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Ontological Modelling of FEST with support for DDI Reasoning

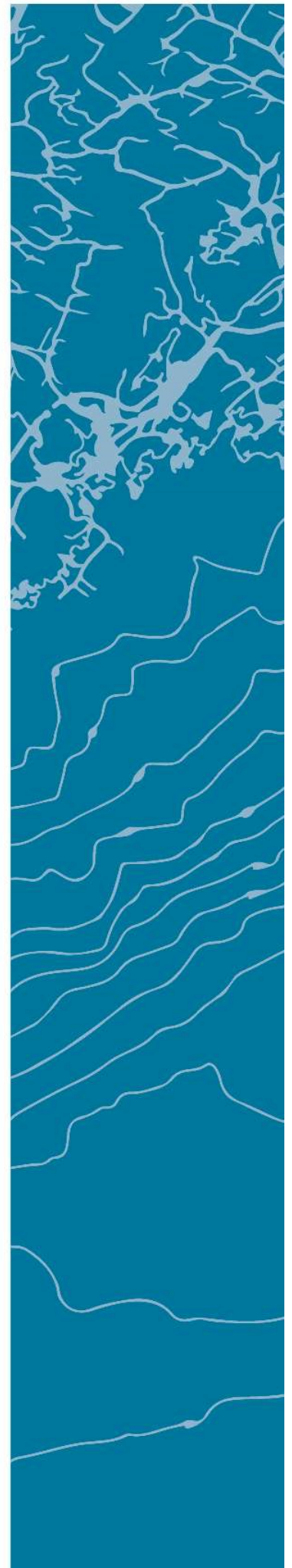
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UNIVERSITY OF AGDER

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DDI Reasoning

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ABSTRACT:

FEST is a Norwegian database and information service aimed towards providing all the required pharmaceutical data to different stakeholders such as hospitals, pharmaceutical companies, and practitioners. FEST being a complete pharmaceutical database, ensures every information related to drugs such as dosage, form of drug, interactions, and brand. FEST database is represented as an XML and schema files. In this master thesis, we propose an open and linked data representation approach of FEST database by modelling it as an Ontology. We propose the integration of FEST ontology with other systems and ontologies for semantic interoperability which is one of the main challenge in current e-health world. We propose in this thesis a method for the representation of drug-drug interaction in context with patient's family member history. We will use SPARQL queries on existing data in FEST ontology to generate implicit information about possible drug-drug interaction. Using the existing drug interactions in FEST, we will represent a method to classify those interactions according to different interaction mechanisms.

PREFACE

This report summarizes the Master thesis work taken at the Department of Information and Communication Technology (ICT), University of Agder (UiA), Campus Grimstad, Norway, from 2 January 2017 to 21 May 2017. The workload is equivalent to 30 ECTS.

My supervisors have been Associate Professor Jan Pettersen Nytnun, and Assistant Professor Martin Wulf Gerdes, University of Agder. I would like to express my gratitude to both the supervisors for their invaluable and profound guidance throughout the thesis period. I would specially pay my gratitude to Mr. Jan Pettersen for not only supervising the master thesis, but also coordinating and helping through out the master degree. I appreciate how the supervisors allowed me to experiment with new ideas during the thesis. I wish to express my love and gratitude for my parents, my Khaala, brothers, and friends who have directly or indirectly motivated me for the successful completion of this thesis. I would like to dedicate this thesis to Mr. Javed Shaffi who has been a source of enthusiasm for me throughout my studies. A noteworthy appreciation for classmates with whom I have spent my two years.

Production note: We use Microsoft Word as the tool for writing this thesis. Ontology development was done in Protégé environment.

Raes Abbas

21 May 2017

Grimstad, Norway

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1 INTRODUCTION

The current modern world is finding IT solutions for common problems in every field of life, and domain of e-health is no exception. System developers are making tools to provide better healthcare systems for different domains such as hospitals, pharmacies, and patients. When it comes to pharmaceuticals, we find many different systems such as SystemX¹, Kjernejournal², and DINTO³, that are being utilized to represent varied information related to patient journals and drugs such as interactions, dosage, and side effects. FEST is also such a system, used in Norway, that exposes pharmaceutical information to pharmacies, labs, patients, practitioners, and hospitals. HL7 is also working towards defining standard protocols for clinical information exchange between different systems. Representation of FEST as an ontology will help us not only to infer more data from the existing, but also to integrate FEST with other health care systems and ontologies such as DINTO, SNOMED and FHIR.

1.1 Background

Artificial intelligence, automatic decision-making capabilities, and representation of big data is of huge interest [1]for current research community. More and more efforts are being made to make the computers able to make decisions according to defined standards and rules. This results in more meaningful and usable interpretation of stored data. In the e-health world, we see different intelligent systems and technologies such are developed to aid practitioners and health industry. That includes, but is not limited to, databases to store pharmaceutical information, EHR's of patients etc.

Semantic web also enables the machines and computers to read the stored data and extract valuable information. Let's take an example from real world, If we want to retrieve a list containing heads of department of different universities, it may not be possible to do it by simply searching through a search engine. The information is available on the internet, but still is not accessible in form of a list. This is due to the fact that information is stored in such a format that machines are unable to make a meaning of that data. Suppose If the information is stored in such a manner that computers can read it and interpret its meaning according to defined rules. In this case, we do not need to go through multiple webpages to retrieve the

¹ systemx.no

² <https://helsenorge.no/kjernejournal>

³ <https://bioportal.bioontology.org/ontologies/DINTO>

concerned list . Figure below illustrates the example of storing information in machine readable format:

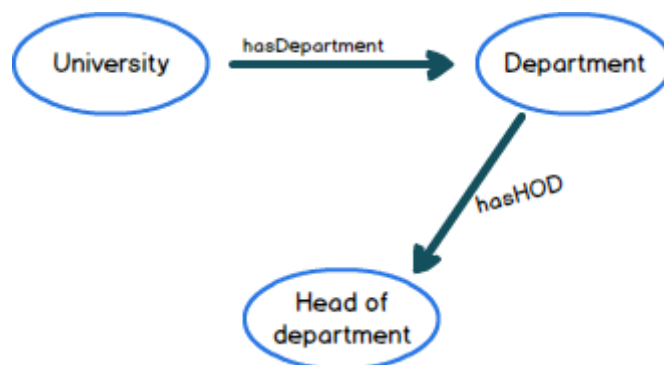


Figure 1.1 Representation of heads of department

Every head of department will be stored with an property hasHOD, and we then simply has to query for all the objects that are linked with this property, which will generate us a list.

This thesis will contribute to the field of e-health and semantic interoperability by utilizing the logics of semantic web. We bring forward a representation of FEST database as an ontology to enable reasoning and inferencing, and to integrate the FEST ontology with other ontologies to provide better solutions for problems such as generating information for drug interactions.

1.2 Motivation

Motivation behind this particular master thesis is mainly to contribute to the health industry of Norway by encouraging use of ontologies for clinical data exchange, and to aid to semantic interoperability. The Norwegian Medicines Agency is also working on a similar concept to enable representation of FEST as open and linked data [2], and a short communication with one of the adviosrs working there also gave us positive feedback about working with the FEST model. We have been working in the fielkd of e-Health from the last two years,and have done three different projects which has motivated us to continue working in this direction because we believe there are several possibilities in this field to explore.

1.3 Problem Statement and Goals

Exposure of pharmaceutical data to different stakeholders such as hospitals, pharmaceutical companies, doctors etc. in Norway is currently done by using FEST database. All the stakeholders have to download the XML files, which are regularly updated, and put them in their systems, or they have to use an automatic system that searches periodically for the updates and downloads the new version by itself. We demonstrate and establish in this thesis that an ontological representation of FEST can lead to many advantages such as semantic

interoperability, and integration with other ontologies. We also expect to exhibit some of the use cases by inferring new information from the existing data. FEST administration is also working on representing the data using an ontology, and so far they have represented 1-2 resources for messaging. This thesis, however, will particularly address the following issues:

- Developing an ontological model of FEST database for the representation of pharmaceutical data
 - Ontology should at least represent all the information related to drugs, i.e. coding system, ingredients/substances etc.
- Using the ontological model to represent implicit drug-drug interaction in context to patient's family member history.
- Using the FEST ontological model to represent drug interaction mechanisms.

1.4 Key suppositions and Limitations

We have made certain constraints and suppositions when it comes to ontological representation of FEST. The ontology mainly focuses on drug related information, and doesn't necessarily deals with the information related to the catalogues such as **Refusjon**, **Vilkår**, **Byttegruppe**, and **Handelsvare**. We also have certain limitations on drug-drug interaction representation also. For example, currently we only represent drug interaction between only two drugs/substances. Moreover, this thesis does not focus on description and in-depth working of FEST XML database. However, we have described the purpose and usage of classes that we have mapped to the ontology in relevant chapter. The classes and attributes in ontology are developed in Norwegian language, because we believe that continuation of this thesis would be to import the data instances from FEST XML, and same language vocabulary will be beneficial. However, for the purpose of understanding, we have added a description of Norwegian words in APPENDIX A.

1.5 Related work

As discussed previously, two of the catalogues that are **VarselfraSLV**, and **Kodeverk** have been represented using an ontology [3] by Norwegian Medicines Agency. At the moment, notifications are sent to pharmacies and hospitals in form of simple text. **Kodeverk** and **Pakning** catalogues are not completely implemented, and the only information from these catalogues which is linked with **VarselfraSLV** is represented as an ontology. The catalogue **VarselfraSLV**, implemented as an ontology is used to send notifications about certain issues such as warnings, drug shortage and safety messages. While catalogue **Kodeverk** is used to

store information related to different coding systems used in FEST. Please refer to section [3.13](#) and [3.14](#) for more information about these catalogues.

In the field of semantic web, a sub group of HL7 ITS work group, known as RDF group is also working on different projects to encourage use of RDF for exchanging healthcare information. One of their project is to represent FHIR resources in RDF format [4].

When it comes to drug-drug interactions, DINTO and DIO are two well-known ontologies used for classification of drug interactions. We also submitted a paper “Mapping FHIR Resources to Ontology for DDI reasoning” in SHI 2017: Scandinavian Conference on Health Informatics and are yet to receive comments. In this paper, along with co-authors, we developed an customized FHIR ontology and used it to infer data about drug interactions.

2 Literature Review

2.1 Theoretical Background

2.1.1 Semantic Web

Semantic web, an approach which differs to the traditional web, is generally termed and described as a “Web of data”. A Web of data may consist of dates, properties, numbers, names, and in general any data that we can imagine and think of. As further described by W3C, fundamental motto of the semantic web is to make the data machine readable, because mostly in the web techniques like HTML, data is only for human consumption. While in semantic web, machines can read the data, deduce meaning from that, and link it with other information through inference to provide more meaningful, and in some cases implicit, information. Technologies (RDF, SPARQL, OWL, SWRL etc.) that are defined under the umbrella of semantic web, enable us to build databases, vocabularies, and rule bases to manipulate the stored information [5].

Benefit of semantic web is realized through Linked and Open data. We have huge amount of data currently available over the internet, and is stored using different schemes and databases. Rules and relations can be defined in a proper and standardized way to link this data and make it available across multiple applications and systems.

Vocabularies or terms are one of the most fundamental part of semantic web and linked data. Imagine, for instance, the vocabulary used in medical industry to describe different information related to drugs, diseases, symptoms and prescriptions [6]. A common and standardized vocabulary, in this case, to represent drug information can enable different institutions, pharmacies, and researchers to exchange data between different platforms, which will enable to create more sophisticated decision support systems for better and enhanced treatment.

Another aspect of semantic web is the powerful query language support. Technologies such as SPARQL, Description Logic, and SWRL Rules are widely used to query and infer data. In some sense, similar to querying relational databases, SPARQL queries are used to retrieve and store data in semantic web.

Inference in the semantic web terminology is effectively used to deduce more information from the already existing data by defining specific rules and restrictions. Inference on semantic data enables to generate implicit data, which means that we don't have to define explicitly all the data related to a particular entity. For example, if we have a database of a family, we don't have to define all the relations between every individual. Let's say if X has father Y, and Y has father

Z, then it's not required to explicitly state that X is grandchild of Z. Instead, we can create a rule base with specific rules about who can be classified as a grandchild, and then through inference we can generate this implicit relation.

