Ontological Representation of Adverse Drug Reactions Using the Fundational Model of Anatomy

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Abstract. In a previous work we proposed a categorial structure for the representation of adverse drug reactions consisting of 16 semantic categories and 20 relations. We present an implementation of this categorial structure in Protégé based on four WHO-ART system organ classes: Gastro-intestinal system disorders, Liver and biliary system disorders, Central & peripheric nervous system disorders, and Psychiatric disorders. We compared classification according to anatomy using SNOMED CT within the PharmARTS tool and the FMA with the Pellet reasoner. This ontology contains 210 concepts for Gastroenterology, 66 concepts for Psychiatry and 85 concepts for Neurology. Classification of disorders located in the upper gastro intestinal tract was similar using both SNOMED CT and the FMA. This work is a first step towards the comparison of two models of anatomy within a common ontology of adverse drug reactions.

Keywords. pharmacovigilance, ontology, anatomy, Foundational Model of anatomy

1. Introduction

Terminologies used for coding of adverse drug reactions are WHO-ART (World Health Organisation-Adverse Reaction Terminology) and MedDRA (Medical Dictionary for Drug Regulatory Activities). In a previous work we assumed that adding formal definitions to both terminologies can improve performances of signal detection algorithms for pharmacovigilance, and proposed a categorial structure for the ontological representation of adverse drug reactions [1].

The CEN Categorial structure is defined as a minimal set of health care domain constraints to represent a biomedical terminology in a precise healthcare domain. These constraints consist of 1) a list of semantic categories; 2) the goal of the Categorial structure; 3) the list of semantic links between semantic categories authorised with their associated semantic categories; 4) the minimal constraints allowing the generation and

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validation of well formed terminological phrases. The categorial structure for pharmacovigilance consists of 20 semantic categories and 16 relations.

When building a new ontology it is recommended to reuse knowledge rather than to reinvent the wheel, and to include other categorial structures to the ontological model whenever this is possible. The Foundational Model of Anatomy is dedicated to the representation of human anatomy [2]. The European standard CATANAT is based on the FMA but allows selecting the desired level of detail for implementation [3]. We are aware of only one study in which the FMA is used for the ontological representation of disorders in ICD-10. This integration is presented from the point of view of a high-level architecture, and does not provide practical details about using the FMA [4].

Our work is part of the VIGITERMS project (http://vigitermes.univ-rennes1.fr) which objective is to build a knowledge management platform for better signal detection in pharmacovigilance. The INSERM partner has developed the PharmARTS tool that allows searching case reports in a pharmacovigilance database [5]. The queries are based on an ontology of adverse drug reaction that was extracted from the UMLS using a mapping between WHO-ART and SNOMED CT [6]. Therefore the current anatomical model in PharmARTS is based on SNOMED CT. One of the research objectives is to evaluate which anatomical model would be the most relevant for querying the pharmacovigilance database. We describe here the first step of this evaluation. The current result consists of two versions of the same ontology where the anatomy is represented by the FMA or SNOMED CT.

2. Material and Method

WHO-ART is the terminology developed and maintained by the WHO collaborating centre for international drug monitoring. The Protégé 3.3.1 editor was used for building the ontology from the categorial structure for pharmacovigilance. Each disorder was defined using six semantic categories: hasCourse, hasForDiagnosticTest, hasFunctionalAbnormality, hasLocation, hasMorphology, and hasSeverity. We describe here the implementation of this categorial structure in Protégé for four WHO-ART system organ classes: Gastroenterology (Gastro-intestinal system disorders, Liver and biliary system disorders), Neurology (Central & peripheric nervous system disorders), and Psychiatry (Psychiatric disorders).

For each Adverse Drug Reaction we used a term from the FMA to describe the anatomical localisation where relevant (most psychiatric disorders do not have an anatomical location). For example the duodenum is described in the FMA as an organ segment which is part of the small intestine, the gastrointestinal tract and the upper gastrointestinal tract (Figure 1). We implemented all semantic categories of the categorial structure with their inverse relations and added the necessary relations for the FMA for example isContainedIn, isContinuousWith and isPartOf.

