A SEMANTIC INTEROPERABILITY FRAMEWORK FOR REINFORCING POST MARKET SAFETY STUDIES

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ABSTRACT

A SEMANTIC INTEROPERABILITY FRAMEWORK FOR REINFORCING POST MARKET SAFETY STUDIES

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Depending mostly on voluntarily sent spontaneous reports, pharmacovigilance studies are hampered by low quantity and quality of patient data. Enabling safety analysts to seamlessly access a wide range of Electronic Health Record (EHR) sources for collecting de-identified medical data sets of selected patient populations and tracing the reported incidents back to original EHRs can provide major improvements for such post market safety studies. The adoption of EHR systems and data exchange among these systems are rapidly increasing due to a number of national and cross-border initiatives. Although the main priority of these systems is improving clinical care, we demonstrate that the same systems and interfaces can be exploited for post market safety studies as well.

We have developed an ontological framework where EHR sources and target clinical research systems can continue to use their own local data models, interfaces and terminology systems; while both structural and semantic interoperability are handled through rule-based reasoning on formal representations of different models and terminology systems maintained in our Semantic Resource Set. The Common Information Model at the core of this set acts as the common mediator.

Our semantic interoperability framework for post market safety studies is scalable. The quantity and quality of the information provided through our framework to the safety analysts is a significant improvement compared to traditional methods. Semantically mediating all the patient data and terminology systems in formalized representations allows us to extend the capabilities of our tools easily.

Keywords: Secondary Use, Post Market Safety Studies, Electronic Health Records, Interoperability, Semantic Web

ÖZ

PAZAR SONRASI GÜVENLİK ÇALIŞMALARINI DESTEKLEMEK İÇİN BİR ANLAMSAL BİRLİKTE ÇALIŞABİLİRLİK SİSTEMİ

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Çoğunlukla gönüllü olarak gönderilen spontan raporlara bağlı olan farmakovijilans çalışmaları, düşük nicelik ve nitelikteki hasta verileri tarafından sekteye uğratılmaktadır. Güvenlik analistlerine seçtikleri hasta popülasyonlarının kimliksizleştirilmiş tıbbi veri setlerini toplamaları ve raporlanmış olayları orijinal Elektronik Sağlık Kayıtlarına (ESK) kadar takip edebilmeleri için geniş bir yelpazedeki ESK kaynaklarına sorunsuz erişmelerini mümkün kılmak, pazar sonrası güvenlik araştırmaları için büyük gelişmeler sağlayabilir. ESK sistemlerinin benimsenmesi ve bu sistemler arasındaki veri alışverişi pek çok ulusal ve sınır ötesi girişim neticesinde hızla artmaktadır. Bu sistemlerin temel önceliği klinik bakımı iyileştirmek olsa da, biz aynı sistemler ve arayüzlerden pazar sonrası güvenlik araştırmaları için de faydalanılabileceğini gösteriyoruz.

ESK kaynakları ve hedef tıbbi araştırma sistemleri kendi yerel veri modellerini, arayüzlerini ve terminoloji sistemlerini kullanmaya devam ederken; yapısal ve anlamsal birlikte çalışabilirliğin Anlamsal Kaynak Kümemizde barındırılan farklı modellerin ve terminoloji sistemlerinin formal ifade edilişleri üzerinde kural tabanlı uslamlama ile üstesinden gelindiği bir ontolojik altyapı geliştirdik. Bu kümenin çekirdeğinde yer alan Ortak Veri Modelimiz uzlaştırıcı olarak görev yapmaktadır.

Pazar sonrası güvenlik çalışmaları için geliştirdiğimiz anlamsal birlikte çalışabilirlik sistemi ölçeklenebilirdir. Altyapımız üzerinden güvenlik analistlerine sunulan bilginin niteliği ve niceliği geleneksel yöntemlere kıyasla kayda değer bir iyileştirmedir. Bütün hasta verilerini ve terminoloji sistemlerini formal ifade edilişleri vasıtasıyla anlamsal olarak uzlaştırmak bize araçlarımızın yeteneklerini kolayca genişletme imkanı sunuyor.

Anahtar Kelimeler: İkincil Kullanım, Pazar Sonrası Güvenlik Araştırmaları, Elektronik Sağlık Kayıtları, Birlikte Çalışabilirlik, Anlamsal Web

To my dear wife, Eda...

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LIST OF ABBREVIATIONS

ADE	Adverse Drug Event
CCD	Continuity of Care Document
CCR	Continuity of Care Record
CDASH	Clinical Data Acquisition Standards Harmonization
CDISC	Clinical Data Interchange Standards Consortium
CDM	Common Data Model
CIM	Common Information Model
CM	Care Management
CSCT	Case Series Characterization Tool
DAM	Domain Analysis Model
DWH	Data Warehouse
eCRF	electronic Case Report Form
EHR	Electronic Health Record
HL7	Health Level Seven
HQMF	Health Quality Measures Format
ICSR	Individual Case Safety Report
IHE	Integrating the Healthcare Enterprise
IT	Information Technology
MI	Myocardial infarction
N3	Notation 3
NLP	Natural Language Processing
OMOP	Observational Medical Outcomes Partnership
OWL	Web Ontology Language
PCC	Patient Care Coordination
PHR	Personal Health Record
QED	Query for Existing Data
QEDExt	Extended IHE QED
RDF	Resource Description Framework
RDFS	RDF Schema
REST	Representational State Transfer
RMIM	Refined Message Information Model
SAQM	Safety Analysis Query Manager

SIL	Semantic Interoperability Layer
SIL-DS	Semantic Interoperability Layer Data Service
SKOS	Simple Knowledge Organization System
TIDSQS	Technical Interoperability Data Source Query Service
UKD	University Hospital of Dresden
UMC	Uppsala Monitoring Centre
UML	Unified Modelling Language
UMLS	Unified Medical Language System
WHO	World Health Organization
XMI	XML Metadata Interchange
XML	eXtensible Markup Language
XSD	XML Schema Definition
XSLT	Extensible Stylesheet Language Transformations

CHAPTER 1

INTRODUCTION

The process of approving pharmaceutical agents (i.e. drugs) for use in humans usually hinges on establishing the efficacy of the agent. This is usually achieved through appropriately designed and rigorously analyzed randomized clinical trials. Whilst certain safety aspects are established though the evaluation of the development program ranging from animal studies to dedicated large trials, for most approved agents however, there are limited data for ensuring the safety of the product at approval. These include, for example, the risk of rare events which are not identified in the clinical trials due to their limited size, or delayed effects of the drug due to the limited duration of the trials. Furthermore, clinical trials usually have exclusion criteria, e.g. the elderly, or pregnant women, and therefore there are little or no data on certain groups available prior to approval, but who may ultimately use the agent. Moreover, the pattern of drug use in clinical trials may not necessarily reflect the real-world use once the drug reaches the population and therefore may impact safety.

For these reasons, while pre-market safety analysis through clinical trials remains vital, there is considerable attention towards improving the reporting and collection of post market data. After authorization, all medicinal products continue to be observed through pharmacovigilance studies to monitor their safety profiles. This phase is known as Phase-IV clinical trials, post market safety studies or observational studies. Current post market safety surveillance and reporting activities are largely based on voluntarily sent spontaneous reports of suspected adverse drug events (ADEs) sent to the regulatory bodies by health professionals, and in some countries by patients themselves. While spontaneous reporting remains a cornerstone of pharmacovigilance in the regulator environment, and is indispensable for signal detection, due to recent examples of drug with-drawals [1] stemming from uncommon adverse events after millions of patients were exposed, the need for a more effective and proactive surveillance is reinforced.

The current post market drug surveillance process has several bottlenecks, the first one being underreporting [2, 3]; it has been estimated that only about 5% of harmful ADEs are reported through spontaneous reporting [4, 5]. This is partially due to fact that overloaded medical personnel do not always see reporting as a priority. Another issue is that detecting adverse events may not always be straightforward, hence can be overlooked. Secondly, the quality of the data collected through spontaneous reporting is low [6], and finally spontaneous reports only report adverse incidents while the information related to other patients who used the drug but not experienced adverse

events, i.e. the denominator data, is missing [7].

As a result, there is a clear need for complementary pharmacovigilance activities. Relative to individual case safety reports (ICSRs) for reporting ADEs, Electronic Health Records (EHRs) cover extended parts of the underlying medical histories, include more complete information on potential risk factors, and are not restricted to patients who have experienced a suspected ADE [8]. It is clear that enabling the secondary use of information from health care settings efficiently will improve the effectiveness of clinical research processes [9]. Hence, there is a great potential in accessing EHRs for tracing safety reports back to medical summaries of patients, and also secondary use of EHRs for complementary pharmacoepidemiology studies for clinical signal evaluation and validation. For example, Uppsala Monitoring Centre (UMC) on behalf of the WHO International Programme for International Drug Monitoring analyzes the WHO global ICSR database, VigiBase, for potential signals [10, 11]. Their objective is to characterize the reported cases in comparison with a selected background population for checking whether there are other explanations more likely to cause the reported adverse event than the exposure to drug of interest. Yet, the data sets used for such studies are limited both in quantity and also considering the extent of medical information covered and geographical spread. Accessing a wide range of EHR sources seamlessly to collect the background information of any selected patient population, more importantly tracing the reported incidents back to original EHRs can provide major improvements for such clinical validation studies, as we demonstrate in our work.

1.1 Objectives

Our objective is to enable safety analysts to seamlessly access EHR data from heterogeneous healthcare systems, so that they are able to trace ICSRs back to EHRs and collect de-identified medical data sets of selected populations to run complementary safety analysis studies for adding meat to the bones of the potential signals. However, there are several challenges:

- The clinical care and the clinical research domains use very different content models as "models of use" for representation of medical data. In contrast to Clinical Data Interchange Standards Consortium (CDISC) [12] and Observational Medical Outcomes Partnership (OMOP) [13] models used in the clinical research domain, in the clinical care domain, the most widely used content standards are by Health Level Seven (HL7) [14] and Integrating the Healthcare Enterprise (IHE) [15].
- Similarly, the transactions that are used for medical data exchange are quite different, led by the same major initiatives above.
- The medical terminology systems as "model of meaning" for representing structured medical data in the two domains are quite different as well. While MedDRA and CDISC Terminology are commonly used in the clinical research domain; the prominent terminology systems in the clinical care domain include SNOMED CT, ICD-10 and LOINC (see Section 3.3).

In this thesis, we have developed a Semantic Interoperability Framework that enables non-disruptive and effective integration and utilization of EHR data to reinforce post market safety studies. The interoperability architecture addresses both structural and semantic interoperability between clinical care and clinical research domains. In our framework, we address the above-mentioned challenges by;

- extending the existing standards-based patient data exchange transactions of the EHR sources for supporting population based queries and data, again based on standards,
- identifying and formalizing the local content models of the EHR sources and target clinical research systems,
- defining a Common Information Model (CIM) by considering i) the local content models of the involved systems, ii) the clinical data requirements of the identified post market safety study methods, and iii) widely-used international content standards, to act as the mediator among different models,
- semantically mediating the formalized representations of the different local content models with the CIM by implementing conversion rules, and thus preventing n-to-n mappings that would be necessary without the CIM as the mediator,
- representing all the required terminology systems as ontologies within our Semantic Resource Set, which include the CIM, local models and conversion rules as well, and linking with the CIM automatically, and
- utilizing reliable mappings among codes from different terminology systems again within our Semantic Resource Set, and then enabling terminology reasoning for achieving semantic interoperability between data sources and the requestors.

We also provide supporting safety analysis tools that run on top of our Semantic Interoperability Framework to query and retrieve de-identified medical data of the defined populations for post market safety studies.

Our work is supported by the European Commission's 7th Framework Programme within the scope of "Scalable, Standard based Interoperability Framework for Sustainable Proactive Post Market Safety Studies" (SALUS) project [16]. On the clinical care side, we have two EHR sources: the Data Warehouse (DWH) of the Lombardy Region in Italy and the ORBIS EHR system of the University Hospital of Dresden (UKD) in Germany (see Section 4.2 for more details). On the clinical research side, we have two end-users: Uppsala Monitoring Centre (UMC) on behalf of the WHO International Programme for International Drug Monitoring as the pharmacovigilance center and ROCHE as the pharmaceutical company.

Post market safety studies is still a wide area where several different analyses can be done by following different approaches. Therefore, as one of the first activities in the SALUS project, we have identified the concrete pilot application scenarios to be implemented, which are presented below under two main headings:

- Suspected ADE Notification and Reporting

  - *Notification of Suspected ADEs:* Running on top of an EHR system, it tries to detect some suspicious ADEs and alert the health professional. Used by Lombardy and UKD.
  - *Semi-automatic ADE Reporting:* Once a suspicious ADE is detected, it assists the health professional by prepopulating the ICSR form to be sent to the regulatory body, with patient data automatically retrieved from the EHR system. Used by Lombardy and UKD.

- Safety Analysis Methods
  - *Case Series Characterization:* The aim is adding meat to the bones by characterizing the cases (i.e. foreground population) and contrasting them to a background population; e.g. what differs between the patients having a myocardial infarction within two weeks of nifedipine intake to all the other patients taking nifedipine? Used by UMC.
  - *Temporal Pattern Characterization:* The aim is again adding meat to the bones, this time by checking a temporal association between a drug of interest and a medical event of interest; e.g. can we see a pattern suggestive of a causal relationship between nifedipine and flushing? This is useful for assessing positive impacts of drugs as well. Used by UMC.
  - *Temporal Association Screening:* The aim is finding needles in the haystack, i.e. discovering new potential signals, by doing an open ended screening of large portions of data; e.g. are the any drugs that might be associated with causing myocardial infarction? Used by UMC.
  - *Post Marketing Safety Studies:* The aim is comparing the observed number of cases of a specific adverse event in a regulated clinical trial with the expected number of cases derived from a similar population (indication) using secondary data sources; e.g. estimate incidence rates of chronic heart failure in diabetic patients with a recent acute coronary syndrome event on different diabetic medications. Used by ROCHE.

Our work in this thesis provides the underlying Semantic Interoperability Framework that is used commonly in all these pilot application scenarios. Furthermore, our work focuses on the scenarios related with safety analysis methods, specifically to the case series characterization scenario for which a Web application to be used by the safety analysts has been developed as a complete solution.

This thesis is organized as follows. Chapter 2 briefly summarizes the background on enabling technologies and standards. The Semantic Resource Set composed of the Common Information Model, local models, terminology systems and the mappings is presented in Chapter 3. The architecture of the Semantic Interoperability Framework is explained in detail in Chapter 4. In order to demonstrate the benefits provided to the safety analysts and to better explain the interactions among the components involved in the architecture, a step by step execution of a complete case series characterization scenario is provided in Chapter 5. Chapter 6 presents the related work in the literature in comparison with our architecture and approach presented in this thesis. Finally, Chapter 7 concludes the thesis supported with some discussions and suggests possible future research directions.

CHAPTER 2

BACKGROUND ON ENABLING TECHNOLOGIES

The main enabling technologies and standards that are used in our work are presented in this chapter, but there is more. Some others such as terminology systems and content models are explained in the next chapter while presenting the Semantic Resource Set.

2.1 HL7 Clinical Document Architecture

Clinical Document Architecture (CDA), previously called Patient Record Architecture (PRA), is a document markup standard that specifies the structure and semantics of a clinical document (such as a discharge summary or progress note) for the purpose of exchange [17]. It is developed by Health Level Seven (HL7) [14], which is a not-for-profit ANSI accredited Standards Developing Organization. Primary goal of HL7 is to provide standards for the exchange of clinical and administrative data among healthcare systems.

A clinical document includes clinical observations and services about care events. A valid CDA document is encoded in XML and conforms to the CDA XML Schema Definition (XSD), once any possible user-specific extensions are removed. HL7 has released two versions of CDA so far. Release 1 (R1) was approved by ANSI in 2000, and Release 2 (R2) in 2005. Throughout the rest of this thesis whenever CDA is mentioned, CDA R2 is referred actually.

A CDA document has two main parts, the header and the body. In the CDA R1, only the header part is derived from the HL7 v3 Reference Information Model (RIM) [18]. In the CDA R2, in addition to the header part, the clinical content in the document body is also derived from the RIM. Therefore CDA R2 model enables the formal representation of clinical statements through CDA entry classes.

The CDA header defines the context of the document by providing information on authentication, the encounter, the patient, and the involved providers whereas the CDA body includes the clinical report. The body part can be either an unstructured blob or a structured hierarchy that involves one or more section components. Within a section, narrative blocks and CDA entries are defined. Machine-processable clinical statements are represented by these CDA entries whereas the narrative blocks are human readable forms of these clinical statements.

CDA has nine entry classes derived from the RIM: Act, Observation, Observation-

Media, SubstanceAdministration, Supply, Procedure, RegionOfInterest, Encounter and Organizer. These entry classes provide a consistent representation of clinical statements across various HL7 v3 specifications. For example, Observation is used for representing clinical observations, SubstanceAdministration is used for representing medication related events, Organizer is used for grouping clinical statements having a common context and Act, as a generic purpose class, is used when the remaining specific entry classes are not appropriate for defining the clinical information. According to their purpose of use, these entry classes enable all the fields to provide information about a clinical statement in a structured and/or coded manner; e.g. SubstanceAdministration has attributes for providing the medicine product, the route of administration, dose, rate and timing of quantity in a structured way.

The generic CDA specification can be constrained through the document-level, section-level and entry-level templates. According to the naming conventions of CDA Release 1, the unconstrained CDA specification is called "CDA Level One". When section-level templates are applied to an unconstrained CDA document, it is called "CDA Level Two". "CDA Level Three" is the CDA specification with entry-level (and optionally section-level) templates applied.

2.2 HL7/ASTM Continuity of Care Document

HL7/ASTM Continuity of Care Document (CCD) [19], one of the most prominent EHR content templates, is defined by constraining the HL7 Clinical Document Architecture, Release 2 (CDA) with requirements set forward in ASTM E2369-05 Standard Specification for Continuity of Care Record (CCR) [20].

CCR was developed to cover information regarding pertinent clinical, demographic and administrative data for a specific patient as a snapshot in time. CCR allows a health professional or systems to collect and aggregate data about a patient and to forward it to other health professionals to support continuity of care. As already described in the previous section, HL7 CDA is a document markup language that specifies the structure and semantics of clinical data for exchange purposes. From a CDA point of view, CCR is a standardized data set (template) by which CDA can be restricted to specify CDA for summary documents. Therefore, CCD is an alternate implementation of the CCR using CDA syntax and format of the proprietary CCR format. CCR specification, itself, also defines an XML schema as a content template for the exchange purposes. However, the HL7 CDA implementation of CCR, that is, Continuity of Care Document (CCD), is more widely-accepted than CCR's own XML schema.

CCD defines a single document template, but there are several section templates and clinical statement templates to be used within this main document template. CCD section templates cover the following health related topics: Payers, Advance Directives, Functional Status, Support, Problems, Family History, Social History, Alerts, Medications, Medical Equipment, Immunizations, Vital Signs, Results, Procedures, Encounters, Plan of Care, Healthcare Providers.

2.3 IHE Patient Care Coordination Templates

EHR content templates are built on top of the well-accepted content standards such as HL7 CDA to further refine these standards by:

- restricting the alternative hierarchical structures to be used within the instances,
- constraining optionality and cardinality of some elements,
- defining the code systems and codes used to classify parts of the document, and
- describing the specific data elements that are included.

We already presented CCD as such a content template in the previous section. Driven by the content module requirements of its integration profiles such as Exchange of Personal Health Record Content (XPHR) [21] and Query for Existing Data (QED) [22], the Integrating the Healthcare Enterprise (IHE) Patient Care Coordination (PCC) Technical Framework further details and multiplies the CCD templates at the document, section and clinical statement levels. Integrating the Healthcare Enterprise (IHE) [15] is a non-profit "integration organization" promoting the coordinated use of established standards such as the HL7 standards to address specific clinical need in support of optimal patient care. For that purpose, IHE develops integration profiles that provide precise definitions of how standards can be implemented to meet specific clinical needs.

Currently, PCC has six main document templates (Discharge Summary, Medical Document, Medical Summary, PHR Extract, PHR Update, Scanned Document) in comparison to the single CCD document template. In addition to document level templates that are defined by IHE PCC, there are many section and entry level templates. Those lists are exhaustive to be presented here. Instead of listing all, a detailed example is provided in this part.

In Figure 2.1, the "Active Problems Section" template of IHE PCC that is based on ASTM/HL7 CCD "Problem Section" template is presented. Each template has at least one template id. The template id of the Active Problems Section is 1.3.6.1.4.1.19376.1.5.-3.1.3.6, and since it refines (i.e. based on) the CCD Problem Section template, it also includes the corresponding CCD template id, which is 2.16.840.1.113883.10.20.1.11. To guarantee a unique meaning, some attributes must have predefined codes from specific terminology systems. For example, the code of the Active Problems Section can have only one value: "11450-4" from the LOINC terminology system [23] corresponding to "PROBLEM LIST". The value of codeSystem attribute presents the unique object identifier (OID) of the LOINC terminology system, which is 2.16.840.1.113883.6.1. A narrative description of the patient conditions is also required to be given through the text element.

HL7 CDA sections are composed of entries. To describe a patient's conditions, the Active Problems Section includes instances of the Problem Concern Entry template. HL7 CDA components are derived from HL7 v3 RIM classes such as "act" or "act-Relationship". In the example, the "Problem Concern Entry" represents a healthcare problem. Therefore it is represented by an act class (<act classCode='ACT') with

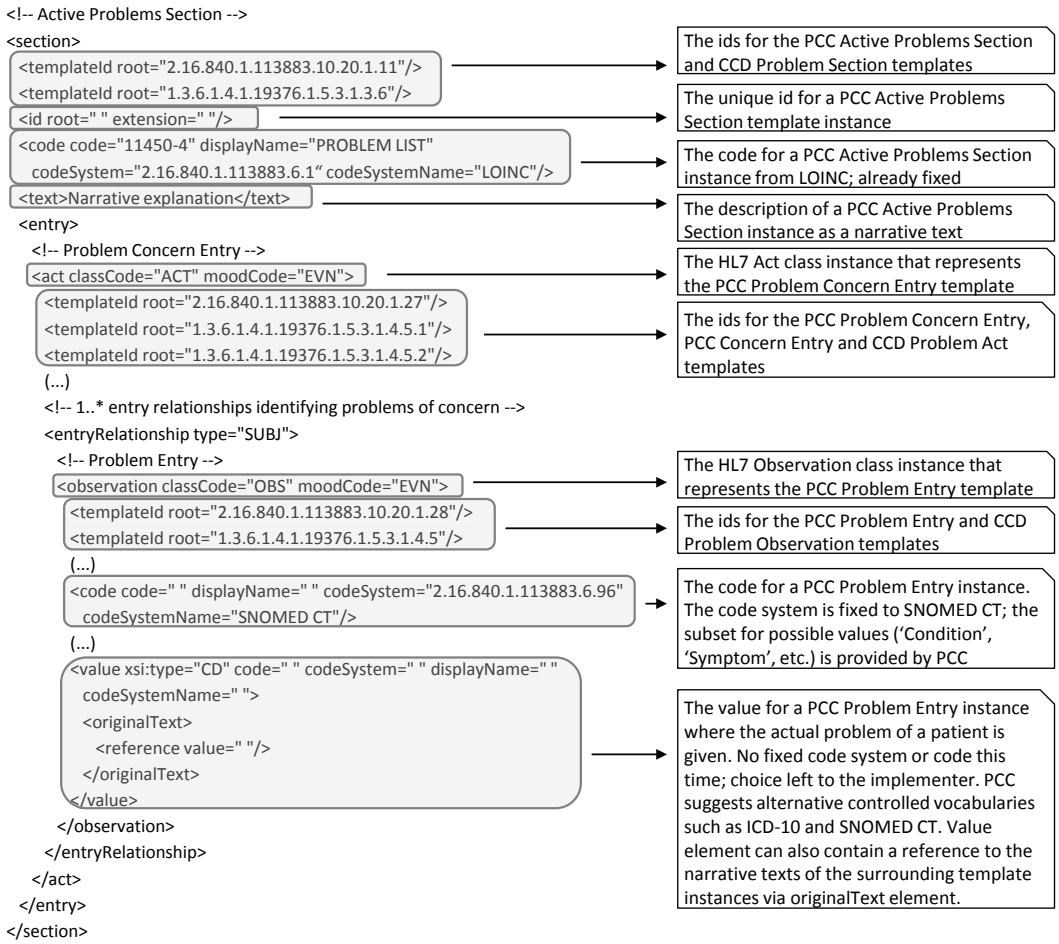

Figure 2.1: IHE PCC Active Problems Section Template based on ASTM/HL7 CCD Problem Section Template

template id 1.3.6.1.4.1.19376.1.5.3.1.4.5.2. Because this problem has already happened, its moodCode is event (moodCode='EVN').

As in the case of Active Problems Section, the Problem Concern Entry template also refines other PCC and CCD templates; hence the corresponding template ids are provided. The Problem Concern Entry allows related problem entries (e.g. coded observations) to be grouped. This makes it possible to represent the history of a concern as a series of observations over time. Each problem entry must be presented within an entry relationship stating that the problem entry is the subject of the concern (<entryRelationship type='SUBJ'>) and should conform to the PCC Problem Entry template with template id 1.3.6.1.4.1.19376.1.5.3.1.4.5, which is actually a refinement of the root CCD Problem Observation template with id 2.16.840.1.113883.10.20.1.28.

Problem Entry template uses the CDA observation element to represent that this observation of a problem (classCode='OBS') has actually taken place (moodCode='EVN'). The code element of Problem Entry template is restricted to a subset from the SNOMED CT terminology system [24] as shown in Table 2.1.

Table2.1: SNOMED CT codes for the code element of the IHE PCC Problem Entry Template

Code	**Description**
64572001	Condition
418799008	Symptom
404684003	Finding
409586006	Complaint
248536006	Functional limitation
55607006	Problem
282291009	Diagnosis

The value element is the place where the actual problem of the patient is given. While the value may be a coded or an un-coded string, its type is always a coded value (xsi:type='CD'). If it is coded, which is essential for the interoperability of the exchanged data, the code attribute should get a value such as a problem, a complaint, a symptom, a finding, a diagnosis or a functional limitation from a controlled vocabulary such as ICD-10 [25], SNOMED CT or others. The Problem Entry template does not restrict the terminology system to be used for the value element; the selection of an appropriate controlled vocabulary is left to the implementers. For example, within the scope of the epSOS project for pan-European piloting of electronic patient summary and prescription data exchange [26], the patient summary template is based on the IHE PCC content templates and for coding the illnesses, syndromes or symptoms of a patient, a subset of the ICD-10 terminology system that consists of 1680 codes (only the 3-digit ICD-10 codes) is selected. Therefore, an epSOS patient summary problem entry instance for a patient with migraine has the following value element: <value code="G43" displayName="Migraine" codeSystem="1.3.6.1.4.1.12559.11.10.1.3.1.44.2" codeSystemName= "ICD-10" xsi:type="CD">. The value element also contains a reference to the originalText in order to link the coded value to the problem narrative text presented within the text element of the root Problem Entry template.

Note that Active Problems Section template is used by several integration profiles of IHE PCC, such as XPHR and QED. Further information about EHR content standards and templates can be found in our Personal Health Record (PHR) interoperability standards survey [27].

In our architecture, PCC and CCD templates are used as content models in the Lombardy Region.

2.4 IHE Query for Existing Data Integration Profile

Using the IHE Query for Existing Data (QED) Profile [22], it is possible to access clinical data sources with predefined queries. There are two actors in this profile, namely the "Clinical Data Consumer" and the "Clinical Data Source", and one transaction, namely, "Query Existing Data" that the consumer uses to query the source. This transaction gets a number of query parameters such as "patientId", "patientName",

"careProvisionCode" and "careRecordTimePeriod". Six different types of queries are defined and each of them is indicated as an option of the "Query Existing Data" transaction. The actor implementing this transaction must support at least one of them: i) Vital Signs Option; ii) Problems and Allergies Option; iii) Diagnostic Results Option; iv) Medications Option; v) Immunizations Option; vi) Professional Services Option. A content template is specified for each result to be returned by the query. Each content template inherits constraints from the CCD and PCC, and defines further constraints such as by setting the units to be used and a specific vocabulary.

For example, a "Clinical Data Consumer" that implements the Problems and Allergies Option can retrieve all problem entries of a specific patient by specifying the code "MEDCCAT", and the result will conform to the PCC Problem Entry template. Similarly, it can specify the code "INTOLIST" which will return the results conforming to the PCC Allergy and Intolerance Concern template.

A "Clinical Data Source" that implements the Problems and Allergies Option, on the other hand, must be able to respond to all vocabulary specified for problems and allergies including "MEDCCAT" and "INTOLIST".

In our architecture, we extend the native QED profile for supporting population based queries and use on top of the Lombardy Data Warehouse. This extension is explained in Section 4.2.1.

2.5 IHE Care Management Integration Profile

IHE Care Management Profile (CM) [28] supports the exchange of information between health IT systems and applications used to manage care for specific conditions. CM describes a publish/subscribe mechanism between source and the consumer systems. It is almost identical with the QED profile but rather than getting an immediate response only for once; the source system keeps sending back the new results that matches the query criteria as they become available. This query is maintained indefinitely and the source system continues to send anything that comes in until the requesting system cancels the subscription.

Some of our pilot application scenarios necessitate subscription to data sources, so we make use of the CM profile for handling subscriptions. As in the case of QED, it is necessary to extend CM as well for supporting population based queries.

2.6 BioPortal

BioPortal [29] is an open repository of biomedical ontologies hosted by the USA National Center for Biomedical Ontology [30]. It gives the ability to browse, search and visualize more than 280 biomedical ontologies including major terminology systems both via Web browsers, REST services and a SPARQL endpoint. It also serves the mapping definitions between these ontologies. BioPortal makes use of the available mappings in the Unified Medical Language System (UMLS) [31] and extends them with natural language processing (NLP) based methods.

In our architecture, we benefit from BioPortal for getting ontological representations of some well-known terminology systems such as SNOMED CT and ICD-10, as explained in detail in Section 3.3. We also use some code mappings among terminology systems provided by BioPortal, but since a majority is created via NLP based methods, they are not totally reliable. Therefore, they are manually reviewed before inclusion in our Semantic Resource Set.

2.7 Semantic Web

Although everything on the Web is machine-readable, they are not readily machine-understandable. This lack of means for machines to automatically process and meaningfully share information on the Web constitutes one of the main barriers to the so called "Semantic Web". In order to fully exploit the opportunities brought by the Web, metadata (semantic representation) of the resources need to be made explicit to make them automatically processable.

The Semantic Web is defined as "a web of data that can be processed directly and indirectly by machines" by its creator Sir Tim Berners-Lee [32]. It is not a replacement, but an extension of the original Web with better methodologies to express meanings of things by representing knowledge in standardized ways, i.e. by defining ontologies [33]. An ontology is a schema for a domain; in other words, is the explicit formal specification of the terms and relations among them in a specific domain.

One of the most important initiatives for describing Semantic Web resources is the Resource Desciption Framework (RDF) [34] developed by the World Wide Web Consortium (W3C). RDF is a general-purpose language for representing information in the Web. Although RDF provides good building blocks for defining a Semantic Web Markup Language, it lacks expressive power. Therefore, for facilitating greater machine interpretability of Web content, the Web Ontology Language (OWL) [35] was introduced by the W3C. More information about RDF and OWL is provided in the following sub-sections.

Through these languages, in the Semantic Web the resources and their relationships are represented with Uniform Resource Identifiers (URIs) [36]. The recommended practice for representing knowledge in the Semantic Web is to use well-known vocabularies (i.e. ontologies) as much as possible. Friend of a Friend (FOAF) [37] is an example popular vocabulary that contains terms and properties related with people such as name, title, phone number and "knows" relationship. It is also possible to use several vocabularies at the same time, by linking one to another, together with the data sets. This is explained further within the scope of Linking Open Data initiative below.

2.7.1 Resource Description Framework

Resource Description Framework (RDF) was developed by the W3C in 1999 as a semantic-network based language to describe Web resources. RDF extends the linking structure of the Web to use URIs to name the relationship between things as well as the two ends of the link (this is usually referred to as a "triple") [34]. A triple is

represented in the *subject (s), predicate (p), object (o)* scheme, where s has a property with value o. In this scheme, s and p shall be represented with URIs, while o can either be a URI (in the case that it refers to another resource) or a literal value. This linking structure forms a directed, labeled graph, where the edges represent the named link between two resources, represented by the graph nodes. In Figure 2.2, a simple RDF graph describing "Eric Miller" as a "Person" identified by `http://www.w3.org/People/EM/contact#me`, with "Dr." as the title and "em@w3.org" as the email address is presented [38].

Figure 2.2: A simple RDF graph describing Eric Miller

RDF Schema (RDFS) [39] was built by the W3C as an extension to RDF, to provide basic elements for the description of ontologies. It defines resources and properties such as "Class", "Property", "subClassOf", "subPropertyOf", "domain", and "range" that are used in specifying application-specific ontologies. RDFS is not very expressive, just allowing the representation of concepts, concept taxonomies and binary relations. For example, it is not possible to restrict the range of properties locally to a class definition, define necessary and sufficient conditions for a class membership, or express the equivalence and disjointness of classes.

2.7.2 Web Ontology Language

The W3C Web Ontology Language (OWL) is a Semantic Web language designed to represent rich and complex knowledge about things, groups of things, and relations between things. OWL is a computational logic-based language such that knowledge expressed in OWL can be reasoned with by computer programs either to verify the consistency of that knowledge or to make implicit knowledge explicit [35].

OWL is a part of the Semantic Web stack of W3C, and it overcomes the limitations

of RDF and RDFS by adding more vocabulary for describing properties and classes: among others, relations between classes (e.g. disjointness), cardinality (e.g. "exactly one"), equality, richer typing of properties, characteristics of properties (e.g. symmetry), and enumerated classes.

Through inferencing, the implicit information hidden in the explicit knowledge can be extracted by making use of the relations among resources. OWL provides three increasingly expressive sub-languages for use by specific communities of implementers and users, according to different requirements [40]:

- *OWL Lite* supports those users primarily needing a classification hierarchy and simple constraints. For example, while it supports cardinality constraints, it only permits cardinality values of 0 or 1.

- *OWL DL* supports those users who want the maximum expressiveness while retaining computational completeness (all conclusions are guaranteed to be computed) and decidability (all computations will finish in finite time). OWL DL includes all OWL language constructs, but they can be used only under certain restrictions (for example, while a class may be a subclass of many classes, a class cannot be an instance of another class). OWL DL is so named due to its correspondence with description logics.

- *OWL Full* is meant for users who want maximum expressiveness and the syntactic freedom of RDF with no computational guarantees. For example, in OWL Full a class can be treated simultaneously as a collection of individuals and as an individual in its own right.

The highest level of expressivity that we use in our architecture is OWL DL in order to preserve computational completeness. We are able to address all of our data representation and reasoning requirements with OWL DL.

2.7.3 SPARQL

SPARQL [41] is a query language for retrieval and manipulation RDF data. SPARQL is to the Semantic Web (RDF data) what SQL is to relational databases. SPARQL can be used to express queries across diverse RDF data sources. The results of SPARQL queries can be results sets or RDF graphs.

```
PREFIX foaf: <http://xmlns.com/foaf/0.1/>
SELECT ?name ?homepage
WHERE {
   ?person a foaf:Person.
   ?person foaf:name ?name.
   ?person foaf:homepage ?homepage.
}
```

Figure 2.3: A simple SPARQL query

A simple SPARQL query to return names and homepage addresses of all persons represented with the FOAF vocabulary is provided in Figure 2.3. In addition to SELECT queries, SPARQL supports CONSTRUCT, ASK and DESCRIBE queries as well.

2.7.4 Linked Data

Linked Data is defined as "a term used to describe a recommended best practice for exposing, sharing, and connecting pieces of data, information, and knowledge on the Semantic Web using URIs and RDF" [42].

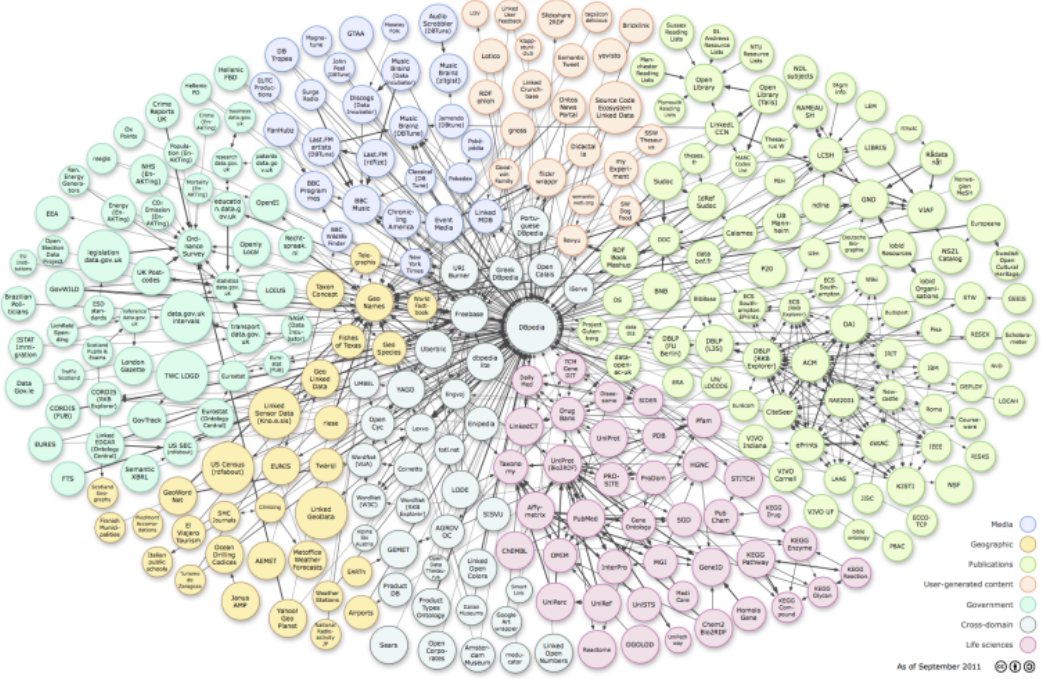

Figure 2.4: Linking Open Data cloud diagram as of September 2011

There are already various interesting open data sets available on the Web. Examples include Wikipedia, Wikibooks, Geonames, WordNet, the DBLP bibliography and many more that are published under permissive licenses. The goal of the W3C Linking Open Data community project is to extend the Web with a data commons by publishing various open data sets as RDF on the Web and by setting RDF links between data items from different data sources [43]. RDF links enable Semantic Web applications to navigate from a data item within one data source to related data items within other sources; thus facilitating the realization of the original "Semantic Web" dream of Sir Tim Berners-Lee.

As of September 2011, in the Linking Open Data initiative, there are 295 data sets consisting of over 31 billion RDF triples, which are interlinked by around 504 million RDF links, as displayed in the cloud diagram in Figure 2.4.

2.8 EYE Reasoning Engine

EYE stands for "Euler Yap Engine" and is a further incremental development of Euler, which is a high-performance inference engine supporting logic based proofs [44]. EYE is a backward-forward-backward chaining reasoner design enhanced with Euler path detection.

