

**Linked2Safety****FP7-288328**

***A Next-Generation, Secure Linked Data Medical  
Information Space for Semantically-Interconnecting  
Electronic Health Records and Clinical Trials  
Systems Advancing Patients Safety in Clinical  
Research***

---

---

**Deliverable D1.4****Semantic EHR Model**

---

---

<b>Editor(s):</b>	Ratnesh Sahay (NUIG), Ronan Fox (NUIG), Dimitrios Ntalaperas (UBITECH), Panagiotis Hasapis (INTRASOFT), Eleni Kamateri (CERTH), Eleni Panopoulou (CERTH)
<b>Responsible Partner:</b>	NUIG
<b>Status-Version:</b>	Final – v0.9
<b>Date:</b>	28/09/2012
<b>EC Distribution:</b>	Public

<b>Project Number:</b>	FP7-288328
<b>Project Title:</b>	Linked2Safety

<b>Title of Deliverable:</b>	D1.4 – Semantic EHR Model
<b>Date of Delivery to the EC:</b>	28/09/2012

<b>Workpackage responsible for the Deliverable:</b>	WP1 – Linked2Safety Requirements and Reference Architecture
<b>Contributor(s):</b>	NUIG, CERTH, UBITECH
<b>Reviewer(s):</b>	SIVECO
<b>Approved by:</b>	All Partners

<b>Abstract:</b>	The objective of this document is to design, implement, and evaluate the Semantic EHR Model based on the requirements analysis conducted in D1.1.
<b>Keyword List:</b>	Healthcare/EHR standards, Medical Vocabularies, Ontology Design, Ontology Development Methodology, Ontology Evaluation.

## Document Description

### Document Revision History

<i>Version</i>	<i>Date</i>	<i>Modifications Introduced</i>	
		<i>Modification Reason</i>	<i>Modified by</i>
v0.1	11/04/2012	Initial Planning and High Level Sketch	NUIG
v0.2	02/07/2012	TOC Definition	NUIG
V0.3	08/08/2012	Semantic EHR Model-Core Version	NUIG
V.04	25/08/2012	Implementing Semantic EHR Model	UBITECH
V.05	19/09/2012	Section 3 completed, merged with the V.04 and further comments provided to the technical partners.	NUIG
v.06	20/09/2012	Section 4 updated by UBITECH	UBITECH, INTRASOFT
v.07	25/09/2012	Section 5 merged with the V.06 and evaluation feedback received.	CERTH
v.08	26/09/2012	Evaluation feedback addressed and D1.4 sent for internal review.	NUIG
v.09	28/09/2012	Addressed the feedback from internal review. Final version submitted.	NUIG

---



---

## Contents

---



---

<b>1. EXECUTIVE SUMMARY .....</b>	<b>9</b>
<b>2. INTRODUCTION .....</b>	<b>10</b>
1.1 DOCUMENT SCOPE .....	10
1.2 MOTIVATION .....	10
1.3 METHODOLOGY .....	11
1.4 DOCUMENT STRUCTURE .....	12
<b>3. DESIGN AND DEVELOPMENT METHODOLOGY .....</b>	<b>13</b>
<b>3.1. ONTOLOGY BUILDING REQUIREMENTS .....</b>	<b>14</b>
<b>3.2. LINKED2SAFETY METHODOLOGY .....</b>	<b>14</b>
3.2.1. SCOPING PHASE .....	15
3.2.2. TECHNOLOGY SUPPORT PHASE .....	17
3.2.3. MODELLING PHASE .....	18
3.2.4. TESTING PHASE .....	23
<b>3.3. ONTOLOGY DOCUMENTATION .....</b>	<b>24</b>
<b>3.4. SUMMARY .....</b>	<b>25</b>
<b>4. IMPLEMENTING THE SEMANTIC EHR MODEL .....</b>	<b>25</b>
<b>4.1. SEMANTIC EHR MODEL: A DOMAIN ONTOLOGY FOR CLINICAL TRIALS .....</b>	<b>25</b>
<b>4.2. NAMESPACES FOR THE SEMANTIC EHR MODEL .....</b>	<b>26</b>
<b>4.3. SEMANTIC EHR MODEL VS. COMMON EHR SCHEMA .....</b>	<b>27</b>
<b>4.4. SEMANTIC EHR MODEL STRUCTURE .....</b>	<b>28</b>
4.4.1. UPPER LAYER ONTOLOGIES .....	28
4.4.2. VARIABLES FROM CLINICAL PARTNERS .....	31
4.4.3 SUMMARY .....	39
<b>5. EVALUATING THE SEMANTIC EHR MODEL .....</b>	<b>39</b>
<b>5.1. EVALUATION APPROACHES .....</b>	<b>40</b>
<b>5.2. EVALUATION METHODOLOGY .....</b>	<b>42</b>
<b>5.3. EVALUATION RESULTS .....</b>	<b>44</b>
5.3.1. CORRECTNESS AND COMPLETENESS EVALUATION .....	44
5.3.2. USABILITY EVALUATION .....	55
<b>6. CONCLUSION .....</b>	<b>56</b>
<b>7. REFERENCES .....</b>	<b>58</b>

I. APPENDIX A: QUESTIONNAIRES .....	63
I.1 CING .....	63
I.2 CHUV.....	71
I.3 ZEINCRO.....	87

---



---

## List of Figures

---



---

<b>FIGURE 1:</b> INPUTS TO LINKED2SAFETY METHODOLOGY .....	11
<b>FIGURE 2:</b> THE PPEPR METHODOLOGY .....	15
<b>FIGURE 3:</b> LIFTING CLINICAL VARIABLES AND DSM-IV CLASSIFICATION .....	19
<b>FIGURE 4:</b> LINKED2SAFETY LAYERING .....	20
<b>FIGURE 5:</b> BFO-UPPER LEVEL ONTOLOGY, ACGT-DOMAIN LEVEL ONTOLOGY, AND DSM-IV ONTOLOGY .....	21
<b>FIGURE 6:</b> LOCAL CLINICAL VARIABLES ADAPTING WITH THE UPPER AND DOMAIN LEVEL ONTOLOGIES .....	22
<b>FIGURE 7:</b> IMPORTING STRUCTURE OF THE SEMANTIC EHR MODEL, DSM-IV, ACGT, COMMONEHR, AND BFO ONTOLOGIES .....	26
<b>FIGURE 8:</b> THE STRUCTURE OF THE UPPER-LAYER LEVEL OF THE ONTOLOGY (IMPORTS FROM BOF AND ACGT ONTOLOGIES) .....	28
<b>FIGURE 9:</b> "INFORMATIONOBJECT" AND SOME OF ITS SUBCLASSES .....	31
<b>FIGURE 10:</b> BREAK-DOWN OF CONCEPT "DISEASE" .....	34
<b>FIGURE 11:</b> "STATEOFAFFAIRS" CONCEPT AND ITS SOME OF ITS SUBCLASSES .....	36

---



---

## List of Tables

---



---

<b>TABLE 1:</b> DEFINITIONS, ACRONYMS AND ABBREVIATIONS .....	7
<b>TABLE 2 :</b> NAMESPACES USED FOR THE L2S SEMANTIC EHR MODEL .....	27
<b>TABLE 3:</b> CLASSIFICATION OF SEMANTIC MODEL EVALUATION INITIATIVES BASED ON THE TYPE OF APPROACH .....	40
<b>TABLE 4:</b> CLASSIFICATION OF SEMANTIC MODEL EVALUATION ACTIVITIES BASED ON THE OBJECT OF APPROACH .....	40
<b>TABLE 5:</b> APPROACHES FOR SEMANTIC MODEL EVALUATION .....	41
<b>TABLE 6:</b> EXPERTS GROUP FOR THE EVALUATION OF THE LINKED2SAFETY SEMANTIC EHR MODEL .....	43
<b>TABLE 7:</b> CHANGES BASED ON CORRECTNESS AND COMPLETENESS EVALUATION .....	44
<b>TABLE 8:</b> USABILITY EVALUATION .....	56

## Definitions, Acronyms and Abbreviations

**Table 1:** Definitions, Acronyms and Abbreviations

Acronym	Title
ADE	Adverse Drug Event
ADL	Archetype Definition Language
AE	Adverse Event
AOM	Archetype Object Model
API	Application Programming Interface
AQL	Archetype-Based Query Language
ATAM	Architecture Tradeoff Analysis Method
CDA	Clinical Document Architecture
CPR	Computerised Patient Record
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
EDC	Electronic Data Capture
EHR	Electronic Health Record
EMR	Electronic Medical Record
EPR	Electronic Patient Record
HIMSS	Healthcare Information and Management Systems Society
HL7	Health Level Seven
ICEHR	Integrated Care HER
LD	Linkage Disequilibrium

MAF	Minor Allele Frequency
NFR	Non-Functional Requirements
OLAP	Online Analytical Processing
OWL	Web Ontology Language
PHR	Personal Health Record
RAIS	Requirements, Architecture, Interoperability Issues and Solutions
RDF	Resource Description Framework
RDFS	RDF Schema
RR	Reporting Ratio
SNOMED	Systematised Nomenclature of Medicine
SNP	Single Nucleotide Polymorphism
SPARQL	SPARQL Protocol and RDF Query Language
SQL	Structured Query Language
URL	Uniform Resource Locator
US	Usage Scenarios
XML	Extensible Markup Language



# 1.Executive Summary

The present document is Deliverable 1.4 “D1.4 – Semantic EHR Model” (henceforth referred to as D1.4) of the Linked2Safety project. The Semantic EHR Model represents the clinical trial domain and describes as a domain level ontology.

The goal of building the Semantic EHR Model is to enable seamless sharing and linking pieces of healthcare, i.e., Electronic Health Records (EHRs) and clinical data/knowledge among the authorised stakeholders. The Semantic EHR Model has a crucial role of sharing consistent knowledge for decision making in medical and clinical research domains. The Semantic EHR Model is a core pillar of the semantically-interlinked Linked2Safety Infrastructure, i.e., Linked Medical Data Space further described in the WP4.

This document presents a step-by-step systematic ontology building methodology for the clinical trial domain where resources from diverse backgrounds (e.g., patient records, drug, cancer) are used in a successful execution of a trial. The ontology building methodology presented in this document is based on the PPEPR Methodology, which we proposed earlier for ontologising the Health Level Seven (HL7) Standard. The Linked2Safety ontology building methodology proposed in this document is an extended and refined version of the PPEPR Methodology.

The Linked2Safety ontology building methodology covers the following five ontology building phases of the PPEPR Methodology: (i) the **scoping** phase establishes the purpose of ontology building and identifies resources that can support the ontology building process; (ii) the **technology support** phase evaluates Semantic Web languages and supporting tools that can fulfil requirements of the scoping phase; (iii) the **modelling** phase provides detailed guidelines for constructing ontologies; (iv) the **alignment** phase resolves ontological heterogeneity; finally (v) the **testing** phase ensures the consistency and correctness of ontologies with respect to previous phases and requirements. Development steps are allocated to each phase, which indicates the order in which the activities should be performed.

The PPEPR Methodology is iterative; therefore, it allows further extension and adaptation of the Semantic EHR Model which might be required due to future changes and different applications scenarios. Furthermore, the evaluation of the Semantic EHR Model is conducted to ensure the correctness and completeness of concepts, properties, and axioms described as part of the Semantic EHR Model. The evaluation process includes clinical data providers, technical partners, and the domain experts. Finally, the maintenance of the Semantic EHR model will be carried throughout the Linked2safety project.

## 2. Introduction

This section presents the work pursued within the Task 1.4, named “Semantic EHR Model”. The Semantic EHR Model covers the healthcare (i.e., Electronic health Records) and clinical research domains to facilitate clinical trials that require diverse and disparate clinical resources for a successful execution. The Semantic EHR Model is a domain level ontology and extends existing upper-level ontologies to meet diverse clinical requirements. The Section 1.1 describes the scope and the key objectives which have guided this work. The Section 1.2 highlights the motivation behind developing this comprehensive Semantic EHR Model. Next, the Section 1.3 briefly introduces the methodology used in building the Semantic EHR Model. Finally, the Section 1.4 presents the overall work performed in Task 1.4 and describes the structure of this document.

### 1.1 Document Scope

The present document is Deliverable 1.4 “D1.4 – Semantic EHR Model” (henceforth referred to as D1.4) of the Linked2Safety project. The main objective of this document is to define, design, implement, and evaluate the Semantic EHR Model. The work presented in this deliverable is based on the state of the art in area of “*EHR-RELATED TECHNOLOGIES, STANDARDS, ONTOLOGIES AND DATA MODEL*” discussed in the Task 1.1.

The deliverable presents the different layers—upper, domain, and application—involved in building the Semantic EHR Model. Moreover, it covers the design, implementation and evaluation processes. The methodology and implementation details provided in this deliverable will be further referenced within the context of WP4.

The development of the Semantic EHR Model is the core step towards the creation of the semantically-interlinked Linked2Safety platform.

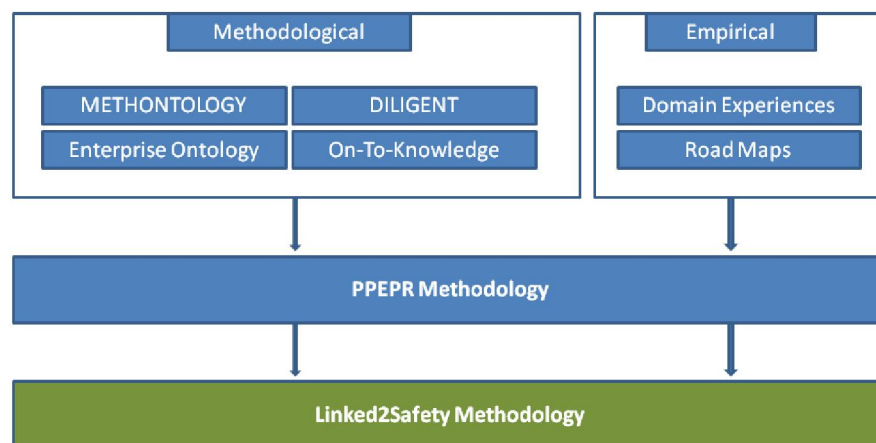
### 1.2 Motivation

The main motivation to build the Semantic EHR Model is to resolve heterogeneities among resources originating from clinical research and EHRs data spaces. To preserve the anonymisation and security of patients (and related stakeholders) these heterogeneous resources are tailored as data-cubes within the Linked2Safety data space. The proposed Semantic EHR Model will act a shared and consistent ontological reference point for the data-cubes originating from various clinical partners.

Furthermore, the above motivation to resolve heterogeneous clinical resources by using an ontological model derives from the functional and non-functional requirements presented in the Requirement Analysis in D1.1. Specifically Table 13 (of D1.1) describes the functional requirements collected from the usage scenarios and the semi-structured interviews; and Table 14 (of D1.1) non-functional requirements collected from the usage scenarios and the semi-structured interviews. At least 10 to 15 functional requirements require a reference ontology in order to be satisfied, and about 5 non-functional requirements related to the interoperability, require the use of Semantic EHR Model.

### 1.3 Methodology

The ontology building methodology used within Task1.4 is a refinement and extension of the PPEPR Methodology [19, 20]. In our past work, we proposed the PPEPR Methodology for ontologising the Health Level Seven (HL7<sup>1</sup>) standard. The clinical scenarios that we consider within the Linked2Safety environment are similar to cases that originally motivated for the development of the PPEPR Methodology. However, the presence of multiple domains (e.g., EHR, Breast Cancer, Diabetes, and Psychiatry) motivated the refinement and extension of the PPEPR Methodology fulfilling the Linked2Safety interoperability requirements.



**Figure 1:** Inputs to Linked2Safety Methodology

In **Figure 1** the Linked2Safety Methodology is grounded on the PPEPR Methodology which is based on existing methodologies and domain experiences:

- **Methodologies and Methods for Building Ontologies:** The PPEPR Methodology inherited where ever possible from the existing methodologies (Enterprise Ontology [13], METHONTOLOGY [14], On-To-Knowledge [15], and DILIGENT [16]). In scope of the Linked2Safety Methodology, we introduce specific guidelines for carrying out development phases and steps.
- **Domain Experiences and Roadmaps:** the RIDE<sup>2</sup> consortium has suggested a roadmap [17, 18] for the interoperability of different healthcare standards and systems. The use of semantic technologies is at the core of the suggested roadmap. From our experiences in RIDE, we obtained a preliminary set of requirements and guidelines about the use of semantics and making healthcare applications interoperable. We incorporated RIDE guidelines within the PPEPR methodology. Further, the PPEPR Methodology is refined and adapted within the Linked2Safety methodology.

<sup>1</sup> <http://www.hl7.org/>

<sup>2</sup> <http://www.srdc.metu.edu.tr/webpage/projects/ride/>

The PPEPR methodology consists of five phases: the **scoping** phase, the **technology support** phase, the **modelling** phase, the **alignment** phase, and the **testing** phase. In the section 3 we will describe phase-by-phase details of the PPEPR methodology and steps adopted in the context of the Linked2Safety methodology.

## 1.4 Document Structure

The remainder of D1.4 is divided into four sections:

Section 3 presents the Linked2Safety design and development methodology for building the Semantic EHR Model.

Section 4 provides the implementation details describing the classes, properties, and axioms used within the Semantic EHR Model.

Section 5 provides the evaluation of the Semantic EHR Model in terms of completeness and correctness of the classes, properties, and axioms described within the Semantic EHR Model.

Section 6 summarises the work carried out in this document and describes the work packages that will utilise the Semantic EHR Model.

### 3. Design and Development Methodology

Ontology building is a set of activities including the ontology development steps, the ontology life cycle, supporting tools, and languages applied coherently for modelling domain knowledge [21]. Several ontology building methodologies have been proposed in the last two decades. The 1990s have witnessed the growing interest of many practitioners in approaches that support the creation and management, as well as the population of single ontologies built from scratch [22]. Until the mid1990s, the ontology development process was an art rather than an engineering activity. Each development team usually followed their own set of principles as well as their own design criteria and phases for manually building the ontology [22]. Thus, the absence of common and structured guidelines slowed the development of ontologies within and between teams, the extension of any ontology, the possibility of ontologies of being reused in others, and the use of ontologies in concrete applications [23]. Until now, a large number of ontologies have been developed by different groups, under different approaches, and with different methods and techniques. However, in comparison to the software engineering counterpart, ontological building is still in its infancy.

Furthermore, the advancement of technology and significant improvement in availability of structured information, ontology practitioners with the goal of speeding up the ontology development process, are starting to reuse [24] as much as possible (i) other ontologies such as UMLS [25], GALEN and ontology modules [26] (ii) ontology statements and ontology design patterns [27], and (iii) non-ontological resources [28] such as thesauri, databases, XML schemas, UML models and classification schemas (e.g., LOINC<sup>3</sup>, SNOMED<sup>4</sup>) built by others and which already have some degree of consensus. Developers realised that such distributed ontology networks should not be developed entirely from scratch, but by reusing and possibly reengineering other ontologies, databases, XML schemas, thesauri, UML models, classification schemes, and other knowledge resources, as well as by taking into account good practices in the development process.

A series of methods and methodologies for developing ontologies from scratch have been reported in [29, 22] and these can be summarised as follows: In 1990, Lenat and Guha published the general steps [30] and some interesting points about the Cyc<sup>5</sup> development. Some years later, in 1995, on the basis of the experience gathered in developing the Enterprise Ontology [31], the first ontology building guidelines were proposed in [33]. The methodology METHONTOLOGY [14] appeared at the same time and was extended in the later paper [34]. Some years later, the On-To-Knowledge methodology appeared as a result of the project with the same name [15]. However, all these methods and methodologies do not consider distributed and layered construction of ontologies. In this respect, in 2004, the DILIGENT methodology [16] was proposed. This new methodology was intended to support domain experts in a distributed setting when they need to engineer and evolve ontologies.

---

<sup>3</sup> <http://loinc.org/>

<sup>4</sup> <http://www.ihtsdo.org/snomed-ct/>

<sup>5</sup> <http://www.cyc.com/>

In this section, sub-section 3.1 briefly describes the requirements discussed in the Task 1.1 for building the Semantic EHR Model. The sub-section 3.2 presents an adapted version of the PPEPR Methodology (i.e., Linked2Safety Methodology) used for building the Semantic EHR Model. Finally the sub-section 3.3 describes a set of ontology documentation tools that are used while building the Semantic EHR Model.

### 3.1. Ontology Building Requirements

Healthcare application scenarios as discussed in the Task 1.2 require inter-department or inter-hospital or inter-clinical system communications which increase the integration complexity. The work done by the Integrating the Healthcare Enterprise (IHE) initiative [35, 36] shows that intra-hospital or inter-clinical system application scenarios are technically very complex and pose interoperability challenges. Thus, a meaningful integration of a patient's medical record and clinical data across healthcare and clinical applications demands interoperability of standard information models, medical vocabularies, and local institute-specific vocabularies.

Widely used ontologies like SNOMED represent the global artefacts of health record components. Similarly, upper-level ontologies like Unified Medical Language System (UMLS<sup>6</sup>) or Basic Formal Ontology (BFO<sup>7</sup>) provide greater abstraction that can be further specialised covering multiple domains. The main purpose of using upper-level (global) ontologies in the healthcare domain is to establish a common agreed set of medical terms used between healthcare institutions. Additionally, local terms or resources (i.e., context-specific terms) need to interoperate with global ones and terms originating from other local sites. In distributed settings, global and local artefacts originating from several sources need interoperation among them, such that messages underlying these artefacts could be transformed, and thus, exchanged meaningfully.

**Key Requirements:** Considering the arrangement of global and local resources in the clinical scenarios discussed in the Task 1.2, an ontology building method (for Semantic EHR Model) will require three main features: (i) **reusability** of existing non-ontological knowledge sources (e.g., UML specifications, XML schemas, and natural text describing classifications); (ii) **layering** of ontological knowledge bases in global and local spaces. As said, a clinical scenario generally has a globally conceptual model or vocabularies as well as a provision for locally designed models and vocabularies that enable the exchange of clinical messages; and (iii) **adaptation** of local knowledge sources with an upper or global conceptual model.

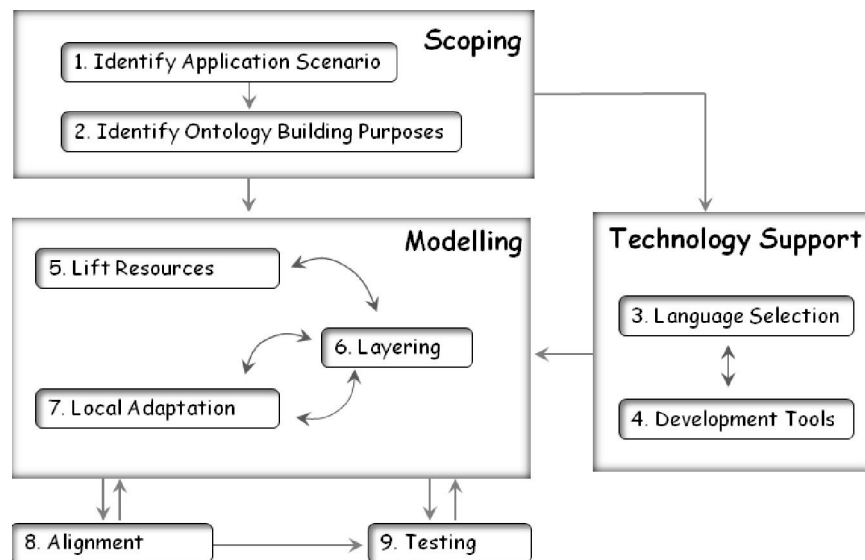
### 3.2. Linked2Safety Methodology

**Figure 2** presents the PPEPR methodology which consists of five phases: (i) the **scoping** phase establishes the purpose of ontology building and identifies resources that can support the ontology building process; (ii) the **technology support** phase evaluates Semantic Web languages and supporting tools that can fulfil the requirements of the scoping phase; (iii) the **modelling** phase provides

<sup>6</sup> <http://www.nlm.nih.gov/research/umls/>

<sup>7</sup> <http://www.ifomis.org/bfo>

detailed guidelines for constructing ontologies; (iv) the **alignment** phase resolves ontological heterogeneity; finally (v) the **testing** phase ensures consistency and correctness of ontologies with respect to the previous phases and requirements. Particular development steps are allocated to each phase, which indicate the order in which the activities should be performed. The modelling, the alignment, and the testing phases are iterative until the required ontologies and their alignments have been constructed. In the following sections we will describe phase-by-phase details of the PPEPR methodology with refinements specifically target to Linked2Safety ontology building requirements.



**Figure 2:** The PPEPR Methodology

### 3.2.1. Scoping Phase

The Scoping phase starts with identifying an application scenario and ends with resources identified within the application scenario and purposes of building Linked2Safety ontology (i.e., Semantic EHR Model).

#### Step 1 (Identify Application Scenario)

This step takes as input: UML interaction (or sequence) diagram; and produces as output: actors, applications, and resources identified within the application scenarios. It is important to first identify an application scenario which drives the need for building the Semantic EHR Model.