Tim Berners-Lee, known as father of world wide web, explains the concept of semantic web in an informal way by stating that *"The Semantic Web is an extension of the current web in which information is given well-defined meaning, better enabling computers and people to work in cooperation."* [7]. A visual representation of the structure realized by Tim Berners-Lee is shown in the figure below which is often termed as Semantic web tower:

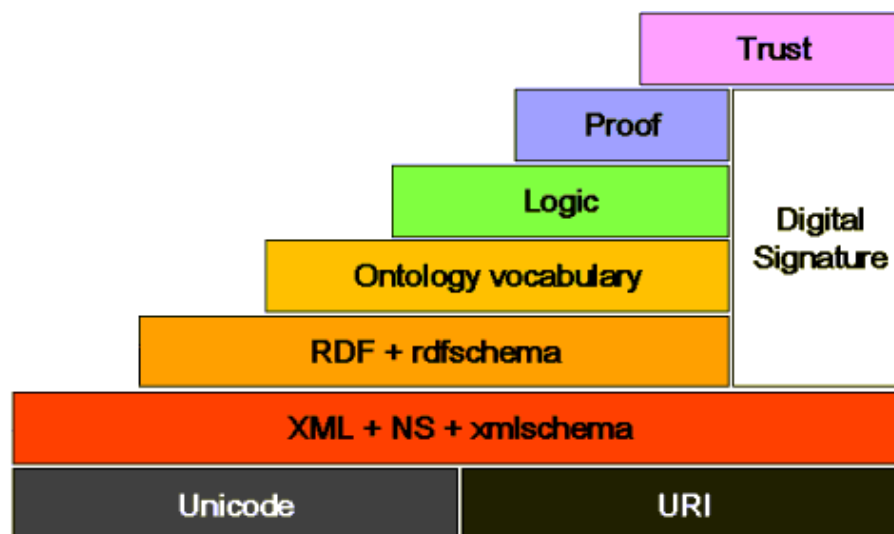


Figure 2.1 Layers of Semantic web tower [7]

The layers in the tower are used to represent concepts at different levels with Unicode and URI's at the lowest level. When we move upwards in the tower, the concepts get more knowledgeable such as Ontology, RDF Schema, and logics. Concepts at higher levels have more detailed description of information.

2.1.2 Ontology

An ontology, as defined by Webster, is a study of metaphysics and explains philosophically the nature of being, and entities that are abstract. [8] An ontology explains the metaphor of realities and concepts, which in some cases are taken as entities.

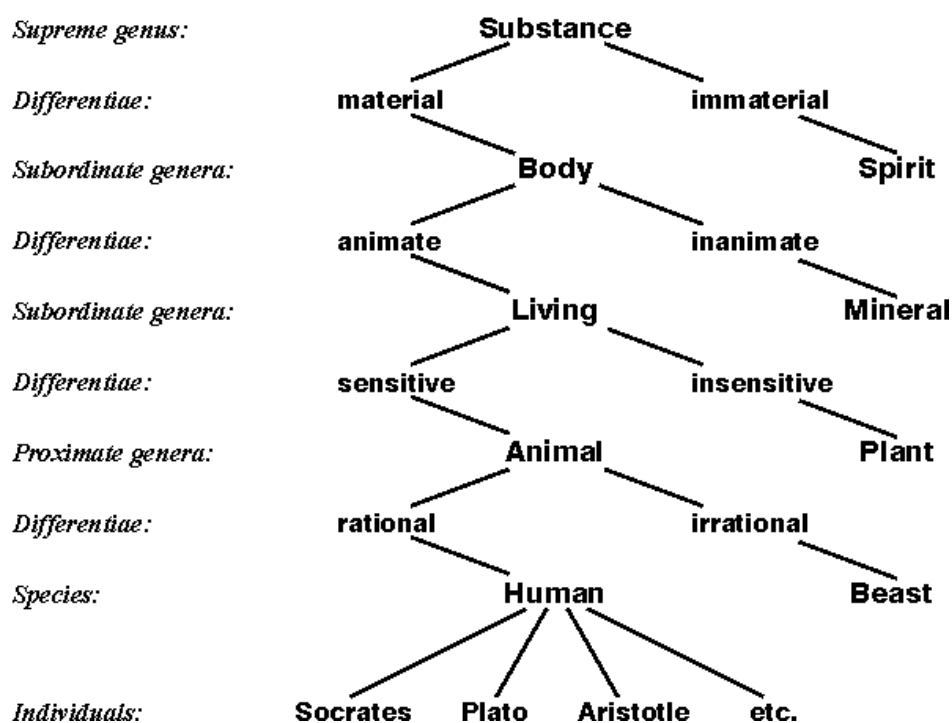


Figure 2.2 Tree of Porphyry [9]

A logician from 13th century, known as Peter of Spain, explained and classified different entities according to their features and properties [9]. Different entities were placed under different categories with all of them having a common supreme category *Substance*. We realize from the Tree of Porphyry that as we move down the structure, the entities get more concrete meaning as opposed to the top level which defines abstract concepts. This same concept is used in the world of computer science today. Classes, in computer science terminology, describe a group of different things having same features, characteristics, and activities. To further describe this concept, take an example of the category Animal in the Tree of Porphyry. In computer world, Animal would be defined as a class, which further has sub classes of Human and Beast differentiated respectively through a quality of being rational and irrational. Humans have further definition known as individuals like Plato, Socrates etc. All of these individuals have some similar features and are thus defined under the class Human. These individuals are defined as Objects or Instances in the world of computer science.

In the field of data representation, ontologies can significantly minimize the complexity of information and arrange the data in a meaningful way. Ontologies can be designed in different standardized formats such as OWL, RDF, and Turtle as shown in the figure 2.2. It is very popular and practicable to build and model data information using ontologies in different sectors such as e-Health, education, agriculture, transportation etc. For example, DINTO is an ontology used to systematically capture drug-drug interaction and related information. DINTO

is not only used to represent the interactions, but also describes different mechanisms that can lead to these drug interactions [10]. We have also used the similar concept of representing DDI mechanisms in this thesis by extending the FEST ontology.

SNOMED CT is also one of the most sophisticated ontology in the medical field, and is used to represent standardized clinical terminologies. At current, SNOMED CT is used by more than 20 different projects overall the world [11], and one of them include an ongoing project at Norwegian Institute of Public Health, which is the mapping of Norwegian national quality registries. Their goal is to systematically map all the existing overlapping variables under national registers such as Medisinsk fødselsregister⁴, Reseptregisteret⁵, and Nasjonalt vaksinasjonsregister⁶. The mapping of such all resources such as archetypes, templates, and other vocabularies is included in the project [12]. The figure below shows an example of classes and properties defined in SNOMED CT ontology.

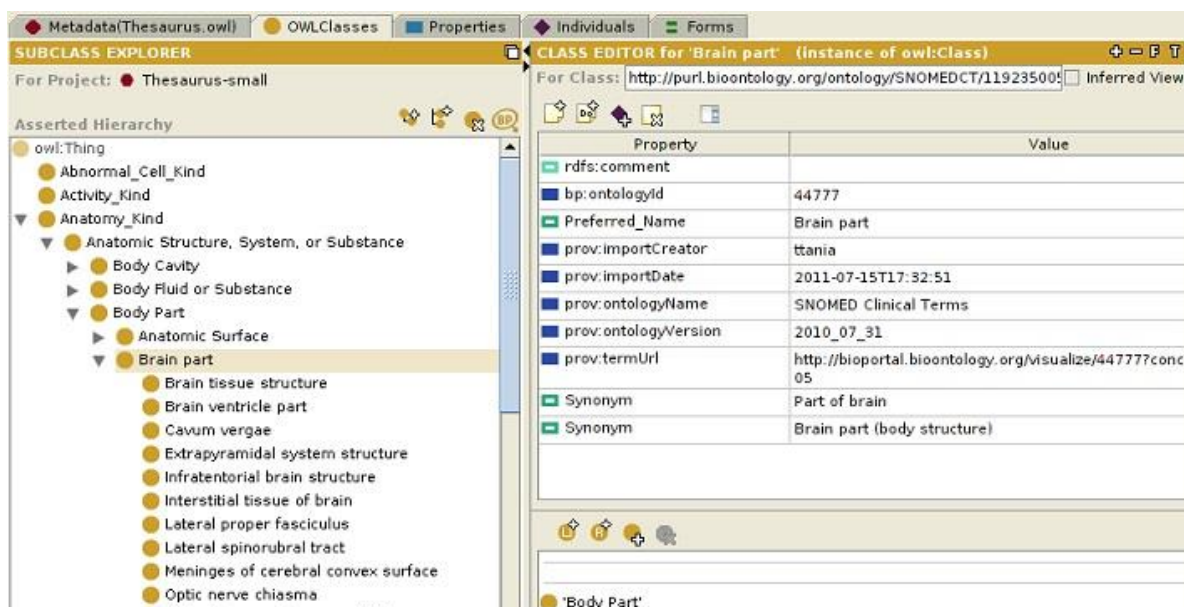


Figure 2.3 Example of SNOMED CT

Use of ontologies in some domains have always been more popular than the others. In a survey published by Jorge Cardoso in IEEE Intelligent Systems in 2007, showed that most popular domain to utilize the ontologies was Education and computer science while the usage of

⁴ <http://www.fhi.no/helseregistre/medisinsk-fodselsregister>

⁵ <http://www.fhi.no/dokumenter/b75ab8ac5b.pdf>

⁶ <http://www.fhi.no/dokumenter/9f01190ee8.pdf>

ontologies among health industry was not much popular as compared with Education [13]. The figure below shows they survey result:

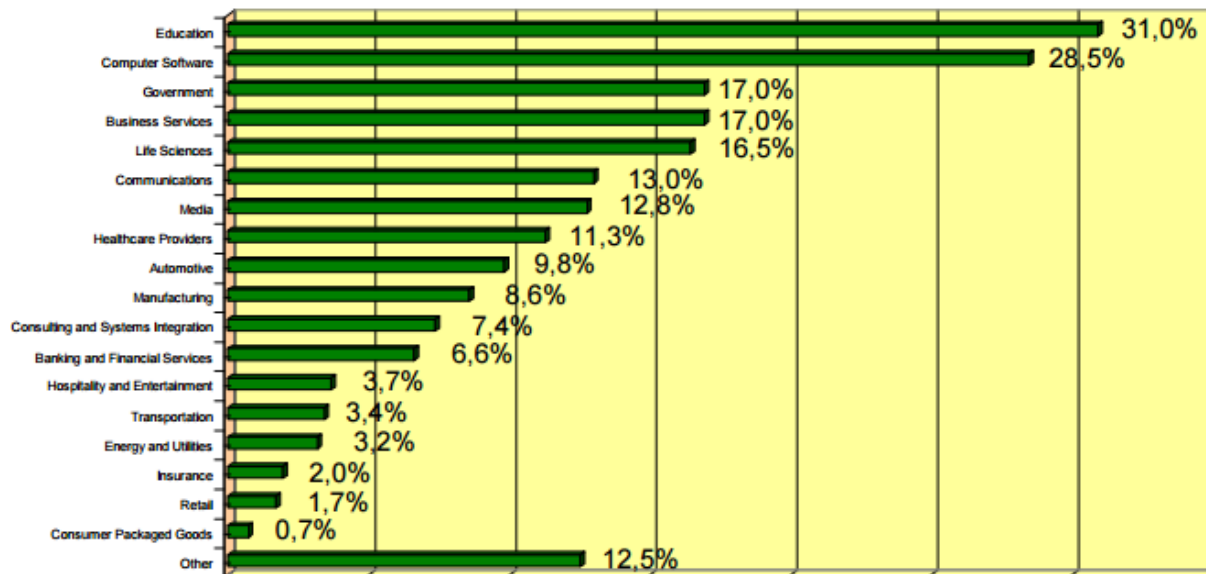


Figure 2.4 Ontologies in different domains 2007 [13]

This trend was shown to be changing by the survey done in 2013 by Sai Baba Magapu [14]. In the journal published in International Journal of Applied Information Systems, he argues that Medical field was one of the most promising field to utilize the ontologies. This shows that there is a great trend in the health sector to represent clinical data using ontologies. Ontologies define concepts and their relations to form a complete model. Most of the ontologies created in current computer world have following core components [15]:

CLASS: core concept, represents individuals having same features. For example, Human is a class to represent all the humans, Man and Woman are subclasses of Human having more specific details.

OBJECT: instances that are described by the concepts defined in Classes. For example, Ole is an object of class Man, thus it possesses all the features of a Man.

PROPERTIES: relations used to connect individuals with other individuals and classes.

Figure 2.5 below shows an example of class structure from our paper “Mapping FHIR resources to ontology for DDI reasoning” that has been submitted to Scandinavian Conference on Health Informatics - SHI 2017. We are yet to receive comments on that submission.

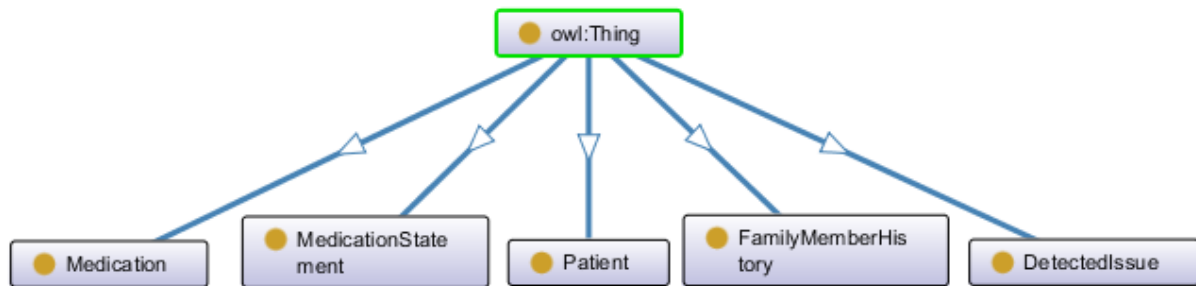


Figure 2.5 Class structure of FHIR ontology

Every class may have further subclasses or individuals. For example, the class Medication represent individuals of particular drugs along with their details.