The backward-forward-backward chaining is realized via an underlying Prolog backward chaining, a forward meta-level reasoning and a backward proof construction. The Euler path detection is roughly "don't step on your own footprints" to avoid vicious cycles, and in that respect there is a similarity with what Leonhard Euler discovered in 1736 for the Königsberg Bridge Problem [45].

The reasoning that EYE performs is grounded in First Order Logic. Keeping a language less powerful than first order predicate calculus is quite reasonable within an application, but not for the Web [46].

EYE supports Notation3 (N3) [47] as the Resource Description Framework (RDF) syntax. N3 is an assertion and logic language which is a superset of RDF. N3 extends the RDF datamodel by adding formulae (literals which are graphs themselves), variables, logical implication, and functional predicates, as well as providing a textual syntax alternative to RDF/XML. EYE consumes RDF data, rules and queries in N3 syntax only. It is possible to use EYE via the command line or a Java wrapper.

EYE is an open source project maintained by AGFA, who is a beneficiary of the SALUS project. In our architecture, we use EYE Reasoning Engine in almost all kinds of semantic processing and reasoning operations.

CHAPTER 3

THE SEMANTIC RESOURCE SET

The Semantic Resource Set is the backbone enabling our Semantic Interoperability Framework to seamlessly mediate clinical data in different models and align them with ontological representations of medical terminology systems to perform terminology reasoning for actually "understanding" the data. Therefore, our Semantic Resource Set achieves a harmonized "model of meaning" as a whole.

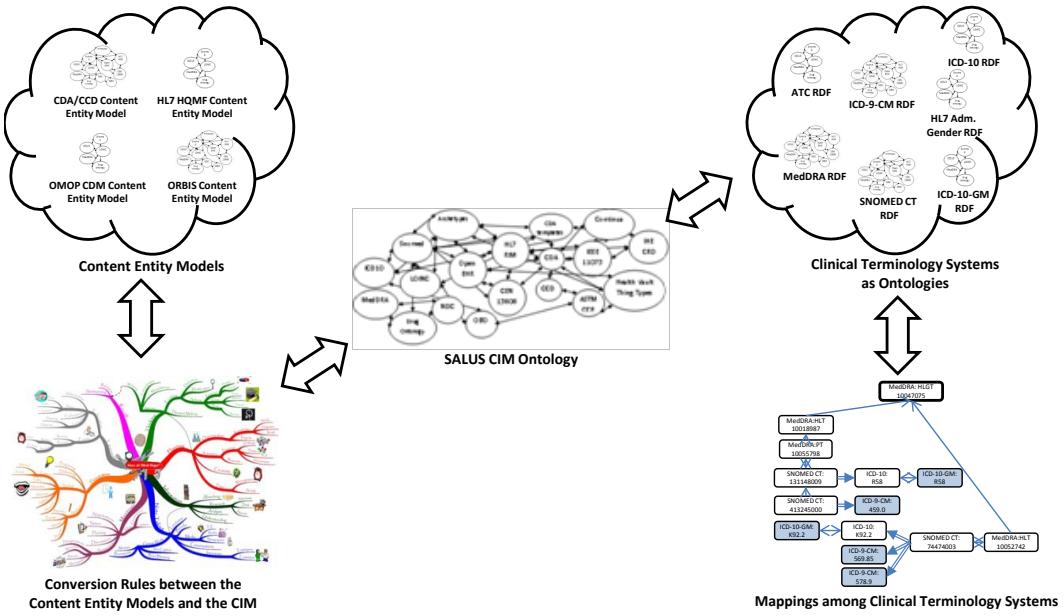

Figure 3.1: The Semantic Resource Set

The Semantic Resource Set is composed of the following artefacts as displayed in Figure 3.1:

1. Formalized representations of the local content models of the EHR sources and target clinical research systems

2. The Common Information Model (CIM) to act as the mediator among different models

3. Ontological representations of medical terminology systems

4. Conversion rules to semantically mediate formalized representations of the native content models with the CIM

5. Reliable mappings among codes from different terminology systems

The first three artefacts are explained in the following sections within this chapter, while the conversion rules are explained in Section 4.3.1 - CDA/CCD Conversion Rules, and mappings among terminology systems in Section 4.7 - Terminology Reasoning Service.

3.1 Content Entity Models

As the first step, we have identified all the local content models of our EHR sources and target post market safety study tools. We have documented all of them in detail, and benefited from them while constructing the Common Information Model (CIM) as well, as explained in the next section. Then, we have created their formalized representations as ontologies to be fed into the Semantic Resource Set. We use the following convention for referring to these artefacts:

- *Content Model:* Local models represented in their native formats, such as XML, SQL, etc.

- *Content Entity Model:* Formalized representation of the Content Models as ontologies with one-to-one correspondence

The Content Entity Models that are involved in our Semantic Resource Set are presented in the following sub-sections.

3.1.1 CDA/CCD Content Entity Model

The Lombardy Region provides the medical summaries of the eligible patient(s) as a response to queries through the entry level HL7 CDA R2 templates, which reuse the existing IHE Patient Care Coordination (PCC) and HL7/ASTM Continuity of Care Document (CCD) templates (see Section 2.2 and Section 2.3). When necessary, we have extended these templates by adding new restrictions in conformance to HL7 CDA Refined Message Information Model (RMIM), to be able to represent additional data items that are required by our pilot applications. In total, we have identified and documented in detail 12 entry level PCC/CCD templates for demographics, conditions, medications, encounters, procedures, coded laboratory results, vital signs, allergies & intolerances, immunizations, pregnancies, social history and family history.

As an example, the PCC/CCD template for coded laboratory results (e.g. blood sugar test) is provided in Table 3.1. The exact locations of the entry template attributes within the generic HL7 CDA R2 schema are provided as XPath expressions.

Table3.1: PCC/CCD template for coded laboratory results

Possible Sections:	Coded Results Section //cda:section[cda:templateId/@root='1.3.6.1.4.1.19376.1.5.3.1.3.28']		
Location in the CDA Document (XPath)	**Definition**	**Card.**	**Data Type**
cda:entry/cda:observation[cda:templateId/@root ='1.3.6.1.4.1.19376.1.5.3.1.4.13']	Observation entry corresponding to the coded result (e.g. a laboratory test result such as blood test)		
cda:code/	Coded name of the result	1..1	CD
cda:originalText/	Free text name of the result	0..1	ED
cda:effectiveTime	Effective time interval of the result (i.e. measured dates)	1..1	IVL<TS>
cda:value	Value of the result, which can be numeric, coded or free text depending on the test	1..1	ANY
cda:interpetationCode	Coded interpretation of the result (e.g. normal, above high threshold, ...)	0..*	SET<CE>
cda:methodCode	Coded specific method used to make the observation	0..*	SET<CE>
cda:targetSiteCode	Coded target body site of the result	0..*	SET<CE>
cda:performer	Health professional that provides the result	0..1	
cda:referenceRange	Reference range of the result (i.e. the safe boundaries)	0..*	
cda:entryRelationship[typeCode='RSON']/ cda:observation [cda:templateId/@root =' 1.3.6.1.4.1.19376.1.5.3.1.4.5']	Condition of the patient that causes result to be measured	0..1	

The CDA/CCD Content Entity Model is the RDF representation of the HL7 CDA R2 schema, automatically converted from the XSD of the CDA document by our Ontmalizer tool, which is explained in detail in Section 4.2.3. Ontmalizer performs comprehensive transformations of XML Schemas (XSD) and XML data to RDF/OWL automatically. Through this tool, it is possible to create an OWL representation of XML Schemas, and XML instances that comply with such XML Schemas. The CDA/CCD Content Entity Model that we have created via Ontmalizer is available in N3 syntax at [48].

In our architecture, the transformation between CDA/CCD Content Entity Model instances and the corresponding native PCC/CCD XML instances is handled by the EHR RDF Service, which is explained in Section 4.2.2.

3.1.2 HL7 HQMF Content Entity Model

HL7 Health Quality Measures Format (HQMF) [49] is a standard for representing a health quality measure as an electronic document. A quality measure is defined as "a quantitative tool that provides an indication of an individual or organization's performance in relation to a specified process or outcome via the measurement of an action, process or outcome of clinical care". HQMF defines a document structure composed of two main parts: i) a body that includes the sections to present measure specific definitions such as data criteria, population criteria, measure period, and ii) a header to present some metadata such as author and verifier of the document.

Although the main objective of HQMF specification is to define health quality e-

measures, which is not directly related with our work; HQMF allows defining inclusion/exclusion criteria (i.e. eligibility criteria) for a specific patient population within its Data Criteria and Population Criteria sections, which is exactly what we need in our work.

It is possible to define eligibility criterions on the following clinical statements, all of which are HL7 v3 Reference Information Model (RIM) classes. HQMF allows grouping these criterions within criteria groups by linking them with logical operators and temporal relationships.

- Patient Demographics
- Problems
- Medications
- Encounters
- Lab Results
- Vital Signs
- Procedures
- Allergies
- Immunizations

As a result of our extensive analysis of the state of the art, we have decided that the declarative eligibility criteria definition mechanism of HQMF is the best fit for meeting our requirements of exchanging and executing population based queries. In our architecture, the native single patient based transactions of IHE Query for Existing Data (QED) and Care Management (CM) profiles are extended for accepting population based queries represented in HQMF. This is explained in Section 4.2.1 - Technical Interoperability Data Source Query Service. Furthermore, the query sub-model of our Common Information Model (CIM) is influenced by the HQMF Content Model.

Since HQMF has an XML Schema, we have created the HL7 HQMF Content Entity Model as RDF representation of this XML Schema automatically via our Ontmalizer tool, just like we created the CDA/CCD Content Entity Model.

3.1.3 OMOP CDM Content Entity Model

In two of our pilot application scenarios, namely temporal pattern characterization and temporal association screening (see Section 1.1), our pilot end user partner Uppsala Monitoring Centre (UMC) has identified the target data model as Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM) [13]. We are expected to provide patient data to Safety Analysis Tools for temporal pattern characterization and temporal association screening in the native OMOP CDM format, which will then store these data in OMOP CDM compliant repositories and run safety analysis algorithms on top.

OMOP is a public-private partnership funded and managed through the Foundation for the National Institutes of Health in the US, with the overall aim to improve the safety monitoring of medicines. OMOP is based on a model where data from various sources is extracted and transformed to a common structure and framework for further analysis. This is referred to as the OMOP Common Data Model (CDM). In addition to defining a fixed structure, OMOP mandates the use of some terminology systems such as SNOMED CT as well.

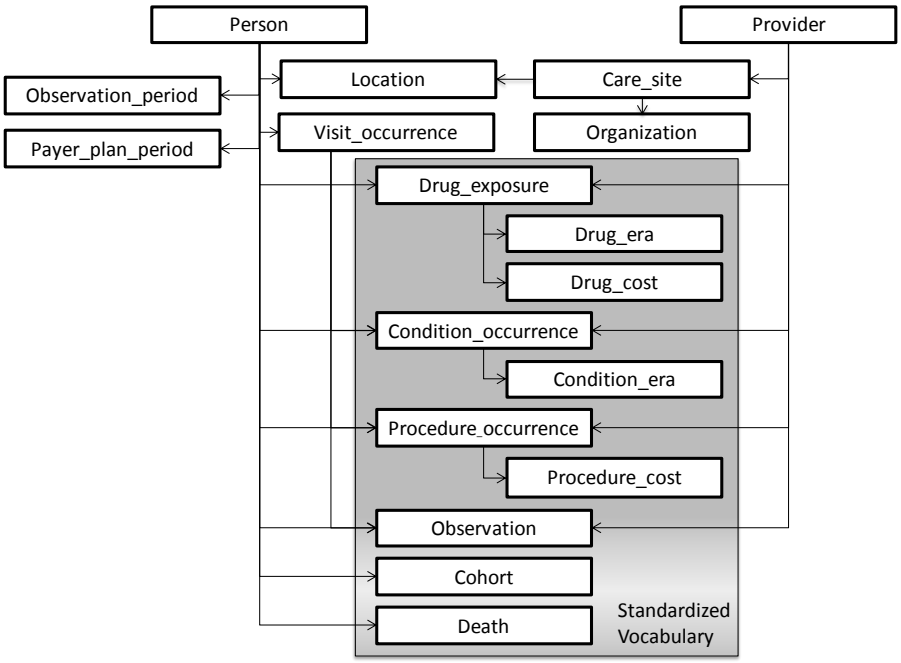

Figure 3.2: OMOP CDM Conceptual Model

Unlike HL7 CDA that has an XML Schema defining the structure, OMOP CDM is defined through human readable tables and SQL scripts for relational database tables. The conceptual model of OMOP CDM can be found in Figure 3.2.

As the first step, we have analyzed all the OMOP CDM tables and their columns that are needed on our side. As an example, Condition Occurrence, which represents a diagnosis or condition that has been recorded about a person at a certain time, is presented in Table 3.2.

Since the model is not complicated, we have created the content entity model of OMOP CDM (i.e. the formalized representation) manually. It is available in N3 syntax at [50]. It is not a 100% direct correspondence of the original OMOP CDM, because during semantic mediation, we need some further information such as the code system identifier for a concept code, before creating the final SQL INSERT statements to be run on an OMOP CDM database. The conversion of patient data in SALUS CIM ontology to OMOP CDM Content Entity Model, and then to native OMOP CDM SQL scripts is the responsibility of the OMOP Converter and Formatter Service in our architecture, which is explained in Section 4.10.

Table3.2: OMOP CDM Condition Occurrence Table

Field	Req.	Type	Description
condition_occurrence_id	yes	integer	A system-generated unique identifier for each condition occurrence event.
person_id	yes	integer	A foreign key identifier to the person who is experiencing the condition. The demographic details of that person are stored in the person table.
condition_concept_id	yes	integer	A foreign key that refers to a standard condition concept identifier in the vocabulary. (refers to SNOMED CT)
condition_start_date	yes	date	The date when the instance of the condition is recorded.
condition_end_date	no	date	The date when the instance of the condition is considered to have ended. This is not typically recorded
condition_type_concept_id	yes	integer	A foreign key to the predefined concept identifier in the vocabulary reflecting the source data from which the condition was recorded, the level of standardization, and the type of occurrence. Conditions are defined as primary or secondary diagnoses, problem lists and person statuses.
stop_reason	no	string (20)	The reason, if available, that the condition was no longer recorded, as indicated in the source data. Valid values include discharged, resolved, etc.
associated_provider_id	no	integer	A foreign key to the provider in the provider table who was responsible for determining (diagnosing) the condition.
visit_occurrence_id	no	integer	A foreign key to the visit in the visit table during which the condition was determined (diagnosed).
condition_source_value	no	string(50)	The source code for the condition as it appears in the source data. This code is mapped to a standard condition concept in the vocabulary and the original code is, stored here for reference. Condition source codes are typically ICD-9-CM diagnosis codes from medical claims or discharge status/disposition codes from EHRs.

3.1.4 ORBIS Content Entity Model

AGFA ORBIS is used as the EHR system in the University Hospital of Dresden (UKD). ORBIS stores all the data in relational database tables. Instead of data exchange through some standard-based content models and transactions, AGFA as a beneficiary of the SALUS project prefers immediate formalization of ORBIS data through a semantic interface they develop directly on top of the ORBIS database.

Therefore, AGFA created the ORBIS Content Entity Model based on the schema of the ORBIS database. The database tables are converted to classes in the ORBIS Content Model Ontology, and the columns in tables are converted to properties. As in the case of our CDA/CCD Content Entity Model, there is one-to-one correspondence between the ORBIS Content Entity Model and the ORBIS Content Model, which is a relational database schema.

In our architecture, the transformation between ORBIS Content Entity Model instances and the corresponding native ORBIS SQL scripts is handled by the UKD SPARQL Endpoint, which is explained in Section 4.2.4.

3.2 The Common Information Model

SALUS semantic interoperability approach has been designed to enable the information exchange between clinical care and clinical research domain applications through a central layer instead of one-to-one transformations between several different content models, by developing a common ontology. SALUS Common Information Model (CIM) ontology forms the core of the SALUS Semantic Resource Set, with the aim of acting as the common mediator to prevent n-to-n mappings among varying content models of data sources and requestors.

During the requirements analysis phase, we have collected all the clinical data requirements of our pilot application scenarios. We have also analyzed the content models that are used by our source EHR systems and target clinical research systems. Although the requirements of our pilot applications were our main driving point, we have analyzed and taken into account content models from other well-known standards and initiatives as well, to provide a common mediator that can interoperate with well-established state of the art. These include:

- HL7/ASTM Continuity of Care Document (CCD) [19] and IHE Patient Care Coordination (PCC) templates [51] which constitute the source model for the data provided by Lombardy Region
- HITSP C32 [52] and C83 [53] components, greenCDA [54] representation of HITSP C32 and Consolidated CDA (C-CDA) Templates Guide [55]
- HL7 Clinical Statement Model [56]
- OMOP CDM [57], which is a target model in two of our pilot application scenarios
- ICH Data Elements for Transmission of Individual Case Safety Reports E2B(R2) [58], which is a target model in our ADE reporting scenario
- Common Data Model of the Mini-Sentinel pilot project [59]
- ISO/CEN EN 13606 archetypes relevant to our scenarios [60]

As a result, we have built a list of Common Data Elements (CDEs) that include elements to be present within a medical summary, such as patient demographics, encounter, condition (problem, diagnosis), allergy, family history, healthcare provider; and their sub-elements. SALUS CDEs can be considered as the semantic dictionary of the SALUS components. The complete list of SALUS CDEs with their descriptions are presented in Appendix A. There are 211 CDEs in total.

After defining and documenting these CDEs, we first created the SALUS Common Information Model (CIM) as an XML Schema Definition (XSD) containing all the CDEs and the relationships among them. In addition to the CDEs, in SALUS CIM, we have used a simple yet satisfactory subset from ISO 21090 data types [61] including the most essential data types such as concept descriptor (CD), interval of timestamp (IVLTS), instance identifier (II), physical quantity (PQ) and interval of physical quantity (IVLPQ). An excerpt from the SALUS CIM XSD is presented in Figure 3.3.

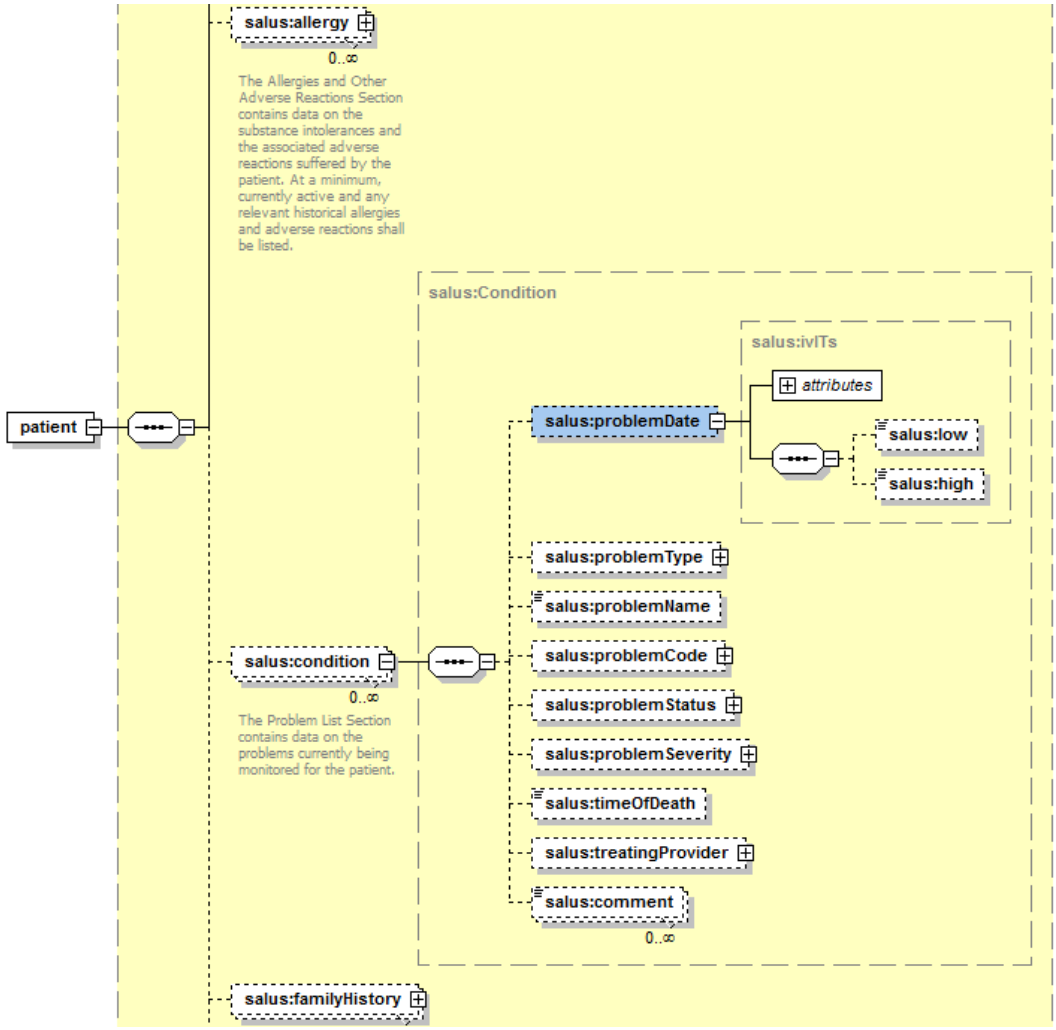

Figure 3.3: An excerpt from the SALUS CIM XSD

Using the Ontmalizer tool (see Section 4.2.3), we have transformed the XSD into the SALUS CIM ontology, to act as a mediator among different content models. The complete SALUS CIM ontology represented in N3 syntax is available at [62]. All the different content entity models of the source and target systems are mapped to the SALUS CIM ontology and instances represented in SALUS CIM ontology are created automatically via our conversion rules at run-time, as explained in Section 4.3.1.

An example SALUS CIM Condition instance in N3 syntax representing an active asthma problem that is being treated by a chest physician is provided in Figure 3.4.

SALUS CIM ontology not only represents entities that can be presented within a medical summary, but also establishes a link with the terminology system ontologies that are used to code patient data. This is explained in detail in Section 4.7. Furthermore, SALUS CIM covers the query model to express eligibility criteria for defining a population of interest, which is an important requirement in carrying out post market safety studies. For this purpose, we mainly benefited from the query model of HL7 Health Quality Measures Format (HQMF) [49], and created its semantic representa-

```
@prefix foaf:  <http://xmlns.com/foaf/0.1/> .
@prefix salus: <http://www.salusproject.eu/ontology/common-information-model#>.

[ rdf:type salus:Condition ;
  salus:problemCode
    [ rdf:type salus:cd ;
      salus:code "493" ;
      salus:codeSystem "2.16.840.1.113883.6.2" ;
      salus:codeSystemName "ICD-9-CM" ;
      salus:displayName "Asthma"
    ] ;
  salus:problemDate
    [ rdf:type salus:ivlTs ;
      salus:low "2003-08-01T00:00:00"^^xsd:dateTime
    ] ;
  salus:problemName "Asthma" ;
  salus:problemSeverity
    [ rdf:type salus:cd ;
      salus:code "H" ;
      salus:codeSystem "2.16.840.1.113883.5.1063" ;
      salus:codeSystemName "ObservationValue" ;
      salus:displayName "High"
    ] ;
  salus:problemStatus
    [ rdf:type salus:cd ;
      salus:code "55561003" ;
      salus:codeSystem "2.16.840.1.113883.6.96" ;
      salus:codeSystemName "SNOMED CT" ;
      salus:displayName "Active"
    ] ;
  salus:treatingProvider
    [ rdf:type salus:HealthcareProvider ;
      salus:providerID
        [ rdf:type salus:ii ;
          salus:extension "54321678906" ;
          salus:root "2.16.840.1.113883.2.9.4.3.2"
        ] ;
      salus:providerRole
        [ rdf:type salus:cd ;
          salus:code "309345004" ;
          salus:codeSystem "2.16.840.1.113883.6.96" ;
          salus:codeSystemName "SNOMED CT" ;
          salus:displayName "Chest Physicians"
        ] ;
      foaf:familyName "Passerini" ;
      foaf:givenName "Fabiola" ;
      foaf:title "Dr."
    ]
]
```

Figure 3.4: An example SALUS CIM Condition instance

tion within the SALUS CIM ontology. The CDEs that are related with the query model are presented in the last part of the table provided in Appendix A.

3.2.1 BRIDG DAM as the Common Information Model

In our very early prototype [63], which was a preparatory work before developing the actual SALUS Common Information Model as described in the previous section, we used BRIDG Domain Analysis Model (DAM) [9] ontology as the common information

model to act as the mediator. In this section, we explain how we developed the semantic representation of BRIDG DAM and used at the core of our very early prototype. At the end, we present why we were not able to proceed with BRIDG DAM as the common information model.

The BRIDG Project has developed a coherent clinical research vocabulary that integrates established domain knowledge from existing standards developed at CDISC, HL7, US Food and Drug Administration (FDA), US National Cancer Institute (NCI) and others. This is achieved through a reverse engineering effort from some of the already existing HL7 Regulated Clinical Research Information Management (RCRIM) messages, and from the CDISC Clinical Data Acquisition Standards Harmonization (CDASH) [64], Study Data Tabulation Model (SDTM) [65] data sets and Operational Data Model (ODM) [66] models. As a result, the latest BRIDG DAM (v3.0.3) is fully aligned with HL7 RIM.

The approach taken by BRIDG involved three tasks:

- Investigating semantically connected domain analysis models;
- Extracting common concepts; and
- Unifying the semantics of these concepts into a coherent information model through explicit knowledge representations based on the general consent among the stakeholders. UML was chosen as the representation language.

In other words, the BRIDG DAM is an implementation independent UML model to represent common shared semantics of regulated clinical research studies which may have different implementations. There have been several implementations of BRIDG DAM built by a number of commercial pharma organizations. In addition to this, BRIDG DAM is also taken as a base model by standardization organizations for the development of message specifications. For example, the CDISC Study/Trial Design Model (SDM) [67] (which is an ODM extension) and the HL7 Study Design RMIM are both implementations of Protocol Representation sub-domain. The mappings of this common semantics to more than one implementation model are provided through spreadsheets. However, these mapping definitions are intended to be used by domain experts, rather than by the computerized systems, as they are not machine processable.

The first challenge of developing our very early prototype was to provide a machine processable semantic representation of the BRIDG DAM together with its mappings to the harmonized standards. Although not referenced in the latest BRIDG Specifications at that time (v3.0.3), an OWL representation of an earlier version of BRIDG DAM (v3.0.1) was available in NCI's SVN Repository. There have been significant changes since v3.0.1 in the BRIDG DAM due to the harmonization of HL7 ICSR Release 2, SDTM Implementation Guide v3.1.2 and CDASH v1.1. As a result, the classes, their attributes and the associations among classes are quite different between DAM v3.0.1 and v3.0.3. On top of this, we noticed that some other properties of the NCI's native OWL representation are not very suitable for our purposes. For example, in the NCI's native OWL representation, associations are unidirectional, however bidirectional associations (i.e. object properties in OWL) are important for our purposes, because

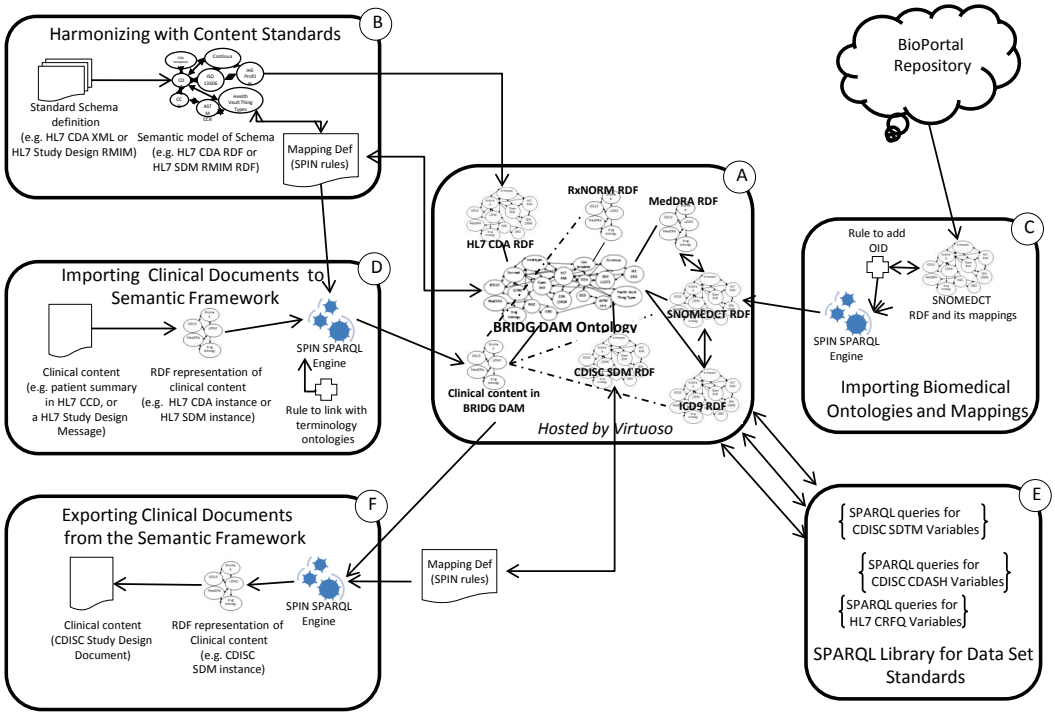

Figure 3.5: Overview of the very early prototype with BRIDG DAM as the core ontology

there is a need to access all the associations of a class (incoming or outgoing). For these reasons, rather than using this earlier version, in this work, we have created a complete RDF representation of BRIDG DAM v3.0.3 through the following steps:

- First, an XMI model [68] of the BRIDG DAM is created through Enterprise Architect tool [69], through which the BRIDG DAM UML models are served. Note that XMI is used as an interchange format for UML models.
- The second step is to export the XMI model as XML Schema Definitions (XSDs). Several tools including Enterprise Architect can export XMI models as XSDs. We have chosen Visual Paradigm tool [70] which, in our experience, performed better with such a complex UML model.
- The BRIDG DAM is using ISO Harmonized Data Types [61], which are created as a result of collaboration of CEN, HL7 and ISO to standardize the data types used in the healthcare domain. The UML model of ISO data types are embedded in the overall DAM UML model; however when the XSDs are created from the corresponding XMI model as described, the ISO data types cause problems due to their complexity. For this reason, we merged the ISO 21090 XSD provided by the HL7 ballot site with the XSD that is generated from the BRIDG DAM. However, the resulting XSD files had to be manually fine-tuned since UML $\Rightarrow$ XMI $\Rightarrow$ XSD conversion missed quite a number of associations and inheritance relationships available in the original BRIDG DAM.
- Finally, we have utilized TopBraid Composer tool [71] to create a complete RDF

representation of the BRIDG DAM via the XSD files that we have generated.

The resulting BRIDG DAM ontology in RDF is accessible from [72]. An overview of our very early prototype displaying the relationships of the BRIDG DAM as the core ontology with other resources is presented in Figure 3.5. It can be understood from this figure that although there are some differences such as the common information model, the foundations of this very early prototype and our current interoperability framework are still the same.

We were planning to proceed with BRIDG DAM in the core of our Semantic Resource Set. However, during in-depth analysis of the pilot application data requirements and the content models, we realized that the common model should be more clinical care oriented in observational studies. Although BRIDG DAM is a harmonization effort, its main focus is regulated clinical research, which is not within the scope of our work. It would not have been possible to map even an encounter if we had proceeded with BRIDG DAM. Therefore, we have developed the SALUS CIM as a harmonization of well-accepted content models in the clinical care and observational study domains.

3.3 Clinical Terminology Systems as Ontologies

In order to align patient data with clinical terminology systems and then to enable terminology reasoning, the first challenge to overcome is the representation of the terminology systems as ontologies. All the clinical terminology systems that are used by the EHR sources and target clinical research systems are maintained within the SALUS Semantic Resource Set as ontologies. We prefer the well-established Simple Knowledge Organization System (SKOS) [73] vocabulary for this purpose.

SKOS provides a model for expressing the basic structure and content of concept schemes such as thesauri, classification schemes, subject heading lists, taxonomies, folksonomies and other similar types of controlled vocabulary. As an application of the Resource Description Framework (RDF), SKOS allows concepts to be composed and published on the World Wide Web, linked with data on the Web and integrated into other concept schemes or ontologies. In SKOS a terminology system is represented as a concept scheme and a set of concepts. URIs are assigned to each concept and the concept scheme itself. In addition to the concept URI to identify a concept, each concept has a notation property to represent the code of the concept in its terminology. Finally, SKOS provides properties for organizing concepts in concept hierarchies and for linking semantically related concepts from different concept schemes, such as "skos:broader" and "skos:exactMatch" that we make use of in our Semantic Resource Set again.

When available, we retrieve the terminology systems from BioPortal [29], and further fine-tune them to stick to SKOS as much as possible. For each code, we create a skos:Concept and define the skos:inScheme property to semantically link the concept to the encapsulating concept scheme, i.e. the terminology system. We preserve the BioPortal URIs, which are persistent and hence easily discoverable in conformance with the Linked Open Data principles [42]. We adapted MedDRA, SNOMED CT Clinical Findings sub-hierarchy, ICD-9-CM, ICD-10, HL7 AdministrativeGender from

BioPortal. When a terminology system is not available in BioPortal, we create its semantic representation ourselves. These include ICD-10-GM (German Modification) and WHO-ATC.

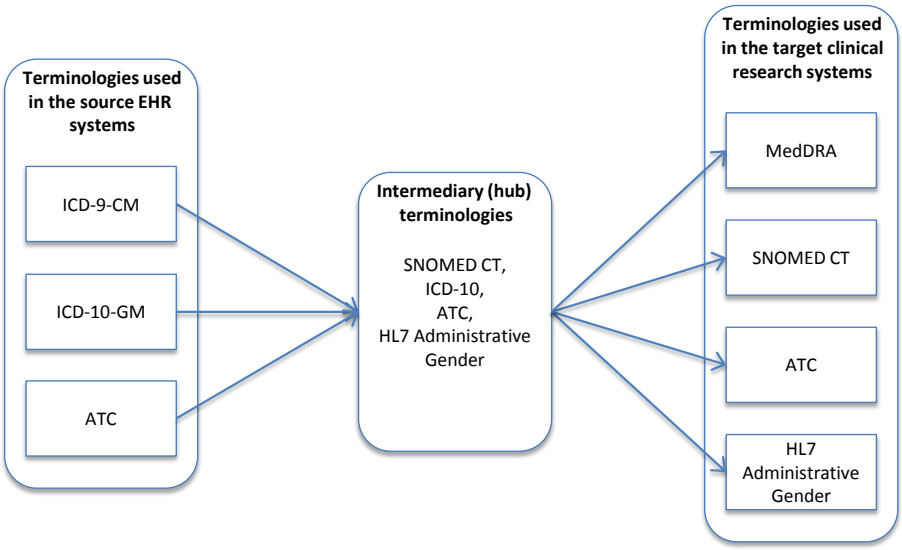

Figure 3.6: The major terminology systems in the SALUS Semantic Resource Set

These major terminology systems that are available in the SALUS Semantic Resource Set and their domain of use are presented in Figure 3.6. Our source EHR systems are the Data Warehouse (DWH) of the Lombardy Region in Italy and the AGFA ORBIS system installed at the University Hospital of Dresden (UKD) in Germany. Our end-users on the clinical research side are WHO Collaborating Centre for International Drug Monitoring, Uppsala Monitoring Centre (UMC) in Sweden and ROCHE in Switzerland. This figure also gives some clues about the terminology system mappings in the SALUS Semantic Resource Set, but these are explained in detail in Section 4.7. It should be noted that, multiple hub terminology systems are preferred according to specific requirements and reliable mapping information that we can utilize in our resource set.

Further information about terminology systems and their representation as ontologies in the SALUS Semantic Resource Set is provided in the following sub-sections. There are some further terminology systems that are used in the local systems (e.g. for gender), but not all of them are provided here.

3.3.1 MedDRA

Medical Dictionary for Regulatory Activities (MedDRA) [74] is a medical terminology used to classify adverse event information associated with the use of biopharmaceuticals and other medical products (e.g., medical devices and vaccines). The purpose of MedDRA is to describe steps of drug development and regulatory issues about human exposure. It includes terms for the description of adverse drug reactions, indications, signs and symptoms, family history, investigations and surgical procedures. Nowadays

this terminology is used for recording and reporting adverse drug event data in most countries. MedDRA terms are organized in 5 levels: System Organ Class (SOC), High Level Group Term (HLGT), High Level Term (HLT), Preferred Term (PT) and Low Level Term (LLT).

In our Semantic Resource Set, we make use of version 13.0 of MedDRA. All terms at the SOC, HLGT, HLT and PT levels are included; LLT terms are discarded since that level of detail is not required by our pilot applications. There are 26 SOC, 335 HLGT, 1709 HLT and 18786 PT terms. In our pilot applications, MedDRA is almost always a target terminology system used on the clinical research side.

Semantic representation of the MedDRA terminology as a SKOS ConceptScheme is provided below in N3 syntax. Since MedDRA (version 12.0) is already available in BioPortal and hence has been assigned a URI, we use the same URI.

```
@prefix MDR:     <http://purl.bioontology.org/ontology/MDR/> .
@prefix foaf:    <http://xmlns.com/foaf/0.1/> .
@prefix iso:     <uri:iso.org:9834#> .
@prefix rdfs:    <http://www.w3.org/2000/01/rdf-schema#> .
@prefix skos:    <http://www.w3.org/2004/02/skos/core#> .

<http://purl.bioontology.org/ontology/MDR>
      rdf:type skos:ConceptScheme ;
      rdfs:label "MedDRA" ;
      foaf:name "Medical Dictionary for Regulatory Activities Terminology, Version 13.0" ;
      iso:oid "2.16.840.1.113883.6.163" .
```

For each skos:ConceptScheme, we define three main properties:

- *rdfs:label* to represent the widely-used abbreviation of the terminology system,
- *foaf:name* to represent the full name of the terminology system, and
- *iso:oid* to provide the unique ISO Object Identifier (OID) of the terminology system, which is critical in establishing the link between the structured patient data and the semantic representation of the corresponding terminology system code.

