen, PhD - Software Research, Development and Consultancy, Ankara, Turkey*

Pre-approval clinical trials cannot possibly ensure that a drug will not have disastrous side effects once it arrives on the market. Post-approval drug safety data gathering was put in place to address this problem, but as implemented, it has not proven to be as effective as hoped. This is due to the fact that, current post market safety studies largely depend on the submission of spontaneous case reports where underreporting is a major problem. The need for a proactive approach is apparent, where safety data from multiple sources are actively monitored, linked and analyzed. Effective integration and utilization of electronic health records (EHR) can help to improve post-market safety activities on a proactive basis. There have been already prototype studies to monitor EHRs for simplifying adverse drug event (ADE) reporting, and also for signal detection by screening multiple EHRs, however these tools are directly built on top of EHR/EMR systems through proprietary interfaces. It is apparent that the promise of proactive, continuous monitoring of multiple sources cannot be achieved through such proprietary integrations. To facilitate wide scale proactive post market safety studies, there is a need for a new capacity enabling accessing the data locked in multiple different heterogenous EHR systems. In SALUS project (www.salusproject.eu), we aim to provide a standard-based interoperability framework that will enable execution of a variety of different intelligent data analysis methods for mining and analyzing real-time patient data in communication with disparate heterogeneous EHR systems. SALUS will provide:

- Functional interoperability profiles based on existing IHE profiles (by extending them when necessary) and supporting open source toolsets enabling EHR systems and clinical research systems to communicate and exchange EHR data for post market safety studies through a common transport protocol
- Semantic interoperability solutions enabling meaningful interpretation of the exchanged EHR data. This will be achieved through the definition of a core common data element set represented as an ontology (based on the existing and evolving standards including CDISC CDASH/ODM, CDISC SHARE, BRIDG Domain model, available HL7 CDA templates, CEN EN 13606 archetypes and OMOP CDM). This core ontology consisting of common data element (CDE) set will be established through a systematic approach by examining the data requirements of the selected SALUS use cases and harmonization of the selected CDEs will be supported through a toolset in conformance to ISO/IEC 11179 standard for metadata registries. On top of this core CDE ontology, we will provide a semantic mediation framework that enables

All participants have agreed to take part on the panel.