2.1.3 Resource Description Framework

In the semantic world, RDF is a framework to represent data information using triples. W3C describes the structure of RDF as set or triples having subject, object and a predicate [16]. Each set of triples is known as RDF Graph which is visually represented in the figure below:

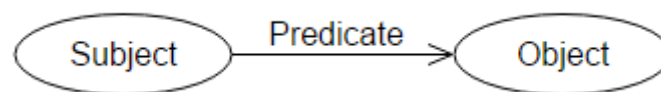


Figure 2.6 A typical RDF graph [16]

Subject in the figure above is used to describe a thing, while Object is a thing on which an action is being performed. Predicate, as visible, is used to define the relation between subject and a particular object. For example, a triple “Ole loves Jenny”, has subject “Ole” and object “Jenny”, while predicate “loves” is used to describe the relation of love between these two objects. Below is an example of an RDF triple from our paper:

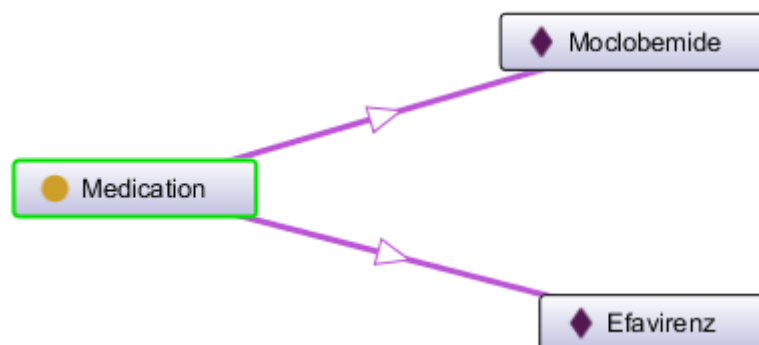


Figure 2.7 Example from FHIR Ontology

The figure above shows that an example of RDF triple with class Medication having two individuals namely Moclobemide and Efavirenz. Two triples are generated that are “Efavirenz

rdf:type Medication” and “Moclobemide rdf:type **Medication** ”. **Medication** is a subject while Efavirenz and Moclobemide are two objects.

RDF Schema, commonly known as RDFS, is an extension of RDF to provide data-modelling vocabulary [17]. As described by W3C, RDFS is complimented by different RDF concepts, RDF semantics, and standardized syntaxes such as JSON-LD and TURTLE [17]. Basic components of an ontology (Class, Object, Property) that we discussed earlier, are defined using RDFS. In case of properties, the domain and range is also defined using RDFS. It is argued that RDFS class, object and property have certain similarities with object oriented concepts. The namespace for RDFS definitions is defined by W3C and is published as IRI www.w3.org/2000/01/rdf-schema#.

2.1.4 Extensive Markup Language

XML is a markup language based on SGML⁷ developed in 1996, and is used to represent structured data and information. This data can belong to any domain such as data from libraries, pharmacies, receipts, etc. XML documents are well defined according to certain rules, and users can create custom tags to give a more logical and meaningful order to the information. One may also say, due to capability of user tags, XML is quiet similar in some aspects with HTML [18]. But when we say XML have similar concepts, it doesn't mean that their purpose of usage is same. HTML was designed predominantly to aid the display of information and data on world wide web, while XML documents are predominantly used for the sharing of data and information between systems running on different machines. Because the data being represented using XML documents has to be well formed, in order to make it machine-readable, implies that any XML document with syntax errors, logical errors will not get compiled without the particular errors being fixed [18]. An example XML code snippet is shown in the figure below which is taken from our paper:

⁷ <https://www.w3.org/TR/html4/intro/sgmltut.html>

```

<code>
  <coding>
    <system value="http://snomed.info/sct"/>
    <code value="116078005"/>
    <display value="Efavirenz 600 mg tablet "/>
  </coding>
  <coding>
    <system value="https://www.whocc.no"/>
    <code value="J05AG03"/>
    <display value="efavirenz"/>
  </coding>
</code>

```

Figure 2.8 Example of XML code

Figure 2.8 shows a code used to associate a drug by using two different coding schemes, ATC and SNOMED CT. All the tags shown in the figure i.e. *code*, *coding* etc. are not pre-defined tags, and are created by the user to give meaning to the stored data. FEST database, which is established by Norwegian Medicines Agency, is also published and delivered in XML format.

2.1.5 SPARQL

We have discussed how RDF is used to build structured database and store information which is readable by machines and computers. One of the most eminent task how efficiently and robustly that data can be retrieved. SPARQL , being a query language to retrieve RDF data, has proven to be of great help in this regard. SPARQL query language consists of different protocols and standard rules to retrieve RDF data, and these set of protocols are maintained and updated by W3C [19].

SPARQL query is also based on concept of triples, i.e. subject, predicate, and object. Similar to RDF, every entity (subject, object, predicate) is identified using IRI's. For example, we discussed the namespace of the IRI for RDFS, and whenever we have to access any class defined with RDFS namespace, we simply use prefixes **rdfs** in combination with colon ":" and property name to access the IRI. Prefixes for a specific IRI can also be defined by the user itself. An example of RDF graph along with SPARQL query is shown below which is taken from one of our projects from 2nd semester.

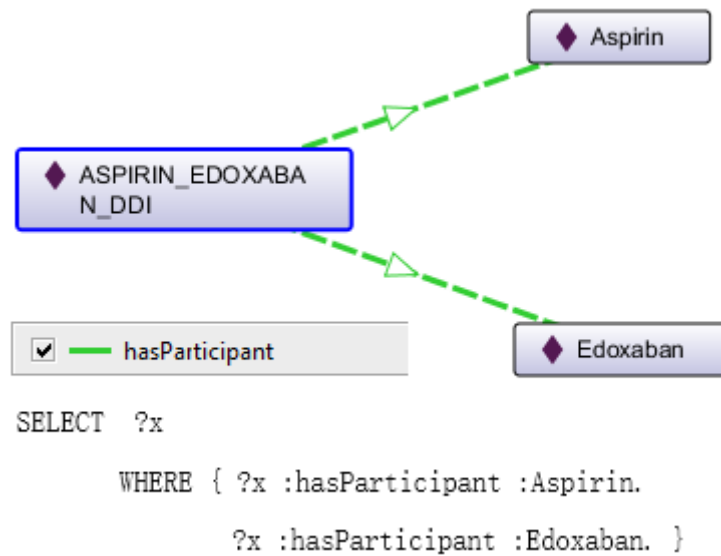


Figure 2.9 Example of a SPARQL query

The query above is used to determine whether there is an interaction between two drugs namely Aspirin, and Edoxaban. For the property and objects, a default blank prefix is used to identify the resource. Value of “x” depends whether both the triples are true or not. Figure below shows result generated in an web application for the query above, which is also taken from our previous project:

Figure 2.10 Query result for drug interaction

The result returned by the query is “ASPIRIN_EDOXABAN_DDI” which classifies that there is an interaction between these two drugs, implying that both the triples in the query were found to be true. SPARQL queries are not only used to retrieve data, but they can also be used to manipulate the stored data and add new information (triples) into the RDF store. We can also

use certain queries to define some rules, and then generate inferred data by implying those rules on the existing data. CONSTRUCT [19] query is used to generate such implicit data based on user defined rules. ASK [19] queries can be used to simply establish whether a particular triple (which may be a fact, date, name etc.) exists or not.

2.1.6 Semantic Interoperability

Semantic Interoperability, being one of the strong motivation behind this master thesis, needs an unambiguous, comprehensible, and explicit interpretation. Interoperability, in general, as defined by oxford dictionary is “*the ability of computer systems or software to exchange and make use of information*” [20]. In terms of computer science, Semantic interoperability can be further explained as the capability of two or more different systems, running independently on different or same networks, to communicate and share data information with each other so that the researchers or stakeholders can take full advantage of every bit of information available on those systems.

Semantic interoperability doesn't only deal with the sharing of data, but also concerns about how the semantic meaning of the information can be shared, and how can metadata and vocabulary can be extended so that the receiving systems can interpret and infer more data [21]. To conceptualize the significance of semantic interoperability, we can consider an example of two healthcare systems using same protocols to exchange clinical information. If a patient moves from one healthcare systems to another, then his patient journal from previous system should be exchanged in such a way that new system can interpret the incoming data and integrate it with current system. In this way, the patient can get better health care service which shows one of the potential benefit of semantic interoperability.

Achieving semantic interoperability is not as simple task as it seems, because every domain needs standardization of multiple factors to truly enable information exchange across systems. Health care industry has been encouraging the utilization of interoperability systems to enable better patient care services. In this regard, RDF was proposed to be top of the line language protocol for the exchange of healthcare and clinical data across systems [22]. This development came when President's Council of Advisors on Science and Technology (PCAST) invited to submit proposals for a universal language for healthcare data exchange. It was called as Yosemite Manifesto, and is signed by more than 100 researchers and representatives of different organizations who are currently working in the field of healthcare information exchange. The figure below summarizes manifesto's prospectus:

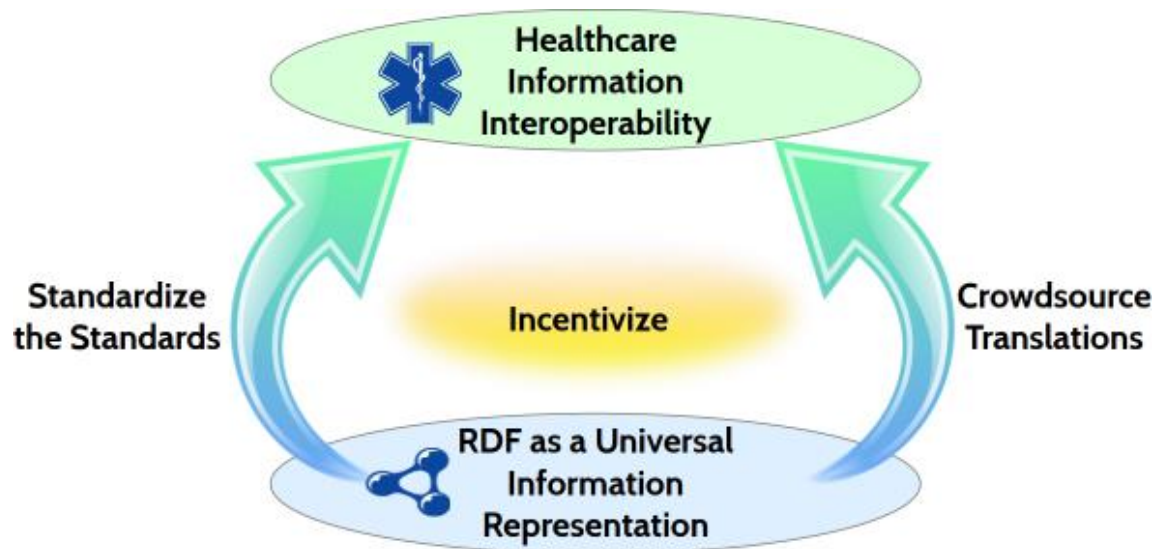


Figure 2.11 Yosemite's interoperability roadmap [22]

The roadmap to enable semantic interoperability for healthcare systems has a fundamental approach to use RDF for the information exchange. As showed in the figure above, and explained by Yosemite's manifesto, clinical or general healthcare information must be exchanged in typical RDF format, or mapping should be done to translate the existing information in RDF format. We can avoid developing new standards for all the existing data models, and define only certain standards which will enable us to connect the existing data models with each other. It is also asserted that, in addition to mapping the existing vocabularies and information to RDF format, new standards and data models should also be presented in RDF format. This semantic interoperability should also be incentivized by governments, health agencies, and corporations. This is to encourage interoperability and counter the business competition hurdles between organizations [22]. However, the claim about RDF, despite of being signed by more than 100 bodies, is not well received by all the researchers. Thomas Beale, a senior architect at openEHR, argues against the use of RDF as a universal and only language for clinical information exchange. He concludes and establishes that we should define certain domains and problems where RDF is applicable and beneficial, and where it is inapplicable [23].

One of the most promising project, in the health care systems, is the ongoing work by HL7 ITS work group for RDF representation of FHIR resources [4]. We also demonstrated a use case in our paper of drug interactions by customizing the unofficial draft ontology of FHIR and extracting clinical data from FHIR servers. The figure below shows an example of using RDF for the representation of clinical information from two different sources.