Similarly, the MedDRA terms are represented via properties from the SKOS vocabulary. Again for the individual MedDRA terms, the URIs that are assigned by BioPortal are used. Unlike BioPortal, we stick to the SKOS vocabulary, and on top, we defined the "MDR:level" property for representing the original MedDRA level information, since there is no SKOS property for representing the level information. Below, the SOC, HLGT, HLT and PT terms hierarchy that leads to "Myocardial infarction" is provided as example SKOS Concepts:

```
<http://purl.bioontology.org/ontology/MDR/10007541>
      a       skos:Concept ;
      MDR:level "SOC" ;
      skos:inScheme <http://purl.bioontology.org/ontology/MDR> ;
      skos:notation "10007541" ;
      skos:prefLabel "Cardiac disorders" .

<http://purl.bioontology.org/ontology/MDR/10011082>
```

```
      a       skos:Concept ;
      MDR:level "HLGT" ;
      skos:broader <http://purl.bioontology.org/ontology/MDR/10007541> ;
      skos:inScheme <http://purl.bioontology.org/ontology/MDR> ;
      skos:notation "10011082" ;
      skos:prefLabel "Coronary artery disorders" .

<http://purl.bioontology.org/ontology/MDR/10011085>
      a       skos:Concept ;
      MDR:level "HLT" ;
      skos:broader <http://purl.bioontology.org/ontology/MDR/10011082> ;
      skos:inScheme <http://purl.bioontology.org/ontology/MDR> ;
      skos:notation "10011085" ;
      skos:prefLabel "Ischaemic coronary artery disorders" .

<http://purl.bioontology.org/ontology/MDR/10028596>
      a       skos:Concept ;
      MDR:level "PT" ;
      skos:broader <http://purl.bioontology.org/ontology/MDR/10011085> ,
            <http://purl.bioontology.org/ontology/MDR/10065875> ;
      skos:inScheme <http://purl.bioontology.org/ontology/MDR> ;
      skos:notation "10028596" ;
      skos:prefLabel "Myocardial infarction" .
```

The common properties that we define for each skos:Concept are:

- *skos:notation* to represent the unique code,
- *skos:prefLabel* to represent the preferred (most common) designation of the code,
- *skos:altLabel* to represent some alternative designations of the code when applicable, e.g. "Classical migraine" as an alternative label for the "Migraine with aura" preferred label,
- *skos:inScheme* to represent the URI of the enclosing skos:ConceptScheme (i.e. terminology system), and
- *:level* to represent the level information of the code within the terminology system when this information is explicitly provided by the terminology system itself as in the case of MedDRA.

Depending on the terminology system, there can be further specific semantic properties again provided by the terminology system itself.

3.3.2 SNOMED CT

Systematized Nomenclature of Medicine Clinical Terms (SNOMED CT) [24] is a broad clinical terminology (the 2011 version includes more than 311,000 concepts), which is sometimes considered as an ontology because of the systematic and logical mode of representations of semantics it promotes. SNOMED CT provides codes, terms, synonyms and definitions covering diseases, findings, procedures, microorganisms, substances, etc. It is one of the most comprehensive, multilingual clinical healthcare terminologies in the World.

In our Semantic Resource Set, for the moment we make use of only the "Clinical finding" sub-hierarchy of SNOMED CT. We retrieved this sub-hierarchy from BioPortal

and then fine-tuned it to get rid of unnecessary properties. There are 97139 SNOMED CT codes in our Semantic Resource Set. In our pilot applications, SNOMED CT is usually neither a source nor target terminology system; but an intermediary (hub) terminology system to link source codes to target codes through mappings and other semantic relationships.

Semantic representation of the SNOMED CT terminology as a SKOS ConceptScheme is provided below. Since SNOMED CT is already available in BioPortal and hence has been assigned a URI, we use the same URI.

```
<http://purl.bioontology.org/ontology/SNOMEDCT>
      rdf:type skos:ConceptScheme ;
      rdfs:label "SNOMED CT" ;
      foaf:name "Systematized Nomenclature of Medicine--Clinical Terms" ;
      iso:oid "2.16.840.1.113883.6.96" .
```

Similarly, the SNOMED CT codes are represented via properties from the SKOS vocabulary. Again for the individual SNOMED CT codes, the URIs that are assigned by BioPortal are used. Unlike BioPortal, we totally stick to the SKOS vocabulary. Below, semantic representation of the SNOMED CT code for "Vascular headache" is provided as an example:

```
<http://purl.bioontology.org/ontology/SNOMEDCT/128187005>
      rdf:type skos:Concept ;
      skos:altLabel "Vascular headache (disorder)" ;
      skos:broader <http://purl.bioontology.org/ontology/SNOMEDCT/230461009> ,
            <http://purl.bioontology.org/ontology/SNOMEDCT/27550009> ;
      skos:inScheme <http://purl.bioontology.org/ontology/SNOMEDCT> ;
      skos:notation "128187005" ;
      skos:prefLabel "Vascular headache" .
```

3.3.3 ICD-9-CM

International Classification of Diseases, 9th Rev., Clinical Modification (ICD-9-CM) [75] is an adaptation created by the U.S. National Center for Health Statistics and used in assigning diagnostic and procedure codes associated with inpatient, outpatient, and physician office utilization in the United States. ICD-9-CM is based on the original ICD-9 by WHO, but provides additional morbidity detail.

In our Semantic Resource Set, we have the semantic representation of the complete ICD-9-CM, version 2007 hierarchy. We retrieved these from BioPortal and then fine-tuned them to get rid of unnecessary properties. There are 21669 ICD-9-CM codes in our Semantic Resource Set. In our pilot applications, ICD-9-CM is a source terminology system that is used within the Lombardy Region EHR system for coding the conditions, allergies, procedures and interventions of the patients.

Semantic representation of the ICD-9-CM terminology as a SKOS ConceptScheme is provided below. Since ICD-9-CM is already available in BioPortal and hence has been assigned a URI, we use the same URI.

```
<http://purl.bioontology.org/ontology/ICD9CM>
```

```
      rdf:type skos:ConceptScheme ;
      rdfs:label "ICD-9-CM" ;
      foaf:name "International Classification of Diseases, Ninth Revision, Clinical
            Modification" ;
      iso:oid "2.16.840.1.113883.6.2" .
```

Similarly, the ICD-9-CM codes are represented via properties from the SKOS vocabulary. Again for the individual ICD-9-CM codes, the URIs that are assigned by BioPortal are used. Unlike BioPortal, we totally stick to the SKOS vocabulary. Below, semantic representation of the ICD-9-CM code for "Overweight and obesity" is provided as an example:

```
<http://purl.bioontology.org/ontology/ICD9CM/278.0>
      a       skos:Concept ;
      skos:broader <http://purl.bioontology.org/ontology/ICD9CM/278> ;
      skos:inScheme <http://purl.bioontology.org/ontology/ICD9CM> ;
      skos:notation "278.0" ;
      skos:prefLabel "Overweight and obesity" .
```

3.3.4 ICD-10

International Statistical Classification of Diseases and Related Health Problems, 10th rev. (ICD-10) [25] is a medical classification list by the World Health Organization (WHO). It codes for diseases, signs and symptoms, abnormal findings, complaints, social circumstances, and external causes of injury or diseases.

In our Semantic Resource Set, we have the semantic representation of the complete ICD-10 hierarchy. We retrieved these from BioPortal and then fine-tuned them to get rid of unnecessary properties. There are 12318 ICD-10 codes in our Semantic Resource Set. In our pilot applications, ICD-10 is usually neither a source nor target terminology system; but an intermediary (hub) terminology system to link source codes to target codes through mappings and other semantic relationships. It is necessary especially for mappings to ICD-10 German Modification (ICD-10-GM), which is used in the University Hospital of Dresden (UKD) as one of our EHR sources.

Semantic representation of the ICD-10 terminology as a SKOS ConceptScheme is provided below. Since ICD-10 is already available in BioPortal and hence has been assigned a URI, we use the same URI.

```
<http://purl.bioontology.org/ontology/ICD10>
      rdf:type skos:ConceptScheme ;
      rdfs:label "ICD-10" ;
      foaf:name "International Statistical Classification of Diseases and Related Health
            Problems. 10th rev." ;
      iso:oid "2.16.840.1.113883.6.3" .
```

Similarly, the ICD-10 codes are represented via properties from the SKOS vocabulary. Again for the individual ICD-10 codes, the URIs that are assigned by BioPortal are used. Unlike BioPortal, we totally stick to the SKOS vocabulary. Below, semantic representation of the ICD-10 code for "Insulin-dependent diabetes mellitus with coma" is provided as an example:

```
<http://purl.bioontology.org/ontology/ICD10/E10.0>
      a       skos:Concept ;
      skos:broader <http://purl.bioontology.org/ontology/ICD10/E10> ;
      skos:inScheme <http://purl.bioontology.org/ontology/ICD10> ;
      skos:notation "E10.0" ;
      skos:prefLabel "Insulin-dependent diabetes mellitus with coma" .
```

3.3.5 ICD-10-GM

Internationale statistische Klassifikation der Krankheiten und verwandter Gesundheitsprobleme, 10. Revision, German Modification (ICD-10-GM) [76] is the German modification of ICD-10. It is the official classification for coding of diagnoses in outpatient and inpatient care in Germany, and hence used in one of our EHR sources, namely the University Hospital of Dresden (UKD) ORBIS system.

The Deutsche Institute Medizinische Dokumentation Information (DIMDI) publishes a new version of ICD-10-GM each year; these different ICD-10-GM versions are classified by the year they are published. Several versions are used in the UKD ORBIS system, so the different versions are modeled as distinct skos:ConceptScheme s as in the example shown below.

```
@prefix ICD10GM:  <http://www.salusproject.eu/terminology/ICD10GM/> .
@prefix clisko:  <http://www.agfa.com/w3c/2009/clinicalSKOSSchemes#> .
@prefix iso:     <uri:iso.org:9834#> .

<http://www.salusproject.eu/terminology/ICD10GM/2007>
      rdf:type skos:ConceptScheme ;
      rdfs:label "icd10gm2007" ;
      iso:oid "1.2.276.0.76.5.318" .
```

Similarly, the ICD-10-GM codes are represented via properties from the SKOS vocabulary. As a local terminology system, ICD-10-GM is not present in BioPortal. Therefore we assign URIs from the SALUS domain. Unlike the other terminology systems, this time we represent several different versions of the terminology system that a code is included in. Below, semantic representation of the ICD-10-GM code for "Acute transmural myocardial infarction of the posterior wall" is provided as an example:

```
<http://www.salusproject.eu/terminology/ICD10GM/I21.1>
      rdf:type skos:Concept ;
      skos:broader ICD10GM:I21 ;
      skos:inScheme <http://www.salusproject.eu/terminology/ICD10GM/2005> ,
            <http://www.salusproject.eu/terminology/ICD10GM/2007> ,
            <http://www.salusproject.eu/terminology/ICD10GM/2009> ,
            <http://www.salusproject.eu/terminology/ICD10GM/2010> ,
            <http://www.salusproject.eu/terminology/ICD10GM/2004> ,
            <http://www.salusproject.eu/terminology/ICD10GM/2012> ,
            <http://www.salusproject.eu/terminology/ICD10GM/2008> ,
            clisko:icd10gm , <http://www.salusproject.eu/terminology/ICD10GM/2006> ,
            <http://www.salusproject.eu/terminology/ICD10GM/2011> ;
      skos:notation "I21.1"^^clisko:icd10gmDT ;
      skos:prefLabel "Akuter transmuraler Myokardinfarkt der Hinterwand"@de .
```

3.3.6 ATC

The Anatomical Therapeutic Chemical (ATC) Classification System [77] is used for the classification of drugs. It is controlled by the WHO Collaborating Centre for Drug Statistics Methodology. ATC divides drugs into different groups according to the organ or system on which they act and/or their therapeutic and chemical characteristics. Each bottom-level ATC code stands for a pharmaceutically used substance, or a combination of substances, in a single indication (or use). This means that one drug can have more than one code. On the other hand, several different brands share the same code if they have the same active substance and indications.

There are 5 levels in the ATC:

1. The first level indicates the anatomical main group and consists of one letter, e.g. **C**: Cardiovascular system.
2. The second level indicates the therapeutic main group and consists of two digits, e.g. C**03**: Diuretics.
3. The third level indicates the therapeutic/pharmacological subgroup and consists of one letter, e.g. C03**C**: High-ceiling diuretics.
4. The fourth level indicates the chemical/therapeutic/pharmacological subgroup and consists of one letter, e.g. C03C**A**: Sulfonamides.
5. The fifth level indicates the chemical substance and consists of two digits, e.g. C03CA**01**: Furosemide.

ATC is a very important terminology system for common understanding of medicinal products through their active ingredients. The same medicinal product can have several different brands and titles in different countries. However, when the active ingredients of these syntactically different but content-wise identical medicinal products are provided through ATC codes, then it is possible to achieve at least a minimum level of cross-border interoperability, as is done in the epSOS project [26] for exchange of structured patient data among the European countries. In our case, ATC is used both by our EHR sources UKD and Lombardy Region, as well as UMC and ROCHE as the end-users on the clinical research side.

The semantic representation of the ATC terminology as a SKOS ConceptScheme is provided below. Since ATC is not available in BioPortal, we have created a URI based on the official WHO ATC web address.

```
<http://www.whocc.no/atc>
      a       skos:ConceptScheme ;
      rdfs:label "ATC" ;
      foaf:name "The Anatomical Therapeutic Chemical Classification System, WHO Collaborating
         Centre for Drug Statistics Methodology (WHOCC)" ;
      iso:oid "2.16.840.1.113883.6.73" .
```

Similarly, the ATC terms are represented via properties from the SKOS vocabulary. Custom URIs based on the official WHO ATC web address are created for the terms

as in the case of the terminology system. We stick to the SKOS vocabulary, and on top, we define the "ATC:level" property for representing the original ATC level information, since there is no SKOS property for representing the level information. Below, a sample hierarchy that includes all the levels leading to "nifedipine" active ingredient is provided as SKOS Concepts:

```
ATC:C
      a       skos:Concept ;
      skos:inScheme <http://www.whocc.no/atc> ;
      skos:notation "C" ;
      skos:prefLabel "CARDIOVASCULAR SYSTEM"@en ;
      ATC:level "1"^^xsd:int .

ATC:C08
      a       skos:Concept ;
      skos:broader ATC:C ;
      skos:inScheme <http://www.whocc.no/atc> ;
      skos:notation "C08" ;
      skos:prefLabel "CALCIUM CHANNEL BLOCKERS"@en ;
      ATC:level "2"^^xsd:int .

ATC:C08C
      a       skos:Concept ;
      skos:broader ATC:C08 ;
      skos:inScheme <http://www.whocc.no/atc> ;
      skos:notation "C08C" ;
      skos:prefLabel "SELECTIVE CALCIUM CHANNEL BLOCKERS WITH MAINLY VASCULAR EFFECTS"@en ;
      ATC:level "3"^^xsd:int .

ATC:C08CA
      a       skos:Concept ;
      skos:broader ATC:C08C ;
      skos:inScheme <http://www.whocc.no/atc> ;
      skos:notation "C08CA" ;
      skos:prefLabel "Dihydropyridine derivatives"@en ;
      ATC:level "4"^^xsd:int .

ATC:C08CA05
      a       skos:Concept ;
      skos:broader ATC:C08CA ;
      skos:inScheme <http://www.whocc.no/atc> ;
      skos:notation "C08CA05" ;
      skos:prefLabel "nifedipine"@en ;
      ATC:level "5"^^xsd:int .
```

3.3.7 HL7 AdministrativeGender

The HL7 AdministrativeGender code system / value set is one of the most simple and widely known vocabularies for representing gender information in a coded manner. It has 3 codes only for defining male, female and undifferentiated. In our pilot applications, it is used both as a hub and target terminology system. Its semantic representation as a SKOS ConceptScheme is provided below:

```
@prefix HL7:     <http://purl.bioontology.org/ontology/HL7/AdministrativeGender/> .
@prefix xsd:     <http://www.w3.org/2001/XMLSchema#> .

<http://purl.bioontology.org/ontology/HL7/AdministrativeGender>
      rdf:type skos:ConceptScheme ;
      rdfs:label "AdministrativeGender" ;
      foaf:name "HL7 Administrative Gender" ;
      iso:oid "2.16.840.1.113883.5.1" .
```

Similarly, the codes are represented via properties from the SKOS vocabulary. All 3 codes are provided below:

```
HL7:M
      rdf:type skos:Concept ;
      skos:inScheme <http://purl.bioontology.org/ontology/HL7/AdministrativeGender> ;
      skos:notation "M" ;
      skos:prefLabel "Male" .

HL7:F
      rdf:type skos:Concept ;
      skos:inScheme <http://purl.bioontology.org/ontology/HL7/AdministrativeGender> ;
      skos:notation "F" ;
      skos:prefLabel "Female" .

HL7:UN
      rdf:type skos:Concept ;
      skos:inScheme <http://purl.bioontology.org/ontology/HL7/AdministrativeGender> ;
      skos:notation "UN" ;
      skos:prefLabel "Undifferentiated" .
```

CHAPTER 4

THE ARCHITECTURE OF THE SEMANTIC INTEROPERABILITY FRAMEWORK

Our Semantic Interoperability Framework enables execution of post market safety studies on distributed EHR sources through a series of integrated semantic interoperability and technical interoperability services, as displayed in Figure 4.1. In the upcoming sections, components of this architecture are presented by focusing on the addressed challenges.

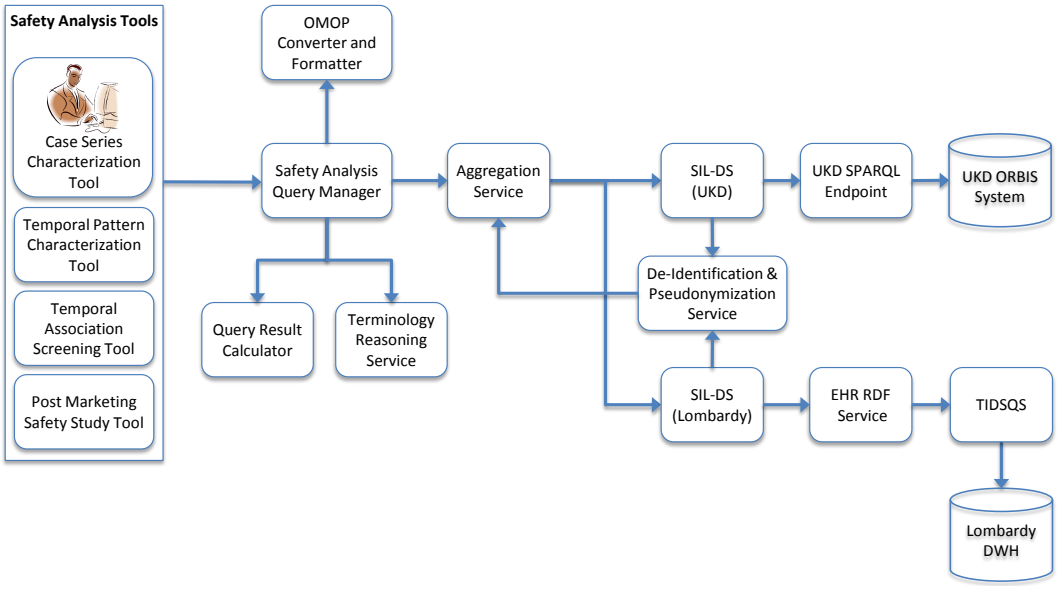

Figure 4.1: The Overall Architecture of the Semantic Interoperability Framework

Furthermore, in order to better explain the interactions among the components involved in the architecture, a step by step execution of a complete case series characterization scenario is provided in Chapter 5.

There are some additional components involved in the architecture such as Adverse Drug Event (ADE) Notification Tool and Individual Case Safety Report (ICSR) Tool for detection and reporting of suspected ADEs, which are not displayed in the architecture diagram. Although, these tools are totally based on our Semantic Interoperability

Framework for access to distributed patient data in an interoperable manner, the implementation of the functionalities of these tools is not within the scope of this thesis work.

4.1 Safety Analysis Tools

As explained in Section 1.1 - Objectives, we have several pilot application scenarios for enabling the safety analysts working at pharmacovigilance centers and pharmaceutical companies to do post market safety studies. For each of these scenarios, we have a dedicated tool in the architecture, which are listed below:

- Case Series Characterization Tool
- Temporal Pattern Characterization Tool
- Temporal Association Screening Tool
- Post Marketing Safety Study Tool

All the Safety Analysis Tools use the same underlying Semantic Interoperability Framework that we have developed. This thesis focuses on the Case Series Characterization Tool, which is explained in the following sub-section. The remaining Safety Analysis Tools are not explained in detail; but while presenting the enabling components and services in our architecture, their different requirements and how they are addressed in the architecture are explained (e.g. OMOP Converter and Formatter Service presented in Section 4.10).

4.1.1 Case Series Characterization Tool

One of the main pilot application scenarios of our work is enabling the safety analysts of the Uppsala Monitoring Centre (UMC) to run a case series characterization study for evaluating the validity of a potential signal, e.g. the effect of nifedipine on myocardial infarction (MI) events. Safety analysts need to access medical data sets of selected populations (e.g. foreground population as patients having MI within two weeks of nifedipine intake, and the background population as patients having nifedipine) from disparate EHR systems to be able to check whether there are other explanations more likely to cause MI than the exposure to nifedipine.

We have developed the Case Series Characterization Tool (CSCT) as a Web application, which enables the safety analyst to evaluate the validity of a potential signal by formally defining the characteristics of foreground and background populations, collecting semantically mediated and de-identified patient data from disperate EHR sources according to the population definitions, and analyzing the results. A screen shot from the tool is provided in Figure 4.2.

It is possible to define eligibility criteria by expressing several different clinical statements, such as conditions, medications, lab results, procedures, which are retrieved

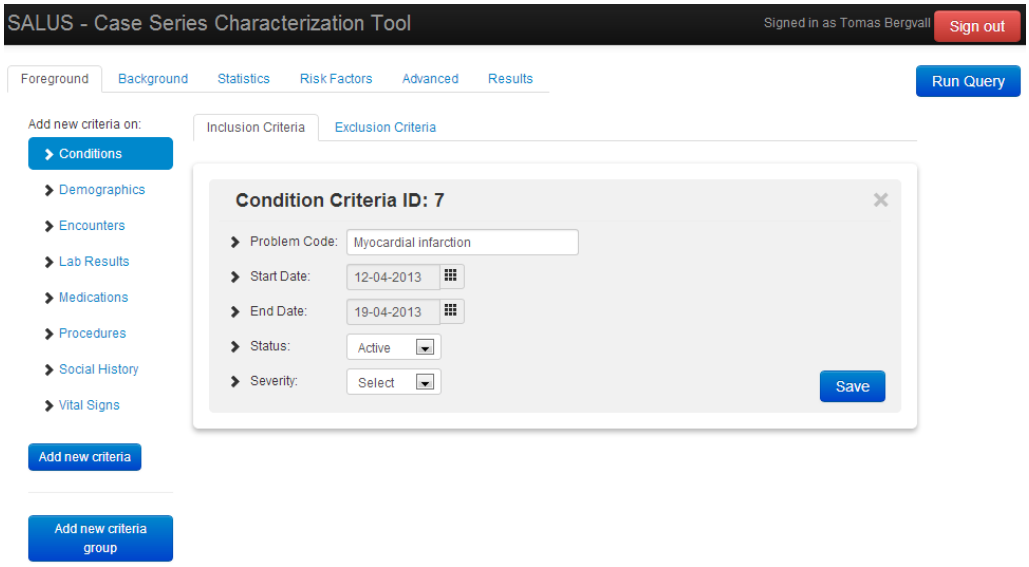

Figure 4.2: A screenshot from the Case Series Characterization Tool

from our common model; the SALUS Common Information Model (CIM) (see Section 3.2). Such criteria are represented by selecting coded values from terminology systems; for example, the medical event of interest can be defined by selecting "myocardial infarction" MedDRA Preferred Term (PT), and medication of interest by selecting "nifedipine" from WHO-ATC. The tool allows configuring the terminology systems to be used in these fields; e.g. another analyst may prefer to use SNOMED CT for defining problem codes. For enabling efficient type-ahead search functionality during code selection, the tool is integrated with a terminology server that indexes medical terminologies. It is also possible to define logical operators such as AND and OR, and temporal constraints among different criteria.

The tool also enables the safety analyst to configure the statistics to be calculated for grouping and stratifying data sets of the eligible populations, such as age, gender, common medications/events before/after medication/event of interest. The coded data can be configured to be grouped under a preferred terminology system and level in the results, for example MedDRA High Level Group Terms (HLGT), no matter which specific terminology system is used in the EHR sources. Finally, it is possible to define a number of coded risk factors to be specifically checked on both populations. These represent the possible confounding factors of the selected conditions in the eligibility criteria that needs to be checked in the medical summaries of the eligible patients.

The eligibility criteria needs to be passed to disparate EHR sources, and the de-identified medical data sets should be retrieved for the eligible patients. After aggregation, these medical data sets need to be analyzed to calculate the statistical information asked by the safety analyst. However, there are several challenges: i) divergent data models are used to represent EHRs, and ii) several different terminology systems are used to code structured patient data. In our architecture, we address these problems by formalizing the local models of EHR sites and semantically aggregating them using a common model, which we call the SALUS Common Information Model

(CIM). SALUS CIM is linked with ontological representations of terminology systems; hence before the statistics are calculated on the aggregated data represented in CIM, terminology reasoning is handled to address not only structural but also semantic mismatches between data sources and the requestor.

A step by step execution of a complete case series characterization scenario is provided in Chapter 5.

Case Series Characterization Tool is implemented following the most popular and stable HTML5 technologies such as Backbone.js [78] and neat graphical user interface experiences like Bootstrap [79]. The communication between the client side (i.e. GUI) and the server side of the tool is handled via RESTful services.

4.2 EHR Sources and Formalizing EHR Data

We have two EHR sources:

- A Regional Health Data Warehouse (DWH) is maintained in Lombardy Region in Italy, which collects and extracts all data necessary for administrative and statistical purposes from almost all the public healthcare providers. It is operational since 2002, covering a population of 9.9 million citizens with about 215 million yearly records. Its main advantage is providing longitudinal data, with the exception of data held in private hospitals. In SALUS, we are using a restricted copy for both eliminating unnecessary data (e.g. financial) and not affecting the regular operation of the system.

- The second source is the AGFA ORBIS installation used as the EHR system at University Hospital of Dresden (Uniklinikum Dresden - UKD), which is the largest hospital structure with 21 clinics in Saxony, Germany. The total number of registered patients in UKD ORBIS is around 820,000. There are more than 2.3 million recorded medical cases, and about 250,000 new medical cases are added each year. For use in SALUS, access to a live backup of the operational database is provided.

We follow a non-disruptive approach and collect EHR data in the local models used by the EHR systems. These can be based on interface standards as in the case of Lombardy DWH, which provides data represented in HL7/ASTM Continuity of Care Document (CCD)/ IHE Patient Care Coordination (PCC) templates; or proprietary formats like ORBIS relational data model as in the case of UKD. In both cases, in order to proceed with semantic mediation, the first thing that has to be done is formalizing the retrieved EHR data by representing them as Resource Description Framework (RDF) entities in local ontologies corresponding to the local models, which we prefer to call "content entity model" (see Section 3.1).

4.2.1 Technical Interoperability Data Source Query Service

Before starting our work, Lombardy Regional Health Infrastructure was already able to produce and exchange patient summary documents complying with CCD/PCC templates within the scope of epSOS project [26]. Building on the results of epSOS, we would like to enable the collection of de-identified medical summaries represented in CCD/PCC templates for the use of clinical research studies through standard based transactions. For this purpose, we have designed an extension of the native IHE Query for Existing Data (QED) [22] transactions to support population based queries and to provide data of all eligible patients represented in CCD/PCC templates as usual.

In the native QED, as explained in Section 2.4, it is possible to query and retrieve some specific medical sections (e.g. allergies, encounters, diagnoses) of a single identified patient. However, this does not cover our needs for supporting population based queries and getting de-identified data of matching patients at once. On the other hand, there is no other standard or profile for population based queries as needed in post market safety studies either. After an extensive analysis of the state of the art, we have decided to extend the QED profile, which we term as QEDExt by replacing its simple query structure with the HL7 Health Quality Measures Format (HQMF) (see Section 3.1.2) to express population based queries. An example population based HQMF query within our extended IHE QED transaction is provided in Appendix B. The response structure is almost identical; the CCD/PCC templates are used for presenting patient data as in the original transaction, but this time it is possible to present data of multiple patients.

We have designed the same extension for IHE Care Management (CM) (see Section 2.5) profile as well, this time for supporting subscription based population queries. The only major difference between the native QED and CM is that the former supports synchronous queries only while the latter supports subscription based queries; apart from that the structures of the transactions are identical.

In our architecture, Technical Interoperability Data Source Query Service (TIDSQS) implements the extended QED and CM profiles on top of Lombardy DWH. Although we have participated actively to the design of these extensions, the actual implementation work belongs to another SALUS beneficiary; hence it is not within the scope of this thesis.

4.2.2 EHR RDF Service

The EHR RDF Service gets the data of the eligible patients from TIDSQS in native XML representation of the CCD/PCC templates, after which data formalization takes place. In order to perform comprehensive transformations of XML Schemas (XSD) and XML data to RDF automatically, we have implemented a generic open source tool named Ontmalizer. Through this tool, the CCD/PCC template instances retrieved from TIDSQS complying with HL7 CDA Schema are automatically RDFized by creating the corresponding ontology instances. The outcome is always a one-to-one correspondence of the input data, but represented as RDF entities to foster further semantic processing. The details of our Ontmalizer tool are presented in the next

section.

In order to demonstrate the formalization of patient data via Ontmalizer, a simple CDA observation instance in its native XML syntax is provided in Figure 4.3. In this example, an "Acute myocardial infarction, of anterolateral wall" problem is presented with the start date of August 1st, 2009.

```
<observation classCode="OBS" moodCode="EVN">
    <code code="55607006" displayName="Problem" codeSystem="2.16.840.1.113883.6.96"
        codeSystemName="SNOMED CT"/>
    <effectiveTime>
        <low value="20090801"/>
    </effectiveTime>
    <value xsi:type="CD" code="410.0" displayName="Acute myocardial infarction, of
        anterolateral wall" codeSystem="2.16.840.1.113883.6.2" codeSystemName="ICD-9-CM">
        <originalText>Acute myocardial infarction, of anterolateral wall</originalText>
    </value>
</observation>
```

Figure 4.3: A simple CDA observation instance in its native XML syntax

Via Ontmalizer, one-to-one semantic correspondence of the simple observation instance in Figure 4.3 is created automatically, as displayed in Figure 4.4.

```
<http://www.srdc.com.tr/ontmalizer/instance#INS7778722_POCD_MT000040.Observation_1>
   a <urn:hl7-org:v3#POCD_MT000040.Observation> ;
   v3:code
      [ a v3:CD ;
        v3:code "55607006"^^v3:csDatatype ;
        v3:codeSystem "2.16.840.1.113883.6.96"^^v3:uidDatatype ;
        v3:codeSystemName "SNOMED CT"^^v3:stDatatype ;
        v3:displayName "Problem"^^v3:stDatatype
      ] ;
   v3:effectiveTime
      [ a v3:IVL_TS ;
        v3:low
          [ a v3:IVXB_TS ;
            v3:value "20090801"^^v3:tsDatatype
          ]
      ] ;
   v3:value
      [ a v3:CD ;
        v3:code "410.0"^^v3:csDatatype ;
        v3:codeSystem "2.16.840.1.113883.6.2"^^v3:uidDatatype ;
        v3:codeSystemName "ICD-9-CM"^^v3:stDatatype ;
        v3:displayName "Acute myocardial infarction, of anterolateral wall"^^v3:stDatatype;
        v3:originalText
          [ a v3:ED ;
            v3:textContent "Acute myocardial infarction, of anterolateral wall"^^xsd:string
          ]
      ] .
```

Figure 4.4: The RDFized (i.e. formalized) CDA observation instance in N3 syntax

As a more detailed example, in Appendix C, an example medical summary in native HL7 CDA format using PCC/CCD templates is provided. This example has basically patient demographics, condition and medication data. Then, in Appendix D, the

one-to-one semantic correspondence of the CCD instance provided in Appendix C is presented.

The EHR RDF Service is also responsible for conversion in the opposite direction during querying. In this case, the EHR RDF Service gets the elibility criteria in RDF/OWL representation of HL7 HQMF and then transforms it to the corresponding native HQMF XML format before passing to the TIDSQS, which will run the query on top of the Lombardy DWH.

4.2.3 Ontmalizer

Ontmalizer performs comprehensive transformations of XML Schemas (XSD) and XML data to RDF/OWL automatically. Through this tool, it is possible to create RDF/OWL representation of XML Schemas, and XML instances that comply with such XML Schemas.

The state of the art open source and/or free tools for RDFizing XSD and XML were not able to handle complex schemas and XML instances such as HL7 Clinical Document Architecture (CDA) R2. Only the commercial versions (standard and maestro) of TopBraid Composer [71] were successfully able to handle such complex schemas. However, we do not want to use such commercial tools in SALUS. Besides, TopBraid Composer is able to RDFize XSDs and XMLs through its GUI; it does not provide an API for easy integration.

As a result, we implemented our own solution. We make use of Sun's XSOM library [80] for processing XML Schemas, Apache Xerces [81] for processing XML data and Apache Jena [82] for managing RDF data. While proceeding with the implementation of Ontmalizer, we noticed that the TopQuadrant / TopBraid Composer team provided their conversion guidelines through a blog entry [83]. In this guideline, the TopBraid team explains how they managed to implement transformations of XML Schemas and XML data to RDF/OWL for version 3.6.0 of TopBraid Composer. We were happy to see that we were following similar approaches, and we continued the implementation by taking into account their guidelines as well.

We explain how we manage to perform conversions from XSD to RDF/OWL, and from XML data to RDF/OWL in the next two sub-sections.

4.2.3.1 Transforming XSD to RDF/OWL

The transformation rules that are used in the Ontmalizer XSD to RDF/OWL algorithm are provided in Table 4.1.

In the implementation, XSD2OWLMapper is the main class to transform XML Schemas to RDF/OWL. The constructor of this class gets the root XSD file to be transformed. Configuration of the transformation operation is quite simple: the caller can set the prefixes for the object property and datatype property names to be created. Then, the call to the convertXSD2OWL() method performs the transformation. XSD2OWLMapper is able to print the output ontology in one of these formats: RDF/XML, RDF/XML-

Table4.1: Conversion from XSD Constructs to OWL Constructs

#	**XSD Constructs**	**OWL Constructs**
1	xs:simpleType	rdfs:Datatype with the suffix "Datatype" on datatype name.
2	xs:simpleType with xs:enumeration	rdfs:Datatype with the suffix "Datatype" on datatype name. In addition, for the enumerations, an owl:Class as a subclass of EnumeratedValue is created. Instances are created for every enumerated value. An instance of Enumeration, referring to all the instances, is created as well as the owl:oneOf union over the instances. These are mostly informative, as they are not used directly during the XML data to RDF/OWL transformation.
3	xs:complexType over xs:complexContent	owl:Class
4	xs:complexType over xs:simpleContent	owl:Class
5	xs:element (global) with complex type	owl:Class and subclass of the class generated from the referenced complex type
6	xs:element (global) with simple type	owl:Datatype
7	xs:element (local to a type)	owl:DatatypeProperty or owl:ObjectProperty depending on the element type. OWL Restrictions are built for the occurrence.
8	xs:group	owl:Class
9	xs:attributeGroup	owl:Class
10	Anonymous Complex Type	As for Complex Type except a URI is constructed as Anon_#. Also, the class is defined as a subclass of Anon.
11	Anonymous Simple Type	As for Simple Type except a URI is constructed as Anon_#.
12	Substitution Groups	Subclass statements are generated for the members.
13	xsi:type on an XML element	Overrides the schema abstract type with the specified type.

ABBREV, N-TRIPLE and N3. An example transformation routine is provided in Figure 4.5 for the HL7 CDA R2 XML Schema.

```
// This part converts XML schema to OWL ontology.
XSD2OWLMapper mapping = new XSD2OWLMapper(new File("src/test/resources/CDA/CDA.xsd"));
mapping.setObjectPropPrefix("");
mapping.setDataTypePropPrefix("");
mapping.convertXSD2OWL();

// This part prints the ontology to the specified file.
FileOutputStream ont;
try {
    File f = new File("src/test/resources/output/cda-ontology.n3");
    f.getParentFile().mkdirs();
    ont = new FileOutputStream(f);
    mapping.writeOntology(ont, "N3");
    ont.close();
} catch (Exception e) {
    e.printStackTrace();
}
```

Figure 4.5: An example XSD to RDF/OWL transformation routine

We benefit from XSD2OWLMapper in several occasions. We created the SALUS Draft Common Information Model (CIM) as an XML Schema first, and we are able to create the CIM ontology by using XSD2OWLMapper. The complete SALUS CIM ontology represented in N3 syntax is available at [62]. Similarly, CDA/CCD Content Entity Model Ontology, which is the outcome of HL7 CDA R2 XML Schema transformation, is available in N3 syntax at [48].

4.2.3.2 Transforming XML to RDF/OWL

In compliance with the transformation rules that are presented in the previous section, this second part takes care of RDFizing XML data. In our implementation, XML2OWLMapper is the main class to transform XML data to RDF/OWL by creating instances of the necessary OWL classes, RDFS datatypes, OWL datatype and object properties. The constructor of this class gets the XML file to be transformed together with an instance of XSD2OWLMapper that is already initialized with the corresponding XML Schema of the XML data. No other configuration is necessary for the transformation operation; the prefixes for the object property and datatype property names to be created are gathered from the XSD2OWLMapper configuration. Then, the call to the convertXML2OWL() method performs the transformation.

Briefly, the XML transformation algorithm is as follows. When convertXML2OWL() method is called:

- The Document element of the XML document is selected,
- A class having the same URI as the document element is selected,
- The root of the model is created according to the type of the class found,
- Then, for each child of document element the traverseChildren method is called. This is a pre-order recursive traversal of the XML DOM tree. For each element the findObjectType method is called.
- The findObjectType method finds the type of the object according to the name of the property in a triple. This is achieved by traversing over class relations of ontology. If we think of sub-class, super-class relationship as a tree, then this function's algorithm resembles a level order traversal. To illustrate from Figure 4.6, the implementation will find Class E as the range of the object property "hasName" when we search starting from the Class A.
- If the method finds a datatype property, then this means the next processed XML node will be a text node. So, in order for traverseChildren to process it properly, we save the property name and its range type to a global variable. An example output for this case is provided below:

```
:INS2007004_IVL_PQ_2
    a v3:IVL_PQ ;
    v3:unit "mg"^^v3:csDatatype ;
    v3:value "250"^^v3:realDatatype .
```

- If the method finds an object property and a text node comes after that XML node and if the type of this property allows mixed content according to the XML Schema definition, then an instance of "textContent" datatype property, which

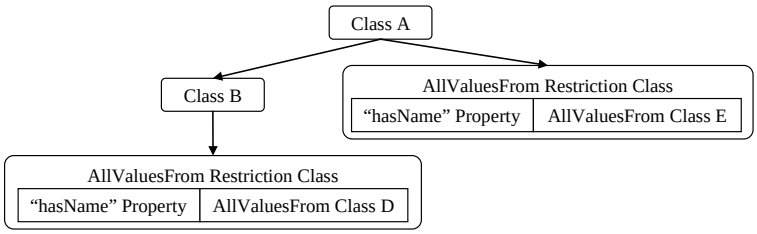

Figure 4.6: An example sub-class / super-class hierarchy representation

does not exist in the original XML Schema, is added. The text is assumed to have xs:string data type. Below, an example for this case is provided:

```
:INS2007004_ST_4
    a v3:ST ;
    v3:textContent "History of medication use"^^xsd:string .
```

Similar to XSD2OWLMapper, XML2OWLMapper is able to print the output ontology instance in one of these formats: RDF/XML, RDF/XML-ABBREV, N-TRIPLE and N3. An example transformation routine is provided in Figure 4.7 for a complete HL7 CDA R2 instance, which is compliant with the HL7/ASTM Continuity of Care Document (CCD) and IHE Patient Care Coordination (PCC) templates.

```
// This part converts XML schema to OWL ontology.
XSD2OWLMapper mapping = new XSD2OWLMapper(new File("src/test/resources/CDA/CDA.xsd"));
mapping.setObjectPropPrefix("");
mapping.setDataTypePropPrefix("");
mapping.convertXSD2OWL();

// This part converts XML instance to RDF data model.
XML2OWLMapper generator = new XML2OWLMapper(
    new File("src/test/resources/CDA/SALUS-sample-full-CDA-instance.xml"), mapping);
generator.convertXML2OWL();

// This part prints the RDF data model to the specified file.
try{
    File f = new File("src/test/resources/output/salus-cda-instance.n3");
    f.getParentFile().mkdirs();
    FileOutputStream fout = new FileOutputStream(f);
    generator.writeModel(fout, "N3");
    fout.close();

} catch (Exception e){
    e.printStackTrace();
}
```

Figure 4.7: An example XML to RDF/OWL transformation routine

Again, XML2OWLMapper plays a very important role in the overall architecture. We use it within the EHR RDF Service for transformation of CCD/PCC entry level XML instances to RDF/OWL; i.e. formalization of EHR data coming from the Lombardy DWH.