The ten use-case scenarios discussed in the Task 1.2 are taken as input this step. An identification of a scenario provides the scope for the resources that may be available from existing applications. We have identified following resources with each of the three clinical partners:



- ❖ **CHUV:** The clinical variables are categorised along two dimensions. The first set of variables corresponds to DSM-IV<sup>8</sup> classification and second is institute specific local variables. The DSM-IV related variables describe the psychiatric disorder (or mental disorder) and use DSM-IV codes for their appropriate interpretation. The scope of DSM-IV classification code is global in the sense that all identified actors and applications must use them as a commonly agreed set of terms. This motivates us to build a DSM-IV global ontology that can be used as a common reference point (for psychiatric cases) in conjunction with the Semantic EHR Model. The scope of institute specific variables is local; therefore, an alignment mechanism is required to establish correspondences between global and local resources. The alignment of global and local resources will allow the consistent and unambiguous use of local resources across different clinical studies and institutes.
- ❖ **CING:** The clinical variables are categorised along three dimensions. The first set of variables corresponds to the breast cancer domain, the second to the diabetic domain and the third to the neurogenetics domain. The scope of these three sets of variables is local and controlled by the publishing institute. Again, an alignment mechanism is required to establish correspondences between global and local resources.
- ❖ **ZEINCRO:** The clinical variables are categorised along three dimensions. They are categorised according to the clinical studies performed (i.e., StudyA, StudyB, and StudyC) for the respiratory domain. Each study includes variables from adverse event (AE), demographic, medical history and concomitant medication details recorded for a patient. The scope of all these three studies is local to the institute. Similar to CHUV's and CING's cases an alignment mechanism is required to establish correspondences between global and local resources.

## Step 2 (Identify Ontology Building Purposes)

This step takes as input the resources identified within the Step 1 (e.g., clinical variables, XML Schemas, Messages, UML Models) and produces as output purposes for building ontologies. We have categorised four major purposes for building the Semantic EHR Model.

- ❖ **Information Exchange and Data Integration:** The Semantic EHR Model can provide formal vocabularies of terms (or clinical variables)

---

<sup>8</sup> <http://www.psychiatry.org/practice/dsm/dsm-iv-tr>; We are aware of the fact that American Psychiatric Association and American Psychiatric Publishing publications and logos are protected by copyright and all rights are reserved. Therefore we are trying to get the written permission from the copyright owner, to be allowed to use and reproduce material from the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) in our project. Until we have the written consent from the copyright owner to do so, we assure that the use and reproduction of DSM-IV is just scheduled only in the event that we obtain this permission. If we don't get the written permission from the copyright owner to use and reproduce DSM-IV we will not do so.



identified in the above Step 1. This consistent set of vocabularies will allow the exchange of data between systems using these vocabularies. In addition to describing concepts and relations, ontology can also describe constraints and additional constructs (e.g., functional properties) that can make the task of data integration much sensible for application integration scenarios.

- ❖ **Vocabulary Sharing:** In certain cases the purpose of an ontology could be to share formal and consistent sets of vocabularies without setting requirements for rigorous data integration or information exchange.
- ❖ **Alignment:** The healthcare domain consists of several sub-domains from the medical and life sciences area. No single domain covers all the concepts required to describe a patient and clinical studies. For example, the Linked2Safety use-cases include clinical variables across various domains such as psychiatrics, breast cancer, diabetic, neurogenetics, and respiratory. Therefore, the cross-domain alignment will allow access to clinical resources across multiple domains and sub-domains.
- ❖ **Reasoning:** The Semantic EHR Model can also be used to reason over concepts and relations between clinical artefacts (e.g., classification, consistency check) as supported by Description Logic (DL) reasoners.

The identification of purposes would ultimately influence the next development phases. For example, in the case of vocabulary sharing, it might be suggested to select light-weight ontology language like RDFS. On the other hand, if reasoning is the main purpose of using ontologies then expressive languages like OWL could be a more appropriate candidate. The output of the scoping phase (i.e., identified clinical resources and ontology building purposes) is input to the Technology Support and modelling phases.

### 3.2.2. Technology Support Phase

The main goal of the Technology Support phase is to identify a list of tools and a language for building the Semantic EHR Model. The Technology Support phase starts with clinical resources (i.e., clinical variables) and ontology building purposes identified within the Scoping phase and ends with list of supporting tools that may automate the overall ontology building process.

Before starting the Modelling phase, it is important to analyse relevant ontology languages and tools support. Language selection depends significantly on constructs supported by the ontology languages and ontology building purposes identified in the scoping phase. The Technology Support phase should also analyse tool support for constructing and testing the ontologies. The selection of ontology languages depends on the richness of axioms that any application scenario may demand. For example, RDFS has limited support to model data types, constraints, and concepts relationships. In the case of modelling advanced data properties and complex relationships between domain concepts, OWL could

be a natural choice. OWL supports advanced data properties for modelling complex Healthcare and Life Sciences (HCLS) use cases [37]. Considering the expressive set of clinical variables obtained in the Step 1, OWL could be a choice to model and implement the Semantic EHR Model. In the case of the DSM-IV classification expressivity is simple, which means that DSM-IV codes primarily use the “subclass” relation with a purpose of sharing the codes among interacting clinical partners. RDFS or OWL both fit well with DSM-IV expressivity.

Tool support is important for the development, maintenance and usage of ontologies in applications. Different types of ontology tool support are emerging. Some of them are specialised for a specific task, but heavyweight integrated-tools are also available. Tools provide the following support for ontology building activities:

- ❖ **Speeding-up** ontology modelling process. User friendly editors support visualisation and ontology construction.
- ❖ **Editing** existing ontologies. Updates and corrections are an essential part of the ontology building process. Tools support ontology change management and version control.
- ❖ **Exporting/importing** ontology in various encoding formats. It is important to use and publish ontologies for healthcare applications using different ontology languages, e.g., RDFS, OWL.
- ❖ **Advanced usages** such as alignment, merging, reasoning, evaluation of ontologies. Integration and quality enhancements like ontology evaluation is supported by specialised plugins or tools that support integrated ontology building environment.
- ❖ **Testing consistency** of the ontologies using reasoners. Ensuring consistency and correctness is at the core of ontology building activities.

The Protégé<sup>9</sup> ontology editor provides most of the support identified above. Therefore, OWL as implementation language and Protégé ontology building environment fit well with the overall design, implementation, and testing of the Semantic EHR Model and DSM-IV classification. The next section describes the Modelling phase which includes three ontology building steps.

### 3.2.3. Modelling Phase

The Modelling phase starts with the task of lifting clinical resources and ends with the local adaptation of ontologies. The overall goal of this phase is to build the Semantic EHR Model and DSM-IV ontology.

---

<sup>9</sup> <http://protege.stanford.edu/>

## Step 5 (Lifting Resources)

In scope the PPEPR Methodology we proposed seven lifting rules that automatically transform structured resources such as a XML schema to a corresponding ontology [20]. However, in Linked2Safety clinical variables and DSM-IV classification are available as unstructured text descriptions. Hence, the lifting of clinical variables and the DSM-IV classification is primarily a manual process. The lifting task involves creating correspondences between unstructured resources (clinical variables and DSM-IV classification) and ontological constructs (class, subclass, property, etc.).

<u>Clinical Variables</u>	<u>DSM-IV</u>
<b>Class:</b> chuv:Poliomyelitis	<b>Class:</b> DSM_292.0
<b>SubClassOf:</b> acgt:ChronicViralInfection	<b>SubClassOf:</b> Nicotine
<b>Annotations:</b> rdfs:comment "Poliomyelitis is a viral disease that can affect nerves and can lead to partial or full paralysis."	<b>Annotations:</b> rdfs:comment "Nicotine Withdrawal"

**Figure 3:** Lifting Clinical Variables and DSM-IV Classification

Figure 3 shows how correspondences ("SubClassOf" inheritance relation) have been identified first and later implemented using OWL. In the case of the local clinical variables (e.g., chuv:Poliomyelitis) a "SubClassOf" relation is created with Advancing Clinico-Genomic Trials on Cancer (ACGT<sup>10</sup>) ontology (prefix "acgt") which is global in the scope of use. The ACGT ontology [38] is developed for clinical trials in the breast cancer domain. The ACGT ontology extends the upper-level Basic Formal Ontology (BFO<sup>11</sup>). Section 4 provides a detailed discussion on the ACGT and BFO ontologies. In Figure 3, a "SubClassOf" relation between "DSM\_292.0" and "Nicotine" is straightforward as both terms are global and applicable to all clinical users.

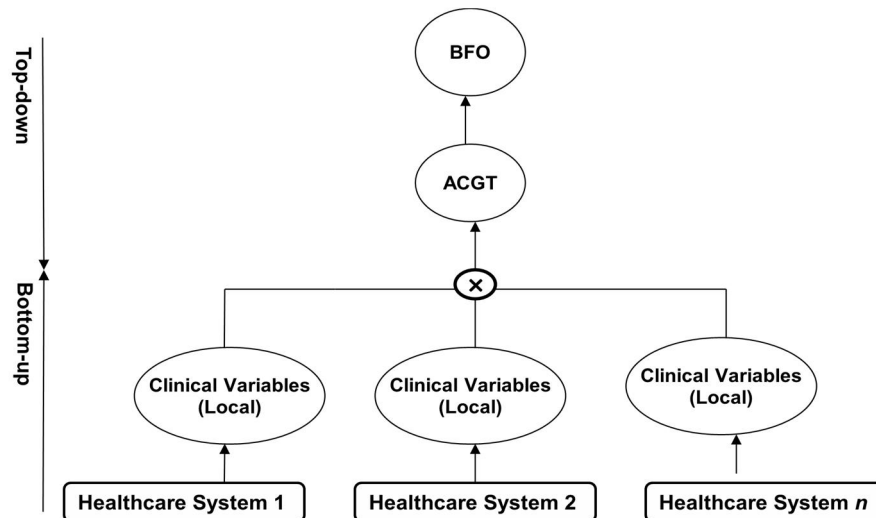
Regardless of resources are structured or unstructured, domain and ontology experts are required to sit together to find and/or verify correspondences between clinic artefacts and ontological constructs. The next section describes the arrangement of the global and local ontologies resulting from core and message schema transformations.

<sup>10</sup> <http://eu-acgt.org/>

<sup>11</sup> <http://www.ifomis.org/bfo/>

## Step 6 (Layering)

The Layering step takes as input global/upper and local ontologies; and produces as output layered global/upper and local ontologies.



**Figure 4:** Linked2Safety Layering

The layering task arranges ontologies into global (shared by all clinical users) and local (used within a particular institute) spaces.

Figure 4 shows that global ontologies are arranged in a top-down fashion where ACGT extends the BFO ontology, while local ontologies are first created from the clinical variables and later aligned with the ACGT ontology. In Figure 4, the  $\otimes$  symbol means alignment of ontologies. The alignment task exists between local and global ontologies. The local ontologies then refer to global ontologies, if matching correspondences are available between them. However, two conceptual ambiguities exist between local ontologies of the same domain: (i) semantically similar concepts are named differently (ii) corresponding concepts are represented at different structural levels. These ambiguities arise because local systems have flexibility and choices in the design of clinical messages. To deal with both issues (i.e., different naming schemes and structural differences) one option is to provide alignments between local ontologies.

The meeting points of the up (bottom-up) and down (top-down) arrows in Figure 4 (left hand side), require extensions within local and global ontologies to find suitable correspondences between them. The next section describes mechanisms and choices for extending both types of ontologies.

## Step 7 (Local Adaptation)

The final Local adaptation step within the Modelling phase takes as input global and local ontologies and has as output extended global and local ontologies meeting local requirements.

The notion of local adaptation was first proposed by DILIGENT methodology.

DILIGENT local users adapt the global ontology by introducing local changes, and a central board controls the contents of the global and local ontologies. On a similar line, Linked2Safety global and local ontologies originate from various sources or clinical partners. The local adaptation step is motivated by normal practices where local clinical applications diverge from the standard (or commonly agreed) guidelines by introducing local vocabularies.

The local adaptation phase ensures that: (i) local ontologies are generalised enough to resemble the concepts defined in global ontology, and (ii) global ontologies are specialised enough to resemble the concepts defined in the local ontologies. We categorise the local ontologies into two parts: (i) local concepts, and (ii) local constraints. As said in previous sections, local concepts generally represent the consensus of a local group. Consequently, their understanding is limited to the local environment.

<u>BFO &amp; ACGT</u>	<u>DSM-IV</u>
<b>Class:</b> acgt:ChronicViralInfection	<b>Class:</b> DSM_292.0
<b>SubClassOf:</b> acgt:ViralInfection	<b>SubClassOf:</b> NicotineSubstanceDisorders
<b>Class:</b> acgt:ViralInfection	<b>Class:</b> DSM_300.23
<b>SubClassOf:</b> acgt:InfectiousDisease	<b>SubClassOf:</b> AnxietyDisorders
<b>Class:</b> acgt:InfectiousDisease	<b>Class:</b> DSM_305.00
<b>SubClassOf:</b> acgt:Disease	<b>SubClassOf:</b> AlcoholSubstanceDisorders
<b>Class:</b> acgt:Disease	<b>Class:</b> DSM_300.21
<b>SubClassOf:</b> snap:Disposition	<b>SubClassOf:</b> PanicDisorder

**Figure 5:** BFO-Upper Level Ontology, ACGT-Domain Level Ontology, and DSM-IV ontology

The PPEPR methodology deals with adaptation of local concepts, i.e., how locally defined concepts fit together with global ontologies. In the case of Linked2Safety, local adaptation step aligns and extends the local ontologies originating from three clinical partners.

<u>CHUV</u>	<u>CING</u>	<u>ZEINCRO</u>
<b>Class:</b>  chuv:HIV	<b>Class:</b>  cingBreastCA:BRCA1	<b>Class:</b>  zeincroAE:AdverseEvent
<b>SubClassOf:</b>  acgt:ChronicViralInfection	<b>SubClassOf:</b>  acgt:GeneExpression	<b>SubClassOf:</b>  acgt:MedicalProcess

**Figure 6:** Local clinical variables adapting with the upper and domain level ontologies

Figure 5 shows a snippet of the ACGT ontology, which describes the top level concepts of local ontologies shown in Figure 6. For example, the "ChronicViralInfection" class represents all types of infections that are viral and chronic. Further, classes such as "ViralInfection" "InfectiousDisease" and "Disease" are abstractions (or super classes) of the "ChronicViralInfection" class. We notice that the "SubClassOf" relation between the "Disease" and "Disposition" classes is a bridge (or alignment) between ACGT and BFO (prefix "snap") ontologies. Similarly, bridges are required between the Semantic EHR Model and ACGT ontology. For example, a local concept such as HBV (Hepatitis B virus) or HCV (hepatitis C virus) or HIV (human immunodeficiency virus) can be inherited from any of the classes, e.g., ChronicViralInfection, InfectiousDisease, or simply from the "Disease" class. To deal with a situation where creating a appropriate (or most suitable) bridge between global and local ontologies could be complex task, the PPEPR methodology suggests three approaches for the adaptation of the local concept such HBV or HCV or HIV.

**Top-Down:** Extend the global ontology with more specialised concepts that resemble the concepts defined in local ontologies. For example, each of the concepts "ChronicViralInfection" or "InfectiousDisease" could be further extended with a lab specific concept like "HBV" or "HIV", to represent that all clinical observations specific to "Infectious" diseases. However, this means that term like "HBV" or "HIV" has a universal acceptability.

**Bottom-Up:** Extend the local ontology with more generalised concepts that resemble the concepts defined in the global ontology. For example, a super class "ChronicViralInfection" for the local concept "HIV" can be added to the local ontology, such that, appropriate inheritance like "HIV" subClassOf "ChronicViralInfection" could be established in the local ontology (see the first column in Figure 6).

**Middle-Out:** As described above, concepts ("ViralInfection" or "Disease") in the global ontology are defined at a higher level of abstraction, which allows a local concept to inherit from all of them. Therefore, instead of specialising or generalising global or local concepts, another approach could be to add a specialised class for the "ViralInfection" class as a sibling of the above two concepts. For example, "ChronicViralInfection" is added to describe all the diseases that are "Chronic" and "Viral" and "Infectious".

The Semantic EHR Model applied these approaches in creating bridges to the ACGT and BFO ontologies. These three approaches could be applied

independently or in combinations depending on requirements from different clinical scenarios. Considering the heterogeneities of different clinical scenarios, we intentionally avoid any fit-for-all suggestion. The next section describes three approaches for testing the ontologies built in the modelling phase.

### 3.2.4. Testing Phase

The Testing phase takes as input global and local ontologies and has as output consistent ontologies.

Once the modelling phase completes, it is important to ensure that ontologies are ready for publishing as well as matching the domain requirements. In the context of the Linked2Safety, three types of testing is performed (i) testing the validity and consistency of an ontology (ii) whether the ontology matches the requirements identified in the scoping phase, and finally (iii) testing correspondences between local and global ontologies.

**Testing validity and consistency:** Validity testing is about ontology correctness, i.e., is the serialisation valid for the chosen ontology language. Ontology editors generally parse input ontologies and report errors in the ontology serialisation. Some dedicated online tools are also available for checking the ontology language syntax. This type of testing can be avoided if the ontology editors ensure that its output is valid syntax. Validity testing is important where ontology markup is edited manually in any standard text editor.

Consistency testing is about the coherence of the conceptual model. It checks the consistency of the conceptual model within the representation formalism (i.e., ontology language) used during the modelling phase. The output of consistency checks generally identifies all conflicting concepts and relationships. Some advanced ontology reasoners can also provide further information on debugging and repairing defects in the ontologies. The Pellet<sup>12</sup> reasoner available as plug-in within the Protégé environment is used for validating the Semantic EHR Model and DSM- IV Ontology. The validity and consistency of the Semantic EHR Model and DSM- IV Ontology has been ensured throughout the modelling phase and the implementation task presented in section 4.

**Requirement Matching:** Requirement Matching is applied for verifying whether the ontology matches requirements of the identified scenario during the scoping phase. The techniques for verifying requirements may differ depending on the complexity of the scenario. For example, in the case of well documented clinical applications, it might be sufficient to compare requirements and ontologies side-by-side. In the case of the Semantic EHR Model, variable descriptions provided by the clinical partners are used for verifying each variable and corresponding ontological entity. Further as part of the evaluation task presented in section 5, evaluation feedback from each partner ensured the suitability of all the ontological entities.

**Testing Correspondences:** In clinical scenarios the number of correspondences between ontologies is generally high. In such cases it is often hard to find the causes of the conceptual conflicts. We performed ontology consistency testing

---

<sup>12</sup> <http://clarkparsia.com/pellet/>

(with or without correspondences between two more ontologies) to identify the causes of the conflicts. For instance, conflicts may occur due to incorrect correspondences or due to errors in structural definitions. This way, errors were identified in the Semantic EHR Model and DSM- IV Ontology at separate levels and corrective measures are applied to the right location.

### 3.3. Ontology Documentation

Documentation is a general task that applies to all phases of the PPEPR methodology. There are several ways documentation could be reused or created for ontologies:

**Integrated Tools:** Ontology editors generally support a documentation function using specialised plugins. The OWLDoc<sup>13</sup> plug-in for Protégé exports HTML documents from ontologies. Similarly, TopBraid<sup>14</sup> and OntoStudio<sup>15</sup> allow creating and editing comprehensive sets of ontology documents in HTML format. Some specialised plug-ins and tools like OWLViz<sup>16</sup> and SWOOP<sup>17</sup> also support the visualisation of ontologies and their graphical documentation.

**Standalone Tools:** Dedicated ontology documentation tools like SpecGen<sup>18</sup> or OntoSpec<sup>19</sup> generate HTML documents from ontology definitions. For example, they identify classes, properties, and other sources to generate templates of definitions and combine them into the main document source.

**Embedding:** One convenient way could be to use RDFa<sup>20</sup>, embedding ontology definitions within a HTML document. In this case the same document acts as the source for the ontology definition and the specification, thus blending together implementation and documentation activities.

In the case of the Semantic EHR Model and DSM-IV Ontology, the first option is primarily used within the Protégé environment. The ontology documentation creates a set of ontology specifications for broad audiences including domain experts, engineers, and non-technical users.

---

<sup>13</sup> <http://www.co-ode.org/downloads/owldoc/>

<sup>14</sup> [http://topquadrant.com/products/TB\\_Suite.html](http://topquadrant.com/products/TB_Suite.html)

<sup>15</sup> <http://www.ontoprise.de/>

<sup>16</sup> <http://www.co-ode.org/downloads/owlviz/>

<sup>17</sup> <http://code.google.com/p/swoop/>

<sup>18</sup> <https://github.com/specgen/specgen>

<sup>19</sup> <http://moustaki.org/ontospec/>

<sup>20</sup> <http://rdfa.info/>



### 3.4. Summary

In this section we have presented the Linked2Safety Methodology for building the Semantic EHR Model and DSM-IV Ontology. The Linked2Safety Methodology is a refinement and extension of the PPEPR Methodology we proposed earlier for ontologising the HL7 standard. The section describes a step-by-step (including various phases) method that transforms unstructured sources (e.g., text, labels, and values) to ontological format. Steps like “Layering” and “Local Adaptation” have been applied for arranging ontologies in the global and local spaces. The next section describes the implementation details for building the Semantic EHR Model and DSM- IV Ontology.

## 4. Implementing the Semantic EHR Model

The implementation of any model in OWL specifies that we need to identify the concepts and properties. Also, there is a need to connect the ontology with an external point of view in a systematic way. In this section, we are going to present what upper layer ontologies we use, as well as how we have incorporated the clinical data variables.

### 4.1. Semantic EHR Model: A domain ontology for clinical trials

One of the main aspects of the Semantic EHR Model is that it is a domain ontology specifically designed for clinical trials. It incorporates upper-layer and domain ontologies. An upper ontology (also known as a top-level ontology) is an ontology (in the sense used in information science) which describes very general concepts that are the same across all knowledge domains. An important function of an upper ontology is to support very broad semantic interoperability between a large number of ontologies which are accessible "under" this upper ontology. It is usually a hierarchy of entities and associated rules that attempts to describe those general entities that do not belong to a specific problem domain.

Over the course of the years, a number of upper-layer ontologies have been created, one of the most first and important being SUMO<sup>21</sup>. Suggested Upper Merged Ontology or SUMO is an upper ontology intended as a foundation ontology for a variety of computer information processing systems. It is considered by some foundations a candidate for the "standard upper ontology". SUMO originally concerned itself with meta-level concepts (general entities that do not belong to a specific problem domain), and thereby would lead naturally to a categorization scheme for encyclopaedias. It has now been considerably expanded to include a mid-level ontology and dozens of domain ontologies.

The Semantic EHR Model is based upon on a upper-layer ontology: IFOMIS Basic Formal Ontology (BFO)<sup>22</sup>. BFO grows out of a philosophical orientation which overlaps with the work done in SUMO. Unlike these, however, it is narrowly focused on the task of providing a genuine upper ontology which can be used in

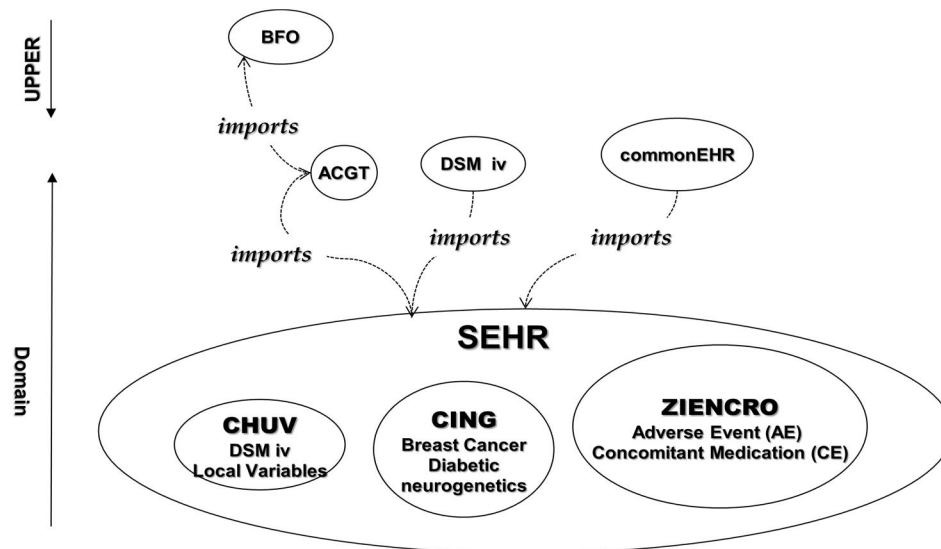
---

<sup>21</sup> <http://www.ontologyportal.org/>

<sup>22</sup> <http://www.ifomis.org/bfo/1.1>

support of domain ontologies developed for scientific research, as for example in biomedicine within the framework of the OBO Foundry. Thus BFO does not contain physical, chemical, biological or other terms which would properly fall within the special sciences domains.

The other upper-layer ontology we use is the Open Biological and Biomedical Ontologies. The OBO Foundry is a collaborative project involving developers of science-based ontologies. Their aim is to establish a set of principles for ontology development with the goal of creating a suite of orthogonal interoperable reference ontologies in the biomedical domain.



**Figure 7:** Importing structure of the Semantic EHR Model, DSM-IV, ACGT, commonEHR, and BFO Ontologies

Figure 7 shows the importing structure of upper-level (BFO), domain ontologies (ACGT, DSM-IV), commonEHR ontology (developed in the Task 1.3) and the Semantic EHR Model (SEHR). The Semantic EHR Model incorporates the best aspects of the upper layer ontologies, providing a way to connect data expressed with these concepts with other external ontologies. The L2S Semantic EHR Model imports ACGT ontology which imports the BFO. As discussed in the Section 3, for psychiatrics cases we have used DSM-IV, which is used in conjunction with the Semantic EHR Model for annotating mental disorder related resources.