Different source formats, same RDF

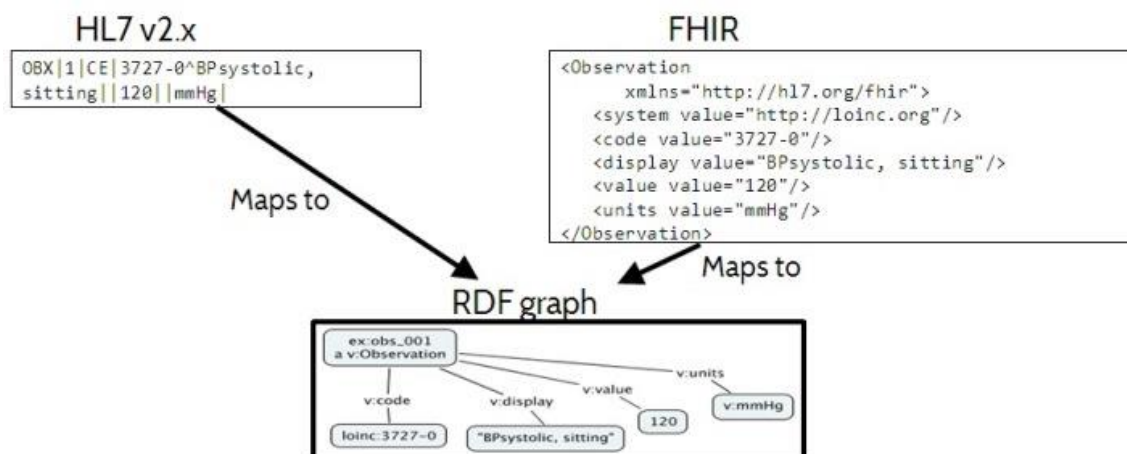


Figure 2.12 RDF graph for FHIR and HL7v2 [10]

The message in HL7 v2.x represents the same information that is represented using the FHIR resources in XML format on the right side. Despite being different formats, by doing precise mapping, the information can be represented by a single RDF graph. To argue more about the advantages, we can define some inference rules to generate new inferred data from the RDF graph represented in the figure above, and which was also successfully demonstrated in our paper.

2.1.7 Norwegian Electronic Prescription Support System (FEST)

FEST is a database, which includes all the information about drugs that are being prescribed in Norway, and is provided as an information system service by Norwegian Medicines Agency to almost all the hospitals, pharmacies, and drug producers. A physician, general practitioner, or a researcher can get all the possible information of a particular drug which can be prescribed in Norway through FEST database. Motivation behind the development of FEST database, as described by Norwegian Medicines Agency, was to encourage and support safe medication and prescription in Norway. FEST makes it possible to endorse safe medication because different stakeholders such as hospitals, pharmacies etc. will be getting all the drug related information from a single source which minimizes the risks of unsafe prescription [24]. Norwegian Medicines Agency encourages the usage of single source for pharmaceutical entities by following arguments:

- Centralized information and regular update enables efficient resource utilization.

- Because the data will be coming from one source (FEST), it will enable standardization and regulation throughout the health industry. It will also enable to generate useful statistics about the usage of certain drugs.
- Communication and collaboration between hospitals, pharmacies, drug manufacturers, and researchers can be more productive.
- End user such as patients will get more benefit through this system as prescriptions will get better and safe through experience and regular updates [24].
- FEST can also be used by researches, working in the field of drug and patient safety, to develop more effective patient safety models by combining it with other systems.
- FEST can also lead towards semantic interoperability, which is also demonstrated in this thesis.

FEST database is mainly developed in XML format, and regular updates are made to it. Because it is developed in XML format, it require systems to use certain applications which can read that XML database and provide user interface according to the stakeholder. FEST is currently used by different stakeholders which are presented in the figure below:

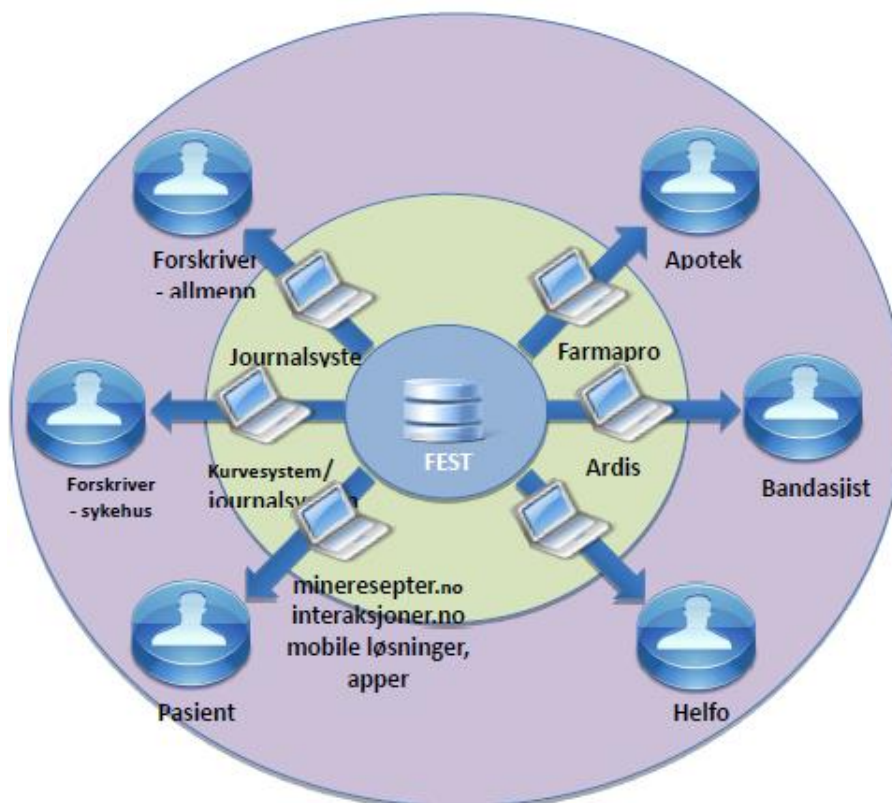


Figure 2.13 FESTA usage by different Stakeholders [25]

Figure 2.13 shows how FEST is used in different services such as patient journals, prescription, and drug interaction services i.e. www.interaksjoner.no. The figure also shows its usage by different stakeholders such as hospitals, pharmacies and Norwegian Health Economics Administration (HELFO).

Doctors and practitioners use FEST while prescribing a medicine, and to check for different aspects of that particular medicine such as side effects, interactions, price etc. They can choose alternatives to a particular drug if it can incur hazardous side effects to certain patients. Hospitals and pharmacies can use FEST to keep track of medicines and equipment. They can send messages to responsible stakeholders in case of emergency such as informing about unregistered side effects of certain medicines or informing about shortage of certain drugs. Norwegian Medicines Agency doesn't alone have the complete information and database related to different drugs, but they collaborate with different state agencies such as Norwegian Directorate of Health, HELFO, and Norwegian Pharmacy Association [26]. Despite the fact that data in FEST itself comes from different organizations, it is still regulated and modelled according to FEST standards to maintain coherence between different systems.

Coming towards the technical aspects of FEST, the figure below shows an overview of the FEST model:

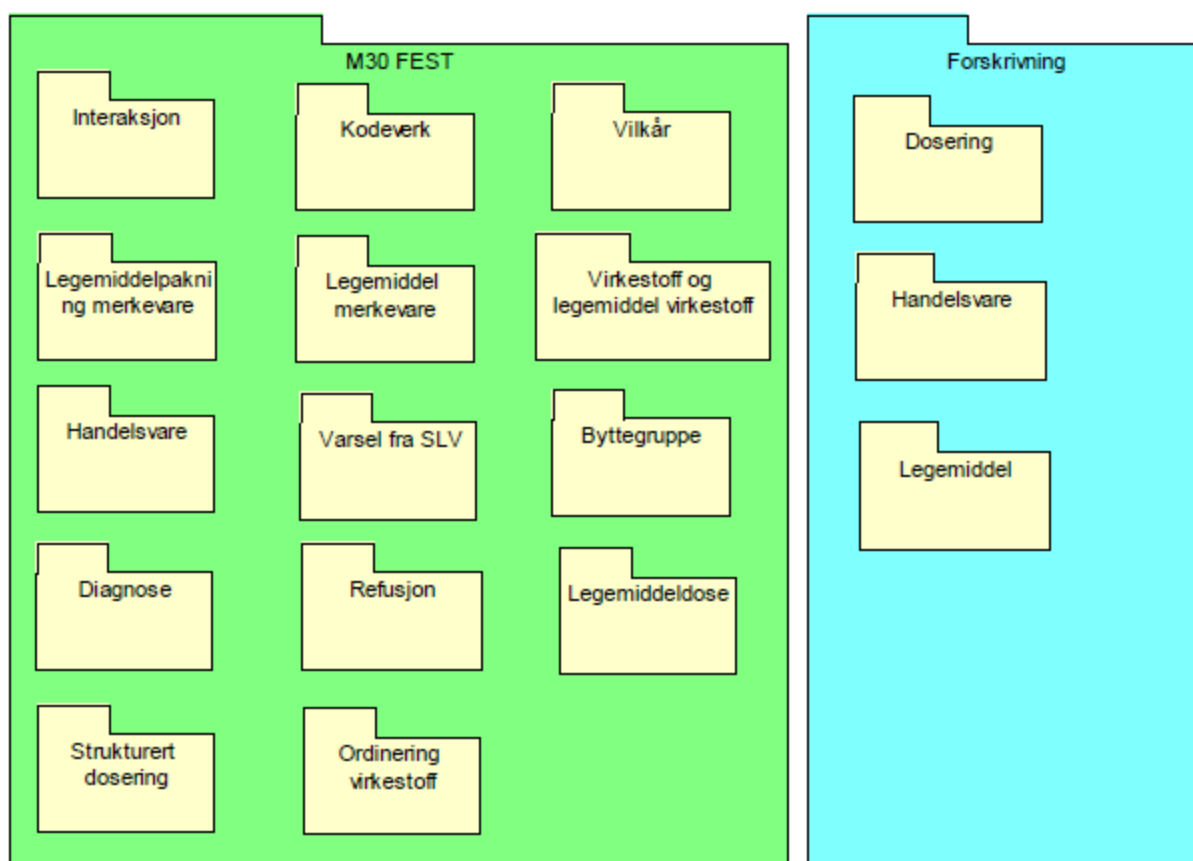


Figure 2.14 FEST overview [25]

For explanation of Norwegian vocabulary used, please refer to Appendix A. The catalogues in blue are generally used for the prescription of a medicine, substance, and to determine whether a particular medicine can be given freely on blue receipt. M30 FEST includes all the catalogues used to describe drug related information, rules for prescription, warnings, dosage information etc. It is important to mention that M30 catalogues are not disjoint with other catalogues and may also depend upon some of the catalogues from Prescription (Forskrivning), and division shown in the figure merely represents the catalogues which are required for different use cases. A detailed information of catalogues is presented in chapter 3, along with their mapping to the ontology.

2.1.8 ATC Classification System (ATC)

ATC classification system, as described by WHOCC, is a widely used drug classification system which is combined with Defined Daily Dosage (DDD) system to provide drug utilization research possibilities across the world. ATC system was an extension and adapted version of Anatomical Classification system (AC-system), developed by Norwegian researchers. Further collaboration with Nordic Council on Medicines (NLN), and then with World Health Organization (WHO) resulted in a very sophisticated ATC/DDD system, and is

currently used effectively to measure and generate statistics about the consumption of drugs [27]. This system didn't only enabled polished research about drug utilization, but also enabled investigators and researchers to make more efficient drugs. Researchers can examine statistics about a particular medicine against a specific disease, which can lead to solid conclusions about the effectiveness of that drug. Pharmacists can make adjustments in drug developing process by improving the quantity of certain substances in a drug.

As discussed concisely about the identification of a drug by ATC codes in section 2.1.4, we can develop more understanding of ATC codes by having a look at the following example which is also used by WHOCC for the illustration of the structure:

A	Alimentary tract and metabolism (1st level, anatomical main group)
A10	Drugs used in diabetes (2nd level, therapeutic subgroup)
A10B	Blood glucose lowering drugs, excl. insulins (3rd level, pharmacological subgroup)
A10BA	Biguanides (4th level, chemical subgroup)
A10BA02	metformin (5th level, chemical substance)

Figure 2.15 Example classification of Metformin [28]

First level in the ATC code describes Anatomical group, which are divided into 14 categories. In the example above, A implies that the drug belongs to Alimentary tract & metabolism group. Second level, consisting of two digits, describes the therapeutic group. In the example, code **A10** describes that the drug is used for the treatment of diabetes. Third level depicts pharmacological group and consists of only one alphabetical letter. In the example above, code **A10 B** shows that this particular drug is used in lowering of glucose in the blood. Fourth and fifth levels indicate chemical group and chemical substance respectively. In the code **A10B A 02** from the example above, **A** is indicating that the drug is actually an Biguanides which is used to treat type II diabetes. The last two digits, in our example **02**, indicates the actual drug substance which is Metformin. At every level, there are groups and subgroups to categorize all the possible substances and concepts, which are maintained by WHO Collaborating Centre for Drug Statistics Methodology [28].

3 Implementation and Solution Architecture

This chapter will include the architecture description of our solution, that is to develop an ontological model of FEST and integrate it with other resources to represent DDI and their mechanisms. FEST XML model is used in Norway, and is therefore represented in Norwegian language, with some of the data having English vocabulary. In our solution, we are also using Norwegian vocabulary for the development of ontology (i.e. classes, properties etc.), as it meant to integrate with Norwegian health systems.