4.2.3.3 Notes about Ontmalizer

Below, some notes (assumptions, limitations) about the current Ontmalizer implementation are provided:

- Valid XML documents with respect to the corresponding XML Schema need to be provided. Ontmalizer does not perform XML validation against the XSD for performance reasons.
- The user needs to supply only the root XML Schema for transformation, the included schemas are automatically imported by Ontmalizer.
- The current implementation does not take into account xsd:import; yet only xsd:include is supported.
- "any", "anyAttribute" elements and "default", "fixed", "nillable" attributes are not taken into account during XSD transformation, as they are not used within XML transformation either.
- Identity constraints of the schema are not processed.
- Default object property prefix is "has", and the default datatype property is "dtp".
- Ontmalizer checks if the URIs are valid. If not http://uri-not-valid.com# is used as the URI. If URI is a relative URI, then http://uri-not-absolute.com# is used.
- To uniquely name the RDF resources, INS<X>_<resourcetypename>_<typeoccurrence> pattern is used, where X is a random number between 0 and 9999999 that is generated for each instance of class XML2OWLMapper and remains the same within a single transformation, resourcetypename is the name of the type of the resource, and finally typeoccurrence is the sequence number of occurrence of that type's instance in a single transformation.

4.2.4 UKD SPARQL Endpoint

A slightly different approach for EHR data formalization is followed on the UKD side. Instead of data exchange through some content standards, as the developer of the system, AGFA exposes a SPARQL endpoint directly on top of the UKD ORBIS System, which is able to retrieve data from the relational tables of ORBIS and return as RDF entities in the ORBIS Content Entity Model according to the SPARQL queries. So, in this case, EHR data formalization immediately takes place on top of the relational database. This work is not within the scope of this thesis, but presented here briefly to explain the differences with our approach, and how these two slightly different approaches work together in our Semantic Interoperability Framework.

4.3 Semantic Interoperability Layer Data Service

In our architecture, Semantic Interoperability Layer - Data Services (SIL-DSs) for Lombardy and UKD are responsible for converting the medical summaries of the eligi-

ble population represented in local ontologies, i.e. CDA/CCD Content Entity Model instances received from EHR RDF Service and ORBIS Content Entity Model instances received from UKD SPARQL Endpoint, to instances represented in SALUS CIM ontology. In order to perform this operation, a set of conversion rules in Notation3 (N3) [47] has been implemented in Euler Yap Engine (EYE), which is an open source and high performance reasoning engine maintained by AGFA [44]. The CDA/CCD conversion rules that we have implemented are explained in more detail in the following sub-section.

Semantic Interoperability Layer - Data Services are implemented as RESTful services with HTTP GET and POST support. The endpoint of the SIL-DS (Lombardy) is:

```
http://localhost:8080/athena/entities/www.salusproject.eu/salus/salus.lispa.it/
    population/medicalsummary
```

4.3.1 CDA/CCD Conversion Rules

Before starting the implementation of the conversion rules, first of all, we have done an extensive study for mapping all the CDA/CCD Content Model elements to the SALUS Common Information Model (CIM) elements. Since we have designed the SALUS CIM to address CDA/CCD Content Model from the very beginning, we were able to find a correspondence for each element of the CDA/CCD Content Model. We have maintained these mappings first in manually created tables. An example mapping from Past Medical History Section or Active Problems Section Entry template to both SALUS Common Data Elements (CDEs) and SALUS CIM ontology entities is provided in Table 4.2.

Once we created these mapping tables, we have implemented the actual conversion rules in N3 to be run on EYE Reasoning Engine. To realize the conversion operations, we feed EYE with patient data in CDA/CCD Content Entity Model and the conversion rules that we have implemented. In a very short time, it provides us with the same clinical data but this time represented as SALUS CIM instances as a result of the conversion operation. As an example, the outcome of the conversion rules applied on top of the simple CDA/CCD observation instance of Figure 4.4 is provided as instances of the SALUS CIM ontology (specifically as salus:Condition) in Figure 4.8.

We can see that the necessary entities are created based on the mapping information provided in Table 4.2. Conversion rules address necessary format transformations as well, such as different datetime formats used in CDA/CCD Content Entity Model and SALUS CIM. As a more comprehensive example, a complete SALUS CIM ontology instance as a direct correspondence of the HL7 CDA instances provided in Appendix C and Appendix D is provided in Appendix E.

We have followed a modular approach while implementing the conversion rules so that there is a root rule matching with the root of the semantic representation of a medical summary. This root rule calls other sub-rules for all possible entries such as allergies, medication, conditions, etc. Such a rule calling mechanism within another rule, just like a function call, is possible since we have implemented the conversion rules as backward rules in EYE.

Table4.2: A part of the mapping from CDA/CCD Problem Entry to SALUS CIM Condition Entity

Past Medical History Section or Active Problems Section Entry		
Location in PCC/CCD in the specified sections	**Common Data Element Name**	**CIM Ontology Entity**
cda:entry/cda:act[cda:templateId/@root= '1.3.6.1.4.1.19376.1.5.3.1.4.5.2']/ cda:entryRelationship[@typeCode='SUBJ']/cda:observation[cda:templateId/@root= '1.3.6.1.4.1.19376.1.5.3.1.4.5']	Condition	Condition
cda:code/	Problem Type	problemType
cda:effectiveTime/low	Start Date	problemDate.low
cda:effectiveTime/high	End Date	problemDate.high
cda:value/cda:originalText	Problem Name	problemName
cda:value/	Problem Code	problemCode
cda:text/	Comments / text describing problem	comment
cda:entryRelationship/cda:observation [cda:templateId/@root = '1.3.6.1.4.1.19376.1.5.3.1.4.1.1']/ value/	Problem Status	problemStatus
cda:entryRelationship/cda:observation [cda:templateId/@root = '1.3.6.1.4.1.19376.1.5.3.1.4.1']/ value/	Severity	problemSeverity

```
_:t0
   a salus:Condition ;
   salus:problemType
      [ rdf:type salus:cd ;
        salus:code "55607006" ;
        salus:codeSystem "2.16.840.1.113883.6.96" ;
        salus:codeSystemName "SNOMED CT" ;
        salus:displayName "Problem"
      ] ;
   salus:problemCode
      [ rdf:type salus:cd ;
        salus:code "410.0" ;
        salus:codeSystem "2.16.840.1.113883.6.2" ;
        salus:codeSystemName "ICD-9-CM" ;
        salus:displayName "Acute myocardial infarction, of anterolateral wall"
      ] ;
   salus:problemDate
      [ rdf:type salus:ivlTs ;
        salus:low "2009-08-01T00:00:00"^^xsd:dateTime
      ] ;
   salus:problemName "Acute myocardial infarction, of anterolateral wall".
```

Figure 4.8: SALUS CIM conversion of the CDA/CCD observation instance in Figure 4.4

A very simple backward rule, which converts the ED data type of CDA into a string literal, is provided in Figure 4.9.

In total, we have 75 high-level conversion rules for mapping the complete CDA/CCD Content Entity Model to SALUS CIM. Both the data type conversion rules and the entry specific rules are reused extensively. For instance, the backward rule in Figure 4.9

```
#ED2String
{?ED :mapED ?STR}
<=
{
    ?ED a cda:ED;
        cda:textContent ?ed_lit.
    (?STR ?datatype) log:dtlit ?ed_lit.
}.
```

Figure 4.9: A simple backward rule to convert ED data type of CDA to string literal

is used in any place where a conversion from ED data type to string literal is needed. The same applies to the high-level CDA/CCD entry based conversion rules as well. For instance, the rule converting CDA/CCD Problem Entry to SALUS CIM Condition is used when both converting the "Past Medical History" and "Active Problems" sections in a CCD document, since both sections use the same entry level CDA/CCD templates. As a more comprehensive example, the set of rules involved in converting CDA/CCD Problem Entry to SALUS CIM Condition is provided in Appendix F.

Similarly, it is easily possible to reuse these conversion rules when PCC/CCD entry level templates are used not necessarily within a CDA document, but other structures such as the response message of the IHE QED and CM integration profiles that we extend and use in our architecture.

Content entity models and conversion rules are part of the SALUS Semantic Resource Set. Whenever a new content model is to be introduced in the SALUS architecture, it is necessary to define the conversion rules from the corresponding entity model (i.e. formalized) to the SALUS CIM ontology as the common mediator.

4.4 De-Identification and Pseudonymization Service

The aim of the De-Identification and Pseudonymization Service is to assure the security and privacy of the patient data exchanged within the SALUS Semantic Interoperability Framework. The EHR sources do not prefer providing identified patient data for post market safety studies. Our safety analysis tools do not need to access identified patient data either. Therefore, the De-Identification and Pseudonymization Service is pre-configured to de-identify some sensitive attributes of the medical summaries before they leave the care zone of the EHR sources. Several de-identification methods are implemented for this purpose, such as generalization for leaving only the year of birth of a patient, or redaction for completely deleting name and surname of the patient. De-Identification and Pseudonymization Service is also able to replace some identifiers (such as patient identifier or health professional identifier) with pseudonyms.

The De-Identification and Pseudonymization Service is used by the Semantic Interoperability Layer Data Services, and hence performs the de-identification and pseudonymization operations on patient data represented in SALUS CIM ontology. It provides the de-identified patient population data represented in SALUS CIM ontology to the Aggregation Service. Within the scope of this thesis, we are the user but not the actual implementer of the De-Identification and Pseudonymization Service.

4.5 Aggregation Service

The Aggregation Service is used to merge multiple entities from different data providers. This takes place through a simple pass through of all the data provided, which is already expressed using the SALUS CIM ontology.

The URL of the Aggregation Service is:

```
http://localhost:8080/athena/entities/www.salusproject.eu/salus/www.salusproject.eu/aggregate
    ?dataUrl=<path_to_population_data_in_cim>
    &dataUrl=<path_to_population_data_in_cim>
```

The Aggregation Service is also a RESTful service and expects references to the entities to aggregate via the dataUrl parameters. Both HTTP GET and POST are supported.

4.6 Running Queries over the Semantic Interoperability Framework

This section depicts the complete transformation and mediation cycle of the query and the results, which is initiated by the Safety Analysis Tools (in particular the Case Series Characterization Tool (CSCT)) by passing the query parameters to the Safety Analysis Query Manager (SAQM). SAQM is a RESTful semantic service managing the workflow among other RESTful semantic services (further details about SAQM are provided in 4.9). Through the Aggregation Service, SAQM is responsible for forwarding the eligibility criteria represented in SALUS CIM ontology to the registered SIL-DSs and getting back the aggregated results again in SALUS CIM. The complete cycle is presented in detail in Figure 4.10.

SIL-DS (Lombardy) converts the eligibility criteria in SALUS CIM ontology to an ontological representation of HQMF (which are quite similar) and passes to the EHR RDF Service, which then translates this to the native HQMF syntax in XML and forwards to TIDSQS. This population query is run on the Lombardy DWH as explained previously, and as a result, first the medical summaries of the eligible patients are provided back to the EHR RDF Service as CDA/CCD XML instances, which then formalizes this data and provides corresponding medical summaries represented in CDA/CCD Content Entity Model to the SIL-DS (Lombardy). By making use of the conversion rules, SIL-DS (Lombardy) represents the medical summaries of the eligible patients in SALUS CIM ontology and returns them to the Aggregation Service via the De-Identification and Pseudonymization Service.

In SIL-DS (UKD), the same query in SALUS CIM ontology is transformed into a SPARQL query compliant with ORBIS Content Entity Model and run directly on top of the SPARQL Endpoint. The data of the eligible patients represented in ORBIS Content Entity Model are provided to the SIL-DS (UKD), which then represents these data as SALUS CIM ontology instances by using the conversion rules and returns them to the Aggregation Service via the De-Identification and Pseudonymization Service.

Aggregation Service simply merges the de-identified population data in SALUS CIM from different sources and provides them to the SAQM. Now, all the patient data in

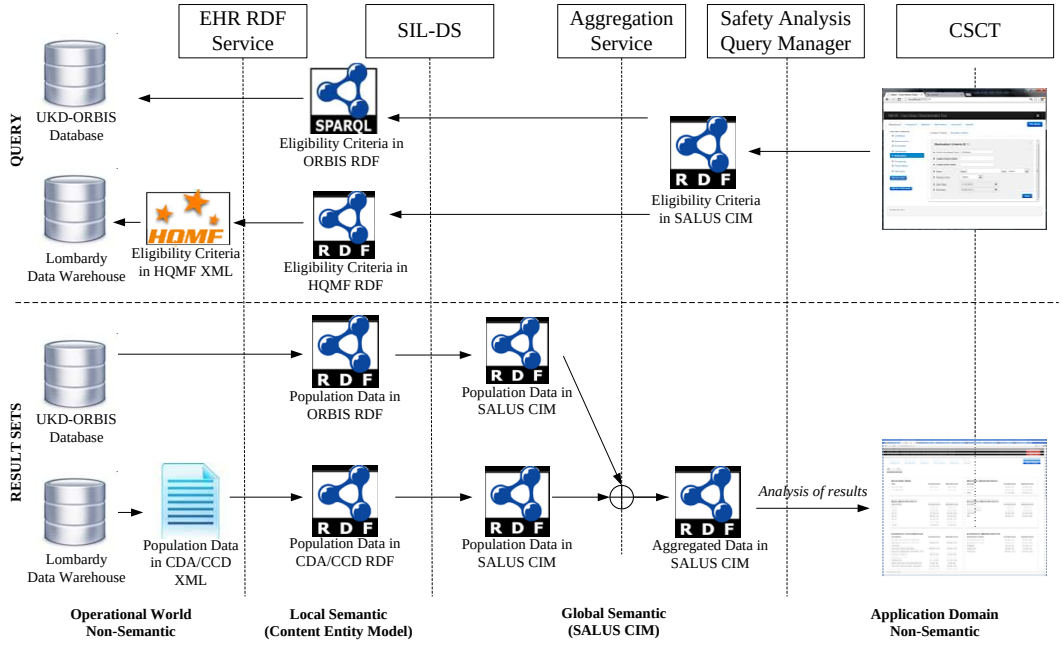

Figure 4.10: The complete transformation and mediation cycle of the eligibility query and the result sets via the SALUS Interoperability Framework

SAQM are represented in SALUS CIM; however, yet it is not possible to "understand" as they are coded with several codes from different terminology systems.

4.7 Terminology Reasoning Service

In all our pilot application scenarios, there is a need for terminology reasoning because the EHR sources on the clinical care side and the end-users on the clinical research side use very different medical terminology systems for coding medical data. For example, for coding conditions (diagnoses, problems, etc.), Lombardy Region uses ICD-9-CM, UKD uses ICD-10-GM and UMC prefers dealing with MedDRA most of the time as well as SNOMED CT. Details about these terminology systems are provided in Section 3.3.

In order to overcome the terminology reasoning challenge, we achieved the following:

- Representation of the terminology systems as ontologies within the SALUS Semantic Resource Set,
- Utilizing reliable terminology system mapping resources,
- Automatically linking coded patient data with terminology system ontologies, and
- Purpose specific materialization for high performance.

Table4.3: Terminology mapping resources that are utilized in the SALUS Semantic Resource Set

Source System	**Target System**	**Type of Mapping**	**Number of Mappings**	**Mapping Resource**
MedDRA	SNOMED CT	exact match	10,648	OntoADR of the PROTECT project; manual improvement of UMLS mappings by PROTECT experts [84]
ICD-9-CM	SNOMED CT	exact or broad match	16,819	OMOP Vocabulary; created manually by OMOP experts
ICD-10-CM	SNOMED CT	exact or broad match	59,122	OMOP Vocabulary; created manually by OMOP experts
ICD-10-GM	ICD-10	exact match	12,318	Identical codes in both systems
ICD-9-CM	SNOMED CT	close match	43,086	BioPortal; manual review by SALUS experts before inclusion
ICD-10-CM	SNOMED CT	close match	45,022	BioPortal; manual review by SALUS experts before inclusion

We already explained the first step, i.e. the representation of the terminology systems as ontologies within the SALUS Semantic Resource Set, in Section 3.3.

For the next step, we utilize the following reliable terminology mapping resources that are presented in Table 4.3.

Like the terminology systems, we provide these mapping information as triples in our Semantic Resource Set as well, by making use of SKOS properties such as skos:exact-Match where possible.

Now that we have the terminology systems and the mapping information available in SALUS Semantic Resource Set, and we are automatically able to link the coded patient data with the terminology system concepts through the commonly used concept and concept scheme identifiers in the patient data instances and semantic representations of terminology systems, we can proceed with terminology reasoning. However, in order to realize terminology reasoning at run time in acceptable durations, it is absolutely necessary to do some in-advance inferencing specific to the reasoning requirements, which is known as materialization in the semantic Web domain.

In our environment, the conditions of the patients are provided with several codes at different levels from ICD-9-CM in Lombardy DWH and ICD-10-GM in UKD. However, the safety analysts working at UMC want the conditions to be grouped under a different terminology system, namely MedDRA, and also at a specific level in the MedDRA hierarchy; e.g. High Level Group Term (HLGT) or High Level Term (HLT). Therefore, we should be able to find either exact or broad correspondences of various source codes from ICD-9-CM and ICD-10-GM to specific MedDRA levels.

As an example, some codes for representing "haemorrhage" (i.e. bleeding) from several different terminology systems and the relations among them, as they are available in SALUS Semantic Resource Set, are presented graphically in Figure 4.11. The actual codes used in the source EHRs are shaded in the figure.

The designations of all the codes in the figure are provided below:

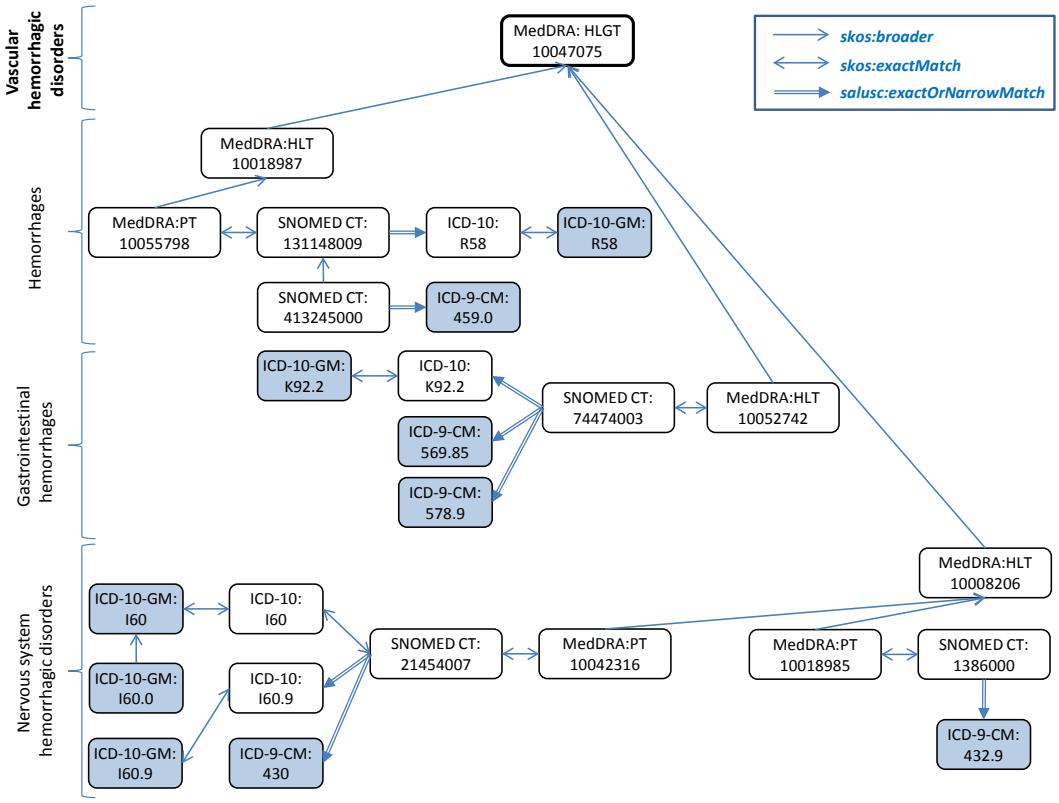

Figure 4.11: Some generic and specific codes for representing "haemorrhage" and the relations among them, as they are available in the SALUS Semantic Resource Set

- ICD-9-CM
  - 430: Subarachnoid hemorrhage
  - 432.9: Unspecified intracranial hemorrhage
  - 459.0: Hemorrhage, unspecified
  - 569.85: Angiodysplasia of intestine with hemorrhage
  - 578.9: Hemorrhage of gastrointestinal tract, unspecified
- ICD-10-GM
  - I60.-: Subarachnoid haemorrhage
  - I60.0: Subarachnoid haemorrhage from carotid siphon and bifurcation
  - I60.9: Subarachnoid haemorrhage, unspecified
  - K92.2: Gastrointestinal haemorrhage, unspecified
  - R58: Haemorrhage, not elsewhere classified
- ICD-10
  - I60: Subarachnoid haemorrhage
  - I60.9: Subarachnoid haemorrhage, unspecified
  - K92.2: Gastrointestinal haemorrhage, unspecified

  - R58: Haemorrhage, not elsewhere classified

- MedDRA
  - 10047075: Vascular haemorrhagic disorders [HLGT]
  - 10018987: Haemorrhages not elsewhere classified (NEC) [HLT]
  - 10055798: Haemorrhage [PT]
  - 10052742: Gastrointestinal haemorrhages [HLT]
  - 10008206: Nervous system haemorrhagic disorders [HLT]
  - 10018985: Haemorrhage intracranial [PT]
  - 10042316: Subarachnoid haemorrhage [PT]

- SNOMED CT
  - 131148009: Bleeding
  - 413245000: Bleeding of unknown origin
  - 74474003: Gastrointestinal hemorrhage
  - 1386000: Intracranial hemorrhage
  - 21454007: Subarachnoid hemorrhage

Both generic codes such as ICD-10-GM:R58 for "Haemorrhage, not elsewhere classified", and more specific codes such as ICD-9-CM:578.9 for "Hemorrhage of gastrointestinal tract, unspecified" take place in the patient data (of course the German and Italian designations are used in our pilots). We are expected to group all such codes under the MedDRA HLGT code "10047075" for "Vascular haemorrhagic disorders", although it does not have a direct link with any of the source codes.

In our Semantic Resource Set, we represent the original hierarchical relationships within a terminology system with skos:broader relationship (see Section 3.3. For the mappings across terminology systems, we use skos:exactMatch for one-to-one mappings, and salusc:exactOrNarrowMatch relationship as a union of skos:exactMatch and skos:narrowMatch when a term is either equal to or broader than the other, which is the case in the mappings provided by OMOP Vocabulary. SKOS does not provide such a property, so we ended up defining salusc:exactOrNarrowMatch to meet our requirements. A very tiny excerpt presenting a few code mappings for the heamorrhage example (Figure 4.11) as triples kept in the SALUS Semantic Resource Set is presented in Figure 4.12.

By using all these relationships, we apply a series of terminology reasoning rules implemented on top of EYE, which calculate the full transitive closure of salusc:narrowOrExactMatch relationship for all the codes in our Semantic Resource Set. We do this in three main steps. The first one is the transitive closure calculation of the skos:broader relationship for all terminology systems, and this is done via execution of the N3 rule provided in Figure 4.13 with EYE reasoning engine. skos:broader is not an owl:TransitiveProperty by definition; but it is a sub-class of skos:broaderTransitive, which is an owl:TransitiveProperty. Also, skos:broader can be used for inserting facts but not for deductions (i.e. inferencing). Therefore, we first create a skos:broaderTransitive correspondent for each skos:broader triple, and then tell the reasoner to calculate the whole transitive closure.

```
# MedDRA and SNOMED CT (OntoADR)
<http://purl.bioontology.org/ontology/MDR/10052742>
    skos:exactMatch <http://purl.bioontology.org/ontology/SNOMEDCT/74474003>.

# ICD-9-CM to SNOMED CT (OMOP Vocabulary)
<http://purl.bioontology.org/ontology/SNOMEDCT/74474003>
    salusc:exactOrNarrowMatch <http://purl.bioontology.org/ontology/ICD9CM/578.9> ,
    <http://purl.bioontology.org/ontology/ICD9CM/569.85> .

# ICD-10 and SNOMED CT (BioPortal + OMOP Vocabulary + manually checked)
<http://purl.bioontology.org/ontology/SNOMEDCT/74474003>
    salusc:exactOrNarrowMatch <http://purl.bioontology.org/ontology/ICD10/K92.2>.

# ICD-10 and ICD-10-GM (equality between the same codes)
ICD10:K92 skos:exactMatch ICD10GM:K92.
<http://purl.bioontology.org/ontology/ICD10/K92.2>
    skos:exactMatch <http://www.salusproject.eu/terminology/ICD10GM/K92.2>.
```

Figure 4.12: A few triples for code mappings in the SALUS Semantic Resource Set

```
{
    ?A skos:broader ?B.
}
=>
{
    ?A skos:broaderTransitive ?B.
}.

{
    ?A skos:broaderTransitive ?B.
    ?B skos:broaderTransitive ?C.
}
=>
{
    ?A skos:broaderTransitive ?C.
}.
```

Figure 4.13: N3 rule for calculating transitive closure of skos:broader

The second rule provided in Figure 4.14 is for calculating the transitive closure of skos:exactMatch, which is an owl:SymmetricProperty by definition. In our Semantic Resource Set, in line with its definition, we use it for one-to-one mappings, which are bidirectional. Therefore, this rule first generates the skos:exactMatch triple in the other direction, and then tell the reasoner to calculate the transitive closure.

The final rule provided in Figure 4.15 merges the outcomes of the first two rules, and then further calculates the transitive closure of salusc:exactOrNarrowMatch. Since salusc:exactOrNarrowMatch is a union of skos:broader (also skos:broaderTransitive) and skos:exactMatch, all of their triples imply salusc:exactOrNarrowMatch relationship as well. Then, in the final part, we tell the reasoner to calculate the transitive closure as usual, this time for salusc:exactOrNarrowMatch.

A small part of the result of executing these materialization rules for the haemorrhage example is provided in Figure 4.16. Now, it is possible reach to the broad MedDRA HLGT term with a single link, not just for ICD-9-CM or ICD-10-GM codes, but all the involved codes from other systems such as SNOMED CT involved in the materialization

```
{
    ?A skos:exactMatch ?B.
}
=>
{
    ?B skos:exactMatch ?A.
}.

{
    ?A skos:exactMatch ?B.
    ?B skos:exactMatch ?C.
    ?A log:notEqualTo ?C.
}
=>
{
    ?A skos:exactMatch ?C.
}.
```

Figure 4.14: N3 rule for calculating transitive closure of skos:exactMatch

```
{
    ?A skos:exactMatch ?B.
}
=>
{
    ?A salusc:exactOrNarrowMatch ?B.
}.

{
    ?A skos:broaderTransitive ?B.
}
=>
{
    ?B salusc:exactOrNarrowMatch ?A.
}.

{
    ?A salusc:exactOrNarrowMatch ?B.
    ?B salusc:exactOrNarrowMatch ?C.
    ?A log:notEqualTo ?C.
}
=>
{
    ?A salusc:exactOrNarrowMatch ?C.
}.
```

Figure 4.15: N3 rule for calculating transitive closure of salusc:exactOrNarrowMatch

process as was displayed in Figure 4.11.

These materialized results are provided to the Terminology Reasoning Service. Whenever a new mapping resource is to be added, it is necessary to recalculate these materialized information, which is easily handled via our N3 rules that we run on EYE.

At run time, having all the patient data in SALUS CIM, Safety Analysis Query Manager (SAQM) calls the Terminology Reasoning Service with these patient data, and the statistics and risk factor configurations provided by the safety analyst. Based on these configurations, Terminology Reasoning Service finds the correspondences of the

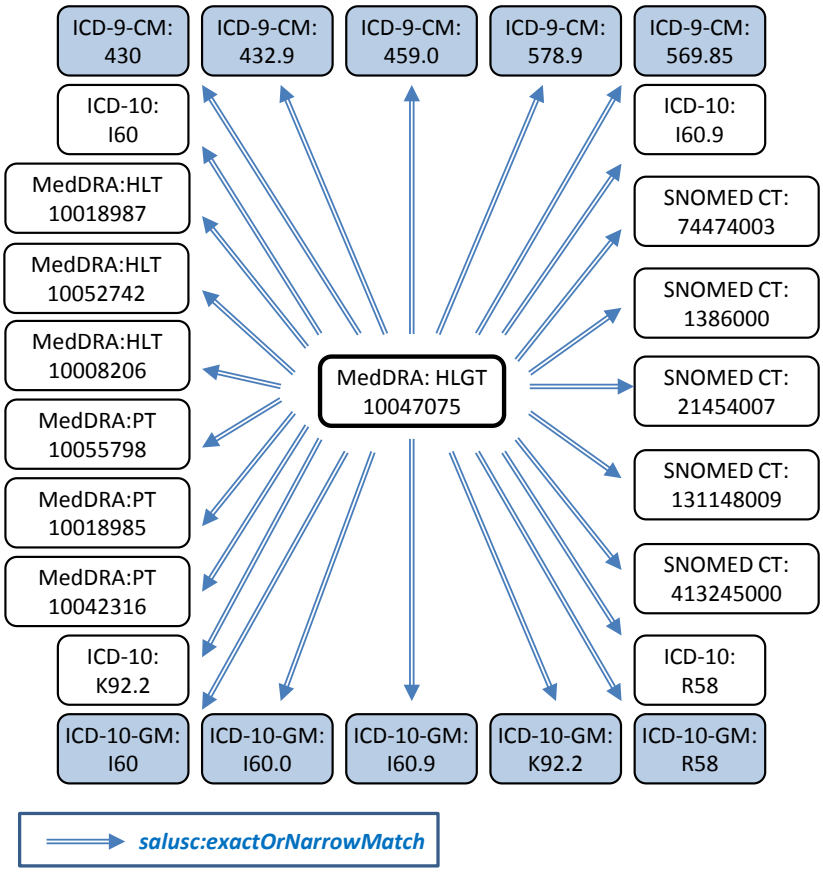

Figure 4.16: An excerpt from the result of salusc:exactOrNarrowMatch relationship transitive closure calculation for the heamorrhage example

coded information such as problem and active ingredient codes. This is implemented through another set of N3 rules that are executed at run time via a call to the RESTful Terminology Reasoning Service deployed at the following URL (this is for the CSCT only):

```
http://localhost:8080/athena/entities/www.salusproject.eu/salus/www.salusproject.eu/
    term-reasoning/csct?dataUrl=<path_to_dynamic_reasoning_rules>
    &dataUrl=<path_to_patient_population_in_cim>
```

The first part of the URL until the first *dataUrl* parameter is a reference to the materialized mapping information among all the terminology systems that exist in the SALUS Semantic Resource Set. The first *dataUrl* parameter indicates a location containing dynamic terminology reasoning rules that are used to calculate an equivalent closure of codes to be obtained from a certain terminology system, e.g. MedDRA, for a certain code included in another terminology system used in the local EHR sources; e.g. ICD-9-CM in Lombardy DWH and ICD-10-GM in UKD ORBIS. These rules have to be dynamically created based on some template rules according to the configurations of the safety analysts, e.g. the specific terminology system and level that she prefers to see the results in. And the last *dataUrl* parameter indicates a location containing the patient population data represented as SALUS CIM instances as an outcome of

the Aggregation Service.

An example dynamic rule to add MedDRA HLGT term correspondences of the source condition codes provided in other terminology systems such as ICD-9-CM, ICD-10-GM and SNOMED CT is presented in Figure 4.17. The first block of this rule gets the unique code and code system identifier of each salus:Condition problem code instance in the patient population data. The second block aligns the problem code in patient data with the semantic representation of the corresponding skos:Concept in the SALUS Semantic Resource Set through these unique identifiers. The value of salus:code shall match with the skos:notation value of a skos:Concept in the SALUS Semantic Resource Set, and salus:codeSystem with the iso:oid value of the skos:ConceptScheme of the same skos:Concept (accessed through skos:inScheme).

```
# prefix declarations are skipped to save space
{
    ?CONDITION a salus:Condition.
    ?CONDITION salus:problemCode ?probcode.
    ?probcode salus:code ?probcode_cd.
    ?probcode salus:codeSystem ?probcode_cs.

    ?sConcept a skos:Concept.
    ?sConcept skos:notation (?probcode_cd ?type)!log:dtlit.
    ?sConcept skos:inScheme ?sConcept_sch.
    ?sConcept_sch iso:oid ?probcode_cs.

    ?tConcept salusc:exactOrNarrowMatch ?sConcept.
    ?tConcept skos:inScheme ?tConcept_sch.
    ?tConcept_sch iso:oid "2.16.840.1.113883.6.163".
    ?tConcept_sch rdfs:label ?targetcode_csn.
    ?tConcept MDR:level "HLGT".
    ?tConcept skos:notation ?targetcode_cd.
    ?tConcept skos:prefLabel ?targetcode_dsn.
}
=>
{
    ?CONDITION salus:problemCode [
        a salus:cd;
        salus:code ?targetcode_cd;
        salus:codeSystem "2.16.840.1.113883.6.163";
        salus:codeSystemName ?targetcode_csn;
        salus:displayName ?targetcode_dsn
    ].
}.
```

Figure 4.17: A dynamic terminology reasoning rule to add MedDRA HLGT term correspondences of source condition codes in varying terminology systems

After identifying the semantic representation of the exact concept in the SALUS Semantic Resource Set, the third block of the rule finds the target concepts that have a salusc:exactOrNarrowMatch relationship with the source concept. While doing so, it restricts the result set by specifying the target code system as MedDRA through **?tConcept_sch iso:oid "2.16.840.1.113883.6.163"** statement, and the level of the target concept as HLGT through **?tConcept MDR:level "HLGT"** statement. In the final part of the rule, the condition is enriched with a new problem code instance for each matching target MedDRA HLGT term. The existing coded data is never modified or removed from the instance, as the analysts might need the original data as well. The enriched CIM instances are returned to the SAQM.

An example enriched SALUS CIM Condition instance in N3 syntax is provided in Figure 4.18. In the original patient data provided to the Terminology Reasoning Service, only the first salus:problemCode with ICD-9-CM code for "Hemorrhage of gastrointestinal tract, unspecified" was present. By making use of the materialized terminology mapping information and the reasoning rule provided in Figure 4.17, the second salus:problemCode with MedDRA HLGT term for "Vascular haemorrhagic disorders" is added to the patient data.

```
[ rdf:type salus:Condition ;
  salus:problemCode
    [ rdf:type salus:cd ;
      salus:code "578.9" ;
      salus:codeSystem "2.16.840.1.113883.6.2" ;
      salus:codeSystemName "ICD-9-CM" ;
      salus:displayName "Hemorrhage of gastrointestinal tract, unspecified"
    ] ;
  salus:problemCode
    [ rdf:type salus:cd ;
      salus:code "10047075" ;
      salus:codeSystem "2.16.840.1.113883.6.163" ;
      salus:codeSystemName "MedDRA" ;
      salus:displayName "Vascular haemorrhagic disorders"
    ] ;
  salus:problemDate
    [ rdf:type salus:ivlTs ;
      salus:low "2003-08-01T00:00:00"^^xsd:dateTime
    ] ;
  salus:problemName "Hemorrhage of gastrointestinal tract, unspecified" ;
]
```

Figure 4.18: An example SALUS CIM Condition instance as the outcome of the Terminology Reasoning Service

Needless to say, our terminology reasoning approach is not specific to problem codes. We are applying the same approach for other coded information as well, such as procedure codes, allergy codes, medication codes, etc. Furthermore, in some cases, we do not need to map the codes in the patient data to another terminology system code; but just do translation of the designations. For example, for providing the structured active ingredients of medications used by the patients, both of our EHR sources use WHO-ATC terminology system, and UMC also prefers to have these information coded with ATC. However, Lombardy DWH uses Italian designations and UKD ORBIS uses German designations for ATC codes; while the safety analysts of UMC work with English designations. We are able to overcome this translation process through N3 rules implemented within Terminology Reasoning Service as well. The rule for ATC code translation is provided in Figure 4.19.

We should note that the materialized mapping information explained here is used while querying the EHRs as well, for query expansion. In Lombardy DWH for example, the original query for "myocardial infarction" (MI) MedDRA code is expanded with all ICD-9-CM codes that are either equal to or children of the MI term, because the Lombardy DWH is unaware of MedDRA.

```
# Rule to get English display name of an ATC code.
{
    ?MEDICATION a salus:Medication.
    ?MEDICATION salus:medicationInformation ?med_info.
    ?med_info salus:codedActiveIngredient ?act_ing_code.
    ?act_ing_code salus:code ?act_ing_code_cd.
    ?act_ing_code salus:codeSystem "2.16.840.1.113883.6.73".

    ?sConcept a skos:Concept.
    ?sConcept skos:notation (?act_ing_code_cd ?type)!log:dtlit.
    ?sConcept skos:inScheme <http://www.whocc.no/atc>.

    ?sConcept skos:prefLabel ?atc_preflabel.
}
=>
{
    ?act_ing_code salus:displayName ?atc_preflabel.
}.
```

Figure 4.19: A terminology reasoning rule to find the English designations of the ATC codes

4.8 Query Result Calculator

The Query Result Calculator is a service that is used to apply additional calculations on the patient population data in SALUS CIM ontology from the EHR sources to extract the characteristics of the population. The Query Result Calculator contains functionalities to be used by safety analysis tools such as the Case Series Characterization Tool and Post Market Safety Study Tool. However, these tools do not communicate with the Query Result Calculator directly. Instead, they communicate with the Safety Analysis Query Manager, which delegates the requests coming from these tools to the Query Result Calculator as explained in Section 4.9. In all cases, terminology reasoning takes place before a call to the Query Result Calculator; hence this service always works on enriched SALUS CIM ontology instances.