## 4.2. Namespaces for the Semantic EHR Model

Linked2Safety aims to incorporate several concepts from different medical domains. There is also a need to incorporate all these things as gracefully as possible, so as to keep track of which concepts come from a particular data provider as well as the medical domain that it is associated. In OWL, one way to achieve this is through the usage of namespaces. Individual spaces have been allocated to each set of variables from the data providers. For example **Table 2** : Namespaces used for the L2S Semantic EHR Model below describes a set of prefix-URI used within the L2S Semantic EHR Model.

Prefix	URI	Description
<b>chuv</b>	http://hcls.der.i.e/l2s/sehr/chuv/1.0#	<i>Namespace encapsulating CHUV variables</i>
<b>cingNg</b>	http://hcls.der.i.e/l2s/sehr/cing/ng/1.0#	<i>CING-Neuro genetics namespace</i>
<b>cingBreastCA</b>	http://hcls.der.i.e/l2s/sehr/cing/BreastCA/1.0#	<i>CING-Breast Cancer namespace</i>
<b>cingDB</b>	http://hcls.der.i.e/l2s/sehr/cing/db/1.0#	<i>CING-Diabetic namespace</i>
<b>zeincroAE</b>	http://hcls.der.i.e/l2s/sehr/zeincro/studyAE/1.0#	<i>Zeincro-Adverse Event (AE) namespace</i>
<b>zeincroConcmed</b>	http://hcls.der.i.e/l2s/sehr/zeincro/Concmed/1.0#	<i>Zeincro-Concomitant Medication namespace</i>
<b>zeincroMedHistStudyA</b>	http://hcls.der.i.e/l2s/sehr/zeincro/respiratory/medicalhistory/studyA/1.0#	<i>Zeincro Medical History for Study A namespace</i>
<b>zeincroMedHistStudyB</b>	http://hcls.der.i.e/l2s/sehr/zeincro/respiratory/medicalhistory/studyB/1.0#	<i>Zeincro Medical History for Study B namespace</i>
<b>zeincroMedHistStudyC</b>	http://hcls.der.i.e/l2s/sehr/zeincro/respiratory/medicalhistory/studyC/1.0#	<i>Zeincro Medical History for Study C namespace</i>
<b>(default)</b>	http://hcls.der.i.e/l2s/sehr/1.0#	<i>Semantic EHR Model namespace</i>

**Table 2 :** Namespaces used for the L2S Semantic EHR Model

Each URI (second column of the above table) ends with “1.0”, which basically describes the version used for ontological entities.

### 4.3. Semantic EHR Model vs. Common EHR Schema

Another important aspect of the ontology is the set of concepts and properties that are specific and/or common to all the participating clinical partners. By studying what the clinical partners are storing for the data they shall provide, we can understand what concepts they are interested in.

As was described in D1.3, the Common EHR Schema incorporates the best attributes from open standards such as openEHR. This latter standard though

does not provide any particular fields that are related to specific medical information for the patient in the project's different medical domains (breast cancer, psychiatric disorders etc) – it just provides a way of declaring the structure for EHR's. By studying the data fields as they were provided by the project's clinical partners, the Common EHR Schema encapsulates only the basic notions and data fields from the clinical partners (which are common to all of them). These are the main points of difference from the Common EHR Model: the SEHR incorporates what has been done in Common EHR Schema along with the rest of the data field's categorized, allowing expressiveness. Also, it goes a step further by combining things that are similar together, either in concepts or in properties, along with a way of "interface" with other external ontologies (by providing the upper-layer part).

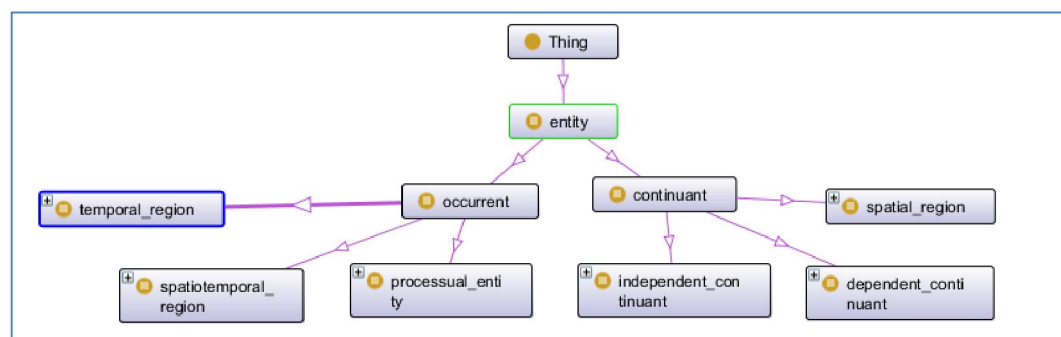
## 4.4. Semantic EHR Model structure

In this section, we will be presenting the implementation of the first version of the Semantic EHR Model. We will start by explaining the structure of the upper layer ontology. Then we will proceed with representing the ontology in layers: first, we will present the upper layer ontologies and their basic concepts and categorization. Secondly, we will present the namespaces we introduced. Last, we present the classes and the properties that were introduced by the studying of the data variables as they were provided by the clinical partners.

### 4.4.1. Upper layer ontologies

The Basic Formal Ontology (*BFO*) consists of a series of sub-ontologies<sup>23</sup> which can be seen as perspectives on reality. The most important of are: a) *SNAP*, a series of ontologies indexed by times and b) *SPAN*, a single video-scopic ontology.

Each element from *SNAP* is a set of all entities existing at a period. *SPAN* is a set of all processes unfolding through time. Each *SNAP* is thus analogous to anatomy, whereas *SPAN* is analogous to physiology. Each snapshot ontology represents entities existing at some given present instant. *SPAN* is a "global point of view" partition of the total of all processes. Processes are invisible in the snapshot view; substances are invisible in the span view.



**Figure 8:** The structure of the upper-layer level of the ontology (imports from BOF and ACGT ontologies)

<sup>23</sup> <http://www.ifomis.org/bfo/overview>

Both *SNAP* and *SPAN* will serve as basis for a series of sub-ontologies at different levels of granularity. The same portion of reality may appear at a plurality of levels of granularity. Sets of things in one case may be aggregates at another and what counts as one unit process at a level may be part of a process-continuum at another. *SPAN* and *SNAP* have their own namespaces on our ontology, as they are imported from BFO.

Another primary division that the ontology provides, has to do with whether the entity is a *continuant* (entity that exists in full at any time in which it exists at all, persists through time while maintaining its identity and has no temporal parts) or an *occurent* (entity that has temporal parts and that happens, unfolds or develops through time). For *continuant* entities, BFO considers the following subclasses (partial list):

### ***Continuant***

**URI** <http://www.ifomis.org/bfo/1.1/snap#Continuant>

**Definition** An entity that exists in full at any time in which it exists at all, persists through time while maintaining its identity and has no temporal parts.

**Examples** A heart, a person, the colour of a tomato, the mass of a cloud, a symphony orchestra, the disposition of blood to coagulate, the lawn and atmosphere in front of our building.

**Sub-class Of** <http://www.ifomis.org/bfo/1.1/snap#Entity>

### ***dependent\_continuant***

**URI** [http://www.ifomis.org/bfo/1.1/snap#dependent\\_continuant](http://www.ifomis.org/bfo/1.1/snap#dependent_continuant)

**Definition** A *continuant* that is either dependent on one or other independent *continuant* bearers or inheres in or is borne by other entities.

**Sub-class Of** <http://www.ifomis.org/bfo/1.1/snap#Continuant>

### ***independent\_continuant***

**URI** [http://www.ifomis.org/bfo/1.1/snap#independent\\_continuant](http://www.ifomis.org/bfo/1.1/snap#independent_continuant)

**Definition** A *continuant* that is a bearer of quality and realizable entity entities, in which other entities inhere and which itself cannot inhere in anything.

**Examples** An organism, a heart, a leg, a person, a symphony orchestra, a chair, the bottom right portion of a human torso, the lawn and atmosphere in front of our building.

**Sub-class Of** <http://www.ifomis.org/bfo/1.1/snap#Continuant>

### ***spatial\_region***

**URI** [http://www.ifomis.org/bfo/1.1/snap#spatial\\_region](http://www.ifomis.org/bfo/1.1/snap#spatial_region)

**Definition** Space and spatial region entities are entities in their own rights which exist independently of any entities which can be located at them. This view of space is sometimes called "absolutist" or "the container view". In BFO, the class site allows for a so-called relational view of space, that is to say, a view according to which spatiality is a matter of relative location between entities and not a matter of being tied to space. The bridge between these two views is secured through the fact that while instances of site are not spatial region entities, they are nevertheless spatial entities.

**Examples** The sum total of all space in the universe, parts of the sum total of all space in the universe

**Sub-class Of** <http://www.ifomis.org/bfo/1.1/snap#Continuant>

For occurrent entities, BFO considers the following subclasses (partial list):

### ***Occurent***

**URI** <http://www.ifomis.org/bfo/1.1/snap#Occurent>

**Definition** An entity that has temporal parts and that happens, unfolds or develops through time. Sometimes also called perdurants.

**Examples** The life of an organism, a surgical operation as processual context for a nosocomical infection, the spatiotemporal context occupied by a process of cellular meiosis.

**Sub-class Of** <http://www.ifomis.org/bfo/1.1/snap#Entity>

### ***processual\_entity***

**URI** [http://www.ifomis.org/bfo/1.1/snap#Processual\\_entity](http://www.ifomis.org/bfo/1.1/snap#Processual_entity)

**Definition** An occurrent that exists in time by occurring or happening, has temporal parts and always involves and depends on some entity.

**Examples** The life of an organism, the process of meiosis, the course of a disease, the flight of a bird.

**Sub-class Of** <http://www.ifomis.org/bfo/1.1/snap#Occurent>

***spatiotemporal\_region***

**URI** [http://www.ifomis.org/bfo/1.1/snap#spatiotemporal\\_region](http://www.ifomis.org/bfo/1.1/snap#spatiotemporal_region)

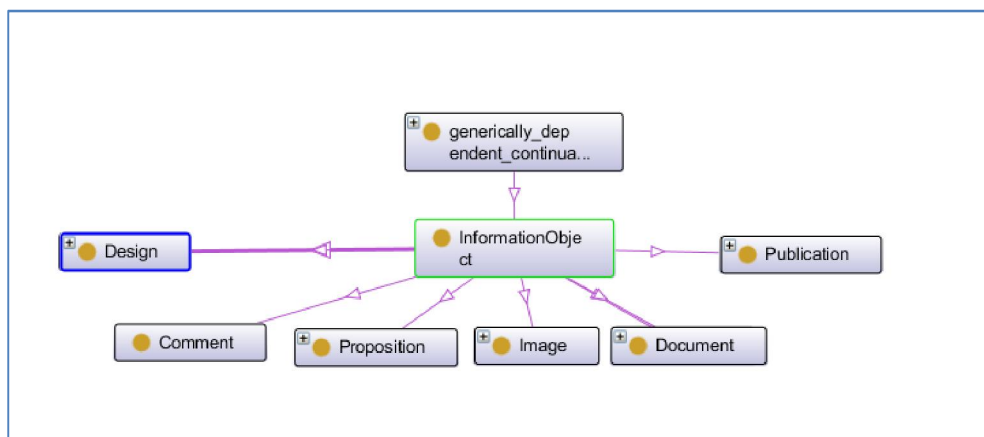
**Definition** All instances of occurrent are spatiotemporal entities, that is, they enter in the relation of (spatiotemporal) location with spatiotemporal region entities. As a particular case, the exact spatiotemporal location of a spatiotemporal region is this region itself.

**Examples** The spatiotemporal region occupied by a human life, the spatiotemporal region occupied by the development of a cancer tumor, the spatiotemporal context occupied by a process of cellular meiosis.

**Sub-class Of** <http://www.ifomis.org/bfo/1.1/snap#Occurent>

**4.4.2. Variables from Clinical Partners**

As it can be seen from Figure 9, all information objects that are related to medicine can be connected the way it is shown.



**Figure 9:** "InformationObject" and some of its subclasses

All classes such as medical information (e.g. "MedicalImage"), as well as knowledge regarding medical texts and therapies ("Publication", "Proposition", "Design" etc), are sub-classes of concept "InformationObject". This latter concept is also sub-class of "*generically\_dependent\_continuant*".

**Sub-classes of *generically\_dependent\_continuant* (sub-class of *dependent\_continuant*):**

**InformationObject**

<b>URI</b>	<a href="http://www.ifomis.org/acgt/1.0#InformationObject">http://www.ifomis.org/acgt/1.0#InformationObject</a>
<b>Definition</b>	Concept that describes any piece of information.
<b>Examples</b>	An image, a publication etc.
<b>Sub-class Of</b>	<a href="http://www.ifomis.org/bfo/1.1/snap#generically_dependent_continuant">http://www.ifomis.org/bfo/1.1/snap#generically_dependent_continuant</a>

**Design**

<b>URI</b>	<a href="http://www.ifomis.org/acgt/1.0#Design">http://www.ifomis.org/acgt/1.0#Design</a>
<b>Definition</b>	Concept that describes any form of definition of an action plan organized by a person.
<b>Examples</b>	A therapy plan, a chemotherapy treatment etc.
<b>Sub-class Of</b>	<a href="http://www.ifomis.org/acgt/1.0#InformationObject">http://www.ifomis.org/acgt/1.0#InformationObject</a>

**Comment**

<b>URI</b>	<a href="http://www.ifomis.org/acgt/1.0#Comment">http://www.ifomis.org/acgt/1.0#Comment</a>
<b>Definition</b>	Concept that describes any form of commentary in a piece of information.
<b>Examples</b>	Commenting in a publication etc.
<b>Sub-class Of</b>	<a href="http://www.ifomis.org/acgt/1.0#InformationObject">http://www.ifomis.org/acgt/1.0#InformationObject</a>

**MedicalImage**

<b>URI</b>	<a href="http://www.ifomis.org/acgt/1.0#MedicalImage">http://www.ifomis.org/acgt/1.0#MedicalImage</a>
<b>Definition</b>	Concept that denotes that a piece of information is a product of medical imaging (the technique and process used to create images of the human body for clinical purposes).
<b>Sub-class Of</b>	<a href="http://www.ifomis.org/acgt/1.0#Image">http://www.ifomis.org/acgt/1.0#Image</a>

**Publication**

<b>URI</b>	<a href="http://www.ifomis.org/acgt/1.0#Publication">http://www.ifomis.org/acgt/1.0#Publication</a>
------------	---



**Definition** Concept that denotes that particular instance information related to a piece of scientific text. Publication is a technical term in legal contexts. The author of a work generally is the initial owner.

**Sub-class Of** <http://www.ifomis.org/acgt/1.0#InformationObject>

### **Specifically\_dependent\_continuant:**

The most important concept in this category is "Quality". This latter class is a specifically dependent continuant that is exhibited if it inheres in an entity or entities at all (a categorical property) – for example the colour of a tomato or the ambient temperature of air.

#### ***BreastCancerDad***

**URI** <http://hcls.der.iie/l2s/sehr/cing/db/1.0#BreastCancerDad>

**Definition** Concept that denotes whether the father of the subject had a breast incident during his lifetime. It subclasses are declaring what has happened in the past.

**Sub-class Of** <http://www.ifomis.org/bfo/1.1/snap#quality>

#### ***FHisFstOC***

**URI** <http://hcls.der.iie/l2s/sehr/cing/db/1.0#FHisFstOC>

**Definition** First degree female family members with ovarian cancer.

**Sub-class Of** <http://www.ifomis.org/bfo/1.1/snap#quality>

#### ***FHisSecBC***

**URI** <http://hcls.der.iie/l2s/sehr/cing/db/1.0#FHisSecBC>

**Definition** Second degree female family members with ovarian cancer

**Sub-class Of** <http://www.ifomis.org/bfo/1.1/snap#quality>

#### ***BreastCancerMom***

**URI** <http://hcls.der.iie/l2s/sehr/cing/db/1.0#BreastCancerMom>

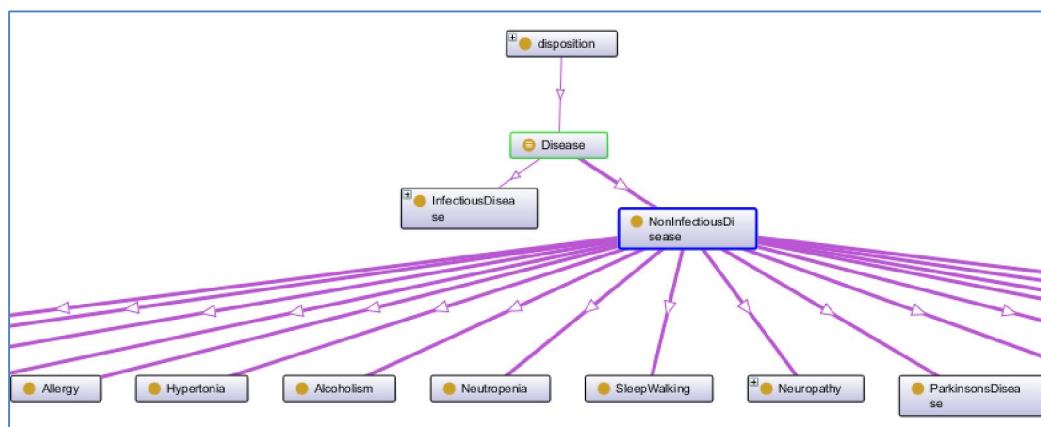
**Definition** Concept that denotes whether the mother of the subject had a breast incident during his lifetime. It subclasses are declaring

what has happened in the past.

**Sub-class Of** <http://www.ifomis.org/bfo/1.1/snap#quality>

## Diseases:

Another important section of concept “Specifically\_dependent\_continuant” are “Diseases”, which is a categorization of medical conditions. The first level breakdown of this concept is two classes: “InfectiousDisease” (diseases that are transferable from one subject/organism to another) and “NonInfectiousDisease” (diseases that are not transferable from one subject/organism to another, such as autoimmune diseases).



**Figure 10:** Break-down of concept “Disease”

### *InfectiousDisease*

**URI** <http://www.ifomis.org/acgt/1.0#InfectiousDisease>

**Definition** Concept that denotes that of disease which are transferable from one organism to another.

**Sub-class Of** <http://www.ifomis.org/acgt/1.0#Disease>

### *NonInfectiousDisease*

**URI** <http://www.ifomis.org/acgt/1.0#NonInfectiousDisease>

**Definition** Concept that denotes that of disease which are not transferable from one organism to another.

**Sub-class Of** <http://www.ifomis.org/acgt/1.0#Disease>

***BacterialInfection***

<b>URI</b>	<a href="http://www.ifomis.org/acgt/1.0#BacterialInfection">http://www.ifomis.org/acgt/1.0#BacterialInfection</a>
<b>Definition</b>	Concept that denotes that of disease which are not transferable from one organism to another, by means of bacterial agents.
<b>Sub-class Of</b>	<a href="http://www.ifomis.org/acgt/1.0#InfectiousDisease">http://www.ifomis.org/acgt/1.0#InfectiousDisease</a>

***ViralInfection***

<b>URI</b>	<a href="http://www.ifomis.org/acgt/1.0#ViralInfection">http://www.ifomis.org/acgt/1.0#ViralInfection</a>
<b>Definition</b>	Concept that denotes that of disease which are not transferable from one organism to another, by means of viral (not bacterial) agents.
<b>Sub-class Of</b>	<a href="http://www.ifomis.org/acgt/1.0#InfectiousDisease">http://www.ifomis.org/acgt/1.0#InfectiousDisease</a>

***HIV***

<b>URI</b>	<a href="http://hcls.der.iie/l2s/sehr/1.0#HIV">http://hcls.der.iie/l2s/sehr/1.0#HIV</a>
<b>Definition</b>	Concept that denotes that of HIV infection.
<b>Sub-class Of</b>	<a href="http://www.ifomis.org/acgt/1.0#ChronicViralInfection">http://www.ifomis.org/acgt/1.0#ChronicViralInfection</a>

***Diabetes***

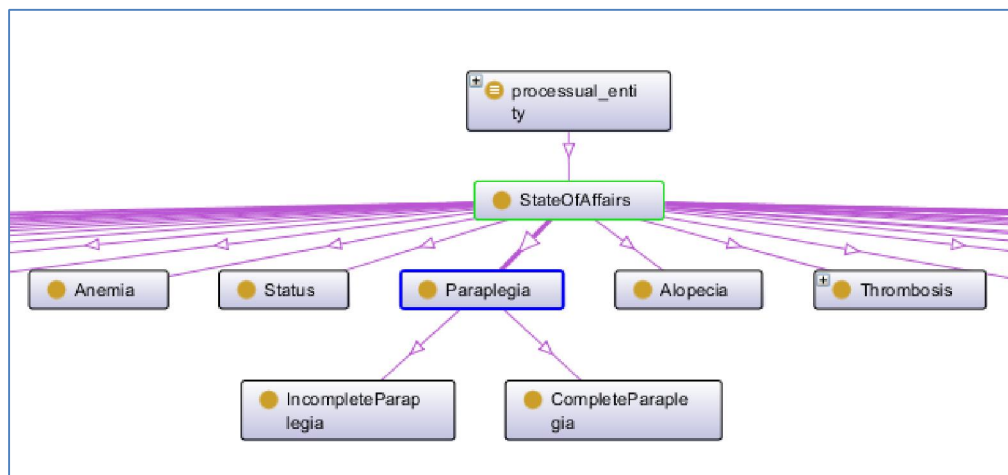
<b>URI</b>	<a href="http://hcls.der.iie/l2s/sehr/1.0#Diabetes">http://hcls.der.iie/l2s/sehr/1.0#Diabetes</a>
<b>Definition</b>	Concept that denotes that of Diabetes-related conditions.
<b>Sub-class Of</b>	<a href="http://www.ifomis.org/acgt/1.0#NonInfectionDisease">http://www.ifomis.org/acgt/1.0#NonInfectionDisease</a>

***Neuropathy***

<b>URI</b>	<a href="http://www.ifomis.org/acgt/1.0#Neuropathy">http://www.ifomis.org/acgt/1.0#Neuropathy</a>
<b>Definition</b>	Concept that denotes that of neuropathic disorders
<b>Sub-class Of</b>	<a href="http://www.ifomis.org/acgt/1.0#NonInfectionDisease">http://www.ifomis.org/acgt/1.0#NonInfectionDisease</a>

**Occurent (Processual\_entity):**

A processual entity is an occurrent that exists in time by occurring or happening, has temporal parts and always involves and depends on some entity for example the life of an organism, the process of meiosis or the course of a disease.



**Figure 11:** "StateOfAffairs" concept and its some of its subclasses

### ***StateOfAffairs***

**URI** <http://www.ifomis.org/acgt/1.0#StateOfAffairs>

**Definition** Concept that denotes the super-class of all symptoms that can occur when a subject (human being) is in a state of physical or psychological distress.