To achieve semantic interoperability and to add support for DDI interaction, we used some customized classes and relations along with FEST ontology. To represent different mechanisms which can trigger a particular drug-drug interaction, we used a set of concepts from DINTO ontology and integrated them with our ontology by using different predicates. The figure below shows an overview of the architecture of our solution:

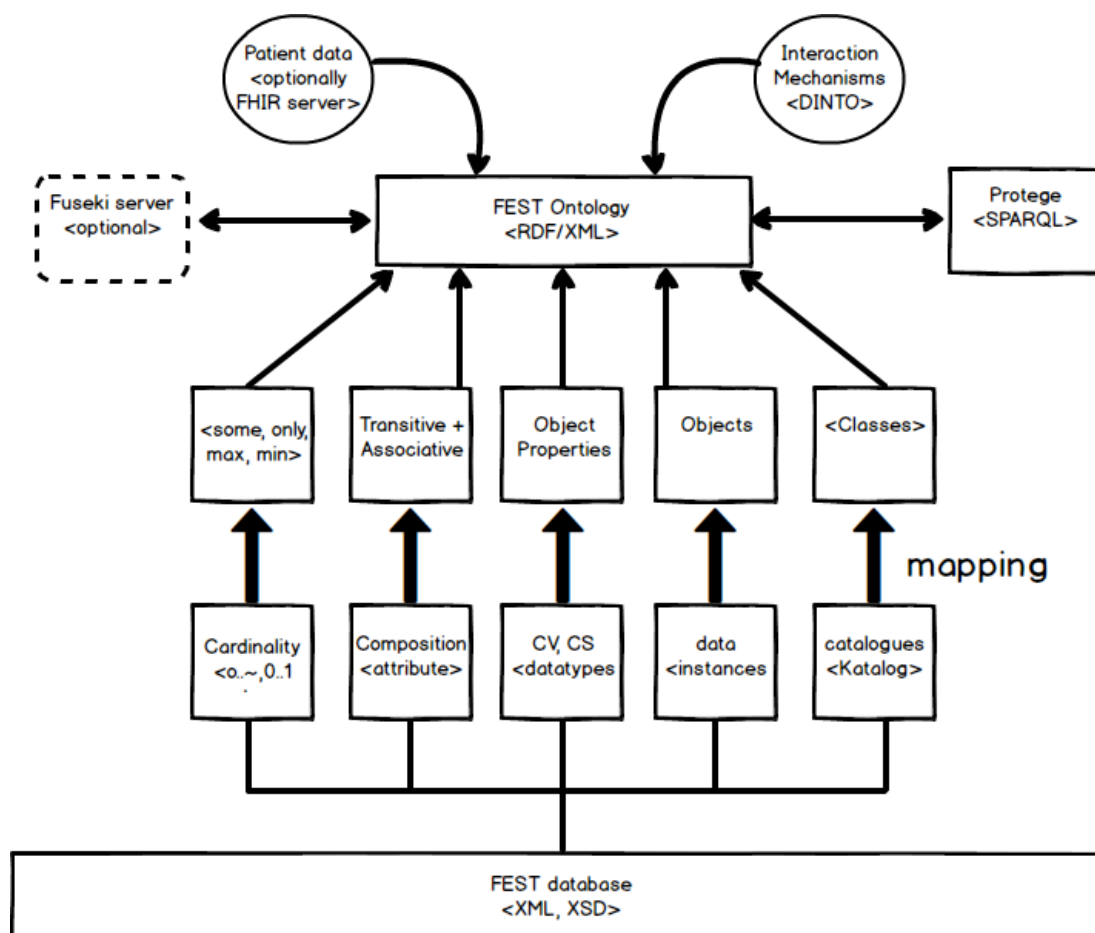


Figure 3.1 Structure overview

The figure above shows an overview of the whole structure of this thesis. Mapping between FEST database and ontology is one-to-one, and we have defined certain directions about which

resource from FEST will correspond to which component in the ontology. Most of the FEST catalogues/resources are represented using UML diagrams which helped us in mapping. All the catalogues from FEST such as LegemiddelMerkevare, LegemiddelDose, Interaksjon and Diagnose are mapped to corresponding classes in the ontology with same notation. For example, a catalogue to represent drug Interaction, represented as **Interaksjon** in FEST, has the same notation and is mapped to **rdfs:Interaksjon** class. All the relevant resources with this catalogue such as **KatInteraksjon** and **OppfInteraksjon** are also mapped to corresponding classes.

Object properties are used to relate an instance with another instance. Attributes in FEST such as CV (coded value), and CS (coded simple) are mapped as to corresponding object properties. These attributes belong to some coding system in the FEST database. All the other attributes such as name, id, and time are mapped as data properties. The notation we have used for object properties and data properties is in accordance with the class that the particular property is intended for. For example, we can interpret that property *interaksjon.id* has its domain as class **Interaksjon** and is only associated with instances of this class. Similar notation is used for object properties.

Cardinality restrictions on different data types from FEST are mapped using cardinalities defined in OWL. For example, $1..∞$ is mapped using owl:minCardinality, and $0..1$ is mapped using owl:maxCardinality which are also presented in a report published by Kilian Kiko und Colin Atkinson [29]. In protégé, these assertions can be defined by using keywords such as min, max, some, exactly and only.

The data instances from FEST are mapped to corresponding owl:object in the ontology. Names of the objects in ontology are mostly *id's* of particular instances in FEST database. The attribute "Composition" is not directly available in OWL or RDF, and has to be mapped by using a combination of relations on property. In a paper [30] presented at EGC 2005-Workshop Modelling of Knowledge presented by Macaire Ahlonsou, Henri Briand and Fabrice Guillet, they exhibited a method to capture composition concept from UML to OWL. A property with Transitive and Antisymmetric relation along with cardinality exactly 1 will correspond to the composition concept of UML. We have also used the same approach, and property enDelAv is defined as both transitive and antisymmetric, and cardinality on the class used is placed to be exactly 1.

The blue arrows represents the property *rdfs:hasSubClass*. The classes marked blue are the main classes in this ontology, and other classes such as **LegemiddelformKort** are only used to represent specific information about a specific entity. For example, the class **LegemiddelformKort** have instances such as tablet, capsule, and powder to represent the form of a medicine or substance. Instances of this class are directly referred to from a particular drug or substance. The actual coding system for to represent the form of a medicine is defined in class **Kodeverk**.

The class **Legemiddel**^[3.6] having 4 subclasses, is used to represent drugs related information and is used in the process of prescribing a drug. The class **Kodeverk**^[3.14] describes and contains all the coding systems used in FEST database and in FEST ontology. For example, a coding system with code 7180 is used to identify medicines based on ATC classification. The class **Diagnose**^[3.12] is used to aid practitioner in the process of prescription. It contains information about the usage of medicine such as recommended dosage, maximum dosage, and approved normal dosage for a particular treatment.

The class **Interaksjon**^[3.15] is used for the identification of all the possible drug interactions .For example, if two drugs are prescribed simultaneously, they may lead to an unwanted side effect. Such information about the potential interaction is represented in class **Interaksjon**. The other two classes **Substans** and **Substansgruppe** are also used in the same context. These two classes contains information about the actual substances and group of substances that lead to a potential drug interaction. The classes **M30Fest** and **EnkeltoppforingsFest**^[3.5] are used to contain all the catalogues and information about entries made in the system. These classes are meant to be used by an API to store and access the information related to a particular entry made in the system such as prescription entry, warning entry, and interaction alert entry.

3.2 Object property hierarchy

The object properties used in the FEST ontology represent relation between two instances, and also imply restrictions and conditions on certain classes. The notations used in this ontology follow the same rule that we have used in our paper, that is to use class name along with the property name separated by a dot. This enables to distinguish quickly between the property usage for human interpretation. For example, *Legemiddel.ATC* represents an ATC code linked with a particular drug and we can quickly differentiate that this ATC code represents individuals of class **Legemiddel**. The figure below shows the hierarchy of object properties in our ontology:

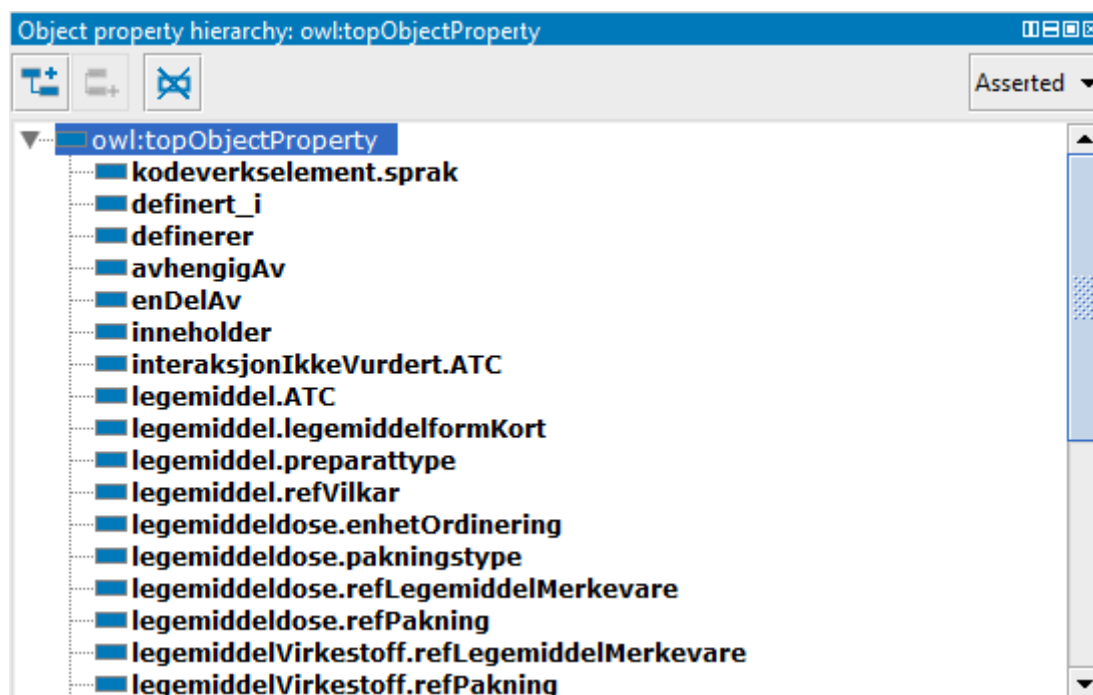


Figure 3.3 Object property hierarchy

Figure 3.2 shows a snippet of some of the object properties that are being used in this ontology. The properties without any class name behind them are used by multiple classes i.e. the object property *definerer* is used by instances of class **KodeverksInfo** to define some elements of class **KodeverksElement**, and the same property is used by instance of class **Varseltype** to define the types of notification. The detailed interpretation of object properties associated with classes, along with their domain and range is given in chapter 3. However their complete usage with respect to different instances and classes is given in the Appendix B in the form of RDF code.

3.3 Data properties hierarchy

The data properties we have used, are also following the same notation to achieve simplicity and consistency. Different information such as names, id's, and codes is captured using data properties. The figure below shows hierarchy of the data properties for FEST ontology.

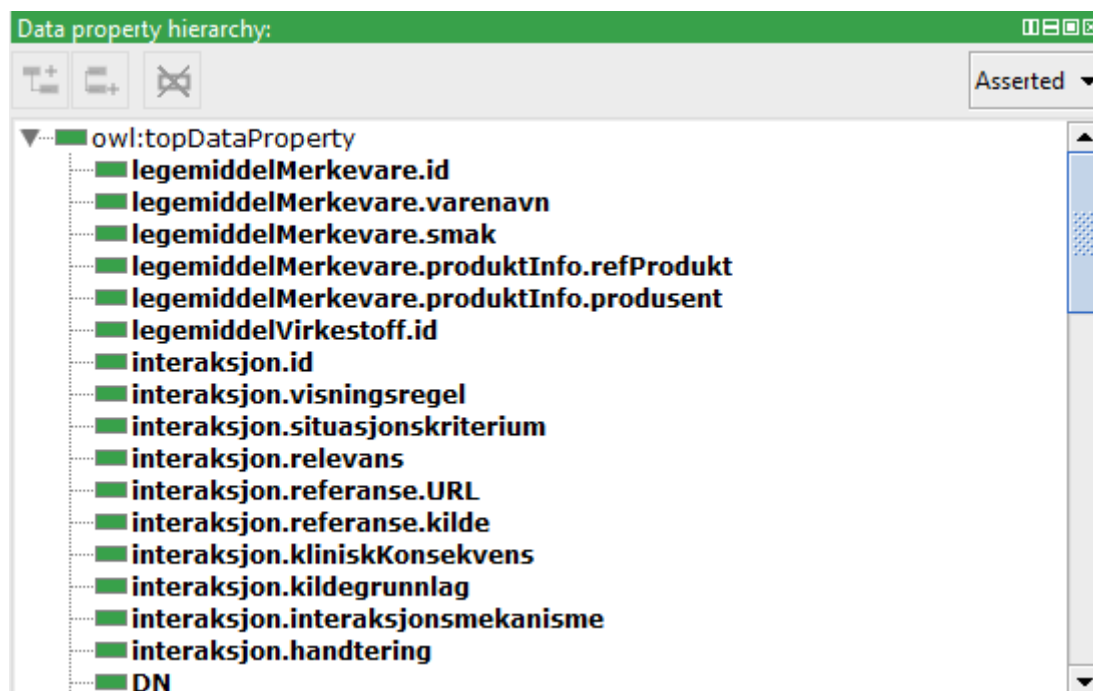


Figure 3.4 Data property hierarchy

There are some data properties that have special description for different scenarios. For example, the data property *interaksjon.relevans* is used to classify the potential risk posed by a drug-drug interaction. The range of this property is `xsd:integer`, and a specific integer should be used with this property, i.e. if a certain drug interaction is very severe which may lead to dangerous side effects, then the code “1” should be used as the range of this property to indicate that this particular combination of drugs should be avoided at any cost. Several other similar attributes are mapped to data properties using similar method instead of using an object property and creating an entire new coding system. The figure below shows the description of scenario described above:

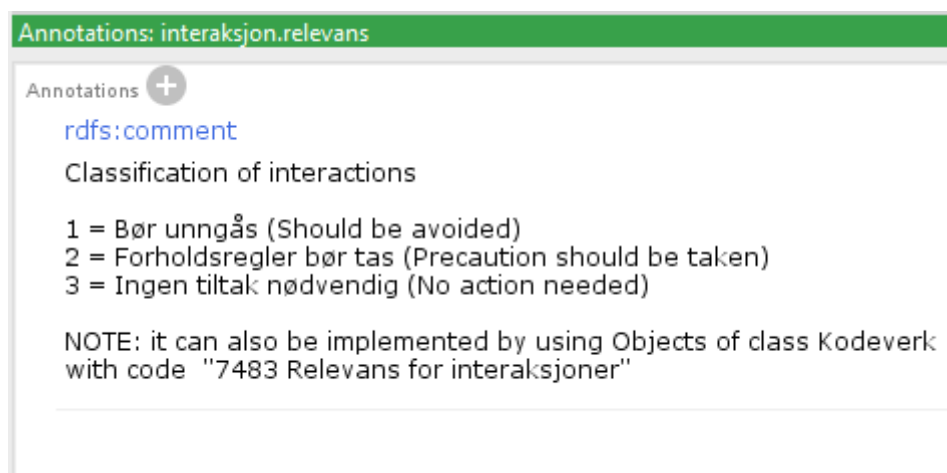


Figure 3.5 Mapping of a data property with special conditions

3.4 Mapping of FEST catalogues to FEST ontology

This sub section explains in detail the mapping from FEST XML database to our FEST ontology.. Refer to Appendix A for description of terms.

3.5 Mapping of M30FEST

M30 FEST contains all the catalogues, and in our ontology we have mapped it to a class **M30Fest**. Refer to the figure 2.13, there we have 14 catalogues to represent different details from drug information to prescription information. As described in chapter 1, in this ontology we are not focusing on **KatRefusjon**, **KatVilkår**, **KatByttegruppe**, and **KatDosering**. All the UML diagrams are taken from “FEST Implementeringsveiledning” document [25]. The UML structure of M30FEST along with its corresponding mapping to the ontology is shown in the figure below:

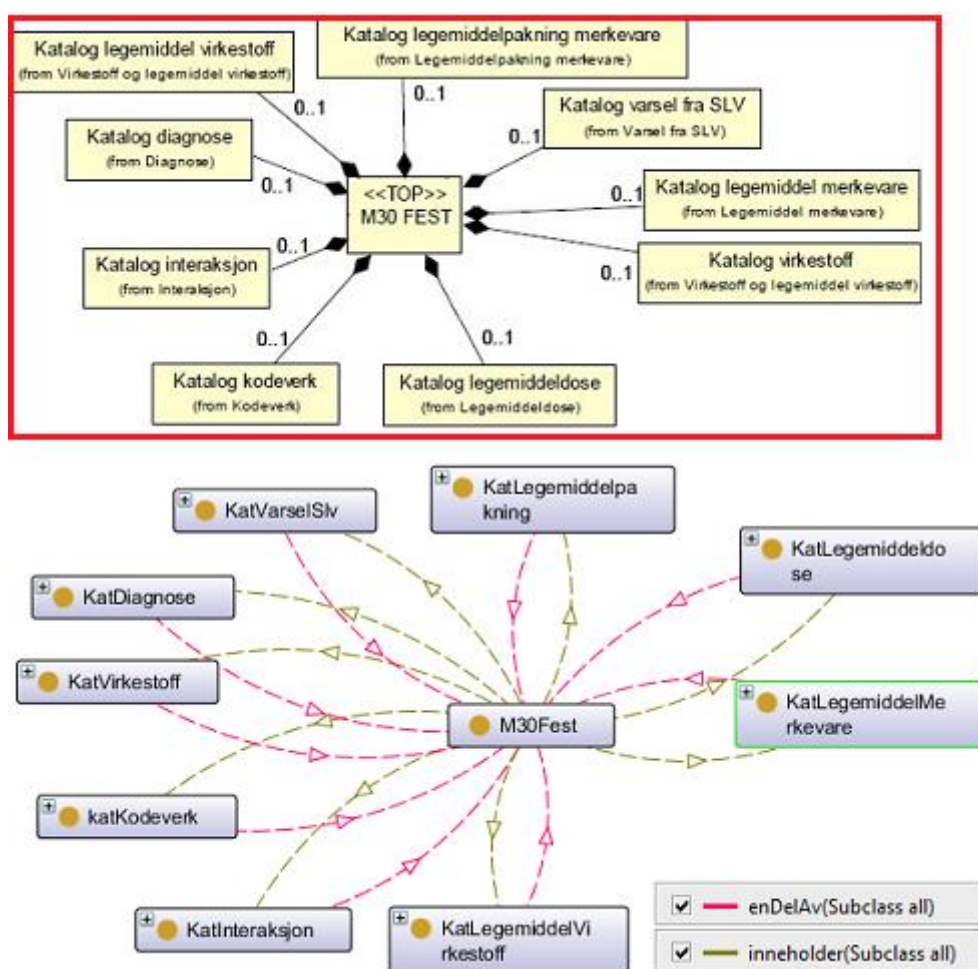


Figure 3.6 Catalogue mapping to Classes

The attributes of M30 FEST to represent date and time are mapped to data property *M30Fest.hentetDato*. To represent all the catalogues, we have used the property *inneholder* which is both transitive and antisymmetric and its cardinality is placed to be exactly “1” to

from the composition relation between M30Fest and catalogues. This concept of composition translation into protégé is presented by Macaire Ahlonsou, Henri Briand, and Fabrice Guillet in a paper [30]. Every catalogue may contain its relevant entry (oppf<className>) class. This mapping is used to keep track of new and previous entries in the system, and is shown in the figure below:

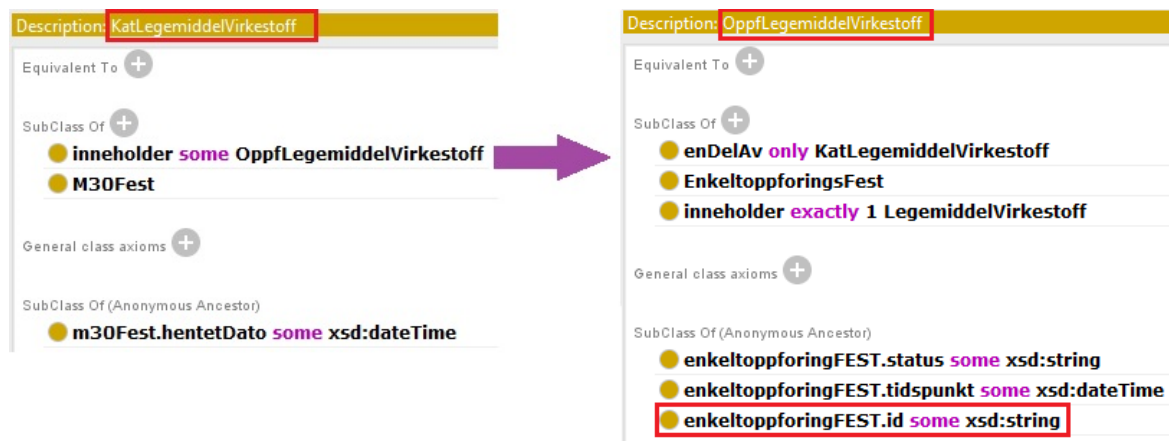


Figure 3.7 Example of mapping from catalogue

Figure 3.7 shows that every instance of class **KatLegemiddelVirkestoff** will include an instance of class **OppfLegemiddelVirkestoff** through the property *inneholder*. The class **OppfLegemiddelVirkestoff** is a subclass of **EnkeltoppforingsFest**, and inherits all the properties from parent class, which are used to record the time, status and id of an entry.

3.6 Mapping of **EnkeltoppforingsFest**

This class is used to store the record of entries, i.e. prescription. For example, every instance of class **OppfLegemiddelVirkestoff** will include an instance of class **LegemiddelVirkestoff** which is used to describe the actual substance. As described by Norwegian Medicines Agency, every new entry will have a new and unique entry-id, time and activity status. If an application (web, API etc.) is made based on this ontology, we will be using this mapping to store every new entry. The figure below shows the UML structure of **EnkeltoppforingsFest** and its corresponding mapping to the ontology:

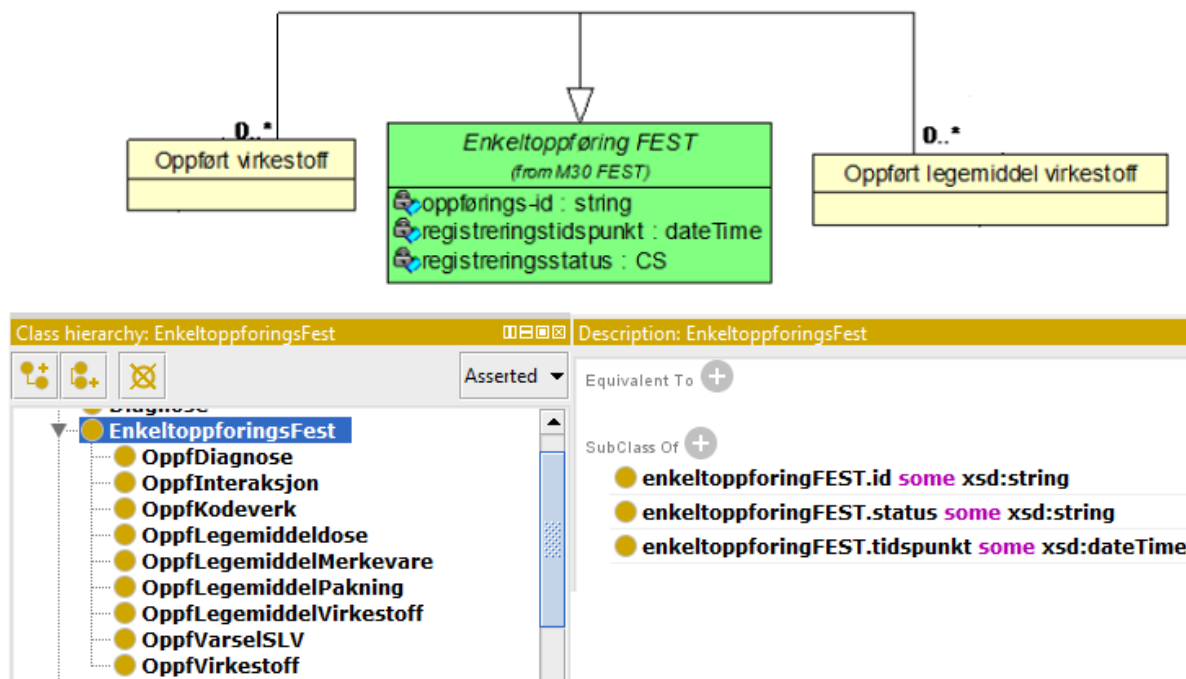


Figure 3.8 Mapping of EnkeltoppforingsFest

Figure 3.8 shows that all the classes used for the entry of specific source are defined as subclasses of **EnkeltoppforingsFest**. The attributes shown in the UML diagram are mapped to this class by using data properties. These data properties are used as conditions on the class **EnkeltoppforingsFest**. The table below summarizes the purpose and definition of data properties used with class **EnkeltoppforingsFest**:

Property	Domain	Range	Short Explanation
<i>enkeltoppforingsFEST.id</i>	EnkeltoppforingsFest	xsd:string	Unique id, used for identification
<i>enkeltoppforingsFEST.status</i>	EnkeltoppforingsFest	xsd:string	Active/Non-active entry
<i>enkeltoppforingsFEST.tidspunkt</i>	EnkeltoppforingsFest	xsd:dateTime	Time and date of an entry

Table 3.1 Properties for class EnkeltoppforingsFest

3.7 Mapping of class Legemiddel

To address the mapping of actual catalogues, we will start with the explanation of class **Legemiddel** which is used to store every information related to a drug or substance. It contains all the medicines that can be prescribed by the practitioner in Norway, including details of

substances, manufacturers, packaging, and dosing. The figure below shows the class structure of **Legemiddel** :

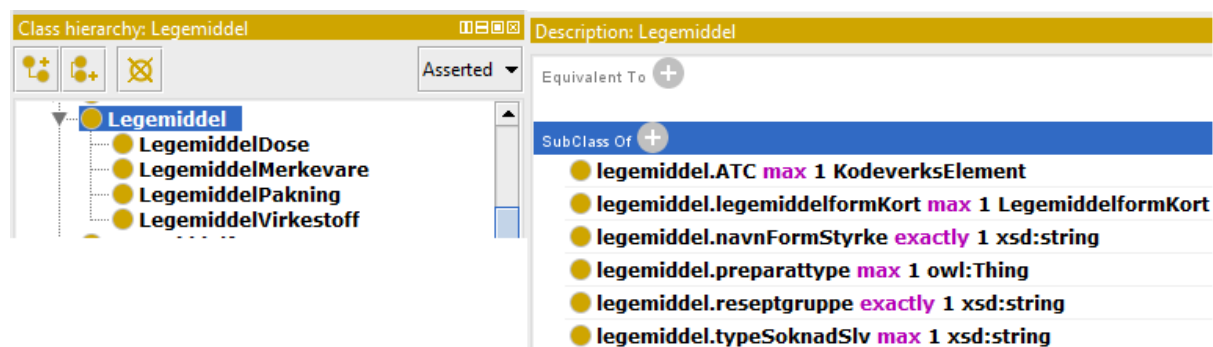


Figure 3.9 Legemiddel class hierarchy

The class **Legemiddel**, as shown in the figure above has four subclasses which are described later in the chapter. Refer to section [4.1](#) for an example of a Legemiddel instance. It should be noted that the class **Legemiddel** itself does not contain any drug or substance, but the subclasses that are associated with this class are used for the representation of a particular drug and relevant information such as dosage, branded medicine, and packaging. The subclasses **LegemiddelDose** and **LegemiddelPakning** are essential in prescription and representation of a specific branded drug or substance, and therefore they are defined as subclasses of **Legemiddel** similar to FEST XML structure.