The Query Result Calculator serves the CSCT by applying N3 rules on top of the population data for different kinds of statistical options that are issued by the safety analyst through the graphical user interface of the CSCT. Some of the possible statistical calculations that can be applied on the foreground and background population data are:

- Average age of patients
- Gender distribution of patients
- Age distribution of patients
- Country distribution of patients
- Risk factors
- Common conditions
- Common medications

- Common conditions prior to medication of interest
- Common conditions post medication of interest
- Common conditions prior to condition of interest
- Common conditions post condition of interest
- Common medications prior to medication of interest
- Common medications post medication of interest
- Common medications prior to condition of interest
- Common medications post condition of interest

The Query Result Calculator requests the following parameters:

- dataUrl: URL of the patient population data enhanced with inferred knowledge produced as a result of terminology reasoning process
- statisticalOptions: Statistical options issued by the safety analyst
- conditionOfInterest: The coded condition of interest provided by the safety analyst
- medicationOfInterest: The coded medication of interest provided by the safety analyst

As in the case of terminology reasoning rules, some of the Query Result Calculator rules have to be dynamically adapted at run time based on the input provided by the safety analyst, e.g. the rule to obtain common conditions prior to medication of interest requires the specific medication of interest (e.g. "nifedipine") that will be used as the pivot for filtering the common conditions. The N3 rule that we have implemented for this case can be seen in Appendix G. All of the Query Result Calculator rules are implemented again as N3 rules, and return the calculated results as RDF triples.

Using the provided configuration information, the required statistical results are prepared to be presented in the graphical user interface of the CSCT. Figure 4.20 depicts an example calculation of the results for the statistics option of "common conditions prior to medication of interest". Although the result for the foreground and background are presented in the same view, the Query Result Calculator calculates results for foreground and background populations in separate processes. The results are merged by the Safety Analysis Query Manager.

The results prepared for each statistical option include the following pieces of information:

- the display name of the item in the first column
- the ratio and number of occurrence of the item in foreground population in the second column
- the ratio and number of occurrence of the item in background population in the third column

Common Conditions Prior to Medication of Interest

Condition	Foreground	Background
Appetite and general nutritional disorders	35.7% (5)	25.0% (10)
Glucose metabolism disorders (incl diabetes mellitus)	28.6% (4)	17.5% (7)
Headaches	14.3% (2)	15.0% (6)
Sleep disorders and disturbances	0.0% (0)	2.5% (1)
Vascular haemorrhagic disorders	14.3% (2)	12.5% (5)
Vascular hypertensive disorders	100.0% (14)	100.0% (40)

Figure 4.20: An example execution result of "common conditions prior to medication of interest" statistics option

4.9 Safety Analysis Query Manager

The Safety Analysis Query Manager (SAQM) is a semantic service managing the workflow among other RESTful semantic services on behalf of the Safety Analysis Tools, such as the Case Series Characterization Tool. SAQM is also a RESTful service, and the endpoint that it provides to the CSCT is:

```
http://localhost:8080/safetyanalysisquerymanager/population
```

This endpoint provides an HTTP POST method that accepts requests in either JSON or RDF/TURTLE format. Once a request is obtained from the CSCT, it is split into the following four parts:

- Eligibility criteria
- Criteria source indicating whether the eligibility criteria are for the foreground or for the background population
- Statistical options to be processed by the Query Result Calculator to apply statistical safety analysis queries on the data sets once they are collected from the EHR sources
- Risk factors to be processed by the Query Result Calculator to apply statistical safety analysis queries on the data sets once they are collected from the EHR sources

Based on the provided parameters, SAQM determines the necessary data sources to query. It collaborates with the Aggregation Service to collect the required population data. The eligibility criteria for the foreground population and for the background population are sent as two separate requests to the Aggregation Service, since the CSCT sends separate queries for foreground and background populations. However, these separate calls to the EHR sources are done in a concurrent way to perform faster.

The merged population data retrieved through the Aggregation Service is now represented as SALUS CIM ontology instances. However, they are all coded with different

terminology systems used by the local EHR sources. Therefore, SAQM calls the Terminology Reasoning Service with the merged population data and with the terminology system preferences of the safety analyst (available within the statistical options and risk factor configurations provided to the SAQM) as explained in Section 4.7.

After the terminology reasoning is done, the statistical safety analysis queries are run by using the Query Result Calculator as explained in Section 4.8. Finally, the statistical results are sent to the caller Safety Analysis Tool; the Case Series Charaterization Tool in this case.

4.10 OMOP Converter and Formatter

Differently from the case series characterization scenario, in two of our pilot application scenarios, namely temporal pattern characterization and temporal association screening, there is a target content model that we need to present the patient data in. This target model is identified as Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM) [57] by the Uppsala Monitoring Centre. OMOP CDM and its Content Entity Model created by us are explained in Section 3.1.3.

OMOP Converter and Formatter is a service that is used by the Safety Analysis Query Manager before providing patient data to the Safety Analysis Tools like Temporal Pattern Characterization Tool and Temporal Association Screening Tool, for transforming the aggregated and enriched (as a result of terminology reasoning) patient data represented in SALUS CIM ontology to OMOP CDM format. Our transformation approach is the same with conversion from local EHR models to SALUS CIM. This time, first we convert SALUS CIM instances to OMOP Content Entity Model instances. Again, we have implemented a set of N3 conversion rules for this purpose that we run on top of EYE Reasoning Engine. A tiny Person entity example in OMOP CDM Content Entity Model as a result of this conversion process is provided in Figure 4.21.

```
@prefix omop: <http://www.salusproject.eu/ontology/omop-cdm#> .

[ a omop:Person ;
  omop:care_site_id "53254132423" ;
  omop:day_of_birth "24" ;
  omop:location
    [ a omop:Location ;
      omop:address_1 "Via Don Giovanni Minzoni" ;
      omop:address_2 "No 34" ;
      omop:city "Milan" ;
      omop:state "MI" ;
      omop:zip "56123"
    ] ;
  omop:month_of_birth "04" ;
  omop:year_of_birth "1967"
].
```

Figure 4.21: A tiny Person entity example in OMOP CDM Content Entity Model

After having the population data as OMOP CDM Content Entity Model instances, OMOP Converter and Formatter transforms these instances to the native OMOP

CDM syntax, which is SQL since OMOP CDM is a relational database schema. The necessary SQL statements are prepared by OMOP Converter and Formatter and passed to the SAQM, which then provides these statements to the requestor Safety Analysis Tool. The Safety Analysis Tool first populates its own OMOP CDM Repository with these SQL statements and then runs the signal detection and verification algorithms on top of this repository.

CHAPTER 5

AN EXAMPLE CASE SERIES CHARACTERIZATION SCENARIO EXECUTION

In this chapter, we present a step by step execution of a complete case series characterization scenario.

During investigation of nifedipine, which is a drug used for the treatment of hypertension, and myocardial infarction (MI) at the Uppsala Monitoring Centre, the safety analyst wants to use the Case Series Characterization Tool (CSCT) to investigate the relation between nifedipine and MI by adding meat to the bones; i.e. supporting cases with background information. In particular, she wants to learn what differs between

- *Foreground:* patients having a myocardial infarction within two weeks of nifedipine intake, and
- *Background:* patients taking nifedipine

The safety analyst wants to check whether there are other explanations more likely to cause MI than the exposure to nifedipine. She logins to the Case Series Characterization Tool (CSCT) for executing such a query. The next steps, which are marked on the architecture diagram provided in Figure 5.1, are explained below.

Step 1

As the first step, the safety analyst defines the inclusion criteria for both background and foreground populations.

- For the background population:
  - She chooses "nifedipine" 5th level term (code C08CA05) from the ATC terminology system as the active ingredient code of a medication by using the typeahead search facility of the tool (which is integrated with our terminology server)
- For the foreground population:
  - She chooses "Myocardial infarction" Preferred Term (PT) (code 10028596) from the MedDRA terminology system as the problem code of a condition by using the typeahead search facility of the tool

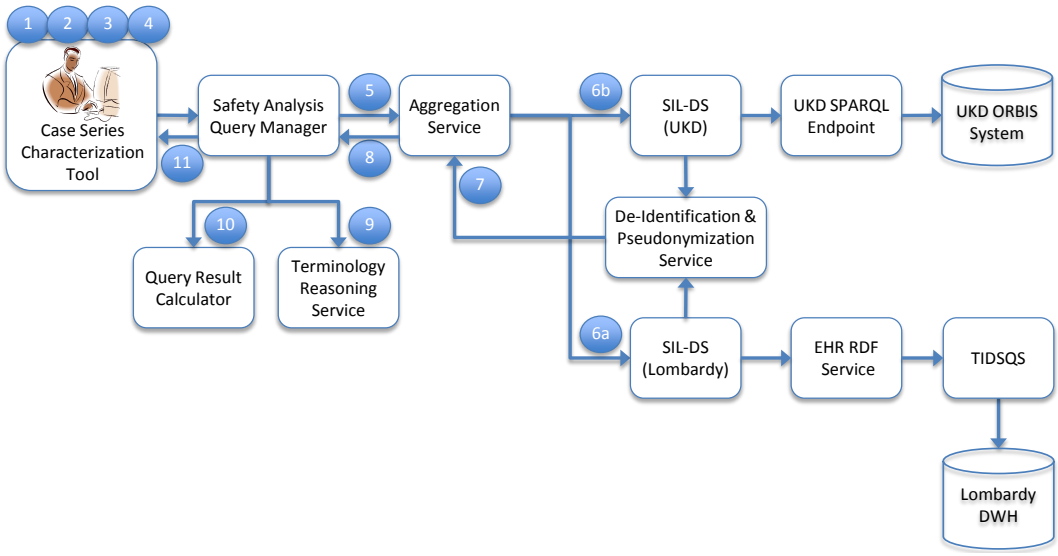

Figure 5.1: CSCT scenario execution steps on the architecture

– She chooses "nifedipine" 5th level term (code C08CA05) from the ATC terminology system as the active ingredient code of a medication by using the typeahead search facility of the tool
– She adds a temporal constraint between the medication and condition statements she just created, for stating that the condition shall occur within two weeks after the medication

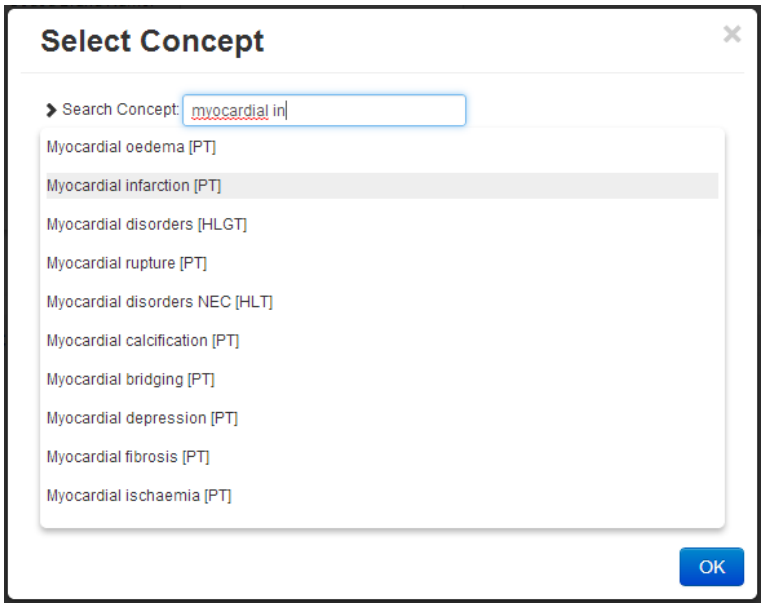

Figure 5.2: Typeahead search in the CSCT

The safety analyst searches for the terminology system codes via the typeahead search

facility as displayed in Figure 5.2 and defines the eligibility criteria as displayed in Figure 5.3 (in this case for foreground population).

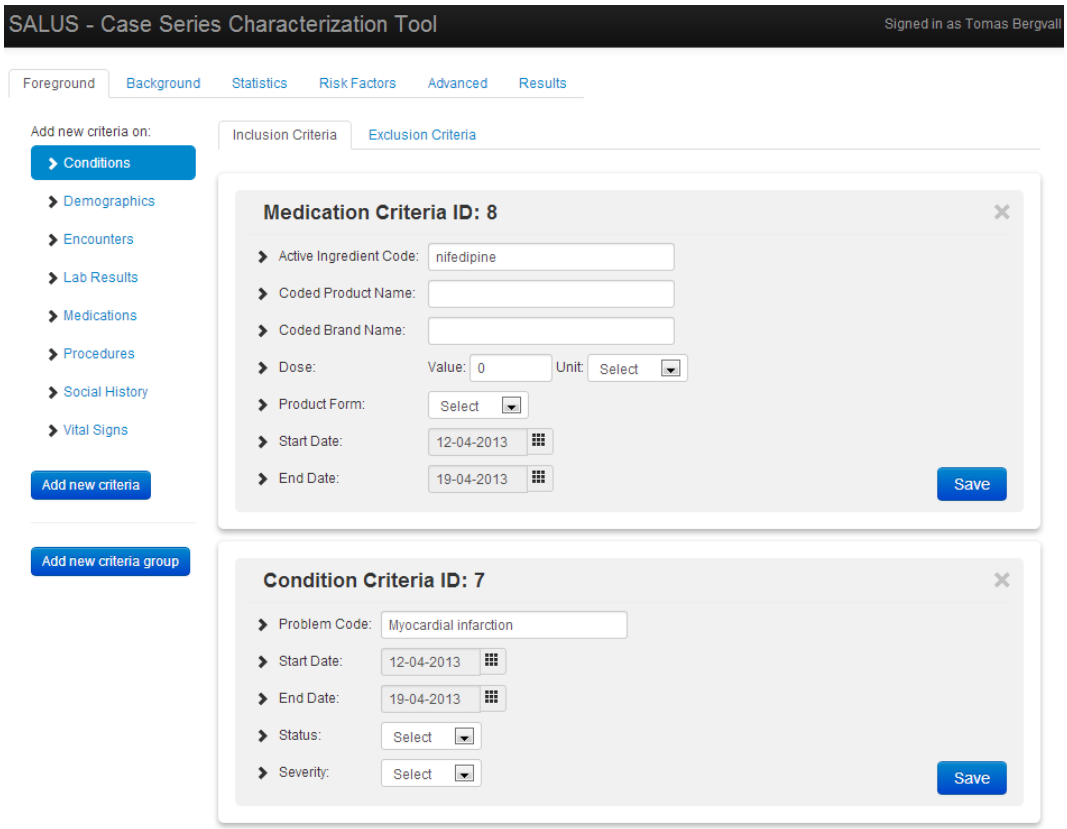

Figure 5.3: Eligibility criteria definition in the CSCT for nifedipine and MI

Step 2

After defining the inclusion/exclusion criteria, the safety analyst configures the statistics to be calculated for grouping and stratifying data sets of the eligible populations, such as age, gender, common medications/conditions before/after medication/condition of interest as displayed in Figure 5.4.

The coded data can be configured to be grouped under a preferred terminology system and level in the results, for example MedDRA High Level Group Terms (HLGT), no matter which specific terminology system is used in the EHR sources. In our case, the safety analyst prefers that the common conditions shall be grouped under MedDRA HLGT terms and the medications under ATC codes.

Step 3

Apart from the common conditions and medications, the safety analyst also wishes to compare the presence of some specific conditions, which are the risk factors (i.e. confounding factors) of the selected conditions in inclusion criteria of foreground and background populations. In our example, the safety analyst defines three risk factors for myocardial infarction again from the Preferred Term (PT) level of the MedDRA

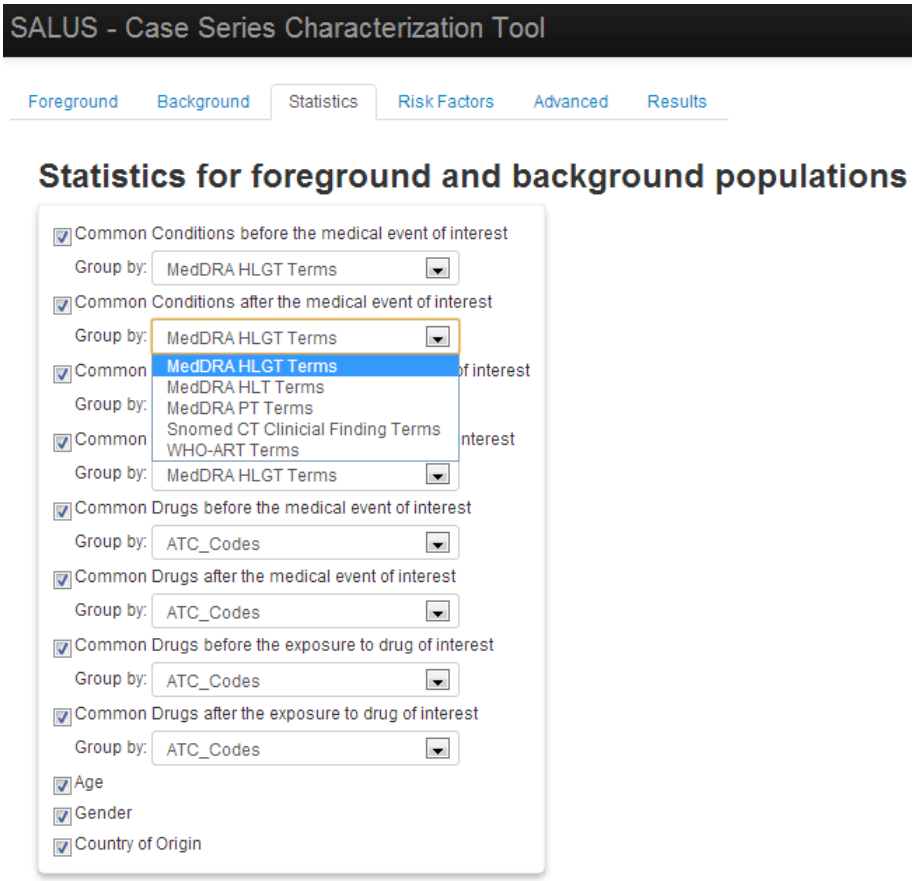

Figure 5.4: Configuring the statistics to be calculated

terminology system. These are "Diabetes mellitus" (code 10012601), "Obesity" (code 10029883) and "Haemorrhage" (code 10055798). This step is similar to defining eligibility criteria as displayed in Figure 5.5.

Step 4

The safety analyst checks the query conditions once again and then submits the query by pushing the "Run Query" button. The Case Series Characterization Tool prepares the query, and passes it to the Safety Analysis Query Manager. In the background, CSCT actually sends to SAQM two separate queries for foreground and background populations; but this is not visible to the user. The SAQM exposes a RESTful service to accept these queries in JSON format via HTTP POST.

Step 5

The Safety Analysis Query Manager processes the query received from CSCT and splits it into four parts: i) eligibility criteria represented in SALUS CIM ontology, ii) criteria source type (i.e. foreground or background), iii) configuration for the statistics to be calculated and iv) configuration for the risk factors to be checked on the medical summaries of the eligible patients. SAQM keeps the latter three for later use, and forwards the eligibility criteria to the data sources, after determining the registered

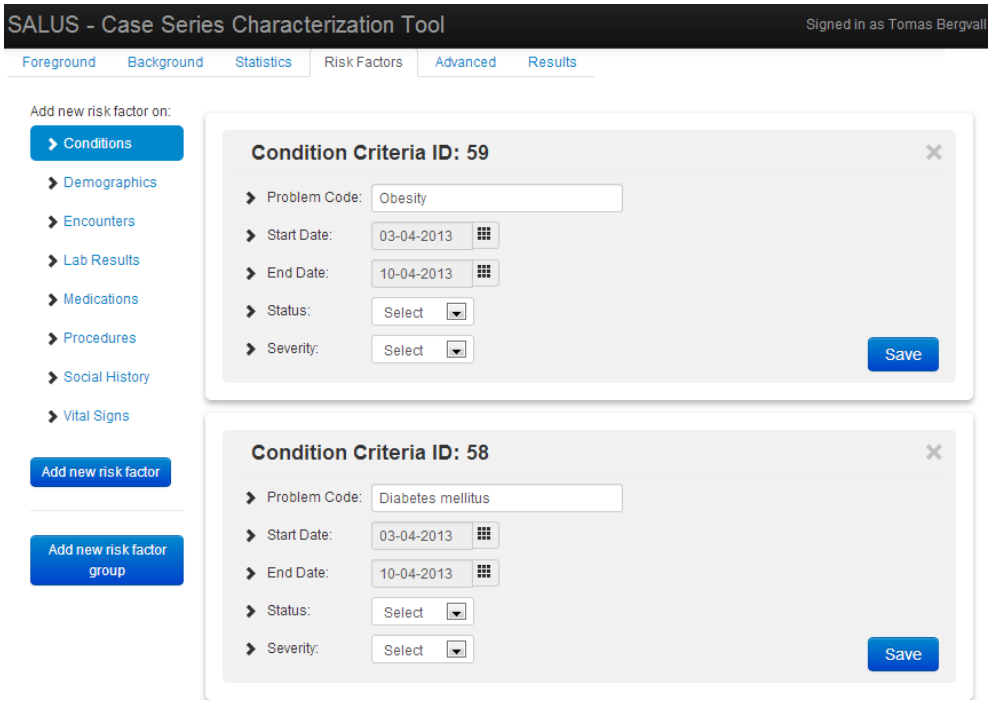

Figure 5.5: Defining risk factors

data sources to query.

SAQM sends the eligibility criteria in SALUS CIM to the Semantic Interoperability Layer Data Services (SIL-DSs) of Lombardy and UKD through the Aggregation Service, again as two separate but concurrent requests for foreground and background populations. The eligibility criteria for the foreground population represented in N3 syntax is provided in Figure 5.6.

As explained previously, the query sub-model of the SALUS CIM ontology is created by benefiting from HL7 HQMF as a declarative means to express elibility criteria. We can see in Figure 5.6 that, the input provided by the safety analyst through the CSCT GUI is transformed into a formal query representation appropriately. There are two criterions each referring to a clinical statement: one salus:Medication instance with active ingredient code referring to nifedipine from the ATC terminology system and one salus:Condition instance with problem code referring to myocardial infarction from the MedDRA terminology system. There is a temporal relation defined from the salus:Condition to the salus:Medication, indicating that the myocardial infarction shall "start after start of" (typeCode: SAS) nifedipine intake, with an allowed time interval of two weeks. Finally, these two criterions are grouped with an AND operator inside a criteria group, and assigned to the inclusion criteria at the beginning of Figure 5.6.

Step 6a

SIL-DS (Lombardy) converts the elibility criteria in SALUS CIM ontology to an ontological representation of HQMF (which are quite similar) and passes to the EHR RDF

```
[]  a salus:EligibilityCriteria ;
    salus:inclusionCriteria [
        a salus:CriteriaGroup ;
        salus:conjunctionCode [ a salus:cd ; salus:code "AND" ] ;
        salus:groupItem _:med , _:cond ;
        salus:negationIndicator "false"^^xsd:boolean
    ].

_:med a salus:Criterion ;
    salus:clinicalStatement [
        a salus:Medication ;
        salus:medicationInformation [
            a salus:MedicationInformation ;
            salus:codedActiveIngredient [
                a salus:cd ;
                salus:code "C08CA05" ;
                salus:displayName "nifedipine" ;
                salus:codeSystem "2.16.840.1.113883.6.73" ;
                salus:codeSystemName "ATC"
            ]
        ]
    ] .

_:cond a salus:Criterion ;
    salus:clinicalStatement [
        a salus:Condition ;
        salus:problemCode [
            a salus:cd ;
            salus:code "10028596" ;
            salus:displayName "Myocardial infarction" ;
            salus:codeSystem "2.16.840.1.113883.6.163" ;
            salus:codeSystemName "MedDRA"
        ] ;
        salus:temporalRelation [
            a salus:TemporalConstraint ;
            salus:targetCriterion _:med ;
            salus:typeCode [ a salus:cd ; salus:code "SAS" ] ;
            salus:pauseQuantity [
                a salus:ivlPq ;
                salus:low [ a salus:pq ; salus:value "2" ; salus:unit "wk" ]
            ]
        ]
    ] .
```

Figure 5.6: The eligibility criteria for the foreground population in SALUS CIM ontology

Service, which then translates this to the native HQMF syntax in XML and forwards to TIDSQS, which implements the extended IHE QED transactions for population based queries. At this phase, the original query is expanded to insert the ICD-9-CM codes that match directly or broad-match with the MedDRA code for myocardial infarction by making use of the materialized terminology mappings available in our Semantic Resource Set, since the conditions are coded with ICD-9-CM but not MedDRA in Lombardy DWH. Lombardy DWH is aware of ATC codes though, so no query expansion is done for the nifedipine code. The HQMF query within our extended IHE QED transaction corresponding to the population based query represented in SALUS CIM ontology (Figure 5.6) is provided in Appendix B.

This expanded population query is run on the Lombardy DWH, and as a result, first the medical summaries of the eligible patients are provided back to the EHR RDF

Service as CDA/CCD XML instances, which then formalizes this data and provides corresponding medical summaries represented in CDA/CCD Content Entity Model to the SIL-DS (Lombardy). In Appendix C, an example medical summary in native HL7 CDA format using PCC/CCD templates is provided. This example has basically patient demographics, condition and medication data. Then, in Appendix D, the one-to-one semantic correspondence of the CCD instance provided in Appendix C is presented.

By making use of the conversion rules, SIL-DS (Lombardy) represents the medical summaries of the eligible patients in SALUS CIM ontology and returns them to the De-Identification and Pseudonymization Service. A complete SALUS CIM ontology instance as a direct correspondence of the HL7 CDA instances provided in Appendix C and Appendix D is provided in Appendix E.

Step 6b

In SIL-DS (UKD), the same query in SALUS CIM ontology is transformed into a SPARQL query compliant with ORBIS Content Entity Model. As in the case of Lombardy, query expansion takes place here as well, this time for inserting the corresponding ICD-10-GM codes exact or broad matching with the MedDRA code for myocardial infarction. Then the expanded SPARQL query is run directly on top of the SPARQL Endpoint. The data of the eligible patients represented in ORBIS Content Entity Model are provided to the SIL-DS (UKD), which then represents these data as SALUS CIM ontology instances by using the conversion rules and returns them to the De-Identification and Pseudonymization Service.

Step 7

According to the previously done de-identification configuration, the De-Identification and Pseudonymization Service de-identifies the population data represented in SALUS CIM ontology. The patient and health professional identifiers are replaced with pseudonyms, names are removed, birth dates and addresses are generalized and so on. This service returns the de-identified data to the Aggregation Service.

Step 8

Aggregation Service simply merges the de-identified population data received from Lombardy and UKD. The merged results are passed to SAQM as SALUS CIM instances.

Step 9

Safety Analysis Query Manager now has all the data sets (i.e. medications, conditions and demographics of all the eligible patients) required for both the foreground and background populations in SALUS CIM ontology. However, yet it is not possible to "understand" these data as they are coded with several codes from different terminology systems such as ICD-9-CM and ICD-10-GM, while the safety analyst wants to deal with MedDRA terms, in some cases specifically with the terms at HLGT level.

Therefore, SAQM calls the Terminology Reasoning Service with the merged population data and with the terminology system preferences of the safety analyst (available within the statistics and risk factor configurations provided to the SAQM). By making

use of the materialized terminology mapping information available in the Semantic Resource Set and dynamically adapting the terminology reasoning rules according to the terminology system preferences, the population data in SALUS CIM is enriched with new coded information and provided back to SAQM.

Step 10

For calculation of the statistics and the risk factors that were requested by the safety analyst, SAQM calls the Query Result Calculator with enriched population data coming from the Terminology Reasoning Service and configurations for statistics and risk factors. By dynamically adapting the template N3 rules according to the configurations provided by the safety analyst, Query Result Calculator calculates the statistics and provides them as RDF entities to SAQM.

Step 11

The final results are sent by SAQM to the CSCT, separately for the foreground and background populations, since the queries were sent separately as well. The server side of the CSCT merges these results and provides them to the client side, i.e. the Web user interface, which then presents them to the safety analyst as seen in Figure 5.7 and Figure 5.8.

Average Age

Age	Foreground	Background
Average Age	64.7 (14)	60.2 (40)

Gender Distribution

Gender	Foreground	Background
Female	42.9% (6)	57.5% (23)
Male	57.1% (8)	42.5% (17)

Age Distribution

Age group	Foreground	Background
35-44	0.0% (0)	12.5% (5)
45-54	21.4% (3)	25.0% (10)
55-64	28.6% (4)	22.5% (9)
65-74	35.7% (5)	27.5% (11)
75-84	14.3% (2)	12.5% (5)

Country Distribution

Country	Foreground	Background
Czech Republic	7.1% (1)	2.5% (1)
Germany	42.9% (6)	47.5% (19)
Italy	50.0% (7)	50.0% (20)

Common Conditions

Condition	Foreground	Background
Appetite and general nutritional disorders	50.0% (7)	35.0% (14)
Coronary artery disorders	100.0% (14)	35.0% (14)
Glucose metabolism disorders (incl diabetes mellitus)	28.6% (4)	20.0% (8)
Headaches	57.1% (8)	47.5% (19)
Sleep disorders and disturbances	0.0% (0)	5.0% (2)
Vascular haemorrhagic disorders	71.4% (10)	40.0% (16)
Vascular hypertensive disorders	100.0% (14)	100.0% (40)

Common Medications

Medication Name	Foreground	Background
acetylsalicylic acid	78.6% (11)	50.0% (20)
losartan	35.7% (5)	42.5% (17)
metformin	28.6% (4)	17.5% (7)
nifedipine	100.0% (14)	100.0% (40)

Common Conditions Prior to Medication of Interest

Condition	Foreground	Background
Appetite and general nutritional disorders	35.7% (5)	25.0% (10)
Glucose metabolism disorders (incl diabetes mellitus)	28.6% (4)	17.5% (7)
Headaches	14.3% (2)	15.0% (6)
Sleep disorders and disturbances	0.0% (0)	2.5% (1)
Vascular haemorrhagic disorders	14.3% (2)	12.5% (5)
Vascular hypertensive disorders	100.0% (14)	100.0% (40)

Common Conditions Post Medication of Interest

Condition	Foreground	Background
Appetite and general nutritional disorders	14.3% (2)	10.0% (4)
Coronary artery disorders	100.0% (14)	35.0% (14)
Glucose metabolism disorders (incl diabetes mellitus)	0.0% (0)	2.5% (1)
Headaches	42.9% (6)	32.5% (13)
Sleep disorders and disturbances	0.0% (0)	2.5% (1)
Vascular haemorrhagic disorders	57.1% (8)	27.5% (11)

Figure 5.7: CSCT results displayed to the safety analyst - part 1

We can see that all the common conditions/medications before/after myocardial infarction / nifedipine are stratified according to the safety analyst's preferences. There are only MedDRA terms at the HLGT level, no matter which specific code is used in

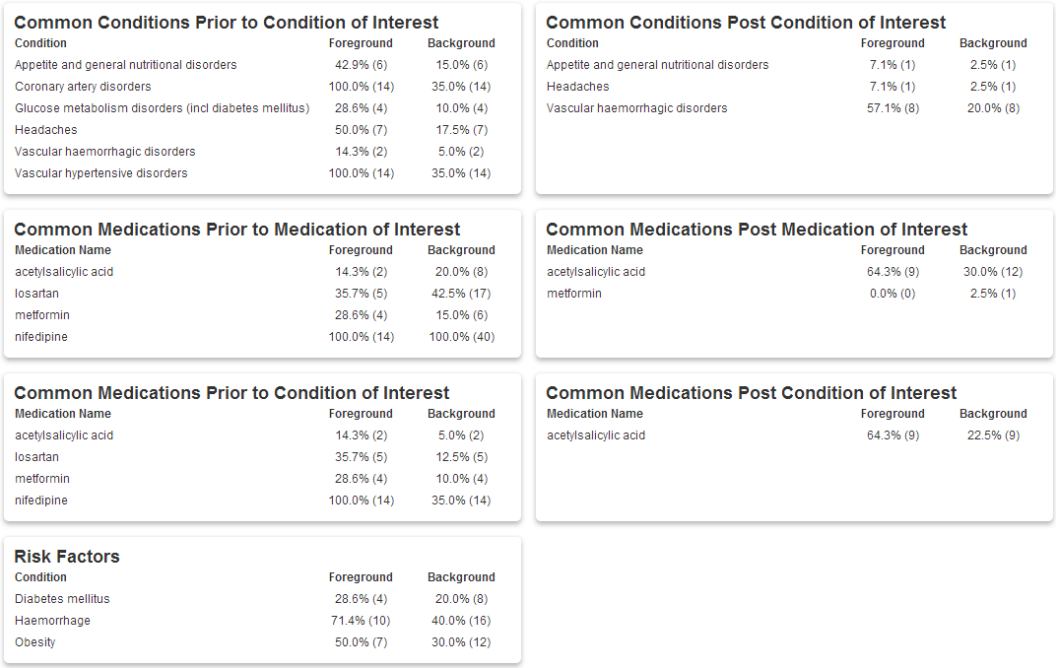

Figure 5.8: CSCT results displayed to the safety analyst - part 2

the original EHR data. In the risk factors though, no extra generalization to HLGT is done since the safety analyst specifically wanted to check these MedDRA PT terms for diabetes mellitus, obesity and haemorrhage.

The analyst notices that the patients who had myocardial infarction after nifedipine intake are older and suffered more from other cardio-metabolic diseases such as diabetes and obesity, before the myocardial infarction event. The analyst decides that these are explanations more likely to cause myocardial infarction than the exposure to nifedipine; hence nifedipine cannot be attributed as the single cause of MI and the potential signal is refuted.

CHAPTER 6

RELATED WORK

Recently, a number of investigators have examined potential use cases for secondary use of EHR data in clinical research and patient safety contexts including eligibility determination, clinical trial data collection, adverse event reporting and conducting epidemiological studies [85, 86, 87, 88, 89, 90, 91, 92, 93, 94]. Murphy et al. [95] describes the potential of using routinely collected clinical data for conducting retrospective observational studies.

Although re-purposing of EHRs for safety studies has a great potential, a major barrier is that information systems in patient care and clinical research domains are not interoperable with each other. This is due to the fact that, different reference information models (as models of use) such as HL7 RIM [18], ISO/CEN 13606 Reference Model [60], CDISC ODM [66], BRIDG DAM [9]; and different terminology systems (as models of meaning) such as ICD-9, SNOMED-CT, MedDRA and CDISC Terminology are used in care and research domains. Hence, although the required information for the safety analysis studies is available in EHR systems, it is not readily available in a structurally and semantically interoperable manner.

There are several efforts for addressing this interoperability challenge. Some projects like OMOP [13], Mini-Sentinel [59], EU-ADR [96, 97] and SHRINE [98] assume that the data is already collected based on a common information model directly from disparate databases to be stored to a central data repository. This central repository has a fixed database schema, and usually the terminology systems that are allowed to be used in this central repository are fixed as well. The EHR sources are responsible for implementing the mechanisms to convert the data in the local EHR system to the schema and terminology systems fixed by the central data repository. This is commonly implemented as extract-transform-load (ETL) processes between two relational database systems. Integration at this very low level is good for performance; however this approach totally neglects the "integration through standardized interfaces" principle; i.e. decoupling, and hence is not sustainable. For example, a slight modification in the schema of either of the source or central database systems might necessitate an update of the integration mediums.

Integrating the Healthcare Enterprise (IHE) profiles [99] select and assume conformance to a well-defined interface standard to communicate with EHR systems, like HL7/ASTM Continuity of Care Document (CCD) [19] to share medical summaries of patients. IHE Drug Safety Content (DSC) [100] and Clinical Research Data Capture (CRD) [101] profiles address the structural interoperability of care and research

domains by proposing Extensible Stylesheet Language Transformations (XSLT) mappings between different information models used in clinical care (HL7/ASTM CCD) and clinical research domains (CDASH [64] annotated CDISC ODM and ICH E2B(R2) [58]). The good thing about DSC and CRD profiles is that they reuse the available standards in clinical care and research domains to facilitate their interoperability. However, the interoperability is achieved through hard-coded XSLT mappings between clinical research and care standards. These profiles do not utilize a semantic mediation approach through an intermediary model. Their XSLT mappings are only valid for the given pre-population data formats defined in the CCD and the ODM models; once these pre-population data templates are modified due to emerging requirements, new mappings will be needed.

This shortcoming is also addressed by the RE-USE architecture [94], where a set of IHE-compliant profiles have been defined and implemented to enable single-source data collection and cross system data reuse through semantic interoperability. In the RE-USE architecture, the electronic Case Report Form (eCRF) templates are shared between Clinical Data Management Systems (CDMS) and EHR systems, and through a semantic mapping algorithm, which uses SNOMED CT as the pivot terminology system and weighted combination of similarity measures, the requested data entries in eCRF forms are linked to the data entries used by the EHR systems. In this way, clinical data reuse between EHRs and CDMSs is achieved. In our approach, we do not stick to a specific terminology to act as the pivot, but achieve a harmonized "model of meaning" through our Semantic Resource Set in which several different content entity models and terminology systems are linked to each other.

To demonstrate the value of the Semantic Web in bridging the divide between clinical practice and clinical research, a W3C task force on Clinical Observations Interoperability (COI) is established [102]. Clinical trial eligibility for patient recruitment is chosen as a use case for the secondary use of Electronic Health Records and a prototype implementation is realized for this use case [103]. In this prototype, the eligibility criteria are specified as SPARQL queries based on an ontology derived from CDISC Study Data Tabulation Model (SDTM) [65] standard. Mappings are defined from SDTM model to the HL7 Reference Information Model (RIM) [18], and from the HL7 RIM to EHR database schema. This way, the relevant data is queried from the database and matching is performed. When necessary, mapping with external ontologies such as drug ontologies is realized. This work is an important effort to show the potential of Semantic Web for bridging the clinical care and clinical research domains. However, in this approach, a direct mapping between SDTM model and the HL7 RIM is proposed, which would not be practical when the number of standards to be harmonized increases: There will be n*n mappings between different standards. In our work, we use the SALUS CIM ontology as the core of our Semantic Resource Set and hence each standard to be harmonized is mapped only to the CIM ontology, reducing the complexity to n*1 mappings. In the CIM ontology, we exploit the results of several widely-used content models as explained in Section 3.2 so that it encompasses a vast amount of domain knowledge.

In the Epoch Framework [104], a clinical trial management system is proposed that natively uses ontologies to define clinical trial protocol, site and specimen definitions, to access the collected clinical trial data and to define temporal constraints. All of this information is stored in a knowledge base, and Semantic Web Rule Language

(SWRL) rules [105] defined on this knowledge base are used for temporal reasoning in the clinical trial management process. Through the Epoch approach, it is successfully demonstrated that semantic modeling and reasoning can facilitate the clinical trial management process; however, it proposes developing a trial management system from scratch in an ontology aware manner. Our approach, in contrast, enables the already existing systems to communicate with each other using industry standards while enabling interoperability between clinical care and clinical research domains through semantic mediation.

In TrialX [106], Semantic Web technologies are used to create a tool on top of Personal Health Record (PHR) systems for matching patients to the open clinical trials. In this system, SNOMED CT, ICD-9 and RxNorm terminology systems are used along with Unified Medical Language System (UMLS) [31] so that semantic mapping can be done between patient information and trial inclusion/exclusion criteria. The patient medical history is collected in the ASTM Continuity of Care Record (CCR) [20] XML format and transformed into semantic models to reason on them and to query the knowledge base to select eligible patients. Although terminology reasoning is included in this approach, the standards used by clinical research, such as those by CDISC have not been included in the study, i.e. the translation of eligibility criteria in CDISC standards to semantic queries has not been addressed. In a similar study by the same authors [107], the medical records of Columbia University Medical Center, which are coded through a MED taxonomy, are transformed into SNOMED CT based ontology instances through custom written rules. The mappings between MED taxonomy and SNOMED CT terms are achieved semi-automatically through UMLS and natural language processing (NLP) based mapping algorithms. The cohort selection is achieved through semantic queries executed on top of this knowledge base supported through an OWL DL reasoner. As in TrialX, the eligibility queries are created manually by examining textual clinical trial documents. In other words, this work, in contrast our approach, does not aim to support semantic mediation among the existing clinical care and clinical research standards; it rather provides a framework for semantically querying clinical care data.