**Sub-class Of** [http://www.ifomis.org/bfo/1.1/span#processual\\_entity](http://www.ifomis.org/bfo/1.1/span#processual_entity)

### ***Alopecia***

**URI** <http://www.ifomis.org/acgt/1.0#Alopecia>

**Definition** Concept related to Alopecia (loss of hair from the head or body)

**Sub-class Of** <http://www.ifomis.org/acgt/1.0#StateOfAffairs>

### ***CardiaMurmur***

**URI** <http://www.ifomis.org/acgt/1.0#CardiacMurmur>

**Definition** Concept related to CardiacMurmur (pathologic heart sounds that are produced as a result of turbulent blood flow that is sufficient to produce audible noise)

**Sub-class Of** <http://www.ifomis.org/acgt/1.0#StateOfAffairs>

## Object Properties:

### *signedBy*

<b>URI</b>	<a href="http://www.ifomis.org/acgt/1.0#signedBy">http://www.ifomis.org/acgt/1.0#signedBy</a>
<b>Definition</b>	Object Property connecting a instance of class "Document" that is signed by an instance of class "HumanBeing"
<b>Domain</b>	<a href="http://www.ifomis.org/acgt/1.0#Document">http://www.ifomis.org/acgt/1.0#Document</a>
<b>Range</b>	<a href="http://www.ifomis.org/acgt/1.0#HumanBeing">http://www.ifomis.org/acgt/1.0#HumanBeing</a>

### *hasTumorClass*

<b>URI</b>	<a href="http://www.ifomis.org/acgt/1.0#hasTumorClass">http://www.ifomis.org/acgt/1.0#hasTumorClass</a>
<b>Definition</b>	Object Property connecting a instance of class "MalignNeoplasm" that is signed by an instance of class "TumorClass"
<b>Domain</b>	<a href="http://www.ifomis.org/acgt/1.0#MalignNeoplasm">http://www.ifomis.org/acgt/1.0#MalignNeoplasm</a>
<b>Range</b>	<a href="http://www.ifomis.org/acgt/1.0#TumorClass">http://www.ifomis.org/acgt/1.0#TumorClass</a>

### *hasDeath*

<b>URI</b>	<a href="http://www.ifomis.org/acgt/1.0#hasDeath">http://www.ifomis.org/acgt/1.0#hasDeath</a>
<b>Definition</b>	Object Property connecting a instance of class "Organism" that is signed by an instance of class "Death"
<b>Domain</b>	<a href="http://www.ifomis.org/acgt/1.0#Organism">http://www.ifomis.org/acgt/1.0#Organism</a>
<b>Range</b>	<a href="http://www.ifomis.org/acgt/1.0#Death">http://www.ifomis.org/acgt/1.0#Death</a>

### *Denies*

<b>URI</b>	<a href="http://www.ifomis.org/acgt/1.0#denies">http://www.ifomis.org/acgt/1.0#denies</a>
<b>Definition</b>	Object Property connecting a instance of class "HumanBeing" that is signed by an instance of class "Consenting"
<b>Domain</b>	<a href="http://www.ifomis.org/acgt/1.0#HumanBeing">http://www.ifomis.org/acgt/1.0#HumanBeing</a>
<b>Range</b>	<a href="http://www.ifomis.org/acgt/1.0#Consenting">http://www.ifomis.org/acgt/1.0#Consenting</a>

## Data Properties:

### *regularExercise*

<b>URI</b>	<a href="http://hcls.der.i.e/l2s/sehr/chuv/1.0#regularExercise">http://hcls.der.i.e/l2s/sehr/chuv/1.0#regularExercise</a>
<b>Definition</b>	Data Property connecting a instance of class "Patient" to a number denoting the regular exercise habits of the subject
<b>Domain</b>	<a href="http://hcls.der.i.e/l2s/sehr/1.0#Patient">http://hcls.der.i.e/l2s/sehr/1.0#Patient</a>
<b>Range</b>	xsd:integer

### *nDRG*

<b>URI</b>	<a href="http://hcls.der.i.e/l2s/sehr/zeincro/Concmed/1.0#nDRG">http://hcls.der.i.e/l2s/sehr/zeincro/Concmed/1.0#nDRG</a>
<b>Definition</b>	Data Property connecting an instance of class "ConcomitantMedication" with a number related to concomitant medication.
<b>Domain</b>	<a href="http://hcls.der.i.e/l2s/sehr/1.0#ConcomitantMedication">http://hcls.der.i.e/l2s/sehr/1.0#ConcomitantMedication</a>
<b>Range</b>	xsd:integer

### *dOSG*

<b>URI</b>	<a href="http://hcls.der.i.e/l2s/sehr/zeincro/Concmed/1.0#dOSG">http://hcls.der.i.e/l2s/sehr/zeincro/Concmed/1.0#dOSG</a>
<b>Definition</b>	Data Property connecting an instance of class "ConcomitantMedication" with date of signature.
<b>Domain</b>	<a href="http://hcls.der.i.e/l2s/sehr/1.0#ConcomitantMedication">http://hcls.der.i.e/l2s/sehr/1.0#ConcomitantMedication</a>
<b>Range</b>	xsd:string

### *ageAtExam*

<b>URI</b>	<a href="http://hcls.der.i.e/l2s/sehr/chuv/1.0#ageAtExam">http://hcls.der.i.e/l2s/sehr/chuv/1.0#ageAtExam</a>
<b>Definition</b>	Date at which psychological interview performed.
<b>Domain</b>	<a href="http://hcls.der.i.e/l2s/sehr/1.0#ConcomitantMedication">http://hcls.der.i.e/l2s/sehr/1.0#ConcomitantMedication</a>
<b>Range</b>	xsd:integer

***FHistFstBCNr***

<b>URI</b>	http://hcls.der.i.e/l2s/sehr/cing/BreastCA/1.0#FHistFstBCNr
<b>Definition</b>	Number of first degree female family members with breast cancer
<b>Domain</b>	http://hcls.der.i.e/l2s/sehr/1.0#HumanBeing
<b>Range</b>	xsd:integer

***FHistSecBCNr***

<b>URI</b>	http://hcls.der.i.e/l2s/sehr/cing/BreastCA/1.0#FHistSecBCNr
<b>Definition</b>	Number of second degree family members with breast cancer
<b>Domain</b>	<a href="http://hcls.der.i.e/l2s/sehr/1.0#HumanBeing">http://hcls.der.i.e/l2s/sehr/1.0#HumanBeing</a>
<b>Range</b>	xsd:integer

**4.4.3 Summary**

In this section we presented the implementation of the basic structure of the Semantic EHR Model. First, we presented the upper layer ontologies and their basic concepts and categorization. We then proceeded on presenting the namespaces we introduced and the classes and the properties that were introduced by the studying of the data variables as they were provided by the clinical partners.

**5. Evaluating the Semantic EHR Model**

Once the implementation of the Linked2Safety Semantic EHR Model has been concluded, an evaluation process is required to validate the accuracy, the completeness, the usability and the understandability of the produced semantic model as well as to provide useful comments and recommendations that will contribute to its general improvement and value. The evaluation process will also review the compliance of the Linked2Safety Semantic EHR Model with the requirements defined in the specification phase (section 3.1) ensuring that they are adequately addressed by the produced model.

The rest of this section is structured as follows: section 5.1 provides the literature background for the current evaluation describing existing approaches and criteria for the ontology and the semantic model evaluation. Section 5.2 presents the methodology followed for the validation of the Linked2Safety Semantic EHR Model. Finally, section 5.3 presents the evaluation results and the amendments made so far.

## 5.1. Evaluation Approaches

Various approaches have been considered in literature for the evaluation of ontologies and semantic models [39-41] depending on the kind of ontology/semantic model is being evaluated and the purpose.

There is no single best or preferred approach to semantic model evaluation; instead, the choice of a suitable approach must depend on the purpose of evaluation, the application in which the semantic model is to be used, and on what aspect of the semantic model we are trying to evaluate. In order to facilitate understanding of evaluation initiatives and select the one that best meets our needs, we adopted a classification provided by Brank et al. [40] which surveys existing initiatives and outlines two sets of criteria based on which semantic model evaluation initiatives can be classified. More specifically, the first classification is based on the type of the approach which is followed by the elicitation activity and the second is based on the object that we are trying to evaluate.

The type of approach is related to the way the evaluation is conducted, specifying the nature of the procedures occurring throughout the evaluation process. Broadly speaking, most evaluation approaches fall into one of the categories described into Table 3, consisting an overview of the “type of approach” criteria.

**Table 3:** Classification of semantic model evaluation initiatives based on the type of approach

Type of approach	Description
<b>Comparison with a standard (“Golden standard”) [42-45]</b>	Syntactic comparison between a semantic model and a standard, which may be another model
<b>Application Based [44, 46, 47]</b>	Use of a semantic model in an application followed by evaluation of the results
<b>Data or corpus driven [48, 49]</b>	Comparison with a data source covered by the proper semantic model
<b>Human assessment and conformity with requirements [50, 51]</b>	Evaluation conducted by people who seek to verify the adherence of a semantic model to criteria and patterns

Further to the above categories of evaluation, we can group the semantic model evaluation approaches based on the level of evaluation or the object of evaluation. A semantic model is a fairly complex structure and it is often more practical to focus on the evaluation of different parts of the structure separately rather than trying to directly evaluate the semantic model as a whole. The individual objects have been defined variously by different authors, but these various definitions tend to be broadly similar. Table 4 presents the objects of evaluation which are usually involved in most semantic model evaluation activities.

**Table 4:** Classification of semantic model evaluation activities based on the object of approach



Object of approach	Description
<b>Lexicon and vocabulary</b> [52, 53]	Emphasizes the handling of concepts and instances and the vocabulary used to identify them
<b>Taxonomy</b> [54, 55]	Emphasizes taxonomic relations (is-a relations)
<b>Semantic relations</b> [44]	Evaluates other relations, which are not taxonomic relations
<b>Context or application</b> [56, 57]	Evaluates semantic models in their context of use and in the context of application of which the semantic model itself is part
<b>Syntax</b> [58]	Evaluates semantic model conformity to syntactical requirements of formal language in which the semantic model was developed
<b>Structure and architecture</b> [51]	Evaluates semantic model conformity to predefined structural requirements

Each type of the evaluation approaches (presented in Table 3) is capable to check some of the evaluation objects (presented in Table 4). Table 5 summarizes which type of evaluation approach is commonly used for which of these evaluation objects.

**Table 5:** Approaches for semantic model evaluation

Object	Type of evaluation approach			
	Golden standard	Application Based	Data or corpus driven	Human assessment and conformity with requirements
<b>Lexicon and vocabulary</b>	✓	✓	✓	✓
<b>Hierarchy, Taxonomy</b>	✓	✓	✓	✓
<b>Semantic relations</b>	✓	✓	✓	✓
<b>Context or application</b>	-	✓	-	✓

<b>Syntax</b>	<input checked="" type="checkbox"/>	-	-	<input checked="" type="checkbox"/>
<b>Structure and architecture</b>	-	-	-	<input checked="" type="checkbox"/>

For the evaluation of the Linked2Safety Semantic EHR Model, the “Golden standard” methodology cannot be used since no standard exists that covers the scope and purpose of the Linked2Safety model. The “Application Based” approach could be used at the maintenance step, once the Linked2Safety platform is complete and evaluation results can be extracted from its use. Therefore, it cannot be used as an evaluation method at this stage where currently no application exists. Furthermore, the “Data or corpus driven” approach has been incorporated in the conceptualization phase of the semantic model creation process where experimental data sets provided by the trial partners have been analyzed to identify and extract concepts and properties. Finally, we conclude that the most appropriate evaluation method at this stage of the semantic model creation process is the “Human assessment and conformity with requirements” approach. As we can see in Table 5, human assessment methodology can take into account all possible objects of evaluation, i.e. Lexicon and vocabulary, Hierarchy, Taxonomy, Semantic relations, Context or application, Syntax and Structure and architecture.

## 5.2. Evaluation Methodology

For evaluating the Linked2Safety Semantic EHR model according to the “Human assessment and conformity with requirements” approach, a series of steps was followed as outlined below:

- ❖ Creation of a separate questionnaire for each trial partner
- ❖ Formation of an expert group that will participate to the evaluation process answering the questionnaires
- ❖ Analysis of the collected data
- ❖ Presentation of the analysis results
- ❖ Refinement of the model based on the analysis results

In order to simplify the evaluation process a questionnaire has been created to check usability and understandability of the model as well as whether it adequately covers data providers’ specific needs. Furthermore, it is important to offer suggestions for improvements through comments and corrections/amendments on the concepts (classes and properties) of the model.

Since each data provider has provided a unique set of variables covering a specific domain (e.g. breast cancer, diabetic, mental disorder, etc.) according to their expertise, they should independently evaluate the respective variables. Therefore, three different questionnaires have been produced to validate data providers’ specific variables (see Appendix A).

The questionnaire includes several questions that have been developed to validate a number of aspects as well as stakeholders’ satisfaction. Specifically, the questionnaire examines the completeness, correctness, usability and the

simplicity of the Linked2Safety Semantic EHR Model. It is separated into two parts:

- ❖ The first part examines the correctness and the completeness of the Linked2Safety Semantic EHR Model in detail. Each section contains questions related to the model's concepts (classes and properties) definition, the subclass hierarchy, the range of the properties and the relations between concepts that exist in the semantic model. Moreover it provides the clinical experts the ability to express any disagreement, detect inconsistencies and weaknesses and propose corrections.
- ❖ The second part examines the usability, the simplicity and the completeness of the model as a whole. In this part, experts are asked to answer a tailored version of the System Usability Scale (SUS) [59] that is proposed by [60] in order to evaluate the understanding and agreement felt according to their general view about the Linked2Safety semantic EHR model. It contains 7 Likert scale questions (stating the degree of agreement or disagreement).

Furthermore, CHUV's data providers were asked to validate the DSM-IV semantic model that was also created for the purposes of the Linked2Safety project.

Meanwhile, the data providers have been asked to decide on the persons to be involved in the evaluation process (to form the expert group) and inform them accordingly. Ideally, these persons should be the ones currently involved in the Linked2Safety requirements analysis (conducted in D1.1) and therefore they will be able to understand whether data sets provided by each data provider are adequately covered by the semantic model. The experts from each trial partner are presented in Table 6.

**Table 6:** Experts group for the evaluation of the Linked2Safety Semantic EHR Model

<b>Interviewee</b>	<b>Partner</b>
Strippoli Marie-Pierre	CHUV
Tozzi Federica	CHUV
Van De Leur Caroline	CHUV
Demetriou Christiana	CING
Kyproula Christodoulou	CING
Kyriacou Kyriacos	CING
Ioannidi Myrto	ZEINCRO
Stavropoulou Thomai	ZEINCRO
Vasiliki Giotaki	ZEINCRO

The questionnaires were circulated to the expert group of each data provider. Overall, we received 9 answered questionnaires, one from each member of the experts' group. Then, the collected responses were analysed, integrated and presented in a perceivable way. Moreover, a documentation table was also created to present the evaluation results including the amendments proposed by the data providers as well as further analysis of what exactly should be corrected or inserted (Section 5.3.1).

The outcomes of the previous analysis have enabled the improvement of the Linked2Safety Semantic EHR Model. In particular, most of the amendments have been already addressed. However, the evaluation will continue to provide feedback during the whole life of the project and additional improvements are going to be included in the Linked2Safety Semantic EHR Model to further address data provider's needs.

### 5.3. Evaluation Results

This section summarizes the results of the Linked2Safety Semantic EHR Model evaluation. In particular, section 5.3.1 reports the amendments that should be adopted by the Linked2Safety Semantic EHR Model based on the examination of the correctness and the completeness of the model. Section 5.3.2 presents how data providers answered the Likert scale questions that examine the understanding and the agreement felt according to their general view about the Linked2Safety semantic EHR model.

#### 5.3.1. Correctness and completeness evaluation

This section presents the results of the correctness and completeness evaluation. The clinical experts generally agreed with the classes and properties of the model but they also proposed changes to definitions, subclass hierarchy as well as addition and deletion of classes and properties. These changes are summarized in Table 7. The majority of these corrections have been already adopted by the Linked2Safety Semantic EHR Model while additional ones are going to be made by data providers during the life of the project.

**Table 7:** Changes based on correctness and completeness evaluation

Change	Description
<b>Changes by CING to Linked2Safety Semantic EHR Model</b>	
Change in the definition of class "cingBreastCA:FHisSecBC"	Remove the word "female" from the definition as it will apply to both sexes. Make it "Second degree <del>female</del> family members with breast cancer"
Change in the definition of class "cingBreastCA:FirstHisFstBC"	Remove the word "female" from the definition as it will apply to both sexes. Make it "First degree <del>female</del> family members with breast cancer"
Change in the definition of class "cingBreastCA:Status"	Make it "Two disease status options, i.e. case, control"
Change in the definition of class "cingBreastCA: SmokingStatus"	Make it "Cigarette smoking, Define three options: never, past, current"

Change in the name of class "cingBreastCA:BreastCancerDadUnavailable"	Make it "cingBreastCA:BreastCancerDadUn <b>available</b> "
Change in the name of class "cingBreastCA:FirstHisFstBCNo"	Make it "cingBreastCA:FirstHisFstBCNo"
Change in the name of class "cingBreastCA:StatusUnavailable"	Make it "cingBreastCA:StatusUnavailable"
Change in the name of class "cingBreastCA:UnavailableInformation"	Make it "cingBreastCA:Unavailable <b>Information</b> "
Change in the hierarchy of class "cingBreastCA:Status"	Class "cingBreastCA:Status" should be a subclass of a class that describes whether a subject is healthy or with the disease of interest (i.e. breast cancer) (Maybe subclass of "acgt:TumorClass" instead of "acgt:StateOfAffairs")
Change in the definition of property "cingBreastCA:breastMos"	Make it "Lifetime duration of breastfeeding <b>in months</b> "
Change in the definition of property "cingBreastCA:FHisFstBCNr"	Make it "Number of first degree <del>female</del> family members with breast cancer"
Change in the definition of property "cingBreastCA:height"	Make it "Adult body height <b>in centimeters</b> "
Change in the definition of property "cingBreastCA:OCMo"	Make it "Lifetime duration of oral contraceptive <b>in months</b> "
Change in the definition of property "cingBreastCA:weight"	Make it "Weight at interview/questionnaire <b>in kilograms</b> "
Change in the range of property "cingBreastCA:mensRsn"	Make the range string "1: natural, 2: surgery – hysterectomy/ovariectomy, 3: other e.g. chemotherapy"
Change in the range of property "cingBreastCA:breastFed"	Make the range "Yes/no"
Change in the range of property "cingBreastCA:parous"	Make the range "Yes/no"
Change in the domain of property "cingBreastCA:Fhscore"	It's not sure if Fhscore has as a domain the class acgt:HumanBeing. This is because a score unit does not always represent a human being. E.g. score=0.5 refers to one second degree relative.
<b>Changes by ZEINCRO to Linked2Safety Semantic EHR Model</b>	
Change in the definition of class "Concmed:ConcomitantMedication"	Make it "A concomitant medication (con-med) is a drug or biological product, other than the study drug, taken by a subject during a clinical trial."
Change in the hierarchy of class "studyAE:AdverseEvent"	The "studyAE:AdverseEvent" is a subclass unintentional event and not Intentional Process. Make it subclass of "acgt:NaturalProcess"
Insert the properties "studyAE:relatcm" and "studyAE: sAEcr"	The properties have definitions "Relationship between Concomitant Medication and AE" and "Seriousness Criteria"
Remove the property "Concmed:dOSG"	This field is of no use and should be removed
Change in the definition of properties 1. "Concmed:contConcomitant" 2. "Concmed:dSTART" 3. "Concmed:indexReason"	Make them 1. "It defines whether the Patient continued to receive the Concomitant Medication at the final visit"

4. "studyAE:cAE" 5. "studyAE:dcMED" 6. "studyAE:randNO" 7. "zeincroMedHistStudyB:BRR" 8. "zeincroMedHistStudyB:CRD" <b>9.</b> "zeincroMedHistStudyB:CRDACT1"	2. "Concomitant Medication Start Date" 3. "Reason for Use" 4. "It defines whether the AE continued in the Last Visit" 5. "It defines whether the patient received Asthma related medication or other Concomitant Medication" 6. "Randomization Number" 7. "Breath Rate (brpmin)" 8. "It defines whether the Patient has any Medical History in Cardiovascular" 9. "It defines whether the Respiratory related Medical History of the Patient is still active"
Remove the properties 1. "zeincroMedHistStudyB:CRDACT2" "zeincroMedHistStudyB:CRDACT3" 2. "zeincroMedHistStudyB:CRDINF2" "zeincroMedHistStudyB:CRDINF3" 3. "zeincroMedHistStudyB:DCRD2" "zeincroMedHistStudyB:DCRD3" 4. "zeincroMedHistStudyB:DHNT2" "zeincroMedHistStudyB:DHNT3" 5. "zeincroMedHistStudyB:DRSP2" "zeincroMedHistStudyB:DRSP3" 6. "zeincroMedHistStudyB:HNTACT2" "zeincroMedHistStudyB:HNTACT3" 7. "zeincroMedHistStudyB:HNTINF2" "zeincroMedHistStudyB:HNTINF3" 8. "zeincroMedHistStudyB:RSPACT2" "zeincroMedHistStudyB:RSPACT3" <b>9.</b> "zeincroMedHistStudyB:RSPINF2" "zeincroMedHistStudyB:RSPINF3"	They are included in: 1. "zeincroMedHistStudyB:CRDACT1" 2. "zeincroMedHistStudyB:CRDINF1" 3. "zeincroMedHistStudyB:DCRD1" 4. "zeincroMedHistStudyB:DHNT1" 5. "zeincroMedHistStudyB:DRSP1" 6. "zeincroMedHistStudyB:HNTACT1" 7. "zeincroMedHistStudyB:HNTINF1" 8. "zeincroMedHistStudyB:RSPACT1" 9. "zeincroMedHistStudyB:RSPINF1"
Change in the name of properties 1. zeincroMedHistStudyB:CRDACT1" 2. "zeincroMedHistStudyB:CRDINF1" 3. "zeincroMedHistStudyB:DCRD1" 4. "zeincroMedHistStudyB:DHNT1" 5. "zeincroMedHistStudyB:DRSP1" 6. "zeincroMedHistStudyB:HNTACT1" 7. "zeincroMedHistStudyB:HNTINF1" 8. "zeincroMedHistStudyB:RSPACT1" 9. "zeincroMedHistStudyB:RSPINF1"	Make them 1. "zeincroMedHistStudyB:CRDACT" 2. "zeincroMedHistStudyB:CRDINF" 3. "zeincroMedHistStudyB:DCRD" 4. "zeincroMedHistStudyB:DHNT" 5. "zeincroMedHistStudyB:DRSP" 6. "zeincroMedHistStudyB:HNTACT" 7. "zeincroMedHistStudyB:HNTINF" 8. "zeincroMedHistStudyB:RSPACT" 9. "zeincroMedHistStudyB:RSPINF"
Change in the definition of properties 1. "zeincroMedHistStudyB:CRDINF1" 2. "zeincroMedHistStudyB:DABDM" 3. "zeincroMedHistStudyB:DCARDV" 4. "zeincroMedHistStudyB:DCRD1" 5. "zeincroMedHistStudyB:DEARS" 6. "zeincroMedHistStudyB:DEYES" 7. "zeincroMedHistStudyB:DGnap" 8. "zeincroMedHistStudyB:DGntr" 9. "zeincroMedHistStudyB:DGST1" 10. "zeincroMedHistStudyB:DHEAD" 11. "zeincroMedHistStudyB:DHNT1" 12. "zeincroMedHistStudyB:DLYMPH"	Make them 1. "More information in case the patient has any cardiovascular related conditions" 2. "Description of abnormal abdomen findings" 3. "Description of abnormal cardiovascular findings" 4. "Onset Date of Cardiovascular Condition" 5. "Description of abnormal ear findings" 6. "Description of abnormal eye findings" 7. "Description of abnormal general appearance findings" 8. "Description of abnormal general

13. "zeincroMedHistStudyB:DNECK"	genitourinary findings"
14. "zeincroMedHistStudyB:DNEUR"	9. "Onset Date of Gastrointestinal related conditions"
15. "zeincroMedHistStudyB:DNOSE"	10. "Description of abnormal head findings"
16. "zeincroMedHistStudyB:DOTHAB"	11. "Onset Date of Head-Ears-Eyes-Nose-Throat (HEENT) related conditions"
17. "zeincroMedHistStudyB:DRSP1"	12. "Description of abnormal general Lymph findings"
18. "zeincroMedHistStudyB:DSKIN"	13. "Description of abnormal general Neck findings"
19. "zeincroMedHistStudyB:EARS"	14. "Description of abnormal general Neurological findings"
20. "zeincroMedHistStudyB:EYES"	15. "Description of abnormal general Nose findings"
21. "zeincroMedHistStudyB:GNAP"	16. "Description of abnormal general Other findings"
22. "zeincroMedHistStudyB:GNTR"	17. "Onset Date of Respiratory related conditions"
23. "zeincroMedHistStudyB:GSTINF1"	18. "Description of abnormal general Skin findings"
24. "zeincroMedHistStudyB:HEAD"	19. "It defines whether the findings in EARS are normal/ abnormal"
25. "zeincroMedHistStudyB:HNT"	20. "It defines whether the findings in EYES are normal/ abnormal"
26. "zeincroMedHistStudyB:HNTACT1"	21. "It defines whether the findings in General Appearance are normal/ abnormal"
27. "zeincroMedHistStudyB:HNTINF1"	22. "It defines whether the findings in Genitourinary are normal/ abnormal"
28. "zeincroMedHistStudyB:LYMPH"	23. "Description of abnormal general gastrointestinal findings"
29. "zeincroMedHistStudyB:NOSE"	24. "It defines whether the findings in Head are normal/ abnormal"
30. "zeincroMedHistStudyB:OTHAB"	25. "It defines whether the patient has any HEENT related conditions"
31. "zeincroMedHistStudyB:OTHST"	26. "It defines whether the HEENT related Medical History of the Patient is still active"
32. "zeincroMedHistStudyB:RSP"	27. "More information in case the patient has any HEENT related conditions"
33. "zeincroMedHistStudyB:RSPACT1"	28. "It defines whether the findings in Lymph are normal/ abnormal"
34. "zeincroMedHistStudyB:RSPINF1"	29. "It defines whether the findings in Nose are normal/ abnormal"
35. "zeincroMedHistStudyB:SKIN"	30. "It defines whether the findings in Other are normal/ abnormal"
36. "zeincroMedHistStudyB:TMP"	31. "More information in case there are findings in Other"
37. "zeincroMedHistStudyC:HEENT"	32. "It defines whether the patient has any Respiratory related conditions"
38. "zeincroMedHistStudyC:HEENT_D1"	33. "It defines whether the Respiratory related Medical History of the Patient is still active"
39. "zeincroMedHistStudyC:INF1_HEENT"	34. "More information in case the patient has any RESPIRATORY related conditions"
40. "zeincroMedHistStudyB:GST"	35. "It defines whether the findings in Skin are normal/ abnormal"
	36. "Temperature"