We have mapped *navnFormStyrke*, *reseptgruppe*, and *typeSoknadSLV* to data properties having range as *xsd:string*. It is asserted that *reseptgruppe*, and *typeSoknadSLV* can also be mapped using an object property similar to the mapping of *ATC*. Attributes like *ATC*, *legemiddelformKort*, and *preparattype* are mapped as object properties to *Legemiddel.ATC*, *Legemiddel.legemiddelformKort*, and *Legemiddel.preparattype* respectively, as shown in the figure 3.9. A particular medicine (an instance of **Legemiddel**) is identified by using a reference to ATC coding system (an instance of class **KodeverksElement**), which has certain attributes and references for further identification of the drug or substance. Please refer to section [3.14](#) for further explanation of class **KodeverksElement** and different coding systems.

Similarly, for the identification of the type of drug or substance, a reference is made to an instance of class **KodeverksElement** having a different coding system. The cardinality of different properties is mostly kept same as was defined by Norwegian Medicines Agency while developing FEST database, and mapping is achieved by assigning certain conditions on a class. In the figure 3.9, property assertion *legemiddel.ATC max 1 KodeverksElement* denotes that the class **Legemiddel** cannot have a reference to more than one instance of *KodeverksElement*.

Similarly, keywords **some** and **exactly** are used for different restrictions. The table below summarizes all the properties associated with class **Legemiddel**.

Property	Domain	Range	Short Explanation
<i>legemiddel.ATC</i>	Legemiddel	ATC	ATC code for identification
<i>legemiddel.legemiddelformKort</i>	Legemiddel	LegemiddelformKort	Used to describe form of a medicine
<i>legemiddel.preparattype</i>	Legemiddel	PreparattypeLegemiddel	Used to identify the formulation of a medicine such as medicine, vaccine, and natural medicine
<i>legemiddel.navnFormStyrke</i>	Legemiddel	<i>xsd:string</i>	A combination of name, type, and strength of drug/substance
<i>legemiddel.reseptgruppe</i>	Legemiddel	<i>xsd:string</i>	Used to describe receipt group of a medicine
<i>legemiddel.typeSoknadSlv</i>	Legemiddel	<i>xsd:integer</i>	Used to identify the application dispenser

Table 3.2 Properties for class *Legemiddel*

3.8 Mapping of class *LegemiddelVirkestoff*

The class **LegemiddelVirkestoff** is used to identify all the active medicine substances/ingredients that can be prescribed in Norway. When practitioner needs to write a substance or an ingredient or a combination of different ingredients, the details of that is available in the class **LegemiddelVirkestoff**. This class inherits all the properties that we have associated with class **Legemiddel** such as ATC code information, and type of substance. The figure below shows the UML architecture of resource **LegemiddelVirkestoff** along with its corresponding mapping to the ontology:

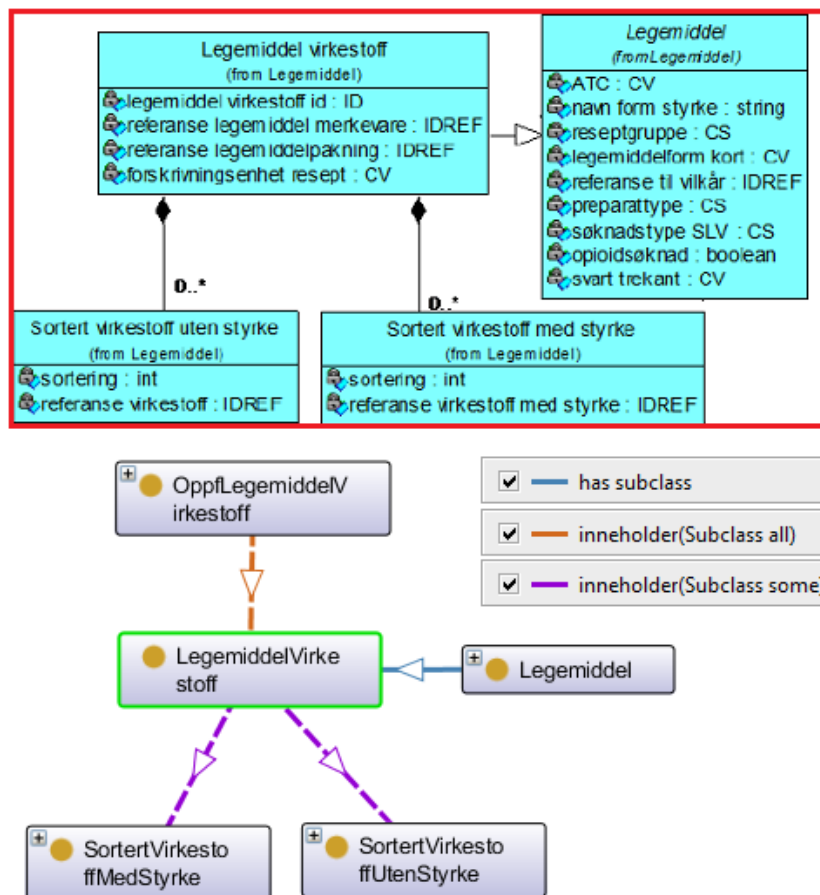


Figure 3.10 Mapping of *LegemiddelVirkestoff*

This class also has direct references to the class **LegemiddelMerkevare** and **LegemiddelPakning**, and is mapped through object properties *legemiddelVirkestoff.refLegemiddelMerkevare* and *legemiddelVirkestoff.refPakning* respectively. This reference makes it possible to identify the brand and packaging type associated with the particular medicine or substance. By using this reference through an object property, we can also query for the particular brand a substance may belong to. The properties and cardinality restrictions that we have placed on the class **LegemiddelVirkestoff** are shown in the figure below:

Description	LegemiddelVirkestoff
SubClass Of	<ul style="list-style-type: none"> ● enDelAv exactly 1 OppfLegemiddelVirkestoff ● inneholder some SortertVirkestoffMedStyrke ● inneholder some SortertVirkestoffUtenStyrke ● Legemiddel ● legemiddelVirkestoff.id exactly 1 xsd:string ● legemiddelVirkestoff.refLegemiddelMerkevare some owl:Thing ● legemiddelVirkestoff.refPakning some owl:Thing
General class axioms	
SubClass Of (Anonymous Ancestor)	<ul style="list-style-type: none"> ● legemiddel.ATC max 1 KodeverksElement ● legemiddel.preparattype max 1 owl:Thing ● legemiddel.reseptgruppe exactly 1 xsd:string ● legemiddel.navnFormStyrke exactly 1 xsd:string ● legemiddel.legemiddelformKort max 1 LegemiddelformKort ● legemiddel.typeSoknadSlv max 1 xsd:string

Figure 3.11 Cardinality restrictions on class LegemiddelVirkestoff

The figure shows that this class is a part of **exactly** one **OppfLegemiddelVirkestoff**, which is used for entry purpose as described earlier. This class may also include **some** instances belonging to class **SortertVirkestoffMedStyrke** and **SortertVirkestoffUtenStyrke** which are used to store information about substances with or without a specific strength. The mapping to these classes is done by using the object property *inneholder*. The table below summarizes the details of properties associated with class **LegemiddelVirkestoff**.

Property	Domain	Range	Short Explanation
<i>legemiddelVirkestoff.id</i>	LegemiddelVirkestoff	<i>xsd:string</i>	Used for identification of a medicine
<i>legemiddelVirkestoff.refLegemiddelMerkevare</i>	LegemiddelVirkestoff	LegemiddelMerkevare	Used to refer to corresponding brand
<i>legemiddelVirkestoff.refPakning</i>	LegemiddelVirkestoff	LegemiddelPakning	Used to refer to corresponding packaging

Table 3.3 Properties for class LegemiddelVirkestoff

3.9 Mapping of class Virkestoff

The class **LegemiddelVirkestoff**, as described earlier, contains information about the active ingredients that can be prescribed or substances that can be used in therapy. The actual

information about a particular substance/ingredient however resides in the class **Virkestoff**, which has all the information such as name of the active substance, strength of the substance, dosage measuring parameters, and reference to therapy related substances (**LegemiddelVirkestoff**). Mapping of class **Virkestoff** to our ontology along with its corresponding UML structure is shown in the figure below:

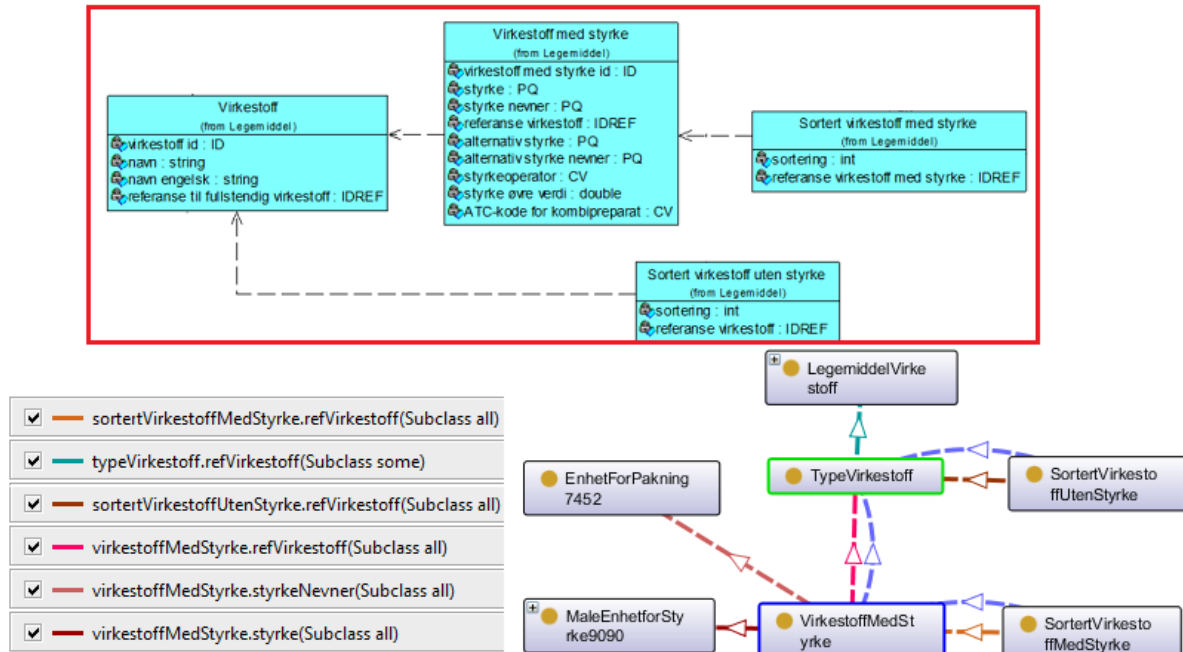


Figure 3.12 Mapping of class **Virkestoff**

Figure above shows similar mapping from **KatVirkestoff** to **OppfVirkestoff** as we have described earlier. It is to be noted that we have not mapped the class **Virkestoff** as a medicine/drug, because as we explained earlier, substances are not actual drugs but are used to prescribe the drugs of a particular brand or packaging. In medical field also, practitioners usually prescribe using formulas and substances, as it is very difficult to remember the names of the brands containing a particular substance. The attributes like *name*, *id*, and *English name* are mapped to data properties, while reference to an actual prescribe-able substance is mapped by using the object property *typeVirkestoff.refVirkestoff*. This object property associates instances of class **Virkestoff** with the instances of class **LegemiddelVirkestoff**. The cardinality restrictions for the class **Virkestoff** are shown in the figure below:

Description: TypeVirkestoff	
SubClass Of	+
●	enDelAv only OppfVirkestoff
●	typeVirkestoff.id exactly 1 xsd:string
●	typeVirkestoff.navn exactly 1 xsd:string
●	typeVirkestoff.navnEngelsk max 1 xsd:string
●	typeVirkestoff.refVirkestoff some LegemiddelVirkestoff
Description: VirkestoffMedStyrke	
SubClass Of	+
●	avhengigAv some TypeVirkestoff
●	enDelAv only OppfVirkestoff
●	virkestoffMedStyrke.alternativStyrke max 1 MaleEnhetforStyrke9090
●	virkestoffMedStyrke.alternativStyrkeNevner max 1 EnhetForPakning7452
●	virkestoffMedStyrke.id exactly 1 xsd:string
●	virkestoffMedStyrke.refVirkestoff exactly 1 TypeVirkestoff
●	virkestoffMedStyrke.styrke exactly 1 MaleEnhetforStyrke9090
●	virkestoffMedStyrke.styrkeNevner max 1 EnhetForPakning7452
●	virkestoffMedStyrke.styrkeoperator exactly 1 xsd:string

Figure 3.13 Cardinality restrictions on class Virkestoff

Every instance of class **Virkestoff** has a reference to instances of **LegemiddelVirkestoff**, because one substance may represent different drugs that can be prescribed. Every substance with some strength depends upon the actual **Virkestoff**, as mapped by property **avhengigAv**. It can also be seen in the picture that substance with a strength have references to different instances such as **EnhetForPakning7452**, and **MaleenhetForPakning9090**. These attributes are defined as coding systems in the class **Kodeverk**.