Several other efforts like Artemis [108], ACGT [109] and DebugIT [110, 111] follow a mediation approach, where the local models are formalized as ontologies and mediated to one another based on a global model. DebugIT aimed at developing and deploying a semantic interoperability platform to connect to different hospitals with different information systems for the purposes of improving antibiotic therapy and reducing antimicrobial resistance. Based on a common set of ontologies, queries are launched to the different systems, results are converted and consolidated into the terms of the common ontology, and finally analysed and visualized in a dashboard. DebugIT dealt with only bacteria data and developed semantic interfaces directly on top of the information system databases (as in the case of our UKD EHR source). Our work complements DebugIT by incorporating the existing data exchange interfaces (e.g. IHE QED, HL7 HQMF) and content models (CDA/CCD Content Model) into the Semantic Interoperability Framework, and by providing seamless access to de-identified patient data.

When it comes to addressing semantic interoperability mismatches due to the use of different terminology systems, in some efforts like epSOS [26], OMOP and DebugIT, specific value sets from identified pivot terminology systems are mandated. For example, epSOS maintains a Master Value Set Catalogue (MVC) in which 45 value sets from

well-known terminology systems such as SNOMED CT, ATC, ICD-10 are selected for coding diagnoses, active ingredients of medications, allergies, procedures, etc. During cross-border patient data exchange within the scope of epSOS, the participating countries are obliged to provide structured data with codes present within the MVC. Mappings from the local terminology systems to the MVC is the responsibility of the participating countries.

Some other efforts handle this separately by calls to external terminology system servers like UMLS and LexEVS [112] as in the case of Artemis, iCARDEA [113] and TrialX [106, 107] projects. The problem when using such external terminology system servers as terminology mapping resources is that, they are not reliable. In our very early prototype [63], for the terminology system mappings we also benefited solely from an external server, BioPortal [29], which reuses and extends the mappings provided by UMLS. We retrieved thousands of terminology mappings from BioPortal, and calculated their transitive closure sets in a similar way that we do in our current implementation. We observed that very misleading and dangerous inferences can be done with these mappings; e.g. when we queried patients who had a myocardial infarction (MI), in addition to MI patients, we retrieved those with bronchitis as well. Therefore, right now we only utilize reliable mapping resources such as OntoADR of the PROTECT project, OMOP Vocabulary and BioPortal supported with manual review by terminology experts, as explained in Section 4.7.

We also believe that addressing syntactic and semantic interoperability cannot be separated from each other, since the binding between models of use and models of meaning has also an impact on semantic interoperability [114, 63]. In this work, we propose an ontological framework where each local system can continue to use their own local models and terminology systems, while both structural and terminology mappings are handled through rule-based reasoning on formal representations of reference models and terminology systems.

TRANSFoRm project also proposes a unified framework for representing structural and semantic models to address the interoperability problem [115], but through a terminology server, LexEVS. In our work, we demonstrate that representing all the knowledge through formal means as ontologies, and establishing the necessary links again through ontological constructs give an enhanced capability of semantic mediation and terminology reasoning.

CHAPTER 7

DISCUSSIONS AND CONCLUSIONS

The adoption of EHR systems and data exchange among these systems are rapidly increasing due to a number of national and cross-border projects in Europe and Meaningful Use in the US [116]. A majority of these initiatives employ well-accepted content and transaction standards/profiles such as CDA, CCD and IHE X* [117]. For example, in Turkey, episodic medical records of the whole population (∼75 million) are collected from the healthcare providers as CDA documents since January 2009 [118]. The daily number of collected records can amount to 4 million. Through epSOS, which is a large scale European pilot for exchange of electronic patient summary and prescription documents across borders, many European national infrastructures are now able to provide and consume patient data in PCC/CCD templates [119]. So, both institutional and regional/national EHR systems become more and more standards compliant.

Although the main priority of these systems is improving clinical care, we demonstrate that the same systems and interfaces can be exploited for post market safety studies as well, with minimum intrusion when necessary, as in the case of our IHE QED extension for population based queries on top of Lombardy Data Warehouse (DWH). Our implementation proves that it is possible to carry these observational studies without developing study specific databases and data warehouses, which is costly and hard to maintain.

Through our Semantic Interoperability Framework, we demonstrate a complementary approach in the University Hospital of Dresden (UKD) case by developing a semantic interface directly on top of the EHR database and formalizing patient data immediately. This approach is of course more capable in the sense that the whole content of the EHR database can be formalized and more complex querying can be done compared to the standard based interfaces for data exchange. However, it necessitates in-depth knowledge of and interaction with the storage structure of the EHR system, in addition to expertise with semantic Web technologies. Our advantage is that AGFA as the developer of the ORBIS system was able to implement such a semantic interface on top of ORBIS, so that we can demonstrate both data integration and formalization approaches work in parallel in integrated scenarios.

The data that we need in our safety analysis tools such as conditions, procedures, allergies, medications of the patients are always available in a structured manner in the EHR sources that are involved in our environment (i.e. Lombardy DWH and UKD ORBIS), and this is usually the case in other EHR systems as well. As a result, we do not have to deal with analysis of free text data in the EHRs, which is very challenging

especially in this domain considering the sensitivity of medical data.

One of the biggest challenges in developing semantic Web applications is to utilizing a satisfactory reasoning engine that is able to perform in reasonable time and space. In our very early prototype [63], we tested several reasoning engines including Jena, OWLim, Fact++, Pellet and Hermit but they were either not even able to load all the ontologies we have, or to complete the reasoning process. At that time, we were able to overcome this challenge by limiting our reasoning requirements to minimum (i.e. reasoning only on subsumption and equivalence of classes) and meeting those with Virtuoso triple store [120], which is a high performance triple store but with very limited reasoning capability. However, when we started the actual implementation of our Semantic Interoperability Framework according to the end-user requirements, we noticed that we have more complex reasoning requirements, which we can resolve by using the open source EYE Reasoning Engine in almost all kinds of semantic processing and reasoning operations in our architecture as explained in detail in Chapter 4. The best thing about EYE is, you get what you ask for; nothing more, nothing less. When not specifically asked, EYE does not perform any inferencing on top of the provided RDF entities. For instance, it does not even try to infer the transitivity of the rdfs:subClassOf property in the provided ontologies. This way, it can process hundreds of thousands of triples in only a few seconds. Then, it can perform inferencing only for the rules provided as input by the user, which again increases performance both in time and space. Another advantage of EYE specific to our work is to have the continuous support of AGFA Advanced Clinical Applications (ACA) Team, our partner in SALUS, who develops and maintains EYE since 2006.

We have developed a scalable Semantic Interoperability Framework for post market safety studies and demonstrated it for case series characterization. The quantity and quality of the information provided by the Case Series Characterization Tool to the safety analysts of the Uppsala Monitoring Centre (UMC) is a significant improvement for informed decision making, compared to what they are able to access using traditional methods. The information that UMC has without our Case Series Characteriation Tool for the example nifedipine followed by myocardial infarction (MI) scenario demonstrated in Chapter 5 is provided in Table 7.1.

Our architecture is designed for all kinds of observational studies, not just for case series characterization. Scalability is due to our semantic mediation approach; whenever a new source or target content model is to be added, only the mappings (i.e. conversion rules) to the SALUS CIM are added in linear time, without affecting the existing resources. This prevents n-to-n mappings. Furthermore, our decoupled RESTful services

Table7.1: Information that UMC has without CSCT for the example nifedipine followed by MI scenario

Information	**Foreground**	**Background**
Male ratio	∼60%	∼40%
Average age	∼65	∼60
MI before nifedipine	∼45%	NA
MI after nifedipine	∼55%	NA
Diabetes	∼20%	NA

allow us to improve the overall performance by multiplying the services for concurrent processing and reasoning.

Overall, the main contributions of this thesis can be summarized as follows:

- Extending the existing standards-based patient data exchange transactions of the EHR sources for supporting population based queries and data; i.e. extension of the IHE QED and CM profiles with HL7 HQMF
- Identifying and formalizing the native content models of the EHR sources and target clinical research systems; i.e. CDA/CCD, OMOP CDM and HL7 HQMF
- Developing the Common Information Model (CIM) by addressing the i) clinical data requirements of various post market safety study methods, ii) widely-used international content standards, and iii) local content models of the involved systems, to be able to represent all the required domain knowledge in all kinds of post market safety studies
- Implementing conversion rules between the content entity models and the CIM in linear time to prevent n-to-n mappings, and utilizing these conversion rules at run time to convert instances in one model to another; e.g. from CDA/CCD instances to OMOP CDM instances through the CIM
- Representing all the required terminology systems and reliable terminology mappings as ontologies within the Semantic Resource Set and linking them with the CIM to achieve semantic interoperability between data sources and the requestors via terminology reasoning
- Developing the scalable Semantic Interoperability Framework through a series of decoupled semantic interoperability and technical interoperability services, which enables execution of post market safety studies on distributed and divergent EHR sources
- Utilizing the high-performance EYE Reasoning Engine inside the Semantic Interoperability Framework to perform the requested operations in acceptable time and space
- Providing an end-to-end solution to the safety analysts working at the Uppsala Monitoring Centre for case series characterization, and improving significantly the quantity and quality of information they are able to access for informed decision making
- Through the same Semantic Interoperability Framework, enabling access to distributed patient data in an interoperable manner to some other tools in the SALUS architecture such as Adverse Drug Event (ADE) Notification Tool and Individual Case Safety Report (ICSR) Tool, although the implementation details of these tools are not within the scope of this thesis

Our work is superior to the similar work in the literature by enabling access to distributed patient data in divergent systems for facilitating post market safety studies in a non-disruptive way (i.e. taking into account the existing content models, data exchange standards and terminology systems, which are mostly different between the

clinical care and clinical research domains), and addressing syntactic and semantic interoperability together through formalized representations of the content models as "models of use", terminology systems as "models of meaning" and the bindings between them through the Common Information Model as the mediator.

Our implementation will be further improved based on existing plans and end-user feedback. For example, right now we are working on introducing further relationships of the terminology systems to querying and reasoning processes, such as "has_finding_site" property of SNOMED CT. Semantically mediating all the patient data and terminology systems in formalized representations allows us to extend the capabilities of our tools via introduction of new rules easily. Soon, we will also add support for ISO/CEN EN 13606 Archetype instances [60] by first creating its formal Content Entity Model and then implementing the conversion rules to SALUS CIM ontology, just like we did with the CDA/CCD Content Model.

All our implementation will be provided as open source software.

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APPENDIX A

THE COMMON DATA ELEMENTS (CDES)

Name	Description
Patient.ID.II	Identifier of the patient
Patient.Title.String	Title/prefix of the patient
Patient.GivenName.String	Given name of the patient
Patient.FamilyName.String	Family name of the patient
Patient.Gender.CD	Gender of the patient
Patient.DateOfBirth.Date	Birth date of the patient
Patient.MaritalStatus.CD	Marital status of the patient
Patient.ReligiousAffiliation.CD	Religion of the patient
Patient.Race.CD	Race of the patient
Patient.Ethnicity.CD	Ethnicity of the patient
Patient.PlaceOfBirth.Address	Birth place of the patient
Patient.Address.Address	Address (e.g. home, work place, postal) of the patient
Patient.Telecom.Tele	Telecommunication means details (i.e. telephone, fax, mobile phone, email) of the patient
Patient.HealthcareProvider. HealthcareProvider	Health professional that takes place in the care of the patient
Patient.ProviderOrganization.Organization	Healthcare provider organization that takes place in the care of the patient
Patient.DataReporter.DataReporter	Human data reporter of the patient. It is a mandatory information in the case of reporting an Adverse Drug Event (ADE).
Patient.InsuranceProvider.InsuranceProvider	Insurance provider of the patient
Patient.Encounter.Encounter	Encounter of the patient
Patient.Allergy.Allergy	Allergy / intolerance / adverse event of the patient
Patient.Condition.Condition	Condition (i.e. problem, diagnosis, finding, symptom) of the patient
Patient.FamilyHistory.FamilyHistory	Family history of the patient
Patient.Immunization.Immunization	Immunization of the patient
Patient.Medication.Medication	Medication of the patient
Patient.PlanOfCare.PlannedEvent	Care plan event of the patient
Patient.Pregnancy.Pregnancy	Pregnancy history of the patient
Patient.Procedure.Procedure	Procedure of the patient
Patient.Result.Result	Lab result of the patient
Patient.SocialHistory.SocialHistory	Social history of the patient
Patient.VitalSign.Result	Vital sign of the patient
Address.NullFlavor.CD	An indicator that the address is null, together with the flavor (i.e. cause) of null.
Address.Use.CD	Type of the address; e.g. home, work place, postal.
Address.StreetAddressLine.String	Street information of the address

Continued on next page

Table A.1 – continued from previous page

Name	Description
Address.PostalCode.String	Postal code of the address
Address.City.String	City of the address
Address.State.String	State (region) of the address
Address.Country.String	Country of the address
Tele.NullFlavor.String	An indicator that the telecom information is null, together with the flavor (i.e. cause) of null.
Tele.Use.CD	Type of the telecom information; e.g. telephone, fax, mobile phone, email.
Tele.Value.String	Value of the telecom information
HealthcareProvider.DateRange.IVLTS	Time interval that the healthcare provider is involved in the care of the patient
HealthcareProvider.ID.II	Identifier of the healthcare provider
HealthcareProvider.Role.CD	Role of the healthcare provider; e.g. GP, surgeon, nurse.
HealthcareProvider.Title.String	Title/prefix of the healthcare provider
HealthcareProvider.GivenName.String	Given name of the healthcare provider
HealthcareProvider.FamilyName.String	Family name of the healthcare provider
HealthcareProvider.Address.Address	Address (e.g. home, work place, postal) of the healthcare provider
HealthcareProvider.Telecom.Tele	Telecommunication means details (i.e. telephone, fax, mobile phone, email) of the healthcare provider
HealthcareProvider.Organization. Organization	Organization that the healthcare provider is associated with
HealthcareProvider.patientID.II	Healthcare provider specific identifier of the patient
HealthcareProvider.Comment.String	Further free text comments / information about the healthcare provider
Organization.ID.II	Identifier of the organization
Organization.Address.Address	Address (e.g. work place, postal) of the organization
Organization.Telecom.Tele	Telecommunication means details (i.e. telephone, fax, mobile phone, email) of the organization
Organization.Name.String	Name of the organization
DataReporter.ID.II	Identifier of the data reporter
DataReporter.Title.String	Title/prefix of the data reporter
DataReporter.GivenName.String	Given name of the data reporter
DataReporter.Familyname.String	Family name of the data reporter
DataReporter.Qualification.CD	Qualification of the data reporter. Suggested values are Physician; Pharmacist; Other Health Professional; Lawyer; Consumer or other non health professional.
DataReporter.Organization.Organization	Organization that the data reporter is associated with
DataReporter.Address.Address	Address (e.g. home, work place, postal) of the data reporter
DataReporter.Telecom.Tele	Telecommunication means details (i.e. telephone, fax, mobile phone, email) of the data reporter
InsuranceProvider.GroupNumber.II	Policy or group contract number identifying the contract between a health plan sponsor and the health plan
InsuranceProvider.HealthInsuranceType.CD	Coded type of the health plan covering the individual
InsuranceProvider.Payer.Organization	Payer organization of the health plan insurance
InsuranceProvider.Member.Member	Patient who is covered by the health plan

Continued on next page

Table A.1 – continued from previous page

Name	Description
InsuranceProvider. FinancialResponsibilityPartyType.CD	Coded type of the financial responsibility party (i.e. guarantor)
InsuranceProvider.Subscriber.Subscriber	Human subscriber (i.e. the actual member or health plan contract holder; the true subscriber) of the health plan
InsuranceProvider.Guarantor.Guarantor	Guarantor of the health plan
InsuranceProvider.HealthPlanName.String	Name of the health plan
InsuranceProvider.Comment.String	Further free text comments / information about the insurance provider / health plan
Encounter.ID.II	Identifier of the encounter
Encounter.Type.CD	Coded type of the encounter (e.g. ambulatory, inpatient, surgical)
Encounter.TimeInterval.IVLTS	Effective time interval of the encounter
Encounter.Provider.HealthcareProvider	Healthcare provider involved in the encounter
Encounter.Organization.Organization	Healthcare provider organization where the encounter takes place
Encounter.ReasonForVisit.Condition	Condition of the patient that causes the encounter
Allergy.AdverseEventType.CD	Coded type of the allergy / intolerance / adverse event (e.g. drug allergy, food intolerance)
Allergy.TimeInterval.IVLTS	Effective time interval of the allergy / intolerance / adverse event
Allergy.Product.CD	Product (i.e. substance) that causes the allergy / intolerance / adverse event (e.g. egg protein, dust, nifedipine)
Allergy.Reaction.Condition	The condition which occur as a reaction to the allergy / intolerance / adverse event; can be any condition
Allergy.Status.CD	Coded status of the allergy / intolerance / adverse event (e.g. active, inactive, resolved)
Allergy.Severity.CD	Coded severity of the allergy / intolerance / adverse event (e.g. low, moderate, high)
Allergy.Comment.String	Further free text comments / information about the allergy / intolerance / adverse event
Condition.TimeInterval.IVLTS	Effective time interval of the condition
Condition.ProblemType.CD	Coded type of the condition (e.g. problem, diagnosis, finding, symptom)
Condition.ProblemName.String	Free text name of the condition
Condition.ProblemCode.CD	Coded name of the condition. In case the Time of Death is provided, this is the coded cause of death.
Condition.ProblemStatus.CD	Coded status of the condition (e.g. active, inactive, resolved)
Condition.ProblemSeverity.CD	Coded severity of the condition (e.g. low, moderate, high)
Condition.TimeOfDeath.Datetime	Time when the patient died
Condition.TreatingProvider. HealthcareProvider	Healthcare provider involved in the diagnosis / treatment of the condition
Condition.Comment.String	Further free text comments / information about the condition
FamilyHistory.ObservationDate.Datetime	Time of entry of the family history
FamilyHistory.KinshipType.CD	Coded type of kinship with the patient
FamilyHistory.ObservationCode.CD	Coded name of the family history observation
FamilyHistory.AgeAtOnset.Integer	Age of the kin when the family history observation became effective

Continued on next page

Table A.1 – continued from previous page

Name	Description
FamilyHistory.Comment.String	Further free text comments / information about the family history
Immunization.AdministeredDate.Datetime	Time when the immunization is applied to the patient
Immunization.MedicationSeriesNumber. Integer	Medication series number of the immunization
Immunization.Route.CD	Coded route of the immunization (e.g. intravenous)
Immunication.Dose.PQ	Dose of the immunization
Immunization.Site.CD	Coded approach site of the immunization (e.g. upper arm structure)
Immunication.Reaction.CD	Coded reaction that the patient has to the immunization
Immunization.Performer.HealthcareProvider	Healthcare provider that applies the immunization to the patient
Immunization.MedicationInformation. MedicationInformation	Details (e.g. coded product name, coded active ingredient, free text brand name) of the immunization
Immunization.Comment.String	Further free text comments / information about the immunization
Medication.TimeInterval.IVLTS	Effective time interval when the medication is used
Medication.AdministeredTiming.PIVLTS	Specific description of use time of the medication
Medication.Route.CD	Coded route of the medication (e.g. oral inhalation)
Medication.Dose.PQ	Dose of the medication
Medication.Site.CD	Coded approach site of the medication (e.g. nose)
Medication.DoseRestriction.IVLPQ	Minimum and maximum doses that the medication can be taken
Medication.ProductForm.CD	Coded product form of the medication (e.g. tablet)
Medication.DeliveryMethod.CD	Coded description of how the medication is administered
Medication.MedicationInformation. MedicationInformation	Details (e.g. coded product name, coded active ingredient, free text brand name) of the medication
Medication.Indication.Condition	Condition of the patient that causes the medication administration
Medication.PatientInstructions.String	Free text instructions to the patient (e.g. "keep in the refrigerator")
Medication.Reaction.CD	Coded reaction that the patient has to the medication
Medication.Order.Order	Details of the order (i.e. prescription)
Medication.FulfillmentInstructions.String	Free text instructions to the dispensing pharmacist or nurse (e.g. "instruct patient on the use of occlusive dressing")
Medication.FulFillmentHistory. FulfillmentHistory	Details of the fulfillment (i.e. dispensation)
Medication.Comment.String	Further free text comments / information about the medication
PlannedEvent.ID.II	Identifier of the care plan event
PlannedEvent.TimeInterval.IVLTS	Effective time interval of the care plan event
PlannedEvent.Type.CD	Coded type of the care plan event
PlannedEvent.EventCode.CD	Coded name of the care plan event
PlannedEvent.Comment.String	Further free text comments / information about the care plan event
Pregnancy.ObservationDate.Datetime	Time of entry of the pregnancy history
Pregnancy.Status.CD	Coded status of the pregnancy

Continued on next page

Table A.1 – continued from previous page

Name	Description
Pregnancy.LastMenstrualPeriodDate.Datetime	Time of last menstrual period of the patient
Pregnancy.DeliveryDate.Datetime	Time of delivery of the patient
Pregnancy.Comment.String	Further free text comments / information about the pregnancy history
Procedure.ID.II	Identifier of the procedure
Procedure.TimeInterval.IVLTS	Time when the procedure is performed
Procedure.Type.CD	Coded name of the procedure
Procedure.Type.String	Free text name of the procedure
Procedure.Status.CD	Coded status of the procedure (e.g. completed, active, aborted, cancelled)
Procedure.Site.CD	Coded target site of the procedure (e.g. hip joint)
Procedure.Provider.HealthcareProvider	Healthcare provider that performs the procedure
Procedure.Indication.Condition	Condition of the patient that causes the procedure
Procedure.RelatedEncounter.Encounter	Associated encounter in which the procedure is performed
Procedure.Comment.String	Further free text comments / information about the procedure
Result.ID.II	Identifier of the lab result / vital sign
Result.TimeInterval.IVLTS	Effective time interval of the lab result / vital sign
Result.Type.CD	Coded name of the lab result / vital sign
Result.Value.CD	Coded value of the lab result / vital sign
Result.Value.String	Free text value of the lab result / vital sign
Result.Value.PQ	Physical quantity value (i.e. value with unit) of the lab result / vital sign
Result.Interpretation.CD	Coded interpretation of the lab result / vital sign (e.g. abnormal, high, below low threshold)
Result.Provider.HealthcareProvider	Healthcare provider that provides the lab result / vital sign value
Result.ReferenceRange.IVLPQ	Referance range of the lab result / vital sign
Result.RelatedCondition.Condition	Condition of the patient that causes the lab result / vital sign to be measured / observed
Result.Comment.String	Further free text comments / information about the lab result / vital sign
SocialHistory.TimeInterval.IVLTS	Effective time interval of the social history
SocialHistory.ObservationCode.CD	Coded name of the social history (e.g. alcohol intake, tobacco use)
SocialHistory.ObservationValue.CD	Coded value of the social history
SocialHistory.ObservationValue.String	Free text value of the social history
SocialHistory.ObservationValue.PQ	Physical quantity value (i.e. value with unit) of the social history
SocialHistory.Comment.String	Further free text comments / information about the social history
Member.HealthPlanCoverageDates.IVLTS	Effective time interval of the health plan covering the member
Member.ID.II	Identifier assigned by the health plan to the member who is covered by the health plan
Member.RelationshipToSubscriber.CD	Coded relationship of the member to the subscriber
Member.Address.Address	Address (e.g. home, work place, postal) of the member
Member.Tele.Tele	Telecommunication means details (i.e. telephone, fax, mobile phone, email) of the member

Continued on next page

Table A.1 – continued from previous page

Name	Description
Member.Title.String	Title/prefix of the member
Member.GivenName.String	Given name of the member
Member.FamilyName.String	Family name of the member
Member.DateOfBirth.Date	Birth date of the member
Subscriber.ID.II	Identifier assigned by the health plan to the actual member or health plan contract holder (the true subscriber)
Subscriber.Address.Address	Address (e.g. home, work place, postal) of the subscriber
Subscriber.Tele.Tele	Telecommunication means details (i.e. telephone, fax, mobile phone, email) of the subscriber
Subscriber.Title.String	Title/prefix of the subscriber
Subscriber.GivenName.String	Given name of the subscriber
Subscriber.FamilyName.String	Family name of the subscriber
Subscriber.DateOfBirth.Date	Birth date of the subscriber
Guarantor.ResponsibilityEffectiveDate. IVLTS	Effective time interval of the responsibility of the guarantor (i.e. financial responsibility party)
Guarantor.Address.Address	Address (e.g. home, work place, postal) of the guarantor
Guarantor.Tele.Tele	Telecommunication means details (i.e. telephone, fax, mobile phone, email) of the guarantor
Guarantor.Title.String	Title/prefix of the guarantor
Guarantor.GivenName.String	Given name of the guarantor
Guarantor.FamilyName.String	Family name of the guarantor
MedicationInformation.ProductName.CD	Coded product name of the medication
MedicationInformation.ProductName.String	Free text product name of the medication
MedicationInformation.ActiveIngredient.CD	Coded active ingredient of the medication
MedicationInformation.BrandName.CD	Coded brand name of the medication
MedicationInformation.BrandName.String	Free text brand name of the medication
MedicationInformation.DrugManufacturer. Organization	Pharmaceuticals organization that manufactured the medication
Order.Number.II	Identifier of the order (i.e. prescription)
Order.Provider.HealthcareProvider	Healthcare provider that wrote this order
Order.FillNumber.Integer	Number of times that the medication can be dispensed
Order.QuantityOrdered.PQ	Amount of product that can be dispensed
Order.ExpirationDateTime.Datetime	Time when the ordering provider wrote the order
Order.Datetime.Datetime	Time when the order is no longer valid
FulfillmentHistory.PrescriptionNumber.II	Identifier of the corresponding order (i.e. prescription)
FulfillmentHistory.DispensingProvider. HealthcareProvider	Healthcare provider that dispensed the medication
FulfillmentHistory.DispenseDate.Datetime	Time when the dispensing provider dispensed the medication
FulfillmentHistory.QuantityDispensed.PQ	Amount of product that was dispensed
FulfillmentHistory.FillNumber.Integer	Fill number of the dispensation
FulfillmentHistory.FillStatus.CD	Coded status of the fill event (e.g. completed, aborted)
EligibilityCriteria.InclusionCriteria. CriteriaGroup	Inclusion criteria definition of the eligibility criteria

Continued on next page

Table A.1 – continued from previous page

Name	Description
EligibilityCriteria.ExclusionCriteria. CriteriaGroup	Exclusion criteria definition of the eligibility criteria
CriteriaGroup.ConjunctionCode.CD	Coded conjunction method of the criteria group. It can be AND, OR, NOR, NAND.
CriteriaGroup.GroupItem.CriterionBase	Members of the criteria group. CriterionBase is an abstract class for Criterion and CriteriaGroup.
CriteriaGroup.NegationIndicator.Boolean	Boolean indicator to negate the complete criteria group
Criterion.ClinicalStatement. ClinicalStatement	Clinical statement defining the criterion. ClinicalStatement is an abstract class for all medical building blocks such as Medication, Condition, Patient, etc.
Criterion.TemporalRelation. TemporalConstraint	Temporal relation of the criterion to a target criterion
Criterion.NegationIndicator.Boolean	Boolean indicator to negate the criterion
TemporalConstraint.TypeCode.CD	Coded type of the temporal constraint (e.g. "starts after start of", "ends before end")
TemporalConstraint.PauseQuantity.IVLPQ	Pause quantity (i.e. the time interval between two criterions) of the temporal constraint
TemporalConstraint.TargetCriterion. Criterion	Target criterion of the temporal constraint

APPENDIX B

AN EXAMPLE HQMF QUERY WITHIN THE EXTENDED IHE QED TRANSACTION

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   <creationTime value=" "/>
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   <processingModeCode code="T"/>
   <acceptAckCode code="AL"/>
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      <device determinerCode="INSTANCE">
         <id/>
         <name/>
      </device>
   </receiver>
   <sender typeCode="SND">
      <device determinerCode="INSTANCE">
         <id/>
         <name/>
      </device>
   </sender>
   <controlActProcess moodCode="RQO">
      <id root=" " extension=" "/>
      <code code="QUPC_TE043100UVExt"/>
      <effectiveTime value=" "/>
      <languageCode code=" "/>
      <authorOrPerformer typeCode=" "/>
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         <responseModalityCode code="R"/>
         <responsePriorityCode code="I"/>
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         <initialQuantityCode code="REPC_RM000100UV" codeSystem="2.16.840.1.113883"/>
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                        <text>This measure document is used to express a population based
                           query in the SALUS project.</text>
                     </measureDescriptionSection>
                  </component>
                  <component>
                     <dataCriteriaSection>
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                           <substanceAdministrationCriteria moodCode="EVN">
                              <id root="0" extension="NifedipineMedication"/>
                              <participation typeCode="CSM">
                                 <role classCode="MANU">
```

```
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                                       codeSystem="2.16.840.1.113883.6.73"
                                       codeSystemName="ATC"/>
                                 </playingMaterial>
                              </role>
                           </participation>
                        </substanceAdministrationCriteria>
                     </entry>
                     <entry>
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                        <observationCriteria>
                           <id root="0" extension="MIEvent"/>
                           <statusCode code="completed"/>
                           <value xsi:type="CD" code="410"
                              displayName="Acute myocardial infarction"
                              codeSystem="2.16.840.1.113883.6.2"
                              codeSystemName="ICD-9-CM"/>
                           <temporallyRelatedInformation typeCode="SAS">
                              <pauseQuantity xsi:type="IVL_PQ">
                                 <any value="2" unit="wk"/>
                              </pauseQuantity>
                              <ObservationReference>
                                 <id root="0" extension="NifedipineMedication"/>
                              </ObservationReference>
                           </temporallyRelatedInformation>
                        </observationCriteria>
                     </entry>
                  </dataCriteriaSection>
               </component>
               <component>
                  <populationCriteriaSection>
                     <entry>
                        <patientPopulationCriteria classCode="OBS" moodCode="EVN">
                           <id root="c75181d0-73eb-11de-8a39-0800200c9a66"/>
                           <code code="IPP" codeSystem="2.16.840.1.113883.5.1063"
                              codeSystemName="HL7 Observation Value">
                              <displayName value="Included in Initial Patient Population"/>
                           </code>
                           <isCriterionInd value="true"/>
                           <precondition typeCode="PRCN">
                              <allTrue>
                                 <precondition>
                                    <observationReference classCode="OBS" moodCode="EVN">
                                       <id root="0" extension="MIEvent"/>
                                    </observationReference>
                                 </precondition>
                                 <precondition>
                                    <substanceAdministrationReference moodCode="EVN">
                                       <id root="0" extension="NifedipineMedication"/>
                                    </substanceAdministrationReference>
                                 </precondition>
                              </allTrue>
                           </precondition>
                        </patientPopulationCriteria>
                     </entry>
                  </populationCriteriaSection>
               </component>
            </QualityMeasureDocument>
         </populationBasedQuery>
         <includeCarePlanAttachment>
            <value value="false"/>
         </includeCarePlanAttachment>
      </parameterList>
   </queryByParameter>
</controlActProcess>
</QUPC_IN043100UVExt>
```

APPENDIX C

AN EXAMPLE MEDICAL SUMMARY IN HL7 CDA FORMAT USING PCC/CCD TEMPLATES

```
<?xml version="1.0" encoding="UTF-8" standalone="yes"?>
<ClinicalDocument xmlns="urn:hl7-org:v3" xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
   <!--
******************************************************
CDA Header
******************************************************
-->
   <typeId root="2.16.840.1.113883.1.3" extension="POCD_HD000040"/>
   <templateId root="2.16.840.1.113883.10.20.1"/>
   <id root="db734647-fc99-424c-a864-7e3cda82e703"/>
   <code code="34133-9" codeSystem="2.16.840.1.113883.6.1" codeSystemName="LOINC"
      displayName="Summarization of episode note"/>
   <title>SALUS Patient Summary Instance</title>
   <effectiveTime value="20130307130000+0200"/>
   <confidentialityCode code="N" codeSystem="2.16.840.1.113883.5.25"/>
   <languageCode code="en-US"/>
   <recordTarget>
      <patientRole>
         <id extension="547001" root="2.16.840.1.113883.2.9.4.3.2"
            assigningAuthorityName="MEF - Italian Citizen Identity Authority"/>
         <addr use="HP">
            <city>Milan</city>
            <state>MI</state>
            <country>Italy</country>
         </addr>
         <patient>
            <name>
               <given>Patient1</given>
               <family>Cremona</family>
            </name>
            <administrativeGenderCode code="M" displayName="Male"
               codeSystem="2.16.840.1.113883.5.1" codeSystemName="AdministrativeGender"/>
            <birthTime value="19450201"/>
         </patient>
         <providerOrganization>
            <id root="2.16.840.1.113883.2.9.4.3.2.4" extension="65432178901"/>
         </providerOrganization>
      </patientRole>
   </recordTarget>
   <author>
      <time value="20130307130000+0200"/>
      <assignedAuthor>
         <id root="2.16.840.1.113883.2.9.4.3.2.5" extension="76543218901"/>
         <assignedAuthoringDevice>
            <softwareName>SALUS LISPA Connector v0.1</softwareName>
         </assignedAuthoringDevice>
         <representedOrganization>
            <id root="2.16.840.1.113883.2.9.4.3.2.4" extension="65432178901"/>
         </representedOrganization>
      </assignedAuthor>
   </author>
```

```
   <custodian>
      <assignedCustodian>
         <representedCustodianOrganization>
            <id root="2.16.840.1.113883.2.9.4.3.2.4" extension="65432178901"/>
            <name>Lombardy Region</name>
         </representedCustodianOrganization>
      </assignedCustodian>
   </custodian>
   <component>
      <structuredBody>
         <!--
*******************************************************
Active problems section
*******************************************************
-->
         <component>
            <section>
               <templateId root="2.16.840.1.113883.10.20.1.11"/>
               <templateId root="1.3.6.1.4.1.19376.1.5.3.1.3.6"/>
               <id root="087e4130-770a-42ee-879e-e60a1fc76110"/>
               <code code="11450-4" codeSystem="2.16.840.1.113883.6.1"
                  codeSystemName="LOINC" displayName="Problem list - Reported"/>
               <title>Problem List</title>
               <text>
                  <table>
                     <thead>
                        <tr>
                           <th>Condition</th>
                           <th>Effective Dates</th>
                        </tr>
                     </thead>
                     <tbody>
                        <tr ID="actprob1">
                           <td ID="actprob1_condition">Malignant essential hypertension</td>
                           <td ID="actprob1_date">01.07.2009</td>
                        </tr>
                        <tr ID="actprob2">
                           <td ID="actprob2_condition">New daily persistent headache</td>
                           <td ID="actprob2_date">25.07.2009</td>
                        </tr>
                        <tr ID="actprob3">
                           <td ID="actprob3_condition">Obesity, unspecified</td>
                           <td ID="actprob3_date">01.06.2006</td>
                        </tr>
                     </tbody>
                  </table>
               </text>
               <entry>
                  <act classCode="ACT" moodCode="EVN">
                     <templateId root="2.16.840.1.113883.10.20.1.27"/>
                     <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.5.1"/>
                     <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.5.2"/>
                     <id root="37e7fef6-2c79-41fe-850e-b1994cdbf869"/>
                     <code nullFlavor="NA"/>
                     <text>
                        <reference value="#actprob1"/>
                     </text>
                     <entryRelationship typeCode="SUBJ">
                        <observation classCode="OBS" moodCode="EVN">
                           <templateId root="2.16.840.1.113883.10.20.1.28"/>
                           <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.5"/>
                           <id root="46190165-a977-4066-be72-1ba9a4f4025c"/>
                           <code code="55607006" displayName="Problem"
                              codeSystem="2.16.840.1.113883.6.96" codeSystemName="SNOMED CT"/>
                           <text>
                              <reference value="#actprob1_condition"/>
                           </text>
                           <statusCode code="completed"/>
                           <effectiveTime>
                              <low value="20090701"/>
```

```
            </effectiveTime>
            <value xsi:type="CD" code="401.0"
               displayName="Malignant essential hypertension"
               codeSystem="2.16.840.1.113883.6.2" codeSystemName="ICD-9-CM">
               <originalText>Malignant essential hypertension</originalText>
            </value>
         </observation>
      </entryRelationship>
   </act>
</entry>
<entry>
   <act classCode="ACT" moodCode="EVN">
      <templateId root="2.16.840.1.113883.10.20.1.27"/>
      <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.5.1"/>
      <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.5.2"/>
      <id root="37e7fef6-2c79-41fe-850e-b1994cdbf869"/>
      <code nullFlavor="NA"/>
      <text>
         <reference value="#actprob2"/>
      </text>
      <entryRelationship typeCode="SUBJ">
         <observation classCode="OBS" moodCode="EVN">
            <templateId root="2.16.840.1.113883.10.20.1.28"/>
            <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.5"/>
            <id root="46190165-a977-4066-be72-1ba9a4f4025c"/>
            <code code="55607006" displayName="Problem"
               codeSystem="2.16.840.1.113883.6.96" codeSystemName="SNOMED CT"/>
            <text>
               <reference value="#actprob2_condition"/>
            </text>
            <statusCode code="completed"/>
            <effectiveTime>
               <low value="20090725"/>
            </effectiveTime>
            <value xsi:type="CD" code="339.42"
               displayName="New daily persistent headache"
               codeSystem="2.16.840.1.113883.6.2" codeSystemName="ICD-9-CM">
               <originalText>New daily persistent headache</originalText>
            </value>
         </observation>
      </entryRelationship>
   </act>
</entry>
<entry>
   <act classCode="ACT" moodCode="EVN">
      <templateId root="2.16.840.1.113883.10.20.1.27"/>
      <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.5.1"/>
      <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.5.2"/>
      <id root="37e7fef6-2c79-41fe-850e-b1994cdbf869"/>
      <code nullFlavor="NA"/>
      <text>
         <reference value="#actprob3"/>
      </text>
      <entryRelationship typeCode="SUBJ">
         <observation classCode="OBS" moodCode="EVN">
            <templateId root="2.16.840.1.113883.10.20.1.28"/>
            <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.5"/>
            <id root="46190165-a977-4066-be72-1ba9a4f4025c"/>
            <code code="55607006" displayName="Problem"
               codeSystem="2.16.840.1.113883.6.96" codeSystemName="SNOMED CT"/>
            <text>
               <reference value="#actprob3_condition"/>
            </text>
            <statusCode code="completed"/>
            <effectiveTime>
               <low value="20060601"/>
            </effectiveTime>
            <value xsi:type="CD" code="278.00"
               displayName="Obesity, unspecified"
               codeSystem="2.16.840.1.113883.6.2" codeSystemName="ICD-9-CM">
```