	<p>37. "It defines whether the patient has any HEENT related Medical Conditions"</p> <p>38. "Onset date of HEENT related conditions"</p> <p>39. "More information in case the patient has any HEENT related conditions"</p> <p>40. "It defines whether the findings in Gastrointestinal are normal/ abnormal"</p>
<p>Insert definitions in properties</p> <ol style="list-style-type: none"> <li>1. "studyAE:aen"</li> <li>2. "studyAE:aeTerm"</li> <li>3. "studyAE:nAE"</li> <li>4. "studyAE:outcum"</li> <li>5. "studyAE:patNo"</li> <li>6. "zeincroMedHistStudyB:ABDM"</li> <li>7. "zeincroMedHistStudyB:DLUNG"</li> <li>8. "zeincroMedHistStudyB:DTHROAT"</li> <li>9. "zeincroMedHistStudyB:EXTR"</li> <li>10. "zeincroMedHistStudyB:LUNG"</li> <li>11. "zeincroMedHistStudyB:MUSC"</li> <li>12. "zeincroMedHistStudyB:NECK"</li> <li>13. "zeincroMedHistStudyB:NEUR"</li> <li>14. "zeincroMedHistStudyB:THROAT"</li> <li>15. "zeincroMedHistStudyB:THYR"</li> </ol>	<p>The definitions are</p> <ol style="list-style-type: none"> <li>1. "A/A of Adverse Event"</li> <li>2. "Type/Term of Adverse Event"</li> <li>3. "It defines whether the patient experiences any AEs"</li> <li>4. "Outcome of AE"</li> <li>5. "Patient Number"</li> <li>6. "It defines whether the findings in Abdominal are normal/ abnormal"</li> <li>7. "Description of Abnormal Lungs"</li> <li>8. "Description of Abnormal Throat"</li> <li>9. "It defines whether the findings in Extremities are normal/ abnormal"</li> <li>10. "It defines whether the findings in Lung are normal/ abnormal"</li> <li>11. "It defines whether the findings in Musculoskeletal are normal/ abnormal"</li> <li>12. "It defines whether the findings in Neck are normal/ abnormal"</li> <li>13. "It defines whether the findings in Neurological are normal/ abnormal"</li> <li>14. "It defines whether the findings in Throat are normal/ abnormal"</li> <li>15. "It defines whether the findings in Thyroid are normal/ abnormal"</li> </ol>
Change in the range of properties "Concmed:nDRG"	It receives an integer value corresponding to a numbered list of drugs
Change in the range of property "studyAE:cae", "studyAE:nAE" and "studyAE:saE"	It receives an integer value among "0" and "1" corresponding to "yes" and "no" respectively
Change in the range of property "studyAE:confr"	It receives an integer value corresponding to a numbered list of actions
Change in the range of property "studyAE:dstAE", "Concmed:dOSG", "Concmed:dSTART", "studyAE:dfAE"	Make the range "date"
Change in the range of property "studyAE:outcum"	It receives an integer value corresponding to a numbered list of outcomes
Change in the range of property "studyAE:sAEcr"	It receives an integer value corresponding to a numbered list of seriousness criteria. In particular: 1) patient died, 2) Life-threatening, 3) Involved persistence of significant disability or significant disability or incapacity, 4) Involved or prolonged inpatient hospitalization, 5) Congenital anomaly, 6) Important medical event
Change in the range of property "studyAE:sevr"	It receives an integer value corresponding to a numbered list of severity conditions



Change in the range of property "zeincroMedHistStudyB:TMP"	Temperature values can also contain decimals
Change in the range of properties 1. "zeincroMedHistStudyB:ABDM" 2. "zeincroMedHistStudyB:CARDV" 3. "zeincroMedHistStudyB:EARS" 4. "zeincroMedHistStudyB:EXTR" 5. "zeincroMedHistStudyB:EYES" 6. "zeincroMedHistStudyB:GNAP" 7. "zeincroMedHistStudyB:GNTR" 8. "zeincroMedHistStudyB:HEAD" 9. "zeincroMedHistStudyB:LUNG" 10. "zeincroMedHistStudyB:LYMPH" 11. "zeincroMedHistStudyB:MUSC" 12. "zeincroMedHistStudyB:NECK" 13. "zeincroMedHistStudyB:NEUR", 14. "zeincroMedHistStudyB:NOSE" 15. "zeincroMedHistStudyB:OTHAB" 16. "zeincroMedHistStudyB:SKIN" 17. "zeincroMedHistStudyB:THROAT" 18. "zeincroMedHistStudyB:THYR"	They receive an integer value among "0", "1" and "3" corresponding to "Normal", "Abnormal", and "NOT DONE" respectively
Change in the range of properties 1. "zeincroMedHistStudyB:CRD" 2. "zeincroMedHistStudyB:CRDACT1" 3. "zeincroMedHistStudyB:CRDACT2" 4. "zeincroMedHistStudyB:CRDACT3" 5. "zeincroMedHistStudyB:DGST1" 6. "zeincroMedHistStudyB:GST" 7. "zeincroMedHistStudyB:HNT" 8. "zeincroMedHistStudyB:HNTACT1" 9. "zeincroMedHistStudyB:HNTACT2" 10. "zeincroMedHistStudyB:HNTACT3" 11. "zeincroMedHistStudyB:RSP", 12. "zeincroMedHistStudyB:RSPACT1" 13. "zeincroMedHistStudyB:RSPACT2" 14. "zeincroMedHistStudyB:RSPACT3" 15. "zeincroMedHistStudyC:HEENT" 16. "Concmed:contConcomitant"	They receives an integer value among "0", "1" and "99" corresponding to "Normal", "Abnormal", and "N/A" respectively
Change in the range of property "Concmed:indexReason"	Make the range "string"
Change in the range of property studyAE:dcMED	It receives an integer value corresponding to "ASTHMA CONCOM.MED.", "OTHER CONCOM.MED.", and "NA"
Change in the domain of property "Concmed:medication"	Remove class "acgt:Patient" from the domain of property "Concmed:medication"
Change in the domain of property "studyAE:randNO"	Include class "acgt:Patient" in the domain of property "studyAE:randNO"
<b>Changes by CHUV to DSM-IV</b>	
Change in the definition of classes 1. DSM_314.00" 2. "DSM_314.01" 3. "DSM_312.81" 4. "DSM_312.82"	Make them 1. "Attention Deficit Hyperactivity Disorder (ADHD), Predominantly Inattentive Subtype" 2. "ADHD Combined Subtype or ADHD"

5. "DSM_300.4" 6. "DSM_295.70" 7. "DSM_301.20" 8. "DSM_305.60"	Predominantly hyperactive-impulsive Subtype" 3. "Conduct Disorder, Childhood Onset Type (before age 10)" 4. "Conduct Disorder, Adolescent Onset Type (after age 10)" 5. "Dysthymic disorder" 6. "Schizo-affective disorder (including both subtypes: bipolar and depressive)" 7. "Schizoid personality" 8. "Cocaine Abuse"
<p style="text-align: center;">Insert the classes</p> 1. "DSM_305.70" 2. "DSM_304.40" 3. "DSM_305.30" 4. "DSM_304.50" 5. "DSM_305.40" 6. "DSM_304.10" 7. "DSM_305.50" 8. "DSM_304.00" 9. "DSM_305.90" 10. "DSM_304.60" 11. "DSM_296.40" 12. "DSM_296.7" 13. "DSM_296.xx" 14. "DSM_307.50" 15. "DSM_312.30" 16. "DSM_314.9" 17. "DSM_301.83" 18. "DSM_301.50" 19. "DSM_301.81" 20. "DSM_301.6" 21. "DSM_301.4" 22. "DSM_295.40" 23. "DSM_297.10" 24. "DSM_298.8" 25. "DSM_295.30" 26. "DSM_295.10" 27. "DSM_295.20" 28. "DSM_295.90" 29. "DSM_295.60"	The definitions of classes are 1. "Stimulant abuse" 2. "Stimulant dependence" 3. "Hallucinogene abuse" 4. "Hallucinogene dependence" 5. "Sedative abuse" 6. "Sedative dependence" 7. "Narcotic abuse" 8. "Narcotic dependence" 9. "Solvent abuse" 10. "Solvent dependence" 11. "Bipolar I Disorder Most Recent Episode Hypomanic" 12. "Bipolar I Disorder, Most recent episode Unspecified" 13. "has definition "Bipolar Disorder I" 14. "Eating Disorder NOS" 15. "Impulse-Control Disorder NOS" 16. "ADHD NOS" 17. "Borderline Personality Disorder" 18. "Histrionic Personality Disorder" 19. "Narcissistic Personality Disorder" 20. "Dependent Personality Disorder" 21. "Obsessive-Compulsive Personality Disorder" 22. "Schizophreniform disorder" 23. "Delusional disorder" 24. "Brief psychotic" 25. "Paranoid type" 26. "Disorganized type" 27. "Catatonic type" 28. "NOS" 29. "Residual type"
Remove the classes DSM_296.56, DSM_296.46, DSM_296.66, DSM_296.06, DSM_296.89, DSM_296.36, DSM_296.26	
Change in the name of class "Bipolar_I_disorder_episode_depressed"	Make the name of the class "DSM_295.5x" with definition "Bipolar I Disorder, Most Recent Episode Depressed"
Change in the name of class "Bipolar_I_disorder_episode_manic_"	Make the name of the class "DSM_296.4x" with definition "Bipolar I Disorder Most Recent Episode Manic"

Change in the name of class "Bipolar_I_disorder_episode_mixed_"	Make the name of the class "DSM_296.6x" with definition "Bipolar I Disorder Most Recent Episode Mixed"
Change in the name of class "Bipolar_I_Disorder_single_manic"	Make the name of the class "DSM_296.0x" with definition "Bipolar I Disorder Single Manic Episode"
Change in the name of class "Bipolar_II_Disorder"	Make the name of the class "DSM_296.89" with definition "Bipolar Disorder II"
Insert the class "Major depressive disorder" and "Suicide attempts"	
Change in the name of class "MajorDepressiveDisorder_Recurrent"	Make the name of the class "DSM 296.3x" with definition "Major depressive disorder, recurrent"
Change in the name of class "MajorDepressiveDisorder_Single"	Make the name of the class "DSM 296.2x" with definition "Major depressive disorder, single episode "
Insert the class "PsychiatricDisorders"	Make it subclass of "acgt:StateOfAffairs" with 2 subclasses: 1) DSM-IV (imported model) 2) Suicide attempts
Change in the definition of class "DSM_307.1"	Make it "Anorexia nervosa"
Change in the definition of class "DSM_307.51"	Make it "Bulimia nervosa"
Change the name of the classes 1. "Current" 2. "LifeTime" 3. "Worst" 4. "ClusterA" 5. "ClusterB" 6. "ClusterC"	Make them 1. "GAF_Current" 2. "GAF_LifeTime" 3. "GAF_Worst" 4. "Personality_ClusterA" 5. "Personality_ClusterB" 6. "Personality_ClusterC"
Change in the subclasses of class "EatingDisorders"	Include also the class "DSM_307.50"
Change in the subclasses of class "ImpulseControlDisorders"	Include also the class "DSM_312.30"
Change in the subclasses of class "MoodDisorders"	Class "MoodDisorders" has 2 subclasses: "DepressiveDisorders" and "BipolarDisorders"
Change in the subclasses of class "BipolarDisorders"	Class "BipolarDisorders" has 3 subclasses: "DSM_296.xx", "DSM_296.89" and "DSM_296.80"
Change in the subclasses of class "DSM_296.xx"	Class "DSM_296.xx" has 5 subclasses: "DSM_296.5x", "DSM_296.40", "DSM_296.4x", "DSM_296.6x", "DSM_296.0x", and "DSM_296.7" and
Change in the subclasses of class "AttentionDeficit_HyperactivityDisorder"	A new subclass should be added which will have the same code "DSM_314.01" but a different definition. At the end, class "AttentionDeficit_HyperactivityDisorder" will have 3 subclasses: "DSM_314.00", "DSM_314.01", "DSM_314.01" and "DSM_314.9"
Change in the subclasses of class "DepressiveDisorders"	The class "DepressiveDisorders" has 2 subclasses: "Major depressive disorder"

	and "DSM_300.4"
Change in the subclasses of class "Major depressive disorder"	The class "Major depressive disorder" has 2 subclasses: "DSM_296.2x" and "DSM_296.3x"
Change in the subclasses of class "ClusterA"	The class "ClusterA" has 3 subclasses: "DSM_301.0", "DSM_301.20", and "DSM_301.22"
Change in the subclasses of class "ClusterB"	The class "ClusterB" has 4 subclasses: "DSM_301.7", "DSM_301.83", "DSM_301.50", and "DSM_301.81"
Change in the subclasses of class "ClusterC"	The class "ClusterC" has 3 subclasses: "DSM_301.82", "DSM_301.6" and "DSM_301.4"
Insert the class Schizophrenia	
Change in the name of class "SchizophreniaDisorder»	Make it "PsychoticDisorders"
Change in the subclasses of class "PsychoticDisorders"	Class "PsychoticDisorder" has 5 subclasses: "Schizophrenia", "DSM_295.40", "DSM_295.70", "DSM_297.10", and "DSM_298.8"
Change in the subclasses of class "Schizophrenia"	Class "Schizophrenia" has 5 subclasses: "DSM_295.30", "DSM_295.10", "DSM_295.20", "DSM_295.90" and "DSM_295.60"
Insert the classes "Stimulant", "Hallucinogene", "Sedative", "Narcotic", and "Solvent"	
Change in the subclasses of class "Drug"	Class "Drug" has 6 subclasses: "Stimulant", "Hallucinogene", "Sedative", "Narcotic", and "Solvent" (where each has 2 subclasses: Abuse /Dependence)
Change in the definition of property "Axis-I"	Make it "Clinical disorders, including major mental disorders, learning disorders and substance use disorders"
Change in the definition of property "Axis-II"	Make it "Personality disorders and intellectual disabilities (although developmental disorders, such as Autism, were coded on Axis II in the previous edition, these disorders are now included on Axis I)"
Change in the definition of property "Axis-III"	Make it "Acute medical conditions and physical disorders"
Change in the definition of property "Axis-IV"	Make it "Psychosocial and environmental factors contributing to the disorder"
Change in the definition of property "Axis-V"	Make it "Global Assessment of Functioning or Children's Global Assessment Scale for children and teens under the age of 18"
<b>Changes by CHUV to Linked2Safety Semantic EHR Model</b>	
Change in the definition of class "chuv:Enuresis"	Make it "Enuresis refers to a repeated inability to control urination (Childhood onset problems)"
Change in the definition of class "chuv:LateMotorDevelopment"	Make it "Motor skills are the abilities usually acquired during infancy and early

	childhood as part of a child's motor development. By the time child reach two years of age, almost all children are able to stand up, walk and run, walk up stairs, etc (Childhood onset problems)"
Change in the definition of class "chuv:Somnambulism"	Make it "Sleep-walking (Childhood onset problems)"
Change the name of class "chuv:AntiparkinsonsDrug"	Make it "chuv:AntipsychoticDrug"
Remove the "class chuv:ATP3"	
Remove the class "chuv:SleepWalking"	It is the same with "chuv:Somnambulism"
<p>Add a definition in classes</p> <ol style="list-style-type: none"> <li>1. "chuv:AuditiveDisorder"</li> <li>2. "chuv:Dyslipidemia"</li> <li>3. "MetabolicSyndrome"</li> <li>4. "chuv:MigraineCumulative"</li> <li>5. "chuv:Nightmare"</li> <li>6. "chuv:BMI (Body mass index)"</li> <li>7. "chuv:SpeechDisorder"</li> <li>8. "chuv:Stuttering"</li> <li>9. "chuv:Ticks"</li> <li>10. "chuv:VisualDisorder"</li> <li>11. "chuv:Hypertension"</li> <li>12. "chuv:Diabetes"</li> <li>13. "chuv:Hyperthymia"</li> <li>14. "chuv:OveranxiousDisorder"</li> <li>15. "chuv:activityType"</li> <li>16. "chuv:ageAtExam"</li> <li>17. "chuv:ageAtInterview"</li> <li>18. "chuv:everSmoking"</li> <li>19. "chuv:firstConsultationAge"</li> <li>20. "chuv:regularExercise"</li> </ol>	<p>The definitions are</p> <ol style="list-style-type: none"> <li>1. "Childhood onset problems"</li> <li>2. "HDL-cholesterol &lt; 1 mmol/l or triglycerides ≥ 2 mmol/l or LDL-cholesterol ≥ 4.1 mmol/l or treatment"</li> <li>3. "ATP III are the criteria used for the definition. According to ATP III (at least 3 criteria of 5)"</li> <li>4. "With or without aura according to International Headache Society"</li> <li>5. "Childhood onset problems"</li> <li>6. "Overweight (BMI ≥ 25 kg/m<sup>2</sup> &lt;30); obese (BMI ≥ 30 kg/m<sup>2</sup>)"</li> <li>7. "Childhood onset problems"</li> <li>8. "Childhood onset problems"</li> <li>9. "Childhood onset problems"</li> <li>10. "Childhood onset problems"</li> <li>11. "Systolic blood pressure ≥ 140 or diastolic ≥90 or treatment"</li> <li>12. "Fasting blood glucose ≥ 7mmol/l or treatment"</li> <li>13. "According to Research diagnostic criteria"</li> <li>14. "According to DSM-III"</li> <li>15. "Types of physical exercise (walking, see CHUV codebook)"</li> <li>16. "Age at somatic exam"</li> <li>17. "Age at psychiatric interview"</li> <li>18. "Have you ever smoked in your lifetime"</li> <li>19. "Age first psychiatric consultation"</li> <li>20. "At least once per week"</li> </ol>
Change the name of class "chuv:Metabolic"	Make it "chuv:MetabolicSyndrome"
Change the name of class "chuv:OverWeight"	Make it "chuv:BMI (Body mass index)"
Change in the hierarchy of class "chuv:MigraineCumulative"	Class "chuv:MigraineCumulative" has two subclasses "chuv:Migrainewithaura" and "chuv:Migrainewithoutaura"
<p>Insert the classes :</p> <ol style="list-style-type: none"> <li>1. chuv:Hypertension</li> <li>2. chuv:Diabetes</li> <li>3. chuv:Diabetes_Type_I</li> <li>4. chuv:Diabetes_Type_II</li> <li>5. chuv:Anemia</li> </ol>	

6. chuv:Cancer 7. chuv:AIDS 8. chuv:Epilepsy 9. chuv:LungDisorder 10. chuv:UrinaryProblems 11. chuv:AllergiesToMedication 12. chuv:HormonalProblems 13. chuv:SkinProblems 14. chuv:Hyperthymia 15. chuv:OveranxiousDisorder 16. chuv:NumberOfPregnancies 17. chuv:EmotionalProblemsDuringPregnan cy 18. chuv:ChangingMoodduringPregnancy 19. chuv:Menopause 20. chuv:EmotionalProblemsLinkedToMeno pause	
Remove the properties 1. "chuv:Ethnicity" 2. "chuv:nationalit" 3. "chuv:AntidepressantOther" 4. "chuv:AntimanicsOther" 5. "chuv:AntiparkinsonsDescription" 6. "chuv:AntipsychoticsOther" 7. "chuv:SedativeDescription"	
Insert property "chuv:gender" Change the range of properties 1. chuv:activityType 2. chuv:AntidepressantExtrapyramidalSid eEffects 3. chuv:AntidepressantGastrointestinalSy mptoms 4. chuv:AntidepressantHeadaches 5. chuv:AntidepressantSexualSymptoms 6. chuv:AntidepressantSleepProblems 7. chuv:AntiDepressantWeightGain 8. chuv:AntidepressantWeightLoss 9. chuv:AntimanicsGastrointestinalsympt oms 10. chuv:AntimanicsHairLoss 11. chuv:AntimanicsHeadaches 12. chuv:AntimanicsSleepProblems 13. chuv:AntimanicsTremblings 14. chuv:AntimanicsWeightGain 15. chuv:AntimanicsWeightLoss 16. chuv:AntiparkisonsSideEffects 17. chuv:AntipsychoticsExtrapyramidalSide Effects 18. chuv:AntipsychoticsMetabolicSyndroms 19. chuv:AntipsychoticsProlactinSymptoms 20. chuv:AntipsychoticsSexualSymptoms 21. chuv:AntipsychoticsSleepProblems 22. chuv:AntipsychoticsWeightGain 23. chuv:AntipsychoticsWeightLoss 24. chuv:SedativeSideEffects	From string to integer

Change the relation between the class "acgt:Patient" and the properties "chuv:everSmoking", "chuv:firstConsultationAge", and "chuv:regularExercise"	They are not patient characteristics
Include "chuv:gender" to "acgt:Patient" properties	The "chuv:gender" is a patient characteristic
Change in the hierarchy of class "chuv:MigraineCumulative"	Make it subclass of "acgt:StateOfAffairs"
Change in the hierarchy of class "chuv:MetabolicSyndrome"	Make it subclass of StateOfAffairs
Insert a class "chuv:CardiacDisease" in "acgt:StateOfAffairs"	Make the classes "chuv:CoronaryHeartDisease", "chuv:MyocardialInfarction", and "chuv:Stroke" subclasses of "chuv:CardiacDisease"
Insert a class "chuv:PerceptiveDisorders" in "acgt:StateOfAffairs"	Make the classes "chuv:VisualDisorder" and "chuv:AuditiveDisorder" subclasses of "chuv:PerceptiveDisorders"
Insert a class "chuv:SleepDisorders" in "acgt:StateOfAffairs"	Make the classes "chuv:Somnambulism" and "chuv:Nightmare" subclasses of "chuv:SleepDisorders"
Change in the definition of class "chuv:HuntingtonsDisease"	Make it "Huntington's disease is an inherited disease that causes the progressive breakdown (degeneration) of nerve cells in the brain. Huntington's disease usually causes movement, cognitive and psychiatric disorders with a wide spectrum of signs and symptoms"

### 5.3.2. Usability evaluation

This section presents the results of the usability evaluation (Table 8). The majority of the clinical experts (33,33% agreement and 33,33% high agreement) declared that they could contribute to the semantic model (Question 1). Most of the clinical experts found the ontology not so easy to understand (Question 2). This is also validated by the fact that several improvements were provided by data providers in the definition of concepts (classes and properties) in order to be clearer. Moreover, most of the experts understand the conceptualization (Question 6) of the semantic model (55.55% agreement and 33.33% indifferent). Regarding Question 3, the answers vary, but most of the users (11.11% high disagreement, 66.66% indifferent and 22.22% high agreement) will need further theoretical support to be able to understand the semantic model. The same conclusion derives also from Question 5, where most of the users agreed that the clinical experts could not easily understand the semantic model (33,33% high disagreement, 22,22% disagreement, 33,33% indifferent, 11,11% agreement). Finally, assuming the completeness (Question 7) and integration (Question 4) of the semantic model most of the users found the concepts of the semantic model well integrated (66,66% indifferent and 33,33% agreement) and they believe that the semantic model covers the needs of the clinical domain (44,44% indifferent, 44,44% agreement, 11,11% high agreement).

**Table 8:** Usability evaluation

N	Question	High disagree	Disagree ment	Indiffe rent	Agree ment	High agree
1	I think that I could contribute to this semantic model	0	11,11	22,22	33,33	33,33
2	I find the semantic model easy to understand	33,33	22,22	44,44	0	0
3	I think that I would need further theoretical support to be able to understand this semantic model	11,11	0	66,66	0	22,22
4	I found that the various concepts in this semantic model were well integrated	0	0	66,66	33,33	0
5	I would imagine that most clinical experts would understand this semantic model very quickly	33,33	22,22	33,33	11,11	0
6	I am confident that I understand the conceptualization of the semantic model	0	11,11	33,33	55,55	0
7	The concepts/properties of the semantic model cover the needs of the clinical trial domain.	0	0	44,44	44,44	11,11
	TOTALS	8,64	7,40	34,56	19,75	7,40

To sum up, data providers faced some difficulties understanding the model due to lack of technical background. However during additional improvements in model definitions, it has become clear that with guidance from the developers' side data providers can understand the model as well as provide clear instructions for its effective development. Nonetheless, the whole evaluation process brought forth additional improvements that increased model's effectiveness and contributed to its general improvement and value.

## 6. Conclusion

This deliverable D1.4 defines, designs, implements and evaluates the Linked2Safety Semantic EHR Model, which is the core conceptual model on which the semantically-interlinked Linked2Safety platform will be built. The deliverable first presents the Linked2Safety design and development methodology for building the Semantic EHR Model. Additionally, one of the clinical partner's involvements in the psychiatric cases motivated us to build the DSM-IV ontology. The Semantic EHR Model and DSM-IV ontology will be used in semantically-enriching the heterogeneous data cubes originating from various clinical partners. Second, the deliverable provides the implementation details describing the classes, properties, and axioms used within the Semantic EHR Model. The model will contribute to the realisation of the Linked2Safety vision by carrying the required semantics in WP3 and 4. Specifically the Semantic EHR Model will be utilized in:



- ❖ WP3: In the semantic enrichment of heterogeneous and distributed data-cubes from various clinical partners.
- ❖ WP4: In the semantic-interlinking, sharing of consistent terminologies and act as a common conceptual framework for the Linked Medical Data Space.

Third, the deliverable provides the evaluation of the Semantic EHR Model in terms of completeness and correctness of the classes, properties, and axioms described within the Semantic EHR Model and DSM-IV ontology.

Finally, maintenance of the Semantic EHR Model and DSM-IV ontology is a continuous process that will be carried throughout the Linked2Safety project. Therefore, any future upgrade suggested by the Linked2Safety consortium members will update (add/remove concepts/properties, change definitions etc) both the ontologies.