Figure 1. Representation of duodenum using the FMA
In order to test the classification of the ontology according to the FMA we used a defined concept PartOfUpperGastroIntestinalTract as the set of all MaterialPhysicalEntities located in the UpperGastroIntestinalTract. Another concept was defined as the set of disorders located in the upper digestive tract (Figure 2). We checked the consistency and classified the ontology with the Pellet reasoner (http://clarkparsia.com/pellet).

Figure 2. Disorders of the upper digestive tract in Protégé

We selected the Upper_gastrointestinal_tract_structure SNOMED CT concept in PharmARTS and found 109 WHO-ART related concepts such as indigestion, haematemesis or haemorrhagic peptic ulcer (Figure 3).

Figure 3. Disorders of the upper digestive tract

3. Results

Figure 4 presents the implementation of the categorial structure using Protégé with the hierarchy of concepts on the left and semantic relations on the right. The semantic categories were: Course, Disorder, Drug, administration, Function, Human anatomy, Investigation, Living organism, Measure, Morphology, Severity, and Value. We chose the name “Human anatomy” instead of “Location” to refer to the FMA. Contrary to the categorial structure, we used “Body substance” instead of “Specimen” because Body substance is a conceptual entity in the FMA. Sign or symptom, Structural disorder and Syndrome were implemented as children of disorders whereas they were semantic categories in the categorial structure. The number of formal definitions was equal to 210 for Gastroenterology, 66 for Psychiatry and 85 for neurology.

When comparing the grouping of disorders located in the upper gastrointestinal tract we found a few abnormal WHOART terms proposed by PharmARTS but not by the classification of our ontology within Protégé. These errors in PharmARTS were observed for disorders located in the anal_structure such as rectal bleeding. This was
not related to an abnormal modelling in SNOMED CT as anal_structure is a lower_gastrointestinal_structure and was probably due to an anomaly in the terminological reasoning within PharmARTS.

4. Discussion and Conclusion

This version of the adverse drug reactions ontology implementing our categorial structure does not take abnormal investigation results into account for example ECG abnormal or ALAT increased. Only six semantic categories and the corresponding semantic links were implemented. We have to include additional WHO-ART system organ classes (SOC) in order to test modelling of terms that are specific to pharmacovigilance. Some examples are related to Modality for example Application
site necrosis (Application site disorders SOC) or Administration for example Overdose effect (Body as a whole – General disorders SOC).

When considering results related to disorders of the upper gastrointestinal tract differences were not related to different models of anatomy between SNOMED CT and the FMA but to an abnormal terminological reasoning in PharmARTS that requires clarification. This work is a first step towards the comparison of two models of anatomy within a common ontology of adverse drug reactions. Bodenreider and Zhang have not noticed any major discrepancies between the FMA and SNOMED CT in their representation of anatomical entities [7]. We do not know any work that describes how the FMA compares with the anatomical model of SNOMED CT when implementing an ontology of disorders.

The FMA contains several part whole relations that add more options for modelling but generate difficulties when performing terminological reasoning [8]. Modelling of anatomy in SNOMED CT is based on SEP triples that allow representing part whole relations as hierarchical relations between structures [9]. For example Stomach_structure is one kind of Upper_gastro_intestinal_structure in SNOMED CT, and Stomach is part of the Upper Gastrointestinal tract in the FMA. We plan to continue this comparison between the FMA and the anatomical model of SNOMED CT by comparing how both models help to represent other WHO-ART system organ classes, and how terminological reasoning is performed using more complex use cases.

Acknowledgment. We acknowledge the French Agence nationale pour la recherche (National Agency for Research) for granting the VigiTerms project ANR-07-TECSAN-026.

References