```
                        <originalText>Obesity, unspecified</originalText>
                     </value>
                  </observation>
               </entryRelationship>
            </act>
         </entry>
      </section>
   </component>
   <!--
*******************************************************
History of past illness section
*******************************************************
-->
   <component>
      <section>
         <templateId root="1.3.6.1.4.1.19376.1.5.3.1.3.8"/>
         <id root="93939ef9-05f7-4ad1-83e3-c23917d51d19"/>
         <code code="11348-0" codeSystem="2.16.840.1.113883.6.1" codeSystemName="LOINC"
            displayName="History of past illness"/>
         <title>History of past illness</title>
         <text>
            <table>
               <thead>
                  <tr>
                     <th>Condition</th>
                     <th>Effective Dates</th>
                  </tr>
               </thead>
               <tbody>
                  <tr ID="pastprob1">
                     <td ID="pastprob1_condition">Acute myocardial infarction</td>
                     <td ID="pastprob1_date">01.08.2009</td>
                  </tr>
               </tbody>
            </table>
         </text>
         <entry>
            <act classCode="ACT" moodCode="EVN">
               <templateId root="2.16.840.1.113883.10.20.1.27"/>
               <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.5.1"/>
               <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.5.2"/>
               <id root="a0fff30c-b94e-4eee-b5f5-bf5a79ebb929"/>
               <code nullFlavor="NA"/>
               <text>
                  <reference value="#pastprob1"/>
               </text>
               <entryRelationship typeCode="SUBJ">
                  <observation classCode="OBS" moodCode="EVN">
                     <templateId root="2.16.840.1.113883.10.20.1.28"/>
                     <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.5"/>
                     <id root="2a29b507-3416-4a50-9e6a-9e05fa9f2af0"/>
                     <code code="55607006" displayName="Problem"
                        codeSystem="2.16.840.1.113883.6.96" codeSystemName="SNOMED CT"/>
                     <text>
                        <reference value="#pastprob1_condition"/>
                     </text>
                     <statusCode code="completed"/>
                     <effectiveTime>
                        <low value="20090801"/>
                        <high value="20090801"/>
                     </effectiveTime>
                     <value xsi:type="CD" code="410"
                        displayName="Acute myocardial infarction"
                        codeSystem="2.16.840.1.113883.6.2" codeSystemName="ICD-9-CM">
                        <originalText>Acute myocardial infarction</originalText>
                     </value>
                  </observation>
               </entryRelationship>
            </act>
         </entry>
```

```
            </section>
         </component>
         <!--
*****************************************************
Medications section
*****************************************************
-->
         <component>
            <section>
               <templateId root="2.16.840.1.113883.10.20.1.8"/>
               <templateId root="1.3.6.1.4.1.19376.1.5.3.1.3.19"/>
               <id root="3876f056-6ed4-4f77-9e6a-fdee4f88411d"/>
               <code code="10160-0" codeSystem="2.16.840.1.113883.6.1"
                  codeSystemName="LOINC" displayName="History of medication use"/>
               <title>History of medication use</title>
               <text>
                  <table>
                     <thead>
                        <tr>
                           <th>Medication</th>
                           <th>Date</th>
                        </tr>
                     </thead>
                     <tbody>
                        <tr ID="med1">
                           <td ID="med1_name">nifedipine</td>
                           <td ID="med1_date">20.07.2009</td>
                        </tr>
                        <tr ID="med2">
                           <td ID="med2_name">acetylsalicylic acid</td>
                           <td ID="med2_date">02.08.2009</td>
                        </tr>
                        <tr ID="med3">
                           <td ID="med3_name">losartan</td>
                           <td ID="med3_date">20.07.2009</td>
                        </tr>
                     </tbody>
                  </table>
               </text>
               <entry>
                  <substanceAdministration classCode="SBADM" moodCode="INT">
                     <templateId root="2.16.840.1.113883.10.20.1.24"/>
                     <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.7"/>
                     <id root="9e4c4be7-0d46-49cf-ba1e-170b5855bb5a"/>
                     <text>
                        <reference value="#med1"/>
                     </text>
                     <statusCode code="completed"/>
                     <effectiveTime xsi:type="IVL_TS">
                        <low value="20090720"/>
                     </effectiveTime>
                     <effectiveTime xsi:type="PIVL_TS" institutionSpecified="true">
                        <period value="8" unit="h"/>
                     </effectiveTime>
                     <routeCode code="PO" codeSystem="2.16.840.1.113883.5.112"
                        codeSystemName="RouteOfAdministration" displayName="Swallow, oral"/>
                     <doseQuantity value="10" unit="mg"/>
                     <consumable>
                        <manufacturedProduct classCode="MANU">
                           <templateId root="2.16.840.1.113883.10.20.1.53"/>
                           <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.7.2"/>
                           <manufacturedMaterial>
                              <code code="316352" codeSystem="2.16.840.1.113883.6.88"
                                 codeSystemName="RxNorm" displayName="Nifedipine 10 MG">
                                 <originalText>Nifedipine 10 MG</originalText>
                                 <translation code="C08CA05" displayName="nifedipine"
                                    codeSystem="2.16.840.1.113883.6.73" codeSystemName="ATC"/>
                              </code>
                           </manufacturedMaterial>
                        </manufacturedProduct>
```

```
            </consumable>
         </substanceAdministration>
      </entry>
      <entry>
         <substanceAdministration classCode="SBADM" moodCode="INT">
            <templateId root="2.16.840.1.113883.10.20.1.24"/>
            <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.7"/>
            <id root="9e4c4be7-0d46-49cf-ba1e-170b5855bb5a"/>
            <text>
               <reference value="#med2"/>
            </text>
            <statusCode code="completed"/>
            <effectiveTime xsi:type="IVL_TS">
               <low value="20090802"/>
            </effectiveTime>
            <effectiveTime xsi:type="PIVL_TS" institutionSpecified="true">
               <period value="1" unit="d"/>
            </effectiveTime>
            <routeCode code="PO" codeSystem="2.16.840.1.113883.5.112"
               codeSystemName="RouteOfAdministration" displayName="Swallow, oral"/>
            <doseQuantity value="250" unit="mg"/>
            <consumable>
               <manufacturedProduct classCode="MANU">
                  <templateId root="2.16.840.1.113883.10.20.1.53"/>
                  <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.7.2"/>
                  <manufacturedMaterial>
                     <code code="335953" codeSystem="2.16.840.1.113883.6.88"
                        codeSystemName="RxNorm" displayName="Aspirin 250 MG">
                        <originalText>Aspirin 250 MG</originalText>
                        <translation code="B01AC06" displayName="acetylsalicylic acid"
                           codeSystem="2.16.840.1.113883.6.73" codeSystemName="ATC"/>
                     </code>
                  </manufacturedMaterial>
               </manufacturedProduct>
            </consumable>
         </substanceAdministration>
      </entry>
      <entry>
         <substanceAdministration classCode="SBADM" moodCode="INT">
            <templateId root="2.16.840.1.113883.10.20.1.24"/>
            <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.7"/>
            <id root="9e4c4be7-0d46-49cf-ba1e-170b5855bb5a"/>
            <text>
               <reference value="#med3"/>
            </text>
            <statusCode code="completed"/>
            <effectiveTime xsi:type="IVL_TS">
               <low value="20090720"/>
            </effectiveTime>
            <effectiveTime xsi:type="PIVL_TS" institutionSpecified="true">
               <period value="1" unit="d"/>
            </effectiveTime>
            <routeCode code="PO" codeSystem="2.16.840.1.113883.5.112"
               codeSystemName="RouteOfAdministration" displayName="Swallow, oral"/>
            <doseQuantity value="50" unit="mg"/>
            <consumable>
               <manufacturedProduct classCode="MANU">
                  <templateId root="2.16.840.1.113883.10.20.1.53"/>
                  <templateId root="1.3.6.1.4.1.19376.1.5.3.1.4.7.2"/>
                  <manufacturedMaterial>
                     <code code="979492" codeSystem="2.16.840.1.113883.6.88"
                        codeSystemName="RxNorm"
                        displayName="Losartan Potassium 50 MG Oral Tablet">
                        <originalText>Losartan Potassium 50 MG Oral Tablet
</originalText>
                        <translation code="C09CA01" displayName="losartan"
                           codeSystem="2.16.840.1.113883.6.73" codeSystemName="ATC"/>
                     </code>
                  </manufacturedMaterial>
               </manufacturedProduct>
```

```
                    </consumable>
                  </substanceAdministration>
                </entry>
              </section>
            </component>
          </structuredBody>
        </component>
      </ClinicalDocument>
```

APPENDIX D

AN EXAMPLE MEDICAL SUMMARY AS AN INSTANCE OF HL7 CDA RDF MODEL

```
@prefix :     <http://www.srdc.com.tr/ontmalizer/instance#> .
@prefix rdfs:    <http://www.w3.org/2000/01/rdf-schema#> .
@prefix v3:   <urn:hl7-org:v3#> .
@prefix owl:     <http://www.w3.org/2002/07/owl#> .
@prefix xsd:     <http://www.w3.org/2001/XMLSchema#> .
@prefix dtype:   <http://www.srdc.com.tr/ontmalizer#> .
@prefix rdf:     <http://www.w3.org/1999/02/22-rdf-syntax-ns#> .

:INS2007004_II_2
   a    v3:II ;
   v3:assigningAuthorityName
        "MEF - Italian Citizen Identity Authority"^^v3:stDatatype ;
   v3:extension "547001"^^v3:stDatatype ;
   v3:root "2.16.840.1.113883.2.9.4.3.2"^^v3:uidDatatype .

:INS2007004_CS_7
   a    v3:CS ;
   v3:code "completed"^^v3:csDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Entry_7>
   a    <urn:hl7-org:v3#POCD_MT000040.Entry> ;
   v3:substanceAdministration
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
SubstanceAdministration_3> .

:INS2007004_ED_3
   a    v3:ED ;
   v3:textContent "Malignant essential hypertension"^^xsd:string .

:INS2007004_TEL_11
   a    v3:TEL ;
   v3:value "#med3"^^v3:urlDatatype .

:INS2007004_IVXB_TS_3
   a    v3:IVXB_TS ;
   v3:value "20060601"^^v3:tsDatatype .

:INS2007004_CE_4
   a    v3:CE ;
   v3:code "11450-4"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.1"^^v3:uidDatatype ;
   v3:codeSystemName "LOINC"^^v3:stDatatype ;
   v3:displayName "Problem list - Reported"^^v3:stDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_37>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.53"^^v3:uidDatatype .

:INS2007004_TEL_4
   a    v3:TEL ;
```

```
   v3:value "#actprob2_condition"^^v3:urlDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_9>
   a    <urn:hl7-org:v3#StrucDoc.Td> ;
   v3:ID   "med1_name"^^xsd:ID ;
   v3:textContent "nifedipine"^^xsd:string .

:INS2007004_CD_13
   a    v3:CD ;
   v3:code "C08CA05"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.73"^^v3:uidDatatype ;
   v3:codeSystemName "ATC"^^v3:stDatatype ;
   v3:displayName "nifedipine"^^v3:stDatatype .

:INS2007004_CS_8
   a    v3:CS ;
   v3:code "completed"^^v3:csDatatype .

:INS2007004_ED_4
   a    v3:ED ;
   v3:reference :INS2007004_TEL_3 .

:INS2007004_CE_5
   a    v3:CE ;
   v3:code "11348-0"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.1"^^v3:uidDatatype ;
   v3:codeSystemName "LOINC"^^v3:stDatatype ;
   v3:displayName "History of past illness"^^v3:stDatatype .

:INS2007004_II_3
   a    v3:II ;
   v3:extension "65432178901"^^v3:stDatatype ;
   v3:root "2.16.840.1.113883.2.9.4.3.2.4"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.CustodianOrganization_1>
   a    <urn:hl7-org:v3#POCD_MT000040.CustodianOrganization> ;
   v3:id   :INS2007004_II_6 ;
   v3:name :INS2007004_ON_1 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Entry_6>
   a    <urn:hl7-org:v3#POCD_MT000040.Entry> ;
   v3:substanceAdministration
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
SubstanceAdministration_2> .

:INS2007004_IVXB_TS_2
   a    v3:IVXB_TS ;
   v3:value "20090725"^^v3:tsDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_1>
   a    <urn:hl7-org:v3#StrucDoc.Tr> ;
   v3:th   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.
Th_1> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Th_2> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_38>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.7.2"^^v3:uidDatatype .

:INS2007004_TEL_3
   a    v3:TEL ;
   v3:value "#actprob2"^^v3:urlDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
SubstanceAdministration_1>
   a    <urn:hl7-org:v3#POCD_MT000040.SubstanceAdministration> ;
   v3:classCode "SBADM"^^v3:ActClassDatatype ;
   v3:consumable <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Consumable_1> ;
   v3:doseQuantity :INS2007004_IVL_PQ_1 ;
```

```
   v3:effectiveTime :INS2007004_IVL_TS_5 , :INS2007004_PIVL_TS_1 ;
   v3:id   :INS2007004_II_18 ;
   v3:moodCode "INT"^^v3:x_DocumentSubstanceMoodDatatype ;
   v3:routeCode :INS2007004_CE_7 ;
   v3:statusCode :INS2007004_CS_6 ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_27> , <http://www.srdc.com.
tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.templateId_28> ;
   v3:text :INS2007004_ED_13 .

:INS2007004_CD_12
   a    v3:CD ;
   v3:code "410"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.2"^^v3:uidDatatype ;
   v3:codeSystemName "ICD-9-CM"^^v3:stDatatype ;
   v3:displayName "Acute myocardial infarction"^^v3:stDatatype ;
   v3:originalText :INS2007004_ED_12 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_en.given_1>
   a    <urn:hl7-org:v3#en.given> ;
   v3:textContent "Patient1"^^xsd:string .

:INS2007004_TEL_6
   a    v3:TEL ;
   v3:value "#actprob3_condition"^^v3:urlDatatype .

:INS2007004_ST_3
   a    v3:ST ;
   v3:textContent "History of past illness"^^xsd:string .

:INS2007004_CE_6
   a    v3:CE ;
   v3:code "10160-0"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.1"^^v3:uidDatatype ;
   v3:codeSystemName "LOINC"^^v3:stDatatype ;
   v3:displayName "History of medication use"^^v3:stDatatype .

:INS2007004_II_10
   a    v3:II ;
   v3:root "37e7fef6-2c79-41fe-850e-b1994cdbf869"^^v3:uidDatatype .

:INS2007004_ED_5
   a    v3:ED ;
   v3:reference :INS2007004_TEL_4 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_20>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.27"^^v3:uidDatatype .

:INS2007004_IVXB_TS_5
   a    v3:IVXB_TS ;
   v3:value "20090801"^^v3:tsDatatype .

:INS2007004_IVL_TS_7
   a    v3:IVL_TS ;
   v3:low  :INS2007004_IVXB_TS_8 .

:INS2007004_CD_11
   a    v3:CD ;
   v3:code "55607006"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.96"^^v3:uidDatatype ;
   v3:codeSystemName "SNOMED CT"^^v3:stDatatype ;
   v3:displayName "Problem"^^v3:stDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
SubstanceAdministration_2>
   a    <urn:hl7-org:v3#POCD_MT000040.SubstanceAdministration> ;
   v3:classCode "SBADM"^^v3:ActClassDatatype ;
   v3:consumable <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
```

```
Consumable_2> ;
   v3:doseQuantity :INS2007004_IVL_PQ_2 ;
   v3:effectiveTime :INS2007004_PIVL_TS_2 , :INS2007004_IVL_TS_6 ;
   v3:id   :INS2007004_II_19 ;
   v3:moodCode "INT"^^v3:x_DocumentSubstanceMoodDatatype ;
   v3:routeCode :INS2007004_CE_9 ;
   v3:statusCode :INS2007004_CS_7 ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_32> , <http://www.srdc.com.
tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.templateId_31> ;
   v3:text :INS2007004_ED_15 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_7>
   a    <urn:hl7-org:v3#StrucDoc.Td> ;
   v3:ID   "pastprob1_condition"^^xsd:ID ;
   v3:textContent "Acute myocardial infarction"^^xsd:string .

:INS2007004_ST_4
   a    v3:ST ;
   v3:textContent "History of medication use"^^xsd:string .

:INS2007004_CE_7
   a    v3:CE ;
   v3:code "PO"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.5.112"^^v3:uidDatatype ;
   v3:codeSystemName "RouteOfAdministration"^^v3:stDatatype ;
   v3:displayName "Swallow, oral"^^v3:stDatatype .

:INS2007004_II_11
   a    v3:II ;
   v3:root "46190165-a977-4066-be72-1ba9a4f4025c"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.AuthoringDevice_1>
   a    <urn:hl7-org:v3#POCD_MT000040.AuthoringDevice> ;
   v3:softwareName :INS2007004_SC_1 .

:INS2007004_II_1
   a    v3:II ;
   v3:root "db734647-fc99-424c-a864-7e3cda82e703"^^v3:uidDatatype .

:INS2007004_ED_6
   a    v3:ED ;
   v3:textContent "New daily persistent headache"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Section_3>
   a    <urn:hl7-org:v3#POCD_MT000040.Section> ;
   v3:code :INS2007004_CE_6 ;
   v3:entry <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Entry_7> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Entry_6> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Entry_5> ;
   v3:id   :INS2007004_II_17 ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_26> , <http://www.srdc.com.
tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.templateId_25> ;
   v3:text <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Text_3> ;
   v3:title :INS2007004_ST_4 .

:INS2007004_IVL_TS_6
   a    v3:IVL_TS ;
   v3:low  :INS2007004_IVXB_TS_7 .

:INS2007004_IVXB_TS_4
   a    v3:IVXB_TS ;
   v3:value "20090801"^^v3:tsDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
SubstanceAdministration_3>
   a    <urn:hl7-org:v3#POCD_MT000040.SubstanceAdministration> ;
   v3:classCode "SBADM"^^v3:ActClassDatatype ;
   v3:consumable <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
```

```
Consumable_3> ;
   v3:doseQuantity :INS2007004_IVL_PQ_3 ;
   v3:effectiveTime :INS2007004_PIVL_TS_3 , :INS2007004_IVL_TS_7 ;
   v3:id   :INS2007004_II_20 ;
   v3:moodCode "INT"^^v3:x_DocumentSubstanceMoodDatatype ;
   v3:routeCode :INS2007004_CE_11 ;
   v3:statusCode :INS2007004_CS_8 ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_36> , <http://www.srdc.com.
tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.templateId_35> ;
   v3:text :INS2007004_ED_17 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_8>
   a    <urn:hl7-org:v3#StrucDoc.Td> ;
   v3:ID   "pastprob1_date"^^xsd:ID ;
   v3:textContent "01.08.2009"^^xsd:string .

:INS2007004_CD_10
   a    v3:CD ;
   v3:nullFlavor "NA"^^v3:NullFlavorDatatype .

:INS2007004_TEL_5
   a    v3:TEL ;
   v3:value "#actprob3"^^v3:urlDatatype .

:INS2007004_CE_10
   a    v3:CE ;
   v3:code "335953"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.88"^^v3:uidDatatype ;
   v3:codeSystemName "RxNorm"^^v3:stDatatype ;
   v3:displayName "Aspirin 250 MG"^^v3:stDatatype ;
   v3:originalText :INS2007004_ED_16 ;
   v3:translation :INS2007004_CD_14 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Component3_1>
   a    <urn:hl7-org:v3#POCD_MT000040.Component3> ;
   v3:section <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Section_1> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Section_2>
   a    <urn:hl7-org:v3#POCD_MT000040.Section> ;
   v3:code :INS2007004_CE_5 ;
   v3:entry <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Entry_4> ;
   v3:id   :INS2007004_II_14 ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_19> ;
   v3:text <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Text_2> ;
   v3:title :INS2007004_ST_3 .

:INS2007004_IVXB_TS_7
   a    v3:IVXB_TS ;
   v3:value "20090802"^^v3:tsDatatype .

:INS2007004_CS_3
   a    v3:CS ;
   v3:code "completed"^^v3:csDatatype .

:INS2007004_ST_1
   a    v3:ST ;
   v3:textContent "SALUS Patient Summary Instance"^^xsd:string .

:INS2007004_II_12
   a    v3:II ;
   v3:root "37e7fef6-2c79-41fe-850e-b1994cdbf869"^^v3:uidDatatype .

:INS2007004_CE_8
   a    v3:CE ;
   v3:code "316352"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.88"^^v3:uidDatatype ;
   v3:codeSystemName "RxNorm"^^v3:stDatatype ;
```

```
   v3:displayName "Nifedipine 10 MG"^^v3:stDatatype ;
   v3:originalText :INS2007004_ED_14 ;
   v3:translation :INS2007004_CD_13 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Th_5>
   a    <urn:hl7-org:v3#StrucDoc.Th> ;
   v3:textContent "Medication"^^xsd:string .

:INS2007004_IVL_PQ_3
   a    v3:IVL_PQ ;
   v3:unit "mg"^^v3:csDatatype ;
   v3:value "50"^^v3:realDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_33>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.53"^^v3:uidDatatype .

:INS2007004_II_6
   a    v3:II ;
   v3:extension "65432178901"^^v3:stDatatype ;
   v3:root "2.16.840.1.113883.2.9.4.3.2.4"^^v3:uidDatatype .

:INS2007004_TEL_8
   a    v3:TEL ;
   v3:value "#pastprob1_condition"^^v3:urlDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_14>
   a    <urn:hl7-org:v3#StrucDoc.Td> ;
   v3:ID   "med3_date"^^xsd:ID ;
   v3:textContent "20.07.2009"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Entry_3>
   a    <urn:hl7-org:v3#POCD_MT000040.Entry> ;
   v3:act  <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Act_3> .

:INS2007004_CD_8
   a    v3:CD ;
   v3:code "55607006"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.96"^^v3:uidDatatype ;
   v3:codeSystemName "SNOMED CT"^^v3:stDatatype ;
   v3:displayName "Problem"^^v3:stDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Thead_3>
   a    <urn:hl7-org:v3#StrucDoc.Thead> ;
   v3:tr   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_7> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_17>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.28"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_4>
   a    <urn:hl7-org:v3#StrucDoc.Tr> ;
   v3:ID   "actprob3"^^xsd:ID ;
   v3:td   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.
Td_6> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_5> .

:INS2007004_II_7
   a    v3:II ;
   v3:root "087e4130-770a-42ee-879e-e60a1fc76110"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Component3_2>
   a    <urn:hl7-org:v3#POCD_MT000040.Component3> ;
   v3:section <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Section_2> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Entry_2>
   a    <urn:hl7-org:v3#POCD_MT000040.Entry> ;
   v3:act  <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Act_2> .
```

```
:INS2007004_CE_11
   a    v3:CE ;
   v3:code "PO"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.5.112"^^v3:uidDatatype ;
   v3:codeSystemName "RouteOfAdministration"^^v3:stDatatype ;
   v3:displayName "Swallow, oral"^^v3:stDatatype .

:INS2007004_CS_4
   a    v3:CS ;
   v3:code "completed"^^v3:csDatatype .

:INS2007004_IVXB_TS_6
   a    v3:IVXB_TS ;
   v3:value "20090720"^^v3:tsDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Section_1>
   a    <urn:hl7-org:v3#POCD_MT000040.Section> ;
   v3:code :INS2007004_CE_4 ;
   v3:entry <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Entry_1> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Entry_2> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Entry_3> ;
   v3:id   :INS2007004_II_7 ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_2> , <http://www.srdc.com.
tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.templateId_3> ;
   v3:text <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Text_1> ;
   v3:title :INS2007004_ST_2 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Th_6>
   a    <urn:hl7-org:v3#StrucDoc.Th> ;
   v3:textContent "Date"^^xsd:string .

:INS2007004_II_13
   a    v3:II ;
   v3:root "46190165-a977-4066-be72-1ba9a4f4025c"^^v3:uidDatatype .

:INS2007004_ST_2
   a    v3:ST ;
   v3:textContent "Problem List"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_34>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.7.2"^^v3:uidDatatype .

:INS2007004_CE_9
   a    v3:CE ;
   v3:code "PO"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.5.112"^^v3:uidDatatype ;
   v3:codeSystemName "RouteOfAdministration"^^v3:stDatatype ;
   v3:displayName "Swallow, oral"^^v3:stDatatype .

:INS2007004_IVL_PQ_2
   a    v3:IVL_PQ ;
   v3:unit "mg"^^v3:csDatatype ;
   v3:value "250"^^v3:realDatatype .

:INS2007004_TEL_7
   a    v3:TEL ;
   v3:value "#pastprob1"^^v3:urlDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tbody_3>
   a    <urn:hl7-org:v3#StrucDoc.Tbody> ;
   v3:tr   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.
Tr_8> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.
Tr_10> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_9> .

:INS2007004_CD_7
   a    v3:CD ;
```

```
   v3:nullFlavor "NA"^^v3:NullFlavorDatatype .

:INS2007004_II_14
   a    v3:II ;
   v3:root "93939ef9-05f7-4ad1-83e3-c23917d51d19"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Material_3>
   a    <urn:hl7-org:v3#POCD_MT000040.Material> ;
   v3:code :INS2007004_CE_12 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.AssignedCustodian_1>
   a    <urn:hl7-org:v3#POCD_MT000040.AssignedCustodian> ;
   v3:representedCustodianOrganization
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
CustodianOrganization_1> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_5>
   a    <urn:hl7-org:v3#StrucDoc.Tr> ;
   v3:th   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.
Th_3> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Th_4> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_18>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.5"^^v3:uidDatatype .

:INS2007004_CS_5
   a    v3:CS ;
   v3:code "completed"^^v3:csDatatype .

:INS2007004_CE_12
   a    v3:CE ;
   v3:code "979492"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.88"^^v3:uidDatatype ;
   v3:codeSystemName "RxNorm"^^v3:stDatatype ;
   v3:displayName "Losartan Potassium 50 MG Oral Tablet"^^v3:stDatatype ;
   v3:originalText :INS2007004_ED_18 ;
   v3:translation :INS2007004_CD_15 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Component3_3>
   a    <urn:hl7-org:v3#POCD_MT000040.Component3> ;
   v3:section <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Section_3>.

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Entry_5>
   a    <urn:hl7-org:v3#POCD_MT000040.Entry> ;
   v3:substanceAdministration
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
SubstanceAdministration_1> .

:INS2007004_ClinicalDocument_1
   a    v3:ClinicalDocument ;
   v3:author <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Author_1> ;
   v3:code :INS2007004_CE_1 ;
   v3:component <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Component2_1> ;
   v3:confidentialityCode
        :INS2007004_CE_2 ;
   v3:custodian <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Custodian_1> ;
   v3:effectiveTime :INS2007004_TS_1 ;
   v3:id   :INS2007004_II_1 ;
   v3:languageCode :INS2007004_CS_1 ;
   v3:recordTarget <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
RecordTarget_1> ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_1> ;
   v3:title :INS2007004_ST_1 ;
   v3:typeId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.typeId_1> .
```

```
<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Th_3>
   a    <urn:hl7-org:v3#StrucDoc.Th> ;
   v3:textContent "Condition"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_35>

   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.24"^^v3:uidDatatype .

:INS2007004_II_4
   a    v3:II ;
   v3:extension "76543218901"^^v3:stDatatype ;
   v3:root "2.16.840.1.113883.2.9.4.3.2.5"^^v3:uidDatatype .

:INS2007004_Anon_3_1
   a    v3:Anon_3 ;
   v3:textContent "MI"^^xsd:string .

:INS2007004_ED_1
   a    v3:ED ;
   v3:reference :INS2007004_TEL_1 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_12>
   a    <urn:hl7-org:v3#StrucDoc.Td> ;
   v3:ID   "med2_date"^^xsd:ID ;
   v3:textContent "02.08.2009"^^xsd:string .

:INS2007004_IVL_PQ_1
   a    v3:IVL_PQ ;
   v3:unit "mg"^^v3:csDatatype ;
   v3:value "10"^^v3:realDatatype .

:INS2007004_II_15
   a    v3:II ;
   v3:root "a0fff30c-b94e-4eee-b5f5-bf5a79ebb929"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_9>

   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.27"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tbody_2>
   a    <urn:hl7-org:v3#StrucDoc.Tbody> ;
   v3:tr   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_6> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_19>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.3.8"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_2>
   a    <urn:hl7-org:v3#StrucDoc.Tr> ;
   v3:ID   "actprob1"^^xsd:ID ;
   v3:td   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.
Td_1> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_2> .

:INS2007004_ED_17
   a    v3:ED ;
   v3:reference :INS2007004_TEL_11 .

:INS2007004_II_20
   a    v3:II ;
   v3:root "9e4c4be7-0d46-49cf-ba1e-170b5855bb5a"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Thead_1>
   a    <urn:hl7-org:v3#StrucDoc.Thead> ;
   v3:tr   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_1> .
```

```
<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Patient_1>
   a    <urn:hl7-org:v3#POCD_MT000040.Patient> ;
   v3:administrativeGenderCode
        :INS2007004_CE_3 ;
   v3:birthTime :INS2007004_TS_2 ;
   v3:name :INS2007004_PN_1 .

:INS2007004_CS_6
   a    v3:CS ;
   v3:code "completed"^^v3:csDatatype .

:INS2007004_IVXB_TS_8
   a    v3:IVXB_TS ;
   v3:value "20090720"^^v3:tsDatatype .

:INS2007004_Anon_2_1
   a    v3:Anon_2 ;
   v3:textContent "Italy"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Entry_4>
   a    <urn:hl7-org:v3#POCD_MT000040.Entry> ;
   v3:act  <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Act_4> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_13>
   a    <urn:hl7-org:v3#StrucDoc.Td> ;
   v3:ID   "med3_name"^^xsd:ID ;
   v3:textContent "losartan"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_10>
   a    <urn:hl7-org:v3#StrucDoc.Tr> ;
   v3:ID   "med3"^^xsd:ID ;
   v3:td   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.
Td_13> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_14> .

:INS2007004_TEL_9
   a    v3:TEL ;
   v3:value "#med1"^^v3:urlDatatype .

:INS2007004_ED_2
   a    v3:ED ;
   v3:reference :INS2007004_TEL_2 .

:INS2007004_II_5
   a    v3:II ;
   v3:extension "65432178901"^^v3:stDatatype ;
   v3:root "2.16.840.1.113883.2.9.4.3.2.4"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Component2_1>
   a    <urn:hl7-org:v3#POCD_MT000040.Component2> ;
   v3:structuredBody <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
StructuredBody_1> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Th_4>
   a    <urn:hl7-org:v3#StrucDoc.Th> ;
   v3:textContent "Effective Dates"^^xsd:string .

:INS2007004_TEL_10
   a    v3:TEL ;
   v3:value "#med2"^^v3:urlDatatype .

:INS2007004_CD_15
   a    v3:CD ;
   v3:code "C09CA01"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.73"^^v3:uidDatatype ;
   v3:codeSystemName "ATC"^^v3:stDatatype ;
   v3:displayName "losartan"^^v3:stDatatype .

:INS2007004_CD_14
   a    v3:CD ;
   v3:code "B01AC06"^^v3:csDatatype ;
```

```
   v3:codeSystem "2.16.840.1.113883.6.73"^^v3:uidDatatype ;
   v3:codeSystemName "ATC"^^v3:stDatatype ;
   v3:displayName "acetylsalicylic acid"^^v3:stDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Custodian_1>
   a    <urn:hl7-org:v3#POCD_MT000040.Custodian> ;
   v3:assignedCustodian
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
AssignedCustodian_1> .

:INS2007004_II_16
   a    v3:II ;
   v3:root "2a29b507-3416-4a50-9e6a-9e05fa9f2af0"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tbody_1>
   a    <urn:hl7-org:v3#StrucDoc.Tbody> ;
   v3:tr   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.
Tr_2> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.
Tr_3> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_4> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.AssignedAuthor_1>
   a    <urn:hl7-org:v3#POCD_MT000040.AssignedAuthor> ;
   v3:assignedAuthoringDevice
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
AuthoringDevice_1> ;
   v3:id   :INS2007004_II_4 ;
   v3:representedOrganization
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Organization_2> .

:INS2007004_CD_9
   a    v3:CD ;
   v3:code "278.00"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.2"^^v3:uidDatatype ;
   v3:codeSystemName "ICD-9-CM"^^v3:stDatatype ;
   v3:displayName "Obesity, unspecified"^^v3:stDatatype ;
   v3:originalText :INS2007004_ED_9 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_8>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.5"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_36>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.7"^^v3:uidDatatype .

:INS2007004_ED_18
   a    v3:ED ;
   v3:textContent "Losartan Potassium 50 MG Oral Tablet"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_3>
   a    <urn:hl7-org:v3#StrucDoc.Tr> ;
   v3:ID   "actprob2"^^xsd:ID ;
   v3:td   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.
Td_4> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_3> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Thead_2>
   a    <urn:hl7-org:v3#StrucDoc.Thead> ;
   v3:tr   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_5> .

:INS2007004_ED_15
   a    v3:ED ;
   v3:reference :INS2007004_TEL_10 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_en.family_1>
   a    <urn:hl7-org:v3#en.family> ;
   v3:textContent "Cremona"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_2>
```

```
   a    <urn:hl7-org:v3#StrucDoc.Td> ;
   v3:ID   "actprob1_date"^^xsd:ID ;
   v3:textContent "01.07.2009"^^xsd:string .

:INS2007004_CD_4
   a    v3:CD ;
   v3:nullFlavor "NA"^^v3:NullFlavorDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Consumable_2>
   a    <urn:hl7-org:v3#POCD_MT000040.Consumable> ;
   v3:manufacturedProduct
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
ManufacturedProduct_2> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_26>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.3.19"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.PatientRole_1>
   a    <urn:hl7-org:v3#POCD_MT000040.PatientRole> ;
   v3:addr :INS2007004_AD_1 ;
   v3:id   :INS2007004_II_2 ;
   v3:patient <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Patient_1> ;
   v3:providerOrganization
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Organization_1> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Act_3>
   a    <urn:hl7-org:v3#POCD_MT000040.Act> ;
   v3:classCode "ACT"^^v3:x_ActClassDocumentEntryActDatatype ;
   v3:code :INS2007004_CD_7 ;
   v3:entryRelationship
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
EntryRelationship_3> ;
   v3:id   :INS2007004_II_12 ;
   v3:moodCode "EVN"^^v3:x_DocumentActMoodDatatype ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_16> , <http://www.srdc.com.
tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_15> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_14> ;
   v3:text :INS2007004_ED_7 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_7>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.28"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Organization_1>
   a    <urn:hl7-org:v3#POCD_MT000040.Organization> ;
   v3:id   :INS2007004_II_3 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_8>
   a    <urn:hl7-org:v3#StrucDoc.Tr> ;
   v3:ID   "med1"^^xsd:ID ;
   v3:td   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.
Td_10> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_9> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_16>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.5.2"^^v3:uidDatatype .

:INS2007004_II_17
   a    v3:II ;
   v3:root "3876f056-6ed4-4f77-9e6a-fdee4f88411d"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Observation_2>
   a    <urn:hl7-org:v3#POCD_MT000040.Observation> ;
```

```
   v3:classCode "OBS"^^v3:ActClassObservationDatatype ;
   v3:code :INS2007004_CD_5 ;
   v3:effectiveTime :INS2007004_IVL_TS_2 ;
   v3:id   :INS2007004_II_11 ;
   v3:moodCode "EVN"^^v3:x_ActMoodDocumentObservationDatatype ;
   v3:statusCode :INS2007004_CS_3 ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_13> , <http://www.srdc.com.
tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.templateId_12> ;
   v3:text :INS2007004_ED_5 ;
   v3:value :INS2007004_CD_6 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Table_2>
   a    <urn:hl7-org:v3#StrucDoc.Table> ;
   v3:tbody <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tbody_2> ;
   v3:thead <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Thead_2> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Th_1>
   a    <urn:hl7-org:v3#StrucDoc.Th> ;
   v3:textContent "Condition"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_11>
   a    <urn:hl7-org:v3#StrucDoc.Td> ;
   v3:ID   "med2_name"^^xsd:ID ;
   v3:textContent "acetylsalicylic acid"^^xsd:string .

:INS2007004_IVL_TS_1
   a    v3:IVL_TS ;
   v3:low  :INS2007004_IVXB_TS_1 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_1>
   a    <urn:hl7-org:v3#StrucDoc.Td> ;
   v3:ID   "actprob1_condition"^^xsd:ID ;
   v3:textContent "Malignant essential hypertension"^^xsd:string .

:INS2007004_ED_16
   a    v3:ED ;
   v3:textContent "Aspirin 250 MG"^^xsd:string .