## 7. References

- [1] D. F. D'Souza and A. C. Wills, "Objects, Components, and Frameworks with UML: The Catalysis Approach," R. Addison-Wesley, Mass., Ed., 1998.
- [2] S. A. Petersen, F. Lillehagen, and M. Anastasiou, "Modelling and Visualisation for Interoperability Requirements Elicitation and Validation," *Enterprise Information Systems, Lecture Notes in Business Information Processing*, vol. 3, pp. 241-253, 2008.
- [3] A. Dogac, G. Laleci, S. Kirbas, Y. Kabak, S. Sinir, and Yildiz A. et al., "Artemis: deploying semantically enriched web services in the healthcare domain," *Information Systems Journal*, vol. 31, pp. 321-339, 2006.
- [4] I. Iakovidis, "Towards personal health record: current situation, obstacles and trends in implementation of electronic healthcare record in Europe," *International Journal of Medical Informatics*, vol. 52, pp. 105-117, 1998.
- [5] A. Dobrev, K. A. Stroetmann, V. N. Stroetmann, J. Artmann, T. Jones, and R. Hammerschmidt, "Report on the conceptual framework of interoperable electronic health record and ePrescribing systems," *EHR Impact project, Deliverable D1.2*, 2008.
- [6] M. Tsiknakis, D. Kafetzopoulos, G. Potamias, A. Analyti, K. Marias, and A. Manganas, "Building a European biomedical grid on cancer: the ACGT Integrated Project," *Studies in Health Technology and Informatics*, vol. 120, pp. 247-258, 2006.
- [7] P. Mitkas, V. Koutkias, and Symeonidis A. et al., "Association studies on cervical cancer facilitated by inference and semantic technologies: the ASSIST approach," *Studies in Health Technology and Informatics*, vol. 136, pp. 241-246, 2008.
- [8] V. Andronikou, E. Karanastasis, E. Chondrogiannis, K. Tserpes, and T. Varvarigou, "Semantically-enabled Intelligent Patient Recruitment in Clinical Trials," in *Proceedings of the 2010 International Conference on P2P, Parallel, Grid, Cloud and Internet Computing (3PGCIC '10)* Washington, DC, USA, 2010, pp. 326-331.
- [9] G. B. Laleci, M. Yuksel, and A. Dogac, *Submitted for publication to IEEE Transactions on Information Technology in Biomedicine*, Providing Semantic Interoperability between Clinical Care and Clinical Research Domains.
- [10] E. Della Valle, D. Cerizza, I. Celino, L. Gadda, and A. Savoldelli, "The COCOON project," in *Demos and Posters of the 2nd European Semantic Web Conference (ESWC 2005)* Heraklion, Greece, 2005.
- [11] V. Koutkias, V. Kilintzis, G. Stalidis, K. Lazou, J. Niès, L. Durand-Texte, P. McNair, R. Beuscart, and N. Maglaveras, "Knowledge engineering for adverse drug event prevention: On the design and development of a uniform, contextualized and sustainable knowledge-based framework," *Journal of Biomedical Informatics*, 2012.
- [12] G. Jiang, H. R. Solbrig, and C. G. Chute, "ADEpedia: a scalable and standardized knowledge base of Advers [1]e Drug Events using semantic web technology," *AMIA Annual Symposium Proceedings*, 2011.
- [13] M. Uschold, "Building Ontologies: Towards a Unified Methodology," in 16th Annual Conference of the British Computer Society Specialist Group on Expert Systems, 1996, pp. 16-18.
- [14] M. Fernandez-Lopez, A. Gomez-Perez, and N. Juristo, "Methontology: from ontological art towards ontological engineering," in *Proceeding Symposium on Ontological Engineering of AAAI*, 1997.

- [15] S. Staab, R. Studer, H.-P. Schnurr, and Y. Sure, "Knowledge Processes and Ontologies," IEEE Intelligent Systems, vol. 16, pp. 26-34, January 2001.
- [16] H. S. Pinto, S. Staab, and C. Tempich, "DILIGENT: Towards a fine-grained methodology for Distributed, Loosely-controlled and Evolving Engineering of Ontologies," in 16th European Conference on AI (ECAI). IOS Press, 2004, pp. 393-397.
- [17] M. Eichelberg, "Requirements Analysis for the RIDE Roadmap," Tech. Rep., Dec. 2007, Deliverable D2.3.1. [Online]. Available: <http://www.srdc.metu.edu.tr/webpage/projects/ride/deliverables/RIDE-D2.3.1-2006-10-13final.pdf>
- [18] A. Dogac, "Vision for a Europe-wide Semantically Interoperable eHealth Infrastructure," Tech. Rep., Dec. 2007, Deliverable D3.2.1. [Online]. Available: <http://www.srdc.metu.edu.tr/webpage/projects/ride/deliverables/RIDED321Vision-v1.5final.doc>
- [19] R. Sahay, W. Akhtar, and R. Fox, "Semantic Service-oriented Design and Development Methodology for Enterprise Healthcare Integration," in WEBIST 2009 - Proceedings of the Fifth International Conference on Web Information Systems and Technologies, Lisbon, Portugal, March 23-26. INSTICC Press, 2009.
- [20] R. Sahay, R. Fox, A. Zimmermann, A. Polleres, and M. Hauswirth, "A Methodological Approach for Ontologising and Aligning Health Level Seven (HL7) Applications," in ARES 2011- Proceedings of the Availability, Reliability and Security for Business, Enterprise and Health Information Systems, Vienna, Austria, August 22-26. Springer LNCS Series, 2011, pp. 102-117.
- [21] A. G´omez-P´erez, O. Corcho, and M. F. L´opez, Ontological Engineering : with examples from the areas of Knowledge Management, e-Commerce and the Semantic Web. First Edition (Advanced Information and Knowledge Processing). Springer, Jul. 2004.
- [22] M. Fern´andez-L´opez and A. G´omez-P´erez, "Overview and analysis of methodologies for building ontologies," Knowledge Engineering Review, 2002.
- [23] M. F. L´opez, A. G´omez-P´erez, and M. D. R. Amaya, "Ontology's Crossed Life Cycles," in Proceedings of the 12th European Workshop on Knowledge Acquisition, Modeling and Man-agement, ser. EKAW '00. London, UK: Springer-Verlag, 2000, pp. 65-79.
- [24] E. Simperl, "Reusing ontologies on the Semantic Web: A feasibility study," Data Knowledge Engineering, vol. 68, pp. 905-925, October 2009.
- [25] D. Lindberg, B. Humphreys, and A. McCray, "The Unified Medical Language System," Methods of Information in Medicine, vol. 32, no. 4, pp. 281-291, 1993.
- [26] B. C. Grau, I. Horrocks, Y. Kazakov, and U. Sattler, "Just the right amount: extracting modules from ontologies," in Proceedings of the 16th International Conference on World Wide Web, ser. WWW07. New York, NY, USA: ACM, 2007, pp. 717-726.

- [27] V. Presutti and A. Gangemi, "Content Ontology Design Patterns as Practical Building Blocks for Web Ontologies," in Proceedings of the 27th International Conference on Conceptual Modeling, ser. ER '08. Berlin, Heidelberg: Springer-Verlag, 2008, pp. 128–141.
- [28] A. J. Yepes, E. J. Ruiz, R. B. Llavori, and D. R. Schuhmann, "Reuse of terminological resources for efficient ontological engineering in Life Sciences," BMC Bioinformatics, vol. 10, no. 10, pp. S4+, 2009.
- [29] O. Corcho, M. Fernández-López, and A. Gómez-Pérez, "Methodologies, tools and languages for building ontologies: where is their meeting point?" Data Knowledge Engineering, vol. 46, pp. 41–64, July 2003.
- [30] D. B. Lenat and R. V. Guha, Building Large Knowledge-Based Systems; Representation and Inference in the Cyc Project, 1st ed. Boston, MA, USA: Addison-Wesley Longman Publishing Co., Inc., 1990.
- [31] M. Uschold and M. King, "Towards a Methodology for Building Ontologies," in In Workshop on Basic Ontological Issues in Knowledge Sharing, held in conjunction with IJCAI-95, 1995.
- [32] M. Fernández-López and A. Gómez-Pérez, "Towards a method to conceptualize domain ontologies," in Proceedings of the ECAI Workshop on Ontological Engineering, 1997.
- [33] M. Uschold, "Building Ontologies: Towards a Unified Methodology," in 16th Annual Conference of the British Computer Society Specialist Group on Expert Systems, 1996, pp. 16–18.
- [34] M. Fernández-López, A. Gómez-Pérez, and N. Juristo, "Methontology: from ontological art to-wards ontological engineering," in Proceeding Symposium on Ontological Engineering of AAAI, 1997.
- [35] S. Kande, N. Jain, T. Briks-Fader, and K. Witting, "IHE IT Infrastructure Technical Framework," Tech. Rep., Jul. 2005, Volume I-II, Revision 2.0. [Online]. Available: [http://www.ihe.net/TechnicalFramework/upload/IHEITI\\_Suppl\\_HPDP\\_Rev1-1\\_TI\\_2010-08-10.pdf](http://www.ihe.net/TechnicalFramework/upload/IHEITI_Suppl_HPDP_Rev1-1_TI_2010-08-10.pdf)
- [36] D. Clunie, "IHE Radiology Technical Framework," Tech. Rep., Jul. 2005, Vol. IIV, Revision 6.0. [Online]. Available: [http://www.ihe.net/TechnicalFramework/upload/IHE-RAD\\_TF\\_Suppl\\_Basic\\_Image\\_Review\\_2009-06-21.pdf](http://www.ihe.net/TechnicalFramework/upload/IHE-RAD_TF_Suppl_Basic_Image_Review_2009-06-21.pdf)
- [37] P. Hitzler, M. Krötzsch, B. Parsia, P. Patel-Schneider, and S. Rudolph, "OWL 2 Web Ontology Language Primer, W3C Recommendation," World Wide Web Consortium (W3C), Tech. Rep., Oct. 27 2009.
- [38] M. Brochhausen, A. D. Spear, C. Cocos, G. Weiler, L. Martín, A. Anguita, H. Stenzhorn, E. Daskalaki, F. Schera, U. Schwarz, S. Sfakianakis, S. Kiefer, M. Doerr, N. M. Graf, and M. Tsiknakis, "The ACGT Master Ontology

and its applications - Towards an ontology-driven cancer research and management system," *Biomedical Informatics*, vol. 44, no. 1, pp. 8–25, 2011.

- [39] M. B. Almeida, "A proposal to evaluate ontology content," *Applied Ontology*, vol. 4, pp. 245–265, 2009.
- [40] J. Brank, M. Grobelnik, and D. Mladenić, "A survey of ontology evaluation techniques," in *Proceedings of the Conference on Data Mining and Data Warehouses (SiKDD 2005)*, 2005.
- [41] G. Maiga and D. Williams, "A Flexible Approach for User Evaluation of Biomedical Ontologies," *International Journal of Computing and ICT Research*, vol. 2, 2008.
- [42] A. Maedche and S. Staab, "Measuring similarity between ontologies," in *Proceedings of the 13th European Conference on Knowledge Acquisition and Management (EKAW 2002)*, Madrid, Spain, 2002.
- [43] J. Brank, M. Grobelnik, and D. Mladenić, "Gold standard based ontology evaluation using instance assignment," in *Proceedings of the 4th International Workshop on Evaluation of Ontologies for the Web (EON 2006) at the 15th International World Wide Web Conference (WWW 2006)* Edinburgh, UK, 2006.
- [44] A. Gangemi, C. Catenacci, M. Ciaramita, and J. Lehmann, "Qood grid: A metaontology-based framework for ontology evaluation and selection," in *Proceeding of the 4th International Workshop on Evaluation of Ontologies for the Web (EON 2006) at the 15th International World Wide Web Conference*, Edinburgh, UK, 2006.
- [45] D. Maynard, Y. Peters, and Y. Li, "Metrics for evaluation of ontology-based information extraction," in *Proceeding of the 4th International Workshop on Evaluation of Ontologies for the Web (EON 2006) at the 15th International World Wide Web Conference (WWW 2006)*, Edinburgh, UK, 2006.
- [46] R. Porzel and R. Malaka, "A task-based approach for ontology evaluation," in *Workshop on Ontology Learning and Population at the 16th European Conference on Artificial Intelligence (ECAI 2004)*, Valencia, Spain, 2004.
- [47] Y. Kalfoglou and B. Hu, "Issues with evaluating and using publicly available ontologies," in *Proceedings of the 4th International Workshop on Evaluation of Ontologies for the Web (EON 2006) at the 15th International World Wide Web Conference* Edinburgh, UK, 2006.
- [48] C. Patel, K. Supekar, L. Yuyung, and E. K. Park, "OntoKhoj: a semantic web portal for ontology searching, ranking and classification," in *Proceedings of the 5th ACM International Workshop on Web Information and Data Management*, 2003, pp. 58–61.
- [49] C. Brewster, H. Alani, S. Dasmahapatra, and Y. Wilk, "Data driven ontology evaluation," in *In International Conference on Language Resources and Evaluation*, Lisbon, Portugal, 2004.
- [50] A. Lozano-Tello and A. Gómez-Pérez, "ONTOMETRIC: A method to choose the appropriate ontology," *Journal of Database Management*, vol. 15, pp. 1–18, 2004.
- [51] A. Gómez-Pérez, *Ontology evaluation*. Berlin: Springer-Verlag, 2004.
- [52] G. A. Aguado, A. Bañón, J. Bateman, S. Bernardos, M. Fernández, A. Gómez-Pérez, E. Nieto, A. Olalla, R. Plaza, and A. Sánchez, "Ontogeneration: Reusing domain and linguistic ontologies for Spanish text generation," in *In Workshop on Applications of Ontologies and Problem-Solving Methods at The European Conference on Artificial Intelligence (ECAI'98)*, Brighton, UK, 1998.

- [53] P. Velardi, R. Navigle, A. Cucchiarelli, and F. Neri, *Evaluation of OntoLearn, a methodology for automatic learning of domain ontologies*: Amsterdam: IOS Press, 2005.
- [54] K. Kozaki, E. Sunagawa, Y. Kitamura, and R. Mizoguchi, "Fundamental consideration of role concepts for ontology evaluation," in *Proceedings of the 4th International Workshop on Evaluation of Ontologies for the Web (EON 2006) at the 15th International World Wide Web Conference (WWW 2006)*, Edinburgh, UK, 2006.
- [55] N. Guarino and C. Welty, "Evaluating ontological decisions with OntoClean," *Communications of the ACM*, vol. 45, pp. 61–65, 2002.
- [56] L. Ding, R. Pan, A. Joshi, C. Kolari, A. Java, and Y. Peng, "Swoogle: a search and metadata engine for the semantic web," in *Proceedings of the 13th ACM Conference of Information and Knowledge Management*, Washington, DC, USA, 2004.
- [57] H. Alani and C. Brewster, "Metrics for ranking ontologies," in *International EON Workshop located at the 15th International World Wide Web Conference*, Edinburgh, UK, 2006.
- [58] A. Gómez-Pérez, "Some ideas and examples to evaluate ontologies," in *Proceedings of the 11th Conference on Artificial Intelligence Applications*, Los Angeles, CA, USA, 1994.
- [59] J. Brooke, *SUS: A "quick and dirty" usability scale*. London: Taylor & Francis, 1996.
- [60] C. Nuria, "Ontology Evaluation through Usability Measures," in *Proceedings of OTM Workshops' 2009*, Vilamoura, Portugal, 2009, pp. 594 - 603.

## I. APPENDIX A: Questionnaires

### I.1 CING

#### Questionnaire for the Evaluation of the Linked2Safety Semantic EHR Model

Name	
Partner/Institution	CING

#### **Part I**

##### Class definition questions

In the table below you can see the classes of the model presented as underlined text. Under each class, there is a definition that has been assigned to each class in the form of comment. In case you don't agree with these descriptions, please revise them accordingly.

N.	Do you agree with the definition of:	Yes	No	If no explain/propose correction or enter a reference for a definition
1	<u>cingBreastCA:BreastCancerDad</u> Father had breast cancer			
2	<u>cingBreastCA:BreastCancerMom</u> Mother had breast cancer			
3	<u>cingBreastCA:EthnicityClass</u> Ethnic origin			
4	<u>cingBreastCA:FHisFstOC</u> First degree female family members with ovarian cancer			
5	<u>cingBreastCA:FHisSecBC</u> Second degree female family members with breast cancer			
6	<u>cingBreastCA:FHisSecOC</u> Second degree female family members with ovarian cancer			
7	<u>cingBreastCA:FirstHisFstBC</u> First degree female family members with breast cancer			
8	<u>cingBreastCA:HormonalReplacementTherapyUsage</u> Use of hormonal replacement therapy (HRT)			
9	<u>cingBreastCA:OralContraceptivesUsage</u> Use of oral contraceptives (OC)			

10	<b><u>cingBreastCA:OvarianCancerMom</u></b> Mother had ovarian cancer			
11	<b><u>cingBreastCA:Sex</u></b> M=male, F=female, U=unknown			
12	<b><u>cingBreastCA:Status</u></b> Discease, i.e, cancer case-control status			
13	<b><u>cingBreastCA: SmokingStatus</u></b> Cigarette smoking			

In the current state of the model, there are no descriptions for the following classes.

N.	Is clear the meaning of the following classes which are not further defined/commented:	Yes	No	If no explain/propose a definition
14	cingNg:ReferralDiagnosis			
15	cingBreastCA:BRCA1			
16	cingBreastCA:BRCA2			
17	cingDB:Diabetes			

#### Questions for subclass hierarchy

The following questions are related to the subclass hierarchy of the model. Each question explains the classification hierarchy of a specific class. In case you don't agree with that, please propose a correction.

N.	Do you agree with the following statements?	Yes	No	If no explain/propose correction
18	The class cingNg:ReferralDiagnosis is subclass of acgt:Diagnosis (acgt:Document-> acgt:Diagnosis)			
19	The class cingBreastCA:EthnicityClass is subclasses of acgt:Identifier			
20	The class cingBreastCA:BreastCancerDad has three subclasses: - cingBreastCA:BreastCancerDadNo - cingBreastCA:BreastCancerDadUnavailable - cingBreastCA:BreastCancerDadYes			
21	The class cingBreastCA:BreastCancerMom has three subclasses: - cingBreastCA:MotherBreastCancerNo - cingBreastCA:MotherBreastCancerUnavailable - cingBreastCA:MotherBreastCancerYes			
22	The class cingBreastCA:FamHistory has three subclasses: - cingBreastCA:FamHistNo - cingBreastCA:FamHistUnavailable - cingBreastCA:FamHistYes			



23	<p>The class cingBreastCA:FHisFstOC has three subclasses:</p> <ul style="list-style-type: none"> <li>- cingBreastCA:FHisFstOCNo</li> <li>- cingBreastCA:FHisFstOCUnavailable</li> <li>- cingBreastCA:FHisFstOCYes</li> </ul>			
24	<p>The class cingBreastCA:FHisSecBC has three subclasses:</p> <ul style="list-style-type: none"> <li>- cingBreastCA:FHisSecBCNo</li> <li>- cingBreastCA:FHisSecBCUnavailable</li> <li>- cingBreastCA:FHisSecBCYes</li> </ul>			
25	<p>The class cingBreastCA:FHisSecOC has three subclasses:</p> <ul style="list-style-type: none"> <li>- cingBreastCA:FHisSecOCNo</li> <li>- cingBreastCA:FHisSecOCUnavailable</li> <li>- cingBreastCA:FHisSecOCYes</li> </ul>			
26	<p>The class cingBreastCA:FirstHisFstBC has three subclasses:</p> <ul style="list-style-type: none"> <li>- cingBreastCA:FirstHisFstBCNo</li> <li>- cingBreastCA:FirstHisFstBCUnavailable</li> <li>- cingBreastCA:FirstHisFstBCYes</li> </ul>			
27	<p>The class cingBreastCA:HormonalReplacementTherapyUsage has three subclasses:</p> <ul style="list-style-type: none"> <li>- cingBreastCA:EverUsedHRT</li> <li>- cingBreastCA:NeverUsedHRT</li> <li>- cingBreastCA:StatusUnavailable</li> </ul>			
28	<p>The class cingBreastCA:OralContraceptivesUsage has three subclasses:</p> <ul style="list-style-type: none"> <li>- cingBreastCA:EverUsed</li> <li>- cingBreastCA:NeverUsed</li> <li>- cingBreastCA:UnavailableInformation</li> </ul>			
29	<p>The class cingBreastCA:OvarianCancerMom has three subclasses:</p> <ul style="list-style-type: none"> <li>- cingBreastCA:OvarianCancerMomNo</li> <li>- cingBreastCA:OvarianCancerMomYes</li> <li>- cingBreastCA:OvarianCancMomUnavailable</li> </ul>			
30	<p>The class cingBreastCA:SmokingStatus has three subclasses:</p> <ul style="list-style-type: none"> <li>- cingBreastCA:CurrentSmoker</li> <li>- cingBreastCA:NeverSmoked</li> <li>- cingBreastCA:PastSmoker</li> </ul>			
31	<p>The classes:</p> <ul style="list-style-type: none"> <li>- cingBreastCA:Sex</li> <li>- cingBreastCA:BreastCancerDad</li> <li>- cingBreastCA:BreastCancerMom</li> <li>- cingBreastCA:FamHistory</li> <li>- cingBreastCA:FHisFstOC</li> <li>- cingBreastCA:FHisSecBC</li> <li>- cingBreastCA:FHisSecOC</li> <li>- cingBreastCA:FirstHisFstBC</li> <li>- cingBreastCA:HormonalReplacementTherapyUsage</li> </ul>			

	<ul style="list-style-type: none"> <li>- cingBreastCA:OralContraceptivesUsage</li> <li>- cingBreastCA:OvarianCancerMom</li> <li>- SmokingStatus</li> </ul> are a subclass of snap:Quality			
32	The class cingDB:Diabetes (acgt:NonInfectiousDisease -> cingDB:Diabetes) has two subclasses: <ul style="list-style-type: none"> <li>- cingDB:DiabetesTypel</li> <li>- cingDB:DiabetesTypell</li> </ul>			
33	The class cingBreastCA:Status is subclass of acgt:StateOfAffairs			
34	The class acgt:GeneExpression (span:Process -> acgt:NaturalProcess -> acgt:OrganismalProcess -> acgt:GeneExpression) has two subclasses: <ul style="list-style-type: none"> <li>- cingBreastCA:BRCA1</li> <li>- cingBreastCA:BRCA2</li> </ul>			

### Properties definition questions

In the following table you can see the definitions assigned to properties of the model with the form of comment. In case you don't agree with these descriptions, please revise them accordingly.

N.	Do you agree with the definition of:	Yes	No	If no explain/propose correction or enter a reference for a definition
35	<u>cingBreastCA:breastFed</u> Ever breastfed			
36	<u>cingBreastCA:ageDiag</u> Age at diagnosis for cases			
37	<u>cingBreastCA:ageFFTP</u> Age at end of first full-term pregnancy			
38	<u>cingBreastCA:ageInt</u> Age at interview/questionnaire for controls and cases			
39	<u>cingBreastCA:ageMenarche</u> Age at menarche			
40	<u>cingBreastCA:BMI</u> Body mass index at interview/questionnaire in kg			
41	<u>cingBreastCA:brCancerDau</u> Number of daughters with breast cancer			
42	<u>cingBreastCA:brCancerSis</u> Number of sisters with breast cancer			
43	<u>cingBreastCA:breastMos</u> Lifetime duration of breastfeeding			
44	<u>cingBreastCA:daughters</u> Total number of daughters			
45	<u>cingBreastCA:eduCat</u> Highest level of education received			

46	<b><u>cingBreastCA:fam1grBC50</u></b> Number of first degree family members with breast ca before age 50			
47	<b><u>cingBreastCA:fam1grOC50</u></b> Number of first degree family members with ovarian ca before age 50			
48	<b><u>cingBreastCA:FHisFstBCNr</u></b> Number of first degree female family members with breast cancer			
49	<b><u>cingBreastCA:FHisFstOCNr</u></b> Number of first degree female family members with ovarian cancer			
50	<b><u>cingBreastCA:FHisSecOCNr</u></b> Number of second degree family members with ovarian cancer			
51	<b><u>cingBreastCA:Fhnumber</u></b> Number of affected (breast cancer) first degree relatives			
52	<b><u>cingBreastCA:Fhscore</u></b> Family history score			
53	<b><u>cingBreastCA:height</u></b> Adult body height			
54	<b><u>cingBreastCA:intDate</u></b> Date at interview/questionnaire for cases and controls			
55	<b><u>cingBreastCA:menoStat</u></b> Menopausal status at reference date (UBITECH-Added intefer for range)			
56	<b><u>cingBreastCA:mensAgeLst</u></b> Age at last menstruation			
57	<b><u>cingBreastCA:mensRsn</u></b> Reason menstruation stopped			
58	<b><u>cingBreastCA:NumberOfPregnancies</u></b> Number Of Pregnancies			
59	<b><u>cingBreastCA:numberOfSisters</u></b> Number of Sisters			
60	<b><u>cingBreastCA:OCMo</u></b> Lifetime duration of oral contraceptive use			
61	<b><u>cingBreastCA:ovCancerDau</u></b> Number of daughters with ovarian cancer			
62	<b><u>cingBreastCA:ovCancerSis</u></b> Number of sisters with ovarian cancer			
63	<b><u>cingBreastCA:parity</u></b> Number of full-term pregnancies			
64	<b><u>cingBreastCA:parous</u></b> Nulliparous v parous			

65	<b><u>cingBreastCA:weight</u></b> Weight at interview/questionnaire			
66	<b><u>cingBreastCA:weightAdult</u></b> Adult body weight in early adulthood (age around 20)			
67	<b><u>cingNg:labTest</u></b> Integer Code (see Columns B & C, sheet 4 for possible values)			

In the current state of the model, the property named cingBreastCA:birthDate is not defined.

N.	Is clear the meaning of the following properties which are not further defined:	Yes	No	If no explain/propose a definition
68	cingBreastCA:birthDate			

#### Questions for the range of properties

In the following questions you can revise the range of the properties. In particular, there are three types set to properties: string, date, and integer.

N.	Do you agree with the range of the following properties?	Yes	No	If no explain/propose correction
	<b>Range: String</b>			
69	cingBreastCA:eduCat			
	<b>Range: Date</b>			
70	cingBreastCA:birthDate			
71	cingBreastCA:intDate			
	<b>Range: Integer</b>			
72	cingBreastCA:ageDiag cingBreastCA:ageFFTP cingBreastCA:ageInt cingBreastCA:ageMenarche cingBreastCA:BMI cingBreastCA:brCancerDau cingBreastCA:brCancerSis cingBreastCA:breastMos cingBreastCA:daughters cingBreastCA:fam1grBC50 cingBreastCA:fam1grOC50 cingBreastCA:FHisFstBCNr cingBreastCA:FHisFstOCNr cingBreastCA:FHisSecOCNr cingBreastCA:Fhnumber			

	cingBreastCA:Fhscore cingBreastCA:height cingBreastCA:menoStat cingBreastCA:mensAgeLst cingBreastCA:NumberOfPregnancies cingBreastCA:numberOfSisters cingBreastCA:OCMo cingBreastCA:ovCancerDau cingBreastCA:ovCancerSis cingBreastCA:parity cingBreastCA:parous cingBreastCA:weight cingBreastCA:weightAdult cingNg:labTest			
--	---	--	--	--

The range of the following properties is not specified. Please define.

	<b>Range: na</b>			
73	cingBreastCA:mensRsn cingBreastCA:breastFed			

#### Questions for relations between concepts

Classes have attributes which describe the instances of each class. Please revise these relations and contribute where needed.

N.	Do you agree with the following statements?	Yes	No	If no explain/propose correction
74	The class acgt:HumanBeing has properties: - cingBreastCA:fam1grBC50 - cingBreastCA:fam1grOC50 - cingBreastCA:FHisFstBCNr - cingBreastCA:FHisFstOCNr - cingBreastCA:FHisSecOCNr - cingBreastCA:Fhnumber - cingBreastCA:Fhscore			
75	The class acgt:FemaleHumanBeing has property: - cingBreastCA:NumberOfPregnancies			

**Part II**Completeness / Usability of the Model

N.	Please rate the following statements (1: high disagreement, 5: high agreement)	1	2	3	4	5
1.	I think that I could contribute to this semantic model					
2.	I find the semantic model easy to understand					
3.	I think that I would need further theoretical support to be able to understand this semantic model					
4.	I found the various concepts in this semantic model were well integrated					
5.	I would imagine that most clinical experts would understand this semantic model very quickly					
6.	I am confident I understand the conceptualization of the semantic model					
7.	The concepts/properties of the semantic model cover the needs of the clinical research domain.					

If the concepts/properties of the semantic model do not cover the needs of the clinical research domain, describe the missing concepts/properties:

.....

.....

.....

.....

.....

.....

.....

.....

.....

## I.2 CHUV

### Questionnaire for the Evaluation of the Linked2Safety Semantic EHR Model

Name	
Partner/Institution	CHUV

#### Part I

##### A. Evaluation of the DSM-IV model

###### Class definition questions

In the table below you can see the classes of the DMS-4 model presented as underlined text. Under each class, there is a definition that has been assigned to the specific class in the form of comment. In case you don't agree with these descriptions, please revise them accordingly.

N.	Do you agree with the definition of:	Yes	No	If no explain/propose correction or enter a reference for a definition
1	<u>DSM 300.02</u> Generalized anxiety disorder			
2	<u>DSM 300.22</u> Agoraphobia without history of panic disorder			
3	<u>DSM 300.23</u> Social Phobia			
4	<u>DSM 300.29</u> Specific Phobia			
5	<u>DSM 300.3</u> Obsessive Compulsive Disorder			
6	<u>DSM 308.3</u> Acute Stress Disorder			
7	<u>DSM 309.81</u> Posttraumatic Stress Disorder			
8	<u>DSM 296.80</u> Bipolar Disorder NOS			
9	<u>DSM 300.01</u> Panic Disorder Without Agoraphobia			
10	<u>DSM 300.21</u> Panic Disorder With Agoraphobia			
11	<u>DSM 309.21</u> Separation Anxiety Disorder			
12	<u>DSM 313.81</u> Oppositional Defiant Disorder			

13	<b><u>DSM 314.00</u></b> Predominantly Inattentive Subtype			
14	<b><u>DSM 314.01</u></b> Combined Subtype			
15	<b><u>DSM 312.81</u></b> Childhood Onset			
16	<b><u>DSM 312.82</u></b> Adolescent Onset			
17	<b><u>DSM 307.1</u></b> Anorexia nervosa : An eating disorder characterized by excessive food restriction and irrational fear of gaining weight, and a distorted body self-perception			
18	<b><u>DSM 307.51</u></b> Bulimia nervosa : An eating disorder characterized by binge eating and purging, or consuming a large amount of food in a short amount of time, followed by an attempt to rid oneself of the food consumed (purging), typically by vomiting, taking a laxative or diuretic and/or excessive exercise, and commonly accompanied with fasting over an extended period of time.			
19	<b><u>GAF</u></b> The Global Assessment of Functioning (GAF) is a numeric scale (0 through 100) used by mental health clinicians and physicians to rate subjectively the social, occupational, and psychological functioning of adults, e.g., how well or adaptively one is meeting various problems-in-living. This can be measured over different time-spans (e.g., current, Life Time, Worst Ever, etc.			
20	<b><u>Current</u></b> Current GAF Score			
21	<b><u>LifeTime</u></b> GAF Life Time Score			
22	<b><u>Worst</u></b> Worst Ever GAF Scope			
23	<b><u>DSM 312.31</u></b> Pathological Gambling			
24	<b><u>DSM 312.32</u></b> Kleptomania			
25	<b><u>DSM 312.33</u></b> Pyromania			
26	<b><u>DSM 312.34</u></b> Intermittent Explosive Disorder			
27	<b><u>DSM 312.39</u></b> Trichotillomania			



28	<b><u>DSM 301.0</u></b> Paranoid personality disorder			
29	<b><u>DSM 301.7</u></b> Antisocial Personality Disorder			
30	<b><u>DSM 300.4</u></b> Dysthymic Disorder or Depressive Personality Disorder			
31	<b><u>DSM 301.82</u></b> Avoidant Personality Disorder			
32	<b><u>DSM 295.70</u></b> Schizo-affective disorder bipolar type			
33	<b><u>DSM 301.20</u></b> Schizo-affective disorder depressive type			
34	<b><u>DSM 301.22</u></b> Schizotypal Personality Disorder			
35	<b><u>DSM 303.90</u></b> Alcohol Dependence			
36	<b><u>DSM 305.00</u></b> Alcohol Abuse			
37	<b><u>DSM 304.20</u></b> Cocaine Dependence			
38	<b><u>DSM 305.60</u></b> Cocaine Abuse or Drug Abuse			
39	<b><u>DSM 292.0</u></b> Nicotine Withdrawal			
40	<b><u>DSM 292.9</u></b> Nicotine Related Disorder NOS			
41	<b><u>DSM 305.10</u></b> Nicotine Dependence			
42	<b><u>DSM 296.56, DSM 296.46, DSM 296.66, DSM 296.06, DSM 296.89, DSM 296.36, DSM 296.26</u></b> In full remission			

In the current state of the DSM-IV model, the following classes are not further described.

N.	Is clear the meaning of the following classes which are not further defined/commented:	Yes	No	If no explain/propose a definition
43	PanicDisorder			
44	Bipolar_I_disorder_episode_depressed			
45	Bipolar_I_disorder_episode_manic_			
46	Bipolar_I_disorder_episode_mixed_			
47	Bipolar_I_Disorder_single_manic			
48	Bipolar_II_Disorder			

49	AttentionDeficit_HyperactivityDisorder			
50	ConductDisorder			
51	DepressiveDisorders			
52	MajorDepressiveDisorder_Recurrent			
53	MajorDepressiveDisorder_Single			
54	ClusterA			
55	ClusterB			
56	ClusterC			

### Questions for subclass hierarchy

The following questions are related to the subclass hierarchy of the DSM-IV model. Each question explains the classification hierarchy of a specific class. In case you don't agree with that, please propose a correction.

N.	Do you agree with the following statements?	Yes	No	If no explain/propose correction
	<b>Class: AnxietyDisorders</b>			
57	The class AnxietyDisorders has 8 subclasses - DSM_300.02 - DSM_300.22 - DSM_300.23 - DSM_300.29 - DSM_300.3 - DSM_308.3 - DSM_309.81 - PanicDisorder			
58	The class PanicDisorder has 2 subclasses: - DSM_300.01 - DSM_300.21			
	<b>Class: BipolarDisorders</b>			
59	The class BipolarDisorders has 6 subclasses: - Bipolar_I_disorder_episode_depressed - Bipolar_I_disorder_episode_manic_ - Bipolar_I_disorder_episode_mixed_ - Bipolar_I_Disorder_single_manic - Bipolar_II_Disorder - DSM_296.80			
	<b>Class: ChildhoodDisorders</b>			
60	The class ChildhoodDisorders has 4 subclasses: - AttentionDeficit_HyperactivityDisorder			

	<ul style="list-style-type: none"> <li>- ConductDisorder</li> <li>- DSM_309.21</li> <li>- DSM_313.81</li> </ul>			
61	<p>The class AttentionDeficit_HyperactivityDisorder has 2 subclasses:</p> <ul style="list-style-type: none"> <li>- DSM_314.00</li> <li>- DSM_314.01</li> </ul>			
62	<p>The class ConductDisorder has 2 subclasses:</p> <ul style="list-style-type: none"> <li>- DSM_312.81</li> <li>- DSM_312.82</li> </ul>			
	<b>Class: EatingDisorders</b>			
63	<p>The class EatingDisorders has 2 subclasses:</p> <ul style="list-style-type: none"> <li>- DSM_307.1</li> <li>- DSM_307.51</li> </ul>			
	<b>Class: GAF</b>			
64	<p>The class GAF has 3 subclasses:</p> <ul style="list-style-type: none"> <li>- Current</li> <li>- LifeTime</li> <li>- Worst</li> </ul>			
	<b>Class: ImpulseControlDisorders</b>			
65	<p>The class ImpulseControlDisorders has 5 subclasses:</p> <ul style="list-style-type: none"> <li>- DSM_312.31</li> <li>- DSM_312.32</li> <li>- DSM_312.33</li> <li>- DSM_312.34</li> <li>- DSM_312.39</li> </ul>			
	<b>Class: Mooodisorders</b>			
66	<p>The class Mooodisorders has one subclass</p> <ul style="list-style-type: none"> <li>- DepressiveDisorders</li> </ul>			
67	<p>The class DepressiveDisorders has 2 subclasses:</p> <ul style="list-style-type: none"> <li>- MajorDepressiveDisorder_Recurrent</li> <li>- MajorDepressiveDisorder_Single</li> </ul>			
	<b>Class: PersonalityDisorders</b>			
68	<p>The class PersonalityDisorders has 3 subclasses:</p> <ul style="list-style-type: none"> <li>- ClusterA</li> <li>- ClusterB</li> <li>- ClusterC</li> </ul>			
69	<p>The class ClusterA has one subclass</p> <ul style="list-style-type: none"> <li>- DSM_301.0</li> </ul>			
70	<p>The class ClusterB has one subclass</p> <ul style="list-style-type: none"> <li>- DSM_301.7</li> </ul>			

71	The class ClusterC has 2 subclasses: - DSM_300.4 - DSM_301.82			
	<b>Class: SchizophreniaDisorder</b>			
72	class SchizophreniaDisorder has 3 subclasses: - DSM_295.70 - DSM_301.20 - DSM_301.22			
	<b>Class: SubstanceDisorders</b>			
73	The class SubstanceDisorders has 3 subclasses: - Alcohol - Drug - Nicotine			
74	The class Alcohol has 2 subclasses: - DSM_303.90 - DSM_305.00			
75	The class Drug as one subclass - Cocaine			
76	The class Cocaine has 2 subclasses: - DSM_304.20 - DSM_305.60			
77	The class Nicotine has 3 subclasses: - DSM_292.0 - DSM_292.9 - DSM_305.10			

### Properties definition questions

In the current state of the DMS-4 model, the following properties are not further described.

N.	Is clear the meaning of the following properties which are not further defined:	Yes	No	If no explain/propose a definition
78	Axis-I			
79	Axis-II			
80	Axis-III			
81	Axis-IV			
82	Axis-V			
83	gaf_score_current			
84	gaf_score_lifetime			
85	gaf_score_worst			

Questions for the range of properties

In the following questions you can revise the range of the properties. In particular, there are two types set to properties: integer and object.

N.	Do you agree with the range of the following properties?	Yes	No	If no explain/propose correction
	<b>Range: Integer</b>			
86	gaf_score_current			
87	gaf_score_lifetime			
88	gaf_score_worst			
	<b>Range: Object</b>			
89	The property Axis-I receives values from classes SchizophreniaDisorder and SubstanceDisorders			
90	The property Axis-II receives values from class PersonalityDisorders			
91	The property Axis-III receives values from classes EatingDisorders and Mooodisorders			
92	The property Axis-IV receives values from classes AnxietyDisorders, EatingDisorders and ImpulseControlDisorders			
93	The property Axis-V receives values from class GAF			

Questions for the relation of concepts

Classes have attributes which describe the instances of each class. Please revise these relations and contribute where needed.

N.	Do you agree with the following statements?	Yes	No	If no explain/propose correction
94	The class Current has property: - gaf_score_current			
95	The class LifeTime has property: - gaf_score_lifetime			
96	The class Worst has property: - gaf_score_worst			

**B Evaluation of the Linked2Safety SEHR model**Class definition questions

In the table below you can see the classes of the Linked2Safety SEHR model presented as underlined text. Under each class, there is a definition that has been assigned to the specific class in the form of comment. In case you don't agree with these descriptions, please revise them accordingly.

N.	Do you agree with the definition of:	Yes	No	If no explain/propose correction or enter a reference for a definition
1	<u>chuv:Enuresis</u> Enuresis refers to a repeated inability to control urination			
2	<u>chuv:Ethnicity</u> Ethnic origin			
3	<u>chuv:HuntingtonsDisease</u> Huntington's disease is a disorder passed down through families in which nerve cells in certain parts of the brain waste away, or degenerate.			
4	<u>chuv:LateMotorDevelopment</u> Motor skills are the abilities usually acquired during infancy and early childhood as part of a child's motor development. By the time child reach two years of age, almost all children are able to stand up, walk and run, walk up stairs, etc			
5	<u>chuv:MultipleSclerosis</u> Multiple sclerosis is an autoimmune disease that affects the brain and spinal cord (central nervous system)			
6	<u>chuv:ParkinsonsDisease</u> Parkinson's disease is a disorder of the brain that leads to shaking (tremors) and difficulty with walking, movement, and coordination.			
7	<u>chuv:Poliomyelitis</u> Poliomyelitis is a viral disease that can affect nerves and can lead to partial or full paralysis.			
8	<u>chuv:Somnambulism</u> Sleep-walking			

In the current state of the Linked2Safety SEHR model, there are no descriptions for the following classes.

N.	Is clear the meaning of the following classes which are not further defined/commented:	Yes	No	If no explain/propose a definition
9	chuv:AntidepressantDrug			
10	chuv:AntimanicDrug			
11	chuv:AntiparkinsonsDrug			
12	chuv:AntiparkinsonsDrug			

13	chuv:ATP3			
14	chuv:AuditiveDisorder			
15	chuv:CoronaryHeartDisease			
16	chuv:DigestiveProblems			
17	chuv:Dyslipidemia			
18	chuv:HIV			
19	chuv:Metabolic			
20	chuv:MigraineCumulative			
21	chuv:MyocardialInfarction			
22	chuv:Nightmare			
23	chuv:OverWeight			
24	chuv:SedativeDrug			
25	chuv:SleepWalking			
26	chuv:SpeechDisorder			
27	chuv:Stimulant			
28	chuv:Stroke			
29	chuv:Stuttering			
30	chuv:Ticks			
31	chuv:VisualDisorder			

### Questions for subclass hierarchy

The following questions are related to the subclass hierarchy of the model. Each question explains the classification hierarchy of a specific class. In case you don't agree with that, please propose a correction.

N.	Do you agree with the following statements?	Yes	No	If no explain/propose correction
32	The class chuv:Ethnicity is subclass of acgt:Identifier			
33	The class acgt:CumulativeDose (snap:Quality –> acgt:Magnitude -> acgt:Dose -> acgt:CumulativeDose) has one subclass: - chuv:MigraineCumulative			
34	The class acgt:ChronicViralInfection (acgt:InfectiousDisease -> acgt:ViralInfection -> acgt:ChronicViralInfection) has two subclasses: - chuv:HIV - chuv:Poliomyelitis			

35	<p>The class <code>acgt:MotorNeuropathy</code> (<code>acgt:NonInfectiousDisease -&gt; acgt:Neuropathy -&gt; acgt:MotorNeuropathy</code>) has one subclass:</p> <ul style="list-style-type: none"> <li>- <code>chuv:LateMotorDevelopment</code></li> </ul>			
36	<p>The class <code>chuv:Metabolic</code> is a subclass of <code>acgt:Syndrome</code> (<code>acgt:NonInfectiousDisease-&gt; acgt:Syndrome</code>)</p>			
37	<p>The class <code>chuv:Metabolic</code> has one subclass:</p> <ul style="list-style-type: none"> <li>- <code>chuv:ATP3</code></li> </ul>			
38	<p>The classes</p> <ul style="list-style-type: none"> <li>- <code>chuv:CoronaryHeartDisease</code>,</li> <li>- <code>chuv:Dyslipidemia</code>,</li> <li>- <code>chuv:HuntingtonsDisease</code>,</li> <li>- <code>chuv:MultipleSclerosis</code>,</li> <li>- <code>chuv:ParkinsonsDisease</code>,</li> <li>- <code>chuv:SleepWalking</code>,</li> <li>- <code>cingDB:Diabetes</code></li> </ul> <p>are subclasses of <code>acgt:NonInfectiousDisease</code></p>			
39	<p>The classes</p> <ul style="list-style-type: none"> <li>- <code>chuv:AntidepressantDrug</code></li> <li>- <code>chuv:AntimanicDrug</code></li> <li>- <code>chuv:AntiparkinsonsDrug</code></li> <li>- <code>chuv:AntipsychoticDrug</code></li> <li>- <code>chuv:SedativeDrug</code></li> <li>- <code>chuv:Stimulant</code></li> </ul> <p>are subclasses of <code>acgt:Drug</code> (<code>snap:Role -&gt; acgt:Drug</code>)</p>			
40	<p>The class <code>acgt:GeneralizedSymptom</code> (<code>snap:Role -&gt; acgt:Symptom -&gt; acgt:GeneralizedSymptom</code>) has 3 subclasses:</p> <ul style="list-style-type: none"> <li>- <code>chuv:AuditiveDisorder</code></li> <li>- <code>chuv:Ticks</code></li> <li>- <code>chuv:VisualDisorder</code></li> </ul>			
41	<p>The class <code>acgt:NervousSystemSymptom</code> (<code>acgt:Symptom -&gt; acgt:SpecificSymptom -&gt; acgt:NervousSystemSymptom</code>) has one subclass:</p> <ul style="list-style-type: none"> <li>- <code>chuv:SpeechDisorder</code></li> </ul>			
42	<p>The class <code>chuv:SpeechDisorder</code> has one subclass:</p> <ul style="list-style-type: none"> <li>- <code>chuv:Stuttering</code></li> </ul>			
43	<p>The class <code>acgt:UrinarySystemSymptom</code> (<code>acgt:Symptom -&gt; acgt:SpecificSymptom -&gt; acgt:UrinarySystemSymptom</code>) has one subclass:</p> <ul style="list-style-type: none"> <li>- <code>chuv:Enuresis</code></li> </ul>			
44	<p>The class <code>chuv:Somnambulism</code> is subclass of <code>acgt:Unconsciousness</code> (<code>acgt:StateOfAffairs -&gt;</code></p>			



	acgt:Unconsciousness)			
45	<p>The classes</p> <ul style="list-style-type: none"> <li>- AllergicReaction</li> <li>- chuv:DigestiveProblems</li> <li>- chuv:MyocardialInfarction</li> <li>- chuv:OverWeight</li> <li>- chuv:Stroke</li> </ul> <p>are subclasses of acgt:StateOfAffairs</p>			
46	<p>The class chuv:Nightmare is a subclass of acgt:OrganismalProcess (span:Process -&gt; acgt:NaturalProcess -&gt; acgt:OrganismalProcess)</p>			

### Properties definition questions

In the following table you can see the definitions assigned to properties of the model in the form of comment. In case you don't agree with these descriptions, please revise them accordingly.

N.	Do you agree with the definition of:	Yes	No	If no explain/propose correction or enter a reference for a definition
47	<u>chuv:AntidepressantExtrapyramidalSideEffects</u> Extrapyramidal Side Effects {@en} Trembling, rigidity, need to move around {@en}			
48	<u>chuv:AntidepressantGastrointestinalSymptoms</u> Gastrointestinal Symptoms {@en} Nausea, diarrhea, constipation {@en}			
49	<u>chuv:AntidepressantHeadaches</u> Headaches {@en}			
50	<u>chuv:AntidepressantOther</u> Other {@en}			
51	<u>chuv:AntidepressantSexualSymptoms</u> Sexual Symptoms {@en} Drop in libido, erectile problems, problems ejaculating {@en}			
52	<u>chuv:AntidepressantSleepProblems</u> Sleep Problems {@en}			
53	<u>chuv:AntiDepressantWeightGain</u> Weight Gain {@en}			
54	<u>chuv:AntidepressantWeightLoss</u> Weight Loss {@en}			
55	<u>chuv:AntimanicsGastrointestinalsymptoms</u> Gastrointestinal symptoms {@en} Nausea, diarrhea, constipation {@en}			
56	<u>chuv:AntimanicsHairLoss</u> Hair Loss {@en}			

57	<b><u>chuv:AntimanicsHeadaches</u></b> Headaches {@en}			
58	<b><u>chuv:AntimanicsOther</u></b> Other {@en}			
59	<b><u>chuv:AntimanicsSleepProblems</u></b> Sleep Problems {@en}			
60	<b><u>chuv:AntimanicsTremblings</u></b> Tremblings {@en}			
61	<b><u>chuv:AntimanicsWeightGain</u></b> Weight Gain {@en}			
62	<b><u>chuv:AntimanicsWeightLoss</u></b> Weight Loss {@en}			
63	<b><u>chuv:AntiparkinsonsDescription</u></b> Description {@en}			
64	<b><u>chuv:AntiparkinsonsSideEffects</u></b> Side Effects {@en}			
65	<b><u>chuv:AntipsychoticsExtrapyramidalSideEffects</u></b> Extrapyramidal Side Effects {@en} Trembling, rigidity, need to move around {@en}			
66	<b><u>chuv:AntipsychoticsMetabolicSyndroms</u></b> Metabolic Syndroms {@en} Diabetes, high cholesterol, high blood sugar {@en}			
67	<b><u>chuv:AntipsychoticsOther</u></b> Other {@en}			
68	<b><u>chuv:AntipsychoticsProlactinSymptoms</u></b> Prolactin Symptoms {@en} Gynecomastia, galactorrhea, amenorrhoea {@en}			
69	<b><u>chuv:AntipsychoticsSexualSymptoms</u></b> Sexual Symptoms {@en} Drop in libido, erectile problems, problems ejaculating {@en}			
70	<b><u>chuv:AntipsychoticsSleepProblems</u></b> Sleep Problems {@en}			
71	<b><u>chuv:AntipsychoticsWeightGain</u></b> Weight Gain {@en}			
72	<b><u>chuv:AntipsychoticsWeightLoss</u></b> Weight Loss {@en}			
73	<b><u>chuv:electrotherapyBenefits</u></b> Ever benefitted from electrotherapy			
74	<b><u>chuv:perWeekCaffeineConsumption</u></b> Number of cups of tea or coffee with caffeine/week			
75	<b><u>chuv:perWeekDrinksCaffeine</u></b> Drinks with caffeine/week			
76	<b><u>chuv:psychiatricHospitalisations</u></b> Number of psychiatric hospitalizations			

77	<b><u>chuv:SedativeDescription</u></b> Description {@en}			
78	<b><u>chuv:SedativeSideEffects</u></b> Side Effects {@en}			

In the current state of the model, the following properties are not further described.

N.	Is clear the meaning of the following properties which are not further defined:	Yes	No	If no explain/propose correction or enter a reference for a definition
79	chuv:activityType			
80	chuv:ageAtExam			
81	chuv:ageAtInterview			
82	chuv:everSmoking			
83	chuv:firstConsultationAge			
84	chuv:regularExercise			
85	chuv:nationality			

#### Questions for the range of properties

In the following questions you can revise the range of the properties. In particular, there are three types set to properties: string, integer and object.