:INS2007004_CD_3
   a    v3:CD ;
   v3:code "401.0"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.2"^^v3:uidDatatype ;
   v3:codeSystemName "ICD-9-CM"^^v3:stDatatype ;
   v3:displayName "Malignant essential hypertension"^^v3:stDatatype ;
   v3:originalText :INS2007004_ED_3 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_6>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.5.2"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Consumable_1>
   a    <urn:hl7-org:v3#POCD_MT000040.Consumable> ;
   v3:manufacturedProduct
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
ManufacturedProduct_1> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_25>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.8"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Organization_2>
   a    <urn:hl7-org:v3#POCD_MT000040.Organization> ;
   v3:id   :INS2007004_II_5 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_9>
   a    <urn:hl7-org:v3#StrucDoc.Tr> ;
   v3:ID   "med2"^^xsd:ID ;
```

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   v3:td   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.
Td_11> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_12> .

:INS2007004_II_18
   a    v3:II ;
   v3:root "9e4c4be7-0d46-49cf-ba1e-170b5855bb5a"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_15>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.5.1"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Act_4>
   a    <urn:hl7-org:v3#POCD_MT000040.Act> ;
   v3:classCode "ACT"^^v3:x_ActClassDocumentEntryActDatatype ;
   v3:code :INS2007004_CD_10 ;
   v3:entryRelationship
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
EntryRelationship_4> ;
   v3:id   :INS2007004_II_15 ;
   v3:moodCode "EVN"^^v3:x_DocumentActMoodDatatype ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_22> , <http://www.srdc.com.tr/ontmalizer/instance
#INS2007004_POCD_MT000040.InfrastructureRoot.templateId_21> , <http://www.srdc.com.
tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.templateId_20> ;
   v3:text :INS2007004_ED_10 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Observation_3>
   a    <urn:hl7-org:v3#POCD_MT000040.Observation> ;
   v3:classCode "OBS"^^v3:ActClassObservationDatatype ;
   v3:code :INS2007004_CD_8 ;
   v3:effectiveTime :INS2007004_IVL_TS_3 ;
   v3:id   :INS2007004_II_13 ;
   v3:moodCode "EVN"^^v3:x_ActMoodDocumentObservationDatatype ;
   v3:statusCode :INS2007004_CS_4 ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_17> , <http://www.srdc.com.tr/ontmalizer/instance#
INS2007004_POCD_MT000040.InfrastructureRoot.templateId_18> ;
   v3:text :INS2007004_ED_8 ;
   v3:value :INS2007004_CD_9 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Entry_1>
   a    <urn:hl7-org:v3#POCD_MT000040.Entry> ;
   v3:act  <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Act_1> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_30>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.7.2"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_10>
   a    <urn:hl7-org:v3#StrucDoc.Td> ;
   v3:ID   "med1_date"^^xsd:ID ;
   v3:textContent "20.07.2009"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Th_2>
   a    <urn:hl7-org:v3#StrucDoc.Th> ;
   v3:textContent "Effective Dates"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Table_1>
   a    <urn:hl7-org:v3#StrucDoc.Table> ;
   v3:tbody <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tbody_1> ;
   v3:thead <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Thead_1> .

:INS2007004_TS_1
   a    v3:TS ;
   v3:value "20130307130000+0200"^^v3:tsDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Material_1>
   a    <urn:hl7-org:v3#POCD_MT000040.Material> ;
```

```
   v3:code :INS2007004_CE_8 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Act_1>
   a    <urn:hl7-org:v3#POCD_MT000040.Act> ;
   v3:classCode "ACT"^^v3:x_ActClassDocumentEntryActDatatype ;
   v3:code :INS2007004_CD_1 ;
   v3:entryRelationship
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
EntryRelationship_1> ;
   v3:id   :INS2007004_II_8 ;
   v3:moodCode "EVN"^^v3:x_DocumentActMoodDatatype ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_5> , <http://www.srdc.com.tr/ontmalizer/instance#
INS2007004_POCD_MT000040.InfrastructureRoot.templateId_4> , <http://www.srdc.com.
tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.templateId_6> ;
   v3:text :INS2007004_ED_1 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_5>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.5.1"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_28>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.7"^^v3:uidDatatype .

:INS2007004_ED_13
   a    v3:ED ;
   v3:reference :INS2007004_TEL_9 .

:INS2007004_II_19
   a    v3:II ;
   v3:root "9e4c4be7-0d46-49cf-ba1e-170b5855bb5a"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_14>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.27"^^v3:uidDatatype .

:INS2007004_CD_6
   a    v3:CD ;
   v3:code "339.42"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.2"^^v3:uidDatatype ;
   v3:codeSystemName "ICD-9-CM"^^v3:stDatatype ;
   v3:displayName "New daily persistent headache"^^v3:stDatatype ;
   v3:originalText :INS2007004_ED_6 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_6>
   a    <urn:hl7-org:v3#StrucDoc.Tr> ;
   v3:ID   "pastprob1"^^xsd:ID ;
   v3:td   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.
Td_8> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_7> .

:INS2007004_Anon_5_1
   a    v3:Anon_5 ;
   v3:textContent "Milan"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_31>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.24"^^v3:uidDatatype .

:INS2007004_ED_12
   a    v3:ED ;
   v3:textContent "Acute myocardial infarction"^^xsd:string .

:INS2007004_CS_2
   a    v3:CS ;
   v3:code "completed"^^v3:csDatatype .
```

```
<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Text_3>
   a    <urn:hl7-org:v3#StrucDoc.Text> ;
   v3:table <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Table_3> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_27>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.24"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Act_2>
   a    <urn:hl7-org:v3#POCD_MT000040.Act> ;
   v3:classCode "ACT"^^v3:x_ActClassDocumentEntryActDatatype ;
   v3:code :INS2007004_CD_4 ;
   v3:entryRelationship
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
EntryRelationship_2> ;
   v3:id   :INS2007004_II_10 ;
   v3:moodCode "EVN"^^v3:x_DocumentActMoodDatatype ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_9> , <http://www.srdc.com.tr/ontmalizer/instance#
INS2007004_POCD_MT000040.InfrastructureRoot.templateId_10> , <http://www.srdc.com.
tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.templateId_11> ;
   v3:text :INS2007004_ED_4 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Material_2>
   a    <urn:hl7-org:v3#POCD_MT000040.Material> ;
   v3:code :INS2007004_CE_10 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_4>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.27"^^v3:uidDatatype .

:INS2007004_CD_5
   a    v3:CD ;
   v3:code "55607006"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.96"^^v3:uidDatatype ;
   v3:codeSystemName "SNOMED CT"^^v3:stDatatype ;
   v3:displayName "Problem"^^v3:stDatatype .

:INS2007004_SC_1
   a    v3:SC ;
   v3:textContent "SALUS LISPA Connector v0.1"^^xsd:string .

:INS2007004_ED_14
   a    v3:ED ;
   v3:textContent "Nifedipine 10 MG"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Observation_1>
   a    <urn:hl7-org:v3#POCD_MT000040.Observation> ;
   v3:classCode "OBS"^^v3:ActClassObservationDatatype ;
   v3:code :INS2007004_CD_2 ;
   v3:effectiveTime :INS2007004_IVL_TS_1 ;
   v3:id   :INS2007004_II_9 ;
   v3:moodCode "EVN"^^v3:x_ActMoodDocumentObservationDatatype ;
   v3:statusCode :INS2007004_CS_2 ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_8> , <http://www.srdc.com.tr/ontmalizer/instance#
INS2007004_POCD_MT000040.InfrastructureRoot.templateId_7> ;
   v3:text :INS2007004_ED_2 ;
   v3:value :INS2007004_CD_3 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tr_7>
   a    <urn:hl7-org:v3#StrucDoc.Tr> ;
   v3:th   <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Th_6> ,
<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Th_5> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_32>
```

```
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.7"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_13>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.5"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.StructuredBody_1>
   a    <urn:hl7-org:v3#POCD_MT000040.StructuredBody> ;
   v3:component <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Component3_2> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Component3_1> , <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Component3_3> .

:INS2007004_CS_1
   a    v3:CS ;
   v3:code "en-US"^^v3:csDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Text_2>
   a    <urn:hl7-org:v3#StrucDoc.Text> ;
   v3:table <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Table_2> .

:INS2007004_II_9
   a    v3:II ;
   v3:root "46190165-a977-4066-be72-1ba9a4f4025c"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.EntryRelationship_4>
   a    <urn:hl7-org:v3#POCD_MT000040.EntryRelationship> ;
   v3:observation <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Observation_4> ;
   v3:typeCode "SUBJ"^^v3:x_ActRelationshipEntryRelationshipDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_6>
   a    <urn:hl7-org:v3#StrucDoc.Td> ;
   v3:ID   "actprob3_date"^^xsd:ID ;
   v3:textContent "01.06.2006"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.ManufacturedProduct_3>
   a    <urn:hl7-org:v3#POCD_MT000040.ManufacturedProduct> ;
   v3:classCode "MANU"^^v3:RoleClassManufacturedProductDatatype ;
   v3:manufacturedMaterial
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Material_3> ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_37> , <http://www.srdc.com.tr/ontmalizer/instance#
INS2007004_POCD_MT000040.InfrastructureRoot.templateId_38> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_3>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.3.6"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_22>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.5.2"^^v3:uidDatatype .

:INS2007004_IVL_TS_5
   a    v3:IVL_TS ;
   v3:low  :INS2007004_IVXB_TS_6 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Text_1>
   a    <urn:hl7-org:v3#StrucDoc.Text> ;
   v3:table <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Table_1> .

:INS2007004_ED_10
   a    v3:ED ;
   v3:reference :INS2007004_TEL_7 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
```

```
templateId_12>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.28"^^v3:uidDatatype .

:INS2007004_II_8
   a    v3:II ;
   v3:root "37e7fef6-2c79-41fe-850e-b1994cdbf869"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_29>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.53"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_5>
   a    <urn:hl7-org:v3#StrucDoc.Td> ;
   v3:ID   "actprob3_condition"^^xsd:ID ;
   v3:textContent "Obesity, unspecified"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.EntryRelationship_3>
   a    <urn:hl7-org:v3#POCD_MT000040.EntryRelationship> ;
   v3:observation <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Observation_3> ;
   v3:typeCode "SUBJ"^^v3:x_ActRelationshipEntryRelationshipDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.ManufacturedProduct_2>
   a    <urn:hl7-org:v3#POCD_MT000040.ManufacturedProduct> ;
   v3:classCode "MANU"^^v3:RoleClassManufacturedProductDatatype ;
   v3:manufacturedMaterial
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Material_2> ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_33> , <http://www.srdc.com.tr/ontmalizer/instance#
INS2007004_POCD_MT000040.InfrastructureRoot.templateId_34> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_2>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.11"^^v3:uidDatatype .

:INS2007004_IVL_TS_4
   a    v3:IVL_TS ;
   v3:high :INS2007004_IVXB_TS_5 ;
   v3:low  :INS2007004_IVXB_TS_4 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_21>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.5.1"^^v3:uidDatatype .

:INS2007004_AD_1
   a    v3:AD ;
   v3:city :INS2007004_Anon_5_1 ;
   v3:country :INS2007004_Anon_2_1 ;
   v3:state :INS2007004_Anon_3_1 ;
   v3:use  "HP"^^v3:set_PostalAddressUseDatatype .

:INS2007004_CE_1
   a    v3:CE ;
   v3:code "34133-9"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.1"^^v3:uidDatatype ;
   v3:codeSystemName "LOINC"^^v3:stDatatype ;
   v3:displayName "Summarization of episode note"^^v3:stDatatype .

:INS2007004_ED_11
   a    v3:ED ;
   v3:reference :INS2007004_TEL_8 .

:INS2007004_IVXB_TS_1
   a    v3:IVXB_TS ;
   v3:value "20090701"^^v3:tsDatatype .
```

```
:INS2007004_PQ_1
   a    v3:PQ ;
   v3:unit "h"^^v3:csDatatype ;
   v3:value "8"^^v3:realDatatype .

:INS2007004_ED_9
   a    v3:ED ;
   v3:textContent "Obesity, unspecified"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_11>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.5.2"^^v3:uidDatatype .

:INS2007004_PIVL_TS_2
   a    v3:PIVL_TS ;
   v3:institutionSpecified
        "true"^^v3:blDatatype ;
   v3:operator "A"^^v3:SetOperatorDatatype ;
   v3:period :INS2007004_PQ_2 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.ManufacturedProduct_1>
   a    <urn:hl7-org:v3#POCD_MT000040.ManufacturedProduct> ;
   v3:classCode "MANU"^^v3:RoleClassManufacturedProductDatatype ;
   v3:manufacturedMaterial
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Material_1> ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_29> , <http://www.srdc.com.tr/ontmalizer/instance#
INS2007004_POCD_MT000040.InfrastructureRoot.templateId_30> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Observation_4>
   a    <urn:hl7-org:v3#POCD_MT000040.Observation> ;
   v3:classCode "OBS"^^v3:ActClassObservationDatatype ;
   v3:code :INS2007004_CD_11 ;
   v3:effectiveTime :INS2007004_IVL_TS_4 ;
   v3:id   :INS2007004_II_16 ;
   v3:moodCode "EVN"^^v3:x_ActMoodDocumentObservationDatatype ;
   v3:statusCode :INS2007004_CS_5 ;
   v3:templateId <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
InfrastructureRoot.templateId_23> , <http://www.srdc.com.tr/ontmalizer/instance#
INS2007004_POCD_MT000040.InfrastructureRoot.templateId_24> ;
   v3:text :INS2007004_ED_11 ;
   v3:value :INS2007004_CD_12 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_4>
   a    <urn:hl7-org:v3#StrucDoc.Td> ;
   v3:ID   "actprob2_date"^^xsd:ID ;
   v3:textContent "25.07.2009"^^xsd:string .

:INS2007004_PN_1
   a    v3:PN ;
   v3:family <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_en.family_1> ;
   v3:given <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_en.given_1> .

:INS2007004_TEL_2
   a    v3:TEL ;
   v3:value "#actprob1_condition"^^v3:urlDatatype .

:INS2007004_CD_2
   a    v3:CD ;
   v3:code "55607006"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.6.96"^^v3:uidDatatype ;
   v3:codeSystemName "SNOMED CT"^^v3:stDatatype ;
   v3:displayName "Problem"^^v3:stDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_1>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1"^^v3:uidDatatype .
```

```
:INS2007004_IVL_TS_3
   a    v3:IVL_TS ;
   v3:low  :INS2007004_IVXB_TS_3 .

:INS2007004_CE_2
   a    v3:CE ;
   v3:code "N"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.5.25"^^v3:uidDatatype .

:INS2007004_TS_2
   a    v3:TS ;
   v3:value "19450201"^^v3:tsDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_24>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.5"^^v3:uidDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_10>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "1.3.6.1.4.1.19376.1.5.3.1.4.5.1"^^v3:uidDatatype .

:INS2007004_ED_8
   a    v3:ED ;
   v3:reference :INS2007004_TEL_6 .

:INS2007004_PQ_2
   a    v3:PQ ;
   v3:unit "d"^^v3:csDatatype ;
   v3:value "1"^^v3:realDatatype .

:INS2007004_PIVL_TS_1
   a    v3:PIVL_TS ;
   v3:institutionSpecified
        "true"^^v3:blDatatype ;
   v3:operator "A"^^v3:SetOperatorDatatype ;
   v3:period :INS2007004_PQ_1 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.EntryRelationship_2>
   a    <urn:hl7-org:v3#POCD_MT000040.EntryRelationship> ;
   v3:observation <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Observation_2> ;
   v3:typeCode "SUBJ"^^v3:x_ActRelationshipEntryRelationshipDatatype .

:INS2007004_TEL_1
   a    v3:TEL ;
   v3:value "#actprob1"^^v3:urlDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
typeId_1>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.typeId> ;
   v3:extension "POCD_HD000040"^^v3:stDatatype ;
   v3:root "2.16.840.1.113883.1.3"^^v3:uidDatatype .

:INS2007004_PIVL_TS_3
   a    v3:PIVL_TS ;
   v3:institutionSpecified
        "true"^^v3:blDatatype ;
   v3:operator "A"^^v3:SetOperatorDatatype ;
   v3:period :INS2007004_PQ_3 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Author_1>
   a    <urn:hl7-org:v3#POCD_MT000040.Author> ;
   v3:assignedAuthor <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
AssignedAuthor_1> ;
   v3:time :INS2007004_TS_3 .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.Consumable_3>
   a    <urn:hl7-org:v3#POCD_MT000040.Consumable> ;
```

```
   v3:manufacturedProduct
        <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
ManufacturedProduct_3> .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.RecordTarget_1>
   a    <urn:hl7-org:v3#POCD_MT000040.RecordTarget> ;
   v3:patientRole <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
PatientRole_1> .

:INS2007004_CD_1
   a    v3:CD ;
   v3:nullFlavor "NA"^^v3:NullFlavorDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Td_3>
   a    <urn:hl7-org:v3#StrucDoc.Td> ;
   v3:ID   "actprob2_condition"^^xsd:ID ;
   v3:textContent "New daily persistent headache"^^xsd:string .

:INS2007004_IVL_TS_2
   a    v3:IVL_TS ;
   v3:low  :INS2007004_IVXB_TS_2 .

:INS2007004_CE_3
   a    v3:CE ;
   v3:code "M"^^v3:csDatatype ;
   v3:codeSystem "2.16.840.1.113883.5.1"^^v3:uidDatatype ;
   v3:codeSystemName "AdministrativeGender"^^v3:stDatatype ;
   v3:displayName "Male"^^v3:stDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.InfrastructureRoot.
templateId_23>
   a    <urn:hl7-org:v3#POCD_MT000040.InfrastructureRoot.templateId> ;
   v3:root "2.16.840.1.113883.10.20.1.28"^^v3:uidDatatype .

:INS2007004_TS_3
   a    v3:TS ;
   v3:value "20130307130000+0200"^^v3:tsDatatype .

:INS2007004_ED_7
   a    v3:ED ;
   v3:reference :INS2007004_TEL_5 .

:INS2007004_ON_1
   a    v3:ON ;
   v3:textContent "Lombardy Region"^^xsd:string .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.EntryRelationship_1>
   a    <urn:hl7-org:v3#POCD_MT000040.EntryRelationship> ;
   v3:observation <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_POCD_MT000040.
Observation_1> ;
   v3:typeCode "SUBJ"^^v3:x_ActRelationshipEntryRelationshipDatatype .

<http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Table_3>
   a    <urn:hl7-org:v3#StrucDoc.Table> ;
   v3:tbody <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Tbody_3> ;
   v3:thead <http://www.srdc.com.tr/ontmalizer/instance#INS2007004_StrucDoc.Thead_3> .

:INS2007004_PQ_3
   a    v3:PQ ;
   v3:unit "d"^^v3:csDatatype ;
   v3:value "1"^^v3:realDatatype .
```

APPENDIX E

AN EXAMPLE MEDICAL SUMMARY EXPRESSED IN SALUS CIM ONTOLOGY

```
@prefix foaf: <http://xmlns.com/foaf/0.1/>.
@prefix owl: <http://www.w3.org/2002/07/owl#>.
@prefix rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>.
@prefix rdfs: <http://www.w3.org/2000/01/rdf-schema#>.
@prefix salus: <http://www.salusproject.eu/ontology/common-information-model#>.

[]    a       salus:Patient ;
      salus:ID
              [ a       salus:ii ;
                salus:extension "547001" ;
                salus:root "2.16.840.1.113883.2.9.4.3.2"
              ] ;
      salus:address
              [ a       salus:addr ;
                salus:city "Milan" ;
                salus:country "Italy" ;
                salus:state "MI"
              ] ;
      salus:condition
              [ a       salus:Condition ;
                salus:problemCode
                        [ a       salus:cd ;
                          salus:code "339.42" ;
                          salus:codeSystem "2.16.840.1.113883.6.2" ;
                          salus:codeSystemName
                                  "ICD-9-CM" ;
                          salus:displayName "New daily persistent headache"
                        ] ;
                salus:problemDate
                        [ a       salus:ivlTs ;
                          salus:low "2009-07-25T00:00:00"^^xsd:dateTime
                        ] ;
                salus:problemName "New daily persistent headache" ;
                salus:problemType
                        [ a       salus:cd ;
                          salus:code "55607006" ;
                          salus:codeSystem "2.16.840.1.113883.6.96" ;
                          salus:codeSystemName
                                  "SNOMED CT" ;
                          salus:displayName "Problem"
                        ]
              ] ;
      salus:condition
              [ a       salus:Condition ;
                salus:problemCode
                        [ a       salus:cd ;
                          salus:code "278.00" ;
                          salus:codeSystem "2.16.840.1.113883.6.2" ;
                          salus:codeSystemName
                                  "ICD-9-CM" ;
                          salus:displayName "Obesity, unspecified"
```

```
                ] ;
          salus:problemDate
                [ a       salus:ivlTs ;
                  salus:low "2006-06-01T00:00:00"^^xsd:dateTime
                ] ;
          salus:problemName "Obesity, unspecified" ;
          salus:problemType
                [ a       salus:cd ;
                  salus:code "55607006" ;
                  salus:codeSystem "2.16.840.1.113883.6.96" ;
                  salus:codeSystemName
                          "SNOMED CT" ;
                  salus:displayName "Problem"
                ]
        ] ;
salus:condition
        [ a       salus:Condition ;
          salus:problemCode
                [ a       salus:cd ;
                  salus:code "401.0" ;
                  salus:codeSystem "2.16.840.1.113883.6.2" ;
                  salus:codeSystemName
                          "ICD-9-CM" ;
                  salus:displayName "Malignant essential hypertension"
                ] ;
          salus:problemDate
                [ a       salus:ivlTs ;
                  salus:low "2009-07-01T00:00:00"^^xsd:dateTime
                ] ;
          salus:problemName "Malignant essential hypertension" ;
          salus:problemType
                [ a       salus:cd ;
                  salus:code "55607006" ;
                  salus:codeSystem "2.16.840.1.113883.6.96" ;
                  salus:codeSystemName
                          "SNOMED CT" ;
                  salus:displayName "Problem"
                ]
        ] ;
salus:condition
        [ a       salus:Condition ;
          salus:problemCode
                [ a       salus:cd ;
                  salus:code "410" ;
                  salus:codeSystem "2.16.840.1.113883.6.2" ;
                  salus:codeSystemName
                          "ICD-9-CM" ;
                  salus:displayName "Acute myocardial infarction"
                ] ;
          salus:problemDate
                [ a       salus:ivlTs ;
                  salus:high "2009-08-01T00:00:00"^^xsd:dateTime ;
                  salus:low "2009-08-01T00:00:00"^^xsd:dateTime
                ] ;
          salus:problemName "Acute myocardial infarction" ;
          salus:problemType
                [ a       salus:cd ;
                  salus:code "55607006" ;
                  salus:codeSystem "2.16.840.1.113883.6.96" ;
                  salus:codeSystemName
                          "SNOMED CT" ;
                  salus:displayName "Problem"
                ]
        ] ;
salus:dateOfBirth "1945-02-01"^^xsd:date ;
salus:gender
        [ a       salus:cd ;
          salus:code "M" ;
          salus:codeSystem "2.16.840.1.113883.5.1" ;
          salus:codeSystemName
```

```
                "AdministrativeGender" ;
          salus:displayName "Male"
        ] ;
salus:medication
        [ a       salus:Medication ;
          salus:administrationTiming
                [ a       salus:pivlTs ;
                  salus:operator "A" ;
                  salus:period
                          [ a       salus:pq ;
                            salus:unit "h" ;
                            salus:value "8"
                          ]
                ] ;
          salus:dose
                [ a       salus:pq ;
                  salus:unit "mg" ;
                  salus:value "10"
                ] ;
          salus:indicateMedicationStartStop
                [ a       salus:ivlTs ;
                  salus:low "2009-07-20T00:00:00"^^xsd:dateTime
                ] ;
          salus:medicationInformation
                [ a       salus:MedicationInformation ;
                  salus:codedActiveIngredient
                          [ a       salus:cd ;
                            salus:code "C08CA05" ;
                            salus:codeSystem "2.16.840.1.113883.6.73" ;
                            salus:codeSystemName
                                    "ATC" ;
                            salus:displayName "nifedipine"
                          ] ;
                  salus:codedProductName
                          [ a       salus:cd ;
                            salus:code "316352" ;
                            salus:codeSystem "2.16.840.1.113883.6.88" ;
                            salus:codeSystemName
                                    "RxNorm" ;
                            salus:displayName "Nifedipine 10 MG"
                          ] ;
                  salus:freeTextProductName
                          "Nifedipine 10 MG"
                ] ;
          salus:route
                [ a       salus:cd ;
                  salus:code "PO" ;
                  salus:codeSystem "2.16.840.1.113883.5.112" ;
                  salus:codeSystemName
                          "RouteOfAdministration" ;
                  salus:displayName "Swallow, oral"
                ]
        ] ;
salus:medication
        [ a       salus:Medication ;
          salus:administrationTiming
                [ a       salus:pivlTs ;
                  salus:operator "A" ;
                  salus:period
                          [ a       salus:pq ;
                            salus:unit "d" ;
                            salus:value "1"
                          ]
                ] ;
          salus:dose
                [ a       salus:pq ;
                  salus:unit "mg" ;
                  salus:value "250"
                ] ;
          salus:indicateMedicationStartStop
```

```
                [ a       salus:ivlTs ;
                  salus:low "2009-08-02T00:00:00"^^xsd:dateTime
                ] ;
          salus:medicationInformation
                [ a       salus:MedicationInformation ;
                  salus:codedActiveIngredient
                          [ a       salus:cd ;
                            salus:code "B01AC06" ;
                            salus:codeSystem "2.16.840.1.113883.6.73" ;
                            salus:codeSystemName
                                    "ATC" ;
                            salus:displayName "acetylsalicylic acid"
                          ] ;
                  salus:codedProductName
                          [ a       salus:cd ;
                            salus:code "335953" ;
                            salus:codeSystem "2.16.840.1.113883.6.88" ;
                            salus:codeSystemName
                                    "RxNorm" ;
                            salus:displayName "Aspirin 250 MG"
                          ] ;
                  salus:freeTextProductName
                          "Aspirin 250 MG"
                ] ;
          salus:route
                [ a       salus:cd ;
                  salus:code "PO" ;
                  salus:codeSystem "2.16.840.1.113883.5.112" ;
                  salus:codeSystemName
                          "RouteOfAdministration" ;
                  salus:displayName "Swallow, oral"
                ]
        ] ;
salus:medication
        [ a       salus:Medication ;
          salus:administrationTiming
                [ a       salus:pivlTs ;
                  salus:operator "A" ;
                  salus:period
                          [ a       salus:pq ;
                            salus:unit "d" ;
                            salus:value "1"
                          ]
                ] ;
          salus:dose
                [ a       salus:pq ;
                  salus:unit "mg" ;
                  salus:value "50"
                ] ;
          salus:indicateMedicationStartStop
                [ a       salus:ivlTs ;
                  salus:low "2009-07-20T00:00:00"^^xsd:dateTime
                ] ;
          salus:medicationInformation
                [ a       salus:MedicationInformation ;
                  salus:codedActiveIngredient
                          [ a       salus:cd ;
                            salus:code "C09CA01" ;
                            salus:codeSystem "2.16.840.1.113883.6.73" ;
                            salus:codeSystemName
                                    "ATC" ;
                            salus:displayName "losartan"
                          ] ;
                  salus:codedProductName
                          [ a       salus:cd ;
                            salus:code "979492" ;
                            salus:codeSystem "2.16.840.1.113883.6.88" ;
                            salus:codeSystemName
                                    "RxNorm" ;
                            salus:displayName "Losartan Potassium 50 MG Oral Tablet"
```

```
                        ] ;
                  salus:freeTextProductName
                        "Losartan Potassium 50 MG Oral Tablet"
                ] ;
          salus:route
                [ a       salus:cd ;
                  salus:code "PO" ;
                  salus:codeSystem "2.16.840.1.113883.5.112" ;
                  salus:codeSystemName
                        "RouteOfAdministration" ;
                  salus:displayName "Swallow, oral"
                ]
        ] ;
salus:providerOrganization
        [ a       salus:OrganizationInformation ;
          salus:organizationID
                [ a       salus:ii ;
                  salus:extension "65432178901" ;
                  salus:root "2.16.840.1.113883.2.9.4.3.2.4"
                ]
        ] ;
foaf:familyName "Cremona" ;
foaf:givenName "Patient1" .
```

APPENDIX F

A SET OF CONVERSION RULES FOR CDA/CCD CONTENT ENTITY MODEL PROBLEM ENTRY

```
@prefix math: <http://www.w3.org/2000/10/swap/math#>.
@prefix salus: <http://www.salusproject.eu/ontology/common-information-model#>.
@prefix e: <http://eulersharp.sourceforge.net/2003/03swap/log-rules#>.
@prefix func: <http://www.w3.org/2007/rif-builtin-function#>.
@prefix xs: <http://www.w3.org/2001/XMLSchema#>.
@prefix log: <http://www.w3.org/2000/10/swap/log#>.
@prefix pred: <http://www.w3.org/2007/rif-builtin-predicate#>.
@prefix cda: <urn:hl7-org:v3#>.
@prefix : <http://www.salusproject.eu/rule/conversion/ccd2saluscim#>.

#functions
######################################################################
#check active problems / past medical history template ids
{?CONDITIONCOMPONENT :checkConditionTemplate ?RESULT}
<=
{
## access to template ids
?CONDITIONCOMPONENT a <urn:hl7-org:v3#POCD_MT000040.Component3>.
?CONDITIONCOMPONENT cda:section ?pc_sec.
?pc_sec cda:templateId ?pc_sec_ti.
?pc_sec_ti cda:root ?ps_sec_ti_root.
?pc_sec cda:entry ?pc_sec_ent.
?pc_sec_ent cda:act ?pc_sec_ent_act.
?pc_sec_ent_act cda:templateId ?pc_sec_act_ti.
?pc_sec_act_ti cda:root ?ps_sec_act_ti_root.
?pc_sec_ent_act cda:entryRelationship ?pc_sec_ent_act_er.
?pc_sec_ent_act_er cda:observation ?pc_sec_ent_act_obs.
?pc_sec_ent_act_obs cda:templateId ?pc_sec_ent_act_obs_ti.
?pc_sec_ent_act_obs_ti cda:root ?ps_sec_ent_act_obs_ti_root.

## section template id check
?SCOPE e:optional {
(?ps_sec_ti_root "1.3.6.1.4.1.19376.1.5.3.1.3.6"^^cda:uidDatatype)
            func:compare ?RESULT.
(?RESULT 0) pred:numeric-equal true.
},{
(?ps_sec_ti_root "1.3.6.1.4.1.19376.1.5.3.1.3.8"^^cda:uidDatatype)
            func:compare ?RESULT.
(?RESULT 0) pred:numeric-equal true.
}.

## act entry template id check
(?ps_sec_act_ti_root "1.3.6.1.4.1.19376.1.5.3.1.4.5.2"^^cda:uidDatatype)
        func:compare ?RESULT2.
(?RESULT2 0) pred:numeric-equal true.

## observation entry template id check
(?ps_sec_ent_act_obs_ti_root "1.3.6.1.4.1.19376.1.5.3.1.4.5"^^cda:uidDatatype)
        func:compare ?RESULT3.
(?RESULT3 0) pred:numeric-equal true.
}.
```

```
########################################################################
########################################################################

{?CONDITIONCOMPONENT :mapConditionComponent ?CONDITION}
<=
{
?CONDITIONCOMPONENT a <urn:hl7-org:v3#POCD_MT000040.Component3>.
?CONDITIONCOMPONENT cda:section ?pc_sec.
?pc_sec cda:entry ?pc_sec_ent.
?pc_sec_ent cda:act ?pc_sec_ent_act.
?pc_sec_ent_act cda:entryRelationship ?pc_sec_ent_act_er.
?pc_sec_ent_act_er cda:observation ?pc_sec_ent_act_obs.
?pc_sec_ent_act_obs :mapCondition ?CONDITION
}.

########################################################################
########################################################################

{?CONDITION :mapConditionGraph {
?CONDITION :mapCondition ?CONDITIONOUT.
?CONDITIONOUT a salus:Condition;
salus:problemDate ?cim_prob_date;
salus:problemType ?cim_prob_type;
salus:problemName ?cim_prob_name;
salus:problemCode ?cim_prob_code;
salus:problemStatus ?cim_prob_status;
salus:problemSeverity ?cim_prob_sever;
salus:timeOfDeath ?cim_prob_tofdeath;
salus:treatingProvider ?cim_prob_hcp;
salus:comment ?cim_prob_comment.
}}
<=
{
?CONDITION a <urn:hl7-org:v3#POCD_MT000040.Observation>.
?CONDITION cda:templateId ?CONDITION_TI.
?CONDITION_TI cda:root ?CONDITION_TI_ROOT.
(?CONDITION_TI_ROOT "1.3.6.1.4.1.19376.1.5.3.1.4.5"^^cda:uidDatatype) func:compare ?RESULT.
(?RESULT 0) pred:numeric-equal true.

## problem date
?SCOPE e:optional {
?CONDITION cda:effectiveTime ?obs_efftime.
?obs_efftime :mapIVLTS ?cim_prob_date.
},{
?cim_prob_date e:tuple (cda:effectiveTime ?CONDITION).
}.

## problem type
?SCOPE e:optional {
?CONDITION cda:code ?obs_cd.
?obs_cd :mapCode ?cim_prob_type.
},{
?cim_prob_type e:tuple (cda:code ?CONDITION).
}.

## problem name
?SCOPE e:optional {
?CONDITION cda:value ?obs_value.
?obs_value cda:originalText ?obs_value_orgt.
?obs_value_orgt :mapED ?cim_prob_name.
},{
?cim_prob_name e:tuple (cda:value ?CONDITION).
}.

## problem code
?SCOPE e:optional {
?CONDITION cda:value ?obs_value.
?obs_value :mapCode ?cim_prob_code.
},{
```

```
?cim_prob_code e:tuple (cda:value ?CONDITION).
}.

## problem status
?SCOPE e:optional {
?CONDITION cda:entryRelationship ?obs_er.
?obs_er cda:observation ?obs_er_obs.
?obs_er :checkERProblemStatus ?RESULT2.
(?RESULT2 0) pred:numeric-equal true.
?obs_er_obs cda:value ?obs_er_obs_val.
?obs_er_obs_val :mapCodeCE ?cim_prob_status.
},{
?cim_prob_status e:tuple (cda:entryRelationship ?CONDITION).
}.

## problem severity
?SCOPE e:optional {
?CONDITION cda:entryRelationship ?obs_er2.
?obs_er2 cda:observation ?obs_er_obs2.
?obs_er2 :checkERProblemSeverity ?RESULT3.
(?RESULT3 0) pred:numeric-equal true.
?obs_er_obs2 cda:value ?obs_er_obs_val2.
?obs_er_obs_val2 :mapCode ?cim_prob_sever.
},{
?cim_prob_sever e:tuple (cda:entryRelationship ?CONDITION).
}.

## time of death
?SCOPE e:optional {
?CONDITION cda:entryRelationship ?obs_er3.
?obs_er3 cda:observation ?obs_er_obs3.
?obs_er3 :checkERTimeOfDeath ?RESULT4.
(?RESULT4 0) pred:numeric-equal true.
?obs_er_obs3 cda:effectiveTime ?obs_er_obs_efftime.
?obs_er_obs_efftime :mapIVLTSToDateTime ?cim_prob_tofdeath.
},{
?cim_prob_tofdeath e:tuple (cda:entryRelationship ?CONDITION).
}.

## treating provider
?SCOPE e:optional {
?CONDITION cda:performer ?obs_per.
?obs_per cda:assignedEntity ?obs_per_assen.
(?obs_per_assen _:BN_1) :mapHealthcareProvider ?cim_prob_hcp.
},{
?cim_prob_hcp e:tuple (cda:performer ?CONDITION).
}.

## comment
?SCOPE e:optional {
?CONDITION cda:text ?obs_text.
?obs_text :mapED ?cim_prob_comment.
},{
?cim_prob_comment e:tuple (cda:text ?CONDITION).
}.

?CONDITIONOUT e:tuple (?CONDITION).
}.

#########################################################################
#########################################################################

# check observation to problem status entry relationship
{?ENTRYRELATIONSHIP :checkERProblemStatus ?RESULT}
<=
{
## entry template id check
?ENTRYRELATIONSHIP a <urn:hl7-org:v3#POCD_MT000040.EntryRelationship>.
?ENTRYRELATIONSHIP cda:observation ?er_obs.
?er_obs cda:templateId ?obs_ti.
```

```
?obs_ti cda:root ?obs_ti_root.
(?obs_ti_root "1.3.6.1.4.1.19376.1.5.3.1.4.1.1"^^cda:uidDatatype) func:compare ?RESULT.
(?RESULT 0) pred:numeric-equal true.
}.

#########################################################################
#########################################################################

# check observation to problem severity entry relationship
{?ENTRYRELATIONSHIP :checkERProblemSeverity ?RESULT}
<=
{
## entry template id check
?ENTRYRELATIONSHIP a <urn:hl7-org:v3#POCD_MT000040.EntryRelationship>.
?ENTRYRELATIONSHIP cda:observation ?er_obs.
?er_obs cda:templateId ?obs_ti.
?obs_ti cda:root ?obs_ti_root.
(?obs_ti_root "1.3.6.1.4.1.19376.1.5.3.1.4.1"^^cda:uidDatatype) func:compare ?RESULT.
(?RESULT 0) pred:numeric-equal true.
}.

#########################################################################
#########################################################################

# check observation to time of death entry relationship
{?ENTRYRELATIONSHIP :checkERTimeOfDeath ?RESULT}
<=
{
## entry template id check
?ENTRYRELATIONSHIP a <urn:hl7-org:v3#POCD_MT000040.EntryRelationship>.
?ENTRYRELATIONSHIP cda:typeCode "CAUS"^^cda:x_ActRelationshipEntryRelationshipDatatype.
?ENTRYRELATIONSHIP cda:observation ?er_obs.
?er_obs cda:code ?obs_cd.
?obs_cd cda:code ?obs_cd_cd.
?obs_cd cda:codeSystem ?obs_cd_cdsys.
(?obs_cd_cd "419620001"^^cda:csDatatype) func:compare ?RESULT.
(?RESULT 0) pred:numeric-equal true.
(?obs_cd_cdsys "2.16.840.1.113883.6.96"^^cda:uidDatatype) func:compare ?RESULT.
(?RESULT 0) pred:numeric-equal true.
}.

#########################################################################
#########################################################################

{?CON :mapConditionGraph ?CONDITION} => ?CONDITION.
```

APPENDIX G

N3 RULE FOR OBTAINING COMMON CONDITIONS PRIOR TO MEDICATION OF INTEREST

```
@prefix e: <http://eulersharp.sourceforge.net/2003/03swap/log-rules#>.
@prefix func: <http://www.w3.org/2007/rif-builtin-function#>.
@prefix list: <http://www.w3.org/2000/10/swap/list#>.
@prefix log: <http://www.w3.org/2000/10/swap/log#>.
@prefix math: <http://www.w3.org/2000/10/swap/math#>.
@prefix pred: <http://www.w3.org/2007/rif-builtin-predicate#>.
@prefix prolog: <http://eulersharp.sourceforge.net/2003/03swap/prolog#>.
@prefix rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#> .
@prefix salus: <http://www.salusproject.eu/ontology/common-information-model#>.
@prefix salusc: <http://www.salusproject.eu/ontology/core#> .
@prefix xs: <http://www.w3.org/2001/XMLSchema#>.
@prefix : <http://www.salusproject.eu/ontology/query-result#>.

# First, calculate the total number of patients and reuse elsewhere
{
    ?SCOPE e:findall (
        1
        {   ?PATIENT rdf:type salus:Patient.
        }
        ?TOTAL
    ).
    ?TOTAL math:memberCount ?PATIENTCOUNT.
} => {
    :root salusc:patientCount ?PATIENTCOUNT.
}.

# Common Conditions Prior to Medication of Interest
{
    :root salusc:patientCount ?PATIENTCOUNT.
    ?SCOPE e:findall (
        ((?CONDITION_NAME) (?PERCENTAGE) (?COUNT))
        {   ?PATIENT rdf:type salus:Patient.
            ?PATIENT salus:condition ?CONDITION.
            ?CONDITION salus:problemCode ?CONDITION_CODE.
            ?CONDITION_CODE salus:code ?CONDITION_CODE_CODE.
            ?CONDITION_CODE salus:codeSystem "2.16.840.1.113883.6.163".
            ?CONDITION_CODE salus:displayName ?CONDITION_NAME.

            # count the number of cases with ?CONDITION_CODE_CODE
            ?SCOPE e:findall (
                (?P ?CONDITION_CODE_CODE)
                {
                    ?P rdf:type salus:Patient.
                    (?P %s) :getPivotMedicationDate ?BMDT.
                    ?P salus:condition ?C.
                    ?C salus:problemCode ?CD.
                    ?CD salus:code ?CONDITION_CODE_CODE.
                    ?C salus:problemDate ?CDT.
                    ?CDT salus:low ?CDTV.
                    (?CDTV ?BMDT) math:difference ?DIFFERENCE.
                    (?DIFFERENCE 0) pred:numeric-less-than-or-equal true.
```

```
                }
                ?LIST
            ).
            ?LIST e:distinct ?DISTINCT_CONDITIONS.
            ?DISTINCT_CONDITIONS math:memberCount ?COUNT.
            (?COUNT 0) pred:numeric-greater-than true.
            (?PATIENTCOUNT 0) pred:numeric-greater-than true.
            ((?COUNT ?PATIENTCOUNT)!math:quotient 100) math:product ?PERCENTAGE.
        }
        ?BAG
    ).
    ?BAG e:distinct ?SETT.
    ((("ccbm"))) ?SETT) list:append ?SET.
} => {
    :ccbm salusc:results ?SET.
}.
```

CURRICULUM VITAE

PERSONAL INFORMATION

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EDUCATION

Degree	Institution	Year of Graduation
M.S.	METU Computer Engineering	2008
B.S.	METU Computer Engineering	2006
High School	Adnan Menderes Anatolian High School	2002
High School	Gazi Anatolian High School	1999

PROFESSIONAL EXPERIENCE

Year	Place	Enrollment
2008-present	SRDC Yazılım Araştırma Geliştirme Ltd. Şti	Researcher / Software Engineer
2006-2008	Software Research and Development Center, METU	Researcher / Software Engineer
2005-2006	Software Research and Development Center, METU	Part-time Software Developer

PUBLICATIONS

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