N.	Do you agree with the range of the following properties?	Yes	No	If no explain/propose correction
	<b>Range: String</b>			
86	chuv:activityType			
87	chuv:AntidepressantExtrapyramidalSideEffects			
88	chuv:AntidepressantGastrointestinalSymptoms			
89	chuv:AntidepressantHeadaches			
90	chuv:AntidepressantOther			
91	chuv:AntidepressantSexualSymptoms			
92	chuv:AntidepressantSleepProblems			
93	chuv:AntiDepressantWeightGain			
94	chuv:AntidepressantWeightLoss			
95	chuv:AntimanicsGastrointestinalsymptoms			
96	chuv:AntimanicsHairLoss			
97	chuv:AntimanicsHeadaches			

98	chuv:AntimanicsOther			
99	chuv:AntimanicsSleepProblems			
100	chuv:AntimanicsTremblings			
101	chuv:AntimanicsWeightGain			
102	chuv:AntimanicsWeightLoss			
103	chuv:AntiparkinsonsDescription			
104	chuv:AntiparkinsonsSideEffects			
105	chuv:AntipsychoticsExtrapyrimalSideEffects			
106	chuv:AntipsychoticsMetabolicSyndroms			
107	chuv:AntipsychoticsOther			
108	chuv:AntipsychoticsProlactinSymptoms			
109	chuv:AntipsychoticsSexualSymptoms			
110	chuv:AntipsychoticsSleepProblems			
111	chuv:AntipsychoticsWeightGain			
112	chuv:AntipsychoticsWeightLoss			
113	chuv:SedativeDescription			
114	chuv:SedativeSideEffects			
	<b>Range: Integer</b>			
115	chuv:ageAtExam			
116	chuv:ageAtInterview			
117	chuv:electrotherapyBenefits			
118	chuv:everSmoking			
119	chuv:firstConsultationAge			
120	chuv:perWeekCaffeineConsumption			
121	chuv:perWeekDrinksCaffeine			
122	chuv:psychiatricHospitalisations			
123	chuv:regularExercise			
	<b>Range: Object</b>			
124	The property chuv:nationality receives values from class acgt:CountryName			

### Questions for relations between concepts

Classes have attributes which describe the instances of each class. Please revise these relations and contribute where needed.

N.	Do you agree with the following statements?	Yes	No	If no explain/propose correction
125	The class acgt:Patient has properties: <ul style="list-style-type: none"> <li>- chuv:nationality</li> <li>- chuv:ageAtExam</li> <li>- chuv:ageAtInterview</li> <li>- chuv:everSmoking</li> <li>- chuv:firstConsultationAge chuv:regularExercise</li> </ul>			
126	The class chuv:AntidepressantDrug has properties: <ul style="list-style-type: none"> <li>- chuv:AntidepressantExtrapyramidalSideEffects</li> <li>- chuv:AntidepressantGastrointestinalSymptoms</li> <li>- chuv:AntidepressantHeadaches</li> <li>- chuv:AntidepressantOther</li> <li>- chuv:AntidepressantSexualSymptoms</li> <li>- chuv:AntidepressantSleepProblems</li> <li>- chuv:AntiDepressantWeightGain</li> <li>- chuv:AntidepressantWeightLoss</li> </ul>			
127	The class chuv:AntimanicDrug has properties: <ul style="list-style-type: none"> <li>- chuv:AntimanicsGastrointestinalsymptoms</li> <li>- chuv:AntimanicsHairLoss</li> <li>- chuv:AntimanicsHeadaches</li> <li>- chuv:AntimanicsOther</li> <li>- chuv:AntimanicsSleepProblems</li> <li>- chuv:AntimanicsTremblings</li> <li>- chuv:AntimanicsWeightGain</li> <li>- chuv:AntimanicsWeightLoss</li> </ul>			
128	The class chuv:AntiparkinsonsDrug has properties: <ul style="list-style-type: none"> <li>- chuv:AntiparkinsonsDescription</li> <li>- chuv:AntiparkinsonsSideEffects</li> </ul>			
129	The class chuv:AntipsychoticDrug has properties: <ul style="list-style-type: none"> <li>- chuv:AntipsychoticsExtrapyramidalSideEffects</li> <li>- chuv:AntipsychoticsMetabolicSyndroms</li> <li>- chuv:AntipsychoticsOther</li> <li>- chuv:AntipsychoticsProlactinSymptoms</li> <li>- chuv:AntipsychoticsSexualSymptoms</li> <li>- chuv:AntipsychoticsSleepProblems</li> <li>- chuv:AntipsychoticsWeightGain</li> <li>- chuv:AntipsychoticsWeightLoss</li> </ul>			
130	The class chuv:SedativeDrug has properties: <ul style="list-style-type: none"> <li>- chuv:SedativeDescription</li> <li>- chuv:SedativeSideEffects</li> </ul>			

**Part II**Completeness / Usability of the Model

N.	Please rate the following statements (1: high disagreement, 5: high agreement)	1	2	3	4	5
1.	I think that I could contribute to this semantic model					
2.	I find the semantic model easy to understand					
3.	I think that I would need further theoretical support to be able to understand this semantic model					
4.	I found the various concepts in this semantic model were well integrated					
5.	I would imagine that most clinical experts would understand this semantic model very quickly					
6.	I am confident I understand the conceptualization of the semantic model					
7.	The concepts/properties of the semantic model cover the needs of the clinical research domain.					

If the concepts/properties of the semantic model do not cover the needs of the clinical research domain, describe the missing concepts/properties:

.....

.....

.....

.....

.....

.....

.....

.....

.....

## I.3 ZEINCRO

### Questionnaire for the Evaluation of the Linked2Safety Semantic EHR Model

Name	
Partner/Institution	ZEINCRO

#### Part I

##### Class definition questions

In the table below you can see the classes of the model presented as underlined text. Under each class, there is a definition that has been assigned to each class in the form of comment. In case you don't agree with these descriptions, please revise them accordingly.

N.	Do you agree with the definition of:	Yes	No	If no explain/propose correction or enter a reference for a definition
1	<u>studyAE:AdverseEvent</u> Similar to OAE Adverse event			
2	<u>Concmed:ConcomitantMedication</u> Concomitant medication is 2 or more treatment methods given during the same time period. This is mostly done in clinical trials. It is also fairly common to combine 2 or more treatment regimes when treating diseases and cancers. For instance, chemoradiotherapy is the concomitant (combining) of chemotherapy and radiation therapy.			

##### Questions for subclass hierarchy

The following questions are related to the subclass hierarchy of the model. Each question explains the classification hierarchy of a specific class. In case you don't agree with that, please propose a correction.

N.	Do you agree with the following statements?	Yes	No	If no explain/propose correction
3	The class studyAE:AdverseEvent is subclass of acgt:MedicalProcess (span:Process -> acgt:IntentionalProcess -> acgt:MedicalProcess)			
4	The class Concmed:ConcomitantMedication is subclass of acgt:TherapeuticProcess			

	(span:Process -> acgt:IntentionalProcess -> acgt:MedicalProcess-> acgt:TherapeuticProcess)			
--	---	--	--	--

### Properties definition questions

In the following table you can see the definitions assigned to properties of the model with the form of comment. In case you don't agree with these descriptions, please revise them accordingly.

N.	Do you agree with the definition of:	Yes	No	If no explain/propose correction or enter a reference for a definition
5	<b><u>studyAE:relat</u></b> RELATIONSHIP TO DRUG STUDY and AE			
6	<b><u>Concmed:contConcomitant</u></b> Medication continuing at final visit			
7	<b><u>Concmed:dose</u></b> Concomitant Medication Dose			
8	<b><u>Concmed:dOSG</u></b> "DATE OF SIGNATURE" for Medication.			
9	<b><u>Concmed:dSTART</u></b> Concomitant Medication Started			
10	<b><u>Concmed:freqDose</u></b> Dose frequency			
11	<b><u>Concmed:indexReason</u></b> REASON FOR USE or MEDICATION			
12	<b><u>Concmed:medication</u></b> Concomitant Medication			
13	<b><u>Concmed:nDRG</u></b> Concomitant Medication Number			
14	<b><u>studyAE:cAE</u></b> CONTINUING AT FINAL VISIT			
15	<b><u>studyAE:confr</u></b> ACTION TAKEN			
16	<b><u>studyAE:dcMED</u></b> ASTHMA OR OTHER CON.MED			
17	<b><u>studyAE:dfAE</u></b> DATE ENDED for AE			
18	<b><u>studyAE:dstAE</u></b> DATE OF ONSET			
19	<b><u>studyAE:randNO</u></b> Patient No for perticular AE			
20	<b><u>studyAE:sAE</u></b> SERIOUS AE			
21	<b><u>studyAE:sevr</u></b> SEVERITY			
22	<b><u>studyAE:siteNO</u></b> SITE NUMBER			



23	<b><u>zeincroMedHistStudyB:BRR</u></b> BreathRate			
24	<b><u>zeincroMedHistStudyB:CRD</u></b> CARDIOVASCULAR			
25	<b><u>zeincroMedHistStudyB:CRDACT1</u></b> ACTIVE RESPIRATORY 1			
26	<b><u>zeincroMedHistStudyB:CRDACT2</u></b> ACTIVE RESPIRATORY 2			
27	<b><u>zeincroMedHistStudyB:CRDACT3</u></b> ACTIVE RESPIRATORY 3			
28	<b><u>zeincroMedHistStudyB:CRDINF1</u></b> PROVIDE INFORMATION CARDIOVASCULAR 1			
29	<b><u>zeincroMedHistStudyB:CRDINF2</u></b> PROVIDE INFORMATION RESPIRATORY 2			
30	<b><u>zeincroMedHistStudyB:CRDINF3</u></b> PROVIDE INFORMATION RESPIRATORY 3			
31	<b><u>zeincroMedHistStudyB:DABDM</u></b> DESCRIBE ABNORMAL. ABDOMEN			
32	<b><u>zeincroMedHistStudyB:DBP</u></b> DBP(mmHg)			
33	<b><u>zeincroMedHistStudyB:DCARDV</u></b> DESCRIBE ABNORMAL. CAR/LAR			
34	<b><u>zeincroMedHistStudyB:DCRD1</u></b> ONSET DATE CARDIOVASCULAR 1			
35	<b><u>zeincroMedHistStudyB:DCRD2</u></b> ONSET DATE RESPIRATORY 2			
36	<b><u>zeincroMedHistStudyB:DCRD3</u></b> ONSET DATE RESPIRATORY 3			
37	<b><u>zeincroMedHistStudyB:DEARS</u></b> Medical History - Study B - DESCRIBE ABNORMAL. EARS			
38	<b><u>zeincroMedHistStudyB:DEYES</u></b> Medical History - Study B			
39	<b><u>zeincroMedHistStudyB:DGNAP</u></b> Medical History - Study B - DESCRIBE ABNORMAL. G.AP.			
40	<b><u>zeincroMedHistStudyB:DGNTR</u></b> Description of GNTR			
41	<b><u>zeincroMedHistStudyB:DGST1</u></b> ONSET DATE GASTROINTESTINAL 1			
42	<b><u>zeincroMedHistStudyB:DHEAD</u></b> Medical History - Study B - DESCRIBE ABNORMAL. HEAD			
43	<b><u>zeincroMedHistStudyB:DHNT1</u></b> ONSET DATE HEENT 1			
44	<b><u>zeincroMedHistStudyB:DHNT2</u></b> ONSET DATE HEENT 2			

45	<b><u>zeincroMedHistStudyB:DHNT3</u></b> ONSET DATE HEENT 3			
46	<b><u>zeincroMedHistStudyB:DLYMPH</u></b> Description of Abnormal Lymph			
47	<b><u>zeincroMedHistStudyB:DNECK</u></b> DESCRIBE ABNORMAL. NECK			
48	<b><u>zeincroMedHistStudyB:DNEUR</u></b> Describe Abnormal Neurological			
49	<b><u>zeincroMedHistStudyB:DNOSE</u></b> DESCRIBE ABNORMAL. NOSE			
50	<b><u>zeincroMedHistStudyB:DOTHAB</u></b> Other Abnormal			
51	<b><u>zeincroMedHistStudyB:DRSP1</u></b> ONSET DATE RESPIRATORY 1			
52	<b><u>zeincroMedHistStudyB:DRSP2</u></b> ONSET DATE RESPIRATORY 2			
53	<b><u>zeincroMedHistStudyB:DRSP3</u></b> ONSET DATE RESPIRATORY 3			
54	<b><u>zeincroMedHistStudyB:DSKIN</u></b> Describe abnormal skin			
55	<b><u>zeincroMedHistStudyB:EARS</u></b> Medical History - Study B - EAR			
56	<b><u>zeincroMedHistStudyB:EYES</u></b> EYES			
57	<b><u>zeincroMedHistStudyB:GNAP</u></b> Medical History - Study B - GENERAL APPEARANCE			
58	<b><u>zeincroMedHistStudyB:GNTR</u></b> GENITOURINARY			
59	<b><u>zeincroMedHistStudyB:GST</u></b> GASTROINTESTINAL			
60	<b><u>zeincroMedHistStudyB:GSTINF1</u></b> PROVIDE INFORMATION GASTROINTESTINAL 1			
61	<b><u>zeincroMedHistStudyB:HEAD</u></b> Medical History - Study B - HEAD			
62	<b><u>zeincroMedHistStudyB:HNT</u></b> HEENT			
63	<b><u>zeincroMedHistStudyB:HNTACT1</u></b> ACTIVE HEENT 1			
64	<b><u>zeincroMedHistStudyB:HNTACT2</u></b> ACTIVE HEENT 2			
65	<b><u>zeincroMedHistStudyB:HNTACT3</u></b> ACTIVE HEENT 3			
66	<b><u>zeincroMedHistStudyB:HNTINF1</u></b> PROVIDE INFORMATION HEENT 1			
67	<b><u>zeincroMedHistStudyB:HNTINF2</u></b> PROVIDE INFORMATION HEENT 2			

68	<b><u>zeincroMedHistStudyB:HNTINF3</u></b> PROVIDE INFORMATION HEENT 3			
69	<b><u>zeincroMedHistStudyB:HR</u></b> HeartRate (in BPM)			
70	<b><u>zeincroMedHistStudyB:LYMPH</u></b> Lymph			
71	<b><u>zeincroMedHistStudyB:NOSE</u></b> Medical History - Study B			
72	<b><u>zeincroMedHistStudyB:OTHAB</u></b> Other			
73	<b><u>zeincroMedHistStudyB:OTHST</u></b> Define Other System			
74	<b><u>zeincroMedHistStudyB:RSP</u></b> RESPIRATORY			
75	<b><u>zeincroMedHistStudyB:RSPACT1</u></b> ACTIVE RESPIRATORY 1			
76	<b><u>zeincroMedHistStudyB:RSPACT2</u></b> ACTIVE RESPIRATORY 2			
77	<b><u>zeincroMedHistStudyB:RSPACT3</u></b> ACTIVE RESPIRATORY 3			
78	<b><u>zeincroMedHistStudyB:RSPINF1</u></b> PROVIDE INFORMATION RESPIRATORY 1			
79	<b><u>zeincroMedHistStudyB:RSPINF2</u></b> PROVIDE INFORMATION RESPIRATORY 2			
80	<b><u>zeincroMedHistStudyB:RSPINF3</u></b> PROVIDE INFORMATION RESPIRATORY 3			
81	<b><u>zeincroMedHistStudyB:SBP</u></b> SBP(mmHg)			
82	<b><u>zeincroMedHistStudyB:SKIN</u></b> Skin - Study B			
83	<b><u>zeincroMedHistStudyB:TMP</u></b> TMP			
84	<b><u>zeincroMedHistStudyC:HEENT</u></b> HEENT HISTORY			
85	<b><u>zeincroMedHistStudyC:HEENT_D1</u></b> ONSET DATE 1			
86	<b><u>zeincroMedHistStudyC:INF1 HEENT</u></b> HEENT HISTORY INFORMATION 1			

In the current state of the model, the following properties are not further described.

N.	Is clear the meaning of the following properties which are not further defined:	Yes	No	If no explain/propose a definition
87	studyAE:aen			
88	studyAE:aeTerm			

89	studyAE:nAE			
90	studyAE:outcum			
91	studyAE:patNo			
92	zeincroMedHistStudyB:ABDM			
93	zeincroMedHistStudyB:DLUNG			
94	zeincroMedHistStudyB:DTHROAT			
95	zeincroMedHistStudyB:EXTR			
96	zeincroMedHistStudyB:LUNG			
97	zeincroMedHistStudyB:MUSC			
98	zeincroMedHistStudyB:NECK			
99	zeincroMedHistStudyB:NEUR			
100	zeincroMedHistStudyB:THROAT			
101	zeincroMedHistStudyB:THYR			

#### Questions for the range of properties

In the following questions you can revise the range of the properties. In particular, there are several types set to properties: string, date, integer, range, and object.

N.	Do you agree with the range of the following properties?	Yes	No	If no explain/propose correction
	<b>Range: String</b>			
102	Concmed:medication			
103	studyAE:aeTerm			
104	Concmed:dose			
105	Concmed:freqDose			
106	zeincroMedHistStudyB:CRDINF1			
107	zeincroMedHistStudyB:CRDINF2			
108	zeincroMedHistStudyB:CRDINF3			
109	zeincroMedHistStudyB:DABDM			
110	zeincroMedHistStudyB:DCARDV			
111	zeincroMedHistStudyB:DEARS			
112	zeincroMedHistStudyB:DEYES			
113	zeincroMedHistStudyB:DGNAP			
114	zeincroMedHistStudyB:DGNTNTR			

115	zeincroMedHistStudyB:DHEAD			
116	zeincroMedHistStudyB:DLUNG			
117	zeincroMedHistStudyB:DLYMPH			
118	zeincroMedHistStudyB:DNECK			
119	zeincroMedHistStudyB:DNEUR			
120	zeincroMedHistStudyB:DNOSE			
121	zeincroMedHistStudyB:DOTHAB			
122	zeincroMedHistStudyB:DSKIN			
123	zeincroMedHistStudyB:DTHROAT			
124	zeincroMedHistStudyB:GSTINF1			
125	zeincroMedHistStudyB:HNTINF1			
126	zeincroMedHistStudyB:HNTINF2			
127	zeincroMedHistStudyB:HNTINF3			
128	zeincroMedHistStudyB:OTHST			
129	zeincroMedHistStudyB:RSPINF1			
130	zeincroMedHistStudyB:RSPINF2			
131	zeincroMedHistStudyB:RSPINF3			
132	zeincroMedHistStudyC:INF1_HEENT			
	<b>Range: Integer</b>			
133	Concmed:nDRG			
134	studyAE:aen			
135	studyAE:cAE			
136	studyAE:confr			
137	studyAE:dstAE			
138	studyAE:nAE			
139	studyAE:outcum			
140	studyAE:patNo			
141	studyAE:randNO			
142	studyAE:sAE			
143	studyAE:sevrt			
144	studyAE:siteNO			
145	zeincroMedHistStudyB:BRR			
146	zeincroMedHistStudyB:DBP			

147	zeincroMedHistStudyB:HR			
148	zeincroMedHistStudyB:SBP			
149	zeincroMedHistStudyB:TMP			
	<b>Range</b>			
150	<u>zeincroMedHistStudyB:ABDM</u> {1,2,3}			
151	<u>zeincroMedHistStudyB:CARDV</u> {1, 2, 3}			
152	<u>zeincroMedHistStudyB:CRD</u> {0, 1, 99}			
153	<u>zeincroMedHistStudyB:CRDACT1</u> {0, 1, 99}			
154	<u>zeincroMedHistStudyB:CRDACT2</u> {0, 1, 99}			
155	<u>zeincroMedHistStudyB:CRDACT3</u> {0, 1, 99}			
156	<u>zeincroMedHistStudyB:DGST1</u> {0, 1, 99}			
157	<u>zeincroMedHistStudyB:EARS</u> {1, 2, 3}			
158	<u>zeincroMedHistStudyB:EXTR</u> {1, 2, 3}			
159	<u>zeincroMedHistStudyB:EYES</u> {1, 2, 3}			
160	<u>zeincroMedHistStudyB:GNAP</u> {1, 2, 3}			
161	<u>zeincroMedHistStudyB:GNTR</u> {"1", "2", "3"}			
162	<u>zeincroMedHistStudyB:GST</u> {0, 1, 99}			
163	<u>zeincroMedHistStudyB:HEAD</u> {1, 2, 3}			
164	<u>zeincroMedHistStudyB:HNT</u> {"0", "1", "99"}			
165	<u>zeincroMedHistStudyB:HNTACT1</u> {"0", "1", "99"}			
166	<u>zeincroMedHistStudyB:HNTACT2</u> {"0", "1", "99"}			
167	<u>zeincroMedHistStudyB:HNTACT3</u> {"0", "1", "99"}			
168	<u>zeincroMedHistStudyB:LUNG</u> {1, 2, 3}			
169	<u>zeincroMedHistStudyB:LYMPH</u> {"1", "2", "3"}			
170	<u>zeincroMedHistStudyB:MUSC</u> {1, 2, 3}			

171	<u>zeincroMedHistStudyB:NECK</u> {1, 2, 3}			
172	<u>zeincroMedHistStudyB:NEUR</u> {"1", "2", "3"}			
173	<u>zeincroMedHistStudyB:NOSE</u> {1, 2, 3}			
174	<u>zeincroMedHistStudyB:OTHAB</u> {"1", "2", "3"}			
175	<u>zeincroMedHistStudyB:RSP</u> {"0", "1", "99"}			
176	<u>zeincroMedHistStudyB:RSPACT1</u> {0, 1, 99}			
177	<u>zeincroMedHistStudyB:RSPACT2</u> {0, 1, 99}			
178	<u>zeincroMedHistStudyB:RSPACT3</u> {0, 1, 99}			
179	<u>zeincroMedHistStudyB:SKIN</u> {"1", "2", "3"}			
180	<u>zeincroMedHistStudyB:THROAT</u> {1, 2, 3}			
181	<u>zeincroMedHistStudyB:THYR</u> {1, 2, 3}			
182	<u>zeincroMedHistStudyC:HEENT</u> {"N/A", "NO", "YES"}			
	<b>Range: Date</b>			
183	zeincroMedHistStudyB:DCRD1			
184	zeincroMedHistStudyB:DCRD2			
185	zeincroMedHistStudyB:DCRD3			
186	zeincroMedHistStudyB:DHNT1			
187	zeincroMedHistStudyB:DHNT2			
188	zeincroMedHistStudyB:DHNT3			
189	zeincroMedHistStudyB:DRSP1			
190	zeincroMedHistStudyB:DRSP2			
191	zeincroMedHistStudyB:DRSP3			
192	zeincroMedHistStudyC:HEENT_D1			
	<b>Range: Object</b>			
193	The property studyAE:relat receives values from class acgt:Drug			

The range of the following properties is not specified. Please define.

	<b>Range: na</b>			
194	Concmed:contConcomitant			

195	Concmed:dOSG			
196	Concmed:dSTART			
197	Concmed:indexReason			
198	studyAE:dcMED			
199	studyAE:dfAE			

### Questions for relations between concepts

Classes have attributes which describe the instances of each class. Please revise these relations and contribute where needed.

N.	Do you agree with the following statements?	Yes	No	If no explain/propose correction
200	<p>The class studyAE:AdverseEvent has properties:</p> <ul style="list-style-type: none"> <li>- studyAE:relat</li> <li>- studyAE:aen</li> <li>- studyAE:aeTerm</li> <li>- studyAE:cAE</li> <li>- studyAE:confr</li> <li>- studyAE:dstAE</li> <li>- studyAE:nAE</li> <li>- studyAE:outcum</li> <li>- studyAE:patNo</li> <li>- studyAE:randNO</li> <li>- studyAE:sAE</li> <li>- studyAE:sevr</li> </ul>			
201	<p>The class Concmed:ConcomitantMedication has properties:</p> <ul style="list-style-type: none"> <li>- Concmed:dose</li> <li>- Concmed:dOSG</li> <li>- Concmed:dSTART</li> <li>- Concmed:freqDose</li> <li>- Concmed:indexReason</li> <li>- Concmed:medication</li> <li>- Concmed:nDRG</li> <li>- studyAE:patNo</li> <li>- studyAE:randNO</li> <li>- studyAE:siteNO</li> </ul>			
202	<p>The class snap:Site has property:</p> <ul style="list-style-type: none"> <li>- studyAE:siteNO</li> </ul>			
203	<p>The class acgt:Patient has properties:</p> <ul style="list-style-type: none"> <li>- Concmed:medication</li> <li>- studyAE:patNo</li> </ul>			



**Part II**Completeness / Usability of the Model

N.	Please rate the following statements (1: high disagreement, 5: high agreement)	1	2	3	4	5
1.	I think that I could contribute to this semantic model					
2.	I find the semantic model easy to understand					
3.	I think that I would need further theoretical support to be able to understand this semantic model					
4.	I found the various concepts in this semantic model were well integrated					
5.	I would imagine that most clinical experts would understand this semantic model very quickly					
6.	I am confident I understand the conceptualization of the semantic model					
7.	The concepts/properties of the semantic model cover the needs of the clinical research domain.					

If the concepts/properties of the semantic model do not cover the needs of the clinical research domain, describe the missing concepts/properties:

.....

.....

.....

.....

.....

.....

.....

.....

.....