Property	Domain	Range	Short Explanation
<i>typeVirkestoff.id</i>	TypeVirkestoff	<i>xsd:string</i>	Used for identification and reference(optional)
<i>typeVirkestoff.navn</i>	TypeVirkestoff	<i>xsd:string</i>	Name of the substance
<i>typeVirkestoff.navnEngelsk</i>	TypeVirkestoff	<i>xsd:string</i>	English name of substance
<i>typeVirkestoff.refVirkestoff</i>	TypeVirkestoff	LegemiddelVirkestoff	Reference to actual medicine including this substance

Table 3.4 Properties for class typeVirkestoff

3.10 Mapping of class **LegemiddelMerkevare**

LegemiddelMerkevare class is used when certain brands are to be identified, which are associated with a particular substance (an instance of **LegemiddelVirkestoff**). This class contains all the information related to a brand such as name of the brand, type of medicine, taste, and manufacturer information. The figure below shows how we mapped this catalogue to the corresponding class in our ontology along with UML structure:

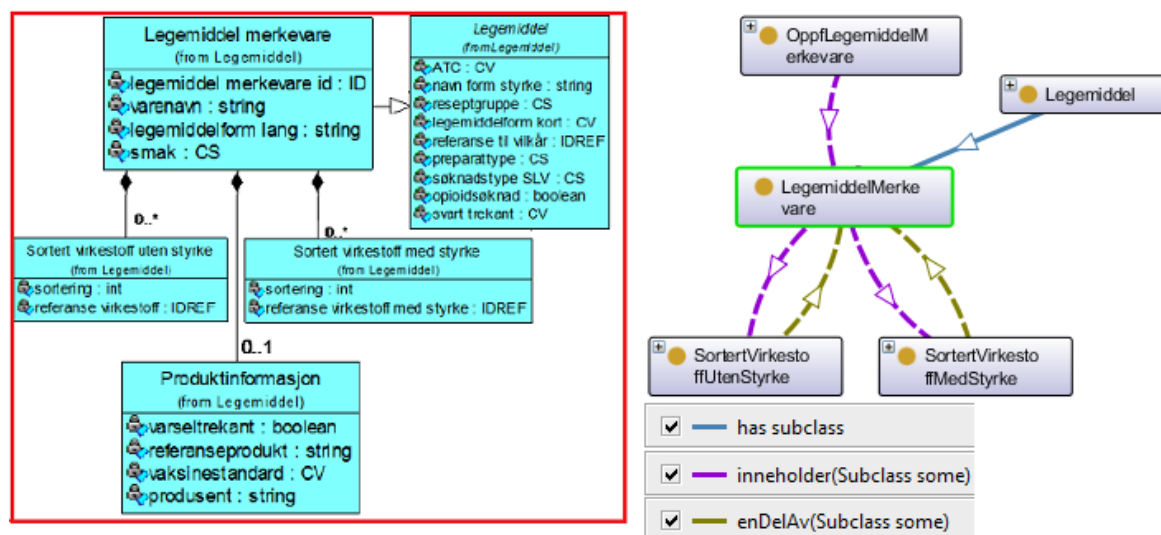


Figure 3.14 Mapping of **LegemiddelMerkevare**

Attributes such as *id*, *vernaven*, and *legemiddelFormLang* are mapped to corresponding data properties with range as *xsd:string*. Mapping to particular catalogues such as **SortertVirkestoffMedStyrke** and **SortertVirkestoffUtenStyrke** is achieved through the object property *Inneholder*, and this mapping is used to point towards actual instance of ingredients/substances (**Virkestoff**) that are connected with these classes. It is also noticeable that we didn't defined a separate class to represent the product information connected with this class, as it is done in the actual FEST UML architecture. Instead we used the data properties *legemiddelMerkevare.produktInfo.produsent*, *legemiddelMerkevare.produktInfo.refProdukt*, and *legemiddelMerkevare.produktInfo.varselTrekant* to store this information. Because it is a subclass of **Legemiddel**, inherited properties from this class are also present in this class. The figure below shows properties and cardinality restrictions that we have assigned to this class:

Description: LegemiddelMerkevare	
Equivalent To	+
SubClass Of	+
● enDelAv	exactly 1 OppfLegemiddelMerkevare
● inneholder	some SortertVirkestoffMedStyrke
● inneholder	some SortertVirkestoffUtenStyrke
●	Legemiddel
● legemiddelMerkevare.id	max 1 xsd:string
● legemiddelMerkevare.legemiddelformLang	max 1 xsd:string
● legemiddelMerkevare.produktInfo.produsent	max 1 xsd:string
● legemiddelMerkevare.produktInfo.refProdukt	max 1 xsd:string
● legemiddelMerkevare.produktInfo.varseltrekant	max 1 xsd:boolean
● legemiddelMerkevare.varenavn	exactly 1 xsd:string

Figure 3.15 Cardinality restrictions on class LegemiddelMerkevare

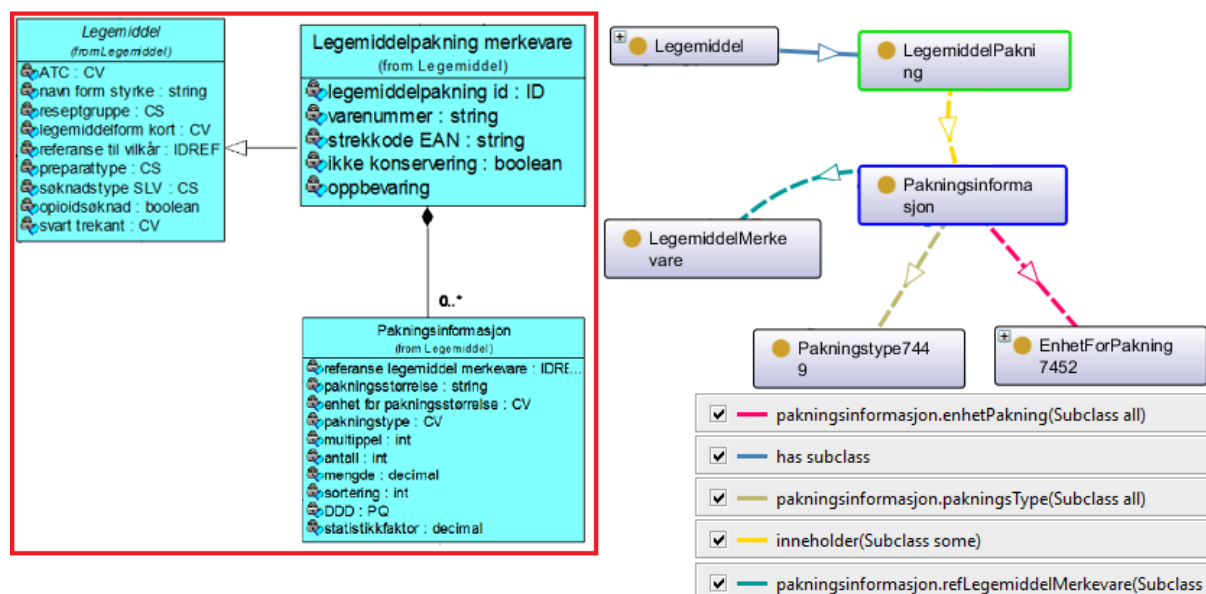
There is no direct reference from this class to the class **LegemiddelPakning**, and to refer to that class we have to use another class **PakningsInformasjon** associated with **LegemiddelPakning**. We propose using a direct reference from class **LegemiddelMerkevare** to **LegemiddelPakning** to reduce the parsing of information, but we haven't implemented this in our ontology to maintain the coherence with the actual structure of FEST, as the ontology is meant to import the real data from FEST database. The properties associated with class **LegemiddelMerkevare** are summarized in the table below:

Property	Domain	Range	Short Explanation
<i>legemiddelMerkevare.id</i>	LegemiddelMerkevare	<i>xsd:string</i>	An ID for identification and reference
<i>legemiddelMerkevare.legemiddelformLang</i>	LegemiddelMerkevare	<i>xsd:string</i>	Detailed description of type
<i>legemiddelMerkevare.smak</i>	LegemiddelMerkevare	<i>xsd:string</i>	Used to describe taste
<i>legemiddelMerkevare.varenavn</i>	LegemiddelMerkevare	<i>xsd:string</i>	Name of the branded medicine
<i>legemiddelMerkevare.produktInfo.produsent</i>	LegemiddelMerkevare	<i>xsd:string</i>	Name of the manufacturer
<i>legemiddelMerkevare.produktInfo.refProdukt</i>	LegemiddelMerkevare	<i>xsd:string</i>	Reference for the real name of medicine in form of string (not branded)
<i>legemiddelMerkevare.produktInfo.varseltrekant</i>	LegemiddelMerkevare	<i>xsd:boolean</i>	Used to identify whether medicine has a triangle mark

Table 3.5 Properties for class *LegemiddelMerkevare*

3.11 Mapping of class *LegemiddelPakningMerkevare*

The class **LegemiddelPakningMerkevare** is mainly used to capture information related to the packaging of a branded medicine (**LegemiddelMerkevare**). Different parameters such as packaging id, size, and design of packaging are described in this class. The figure below shows the mapping of resource **LegemiddelPakningMerkevare** to our ontology along with existing UML structure:

Figure 3.16 Mapping of class *LegemiddelPakningMerkevare*

Every instance of class **LegemiddelPakning** includes an instance of class **PakningsInformasjon** which is used to describe the physical nature of packaging. There is also a reference from class **PakningsInformasjon** to the actual brand (**LegemiddelMerkevare**) and is mapped through property *pakningsinformasjon.refLegemiddelMerkevare* as shown in the figure 3.16 above. The classes with codes 7452 and 7449 are defined in class **Kodeverk**, and are coding systems to describe dosage and packaging type. The cardinality restrictions on the class **LegemiddelPakning** are shown in the figure below:

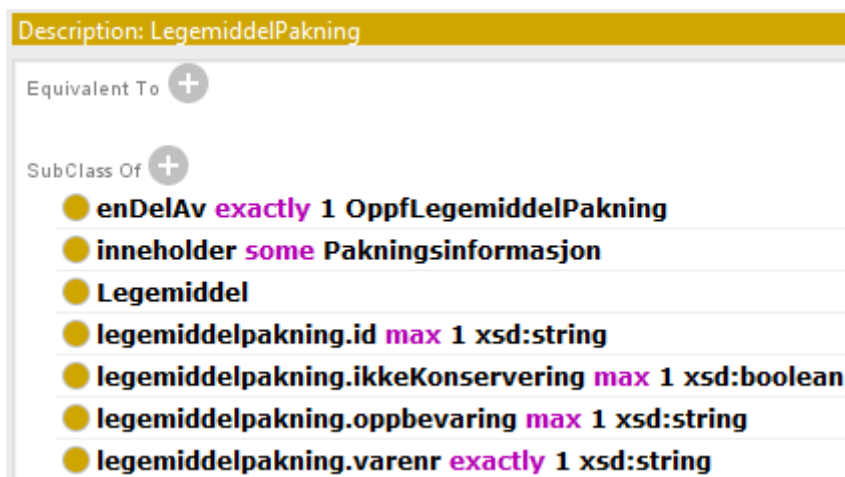


Figure 3.17 Cardinality restrictions on LegemiddelPakning

Every instance of class **LegemiddelPakning** should have a maximum of 1 *id*, which is primarily used for the identification of packaging. Figure 3.17 also shows that every instance of class **LegemiddelPakning** includes some of the instances of **PakningsInformasjon** which further describe the nature of packaging. The table below summarizes the properties associated with class **LegemiddelPakning**:

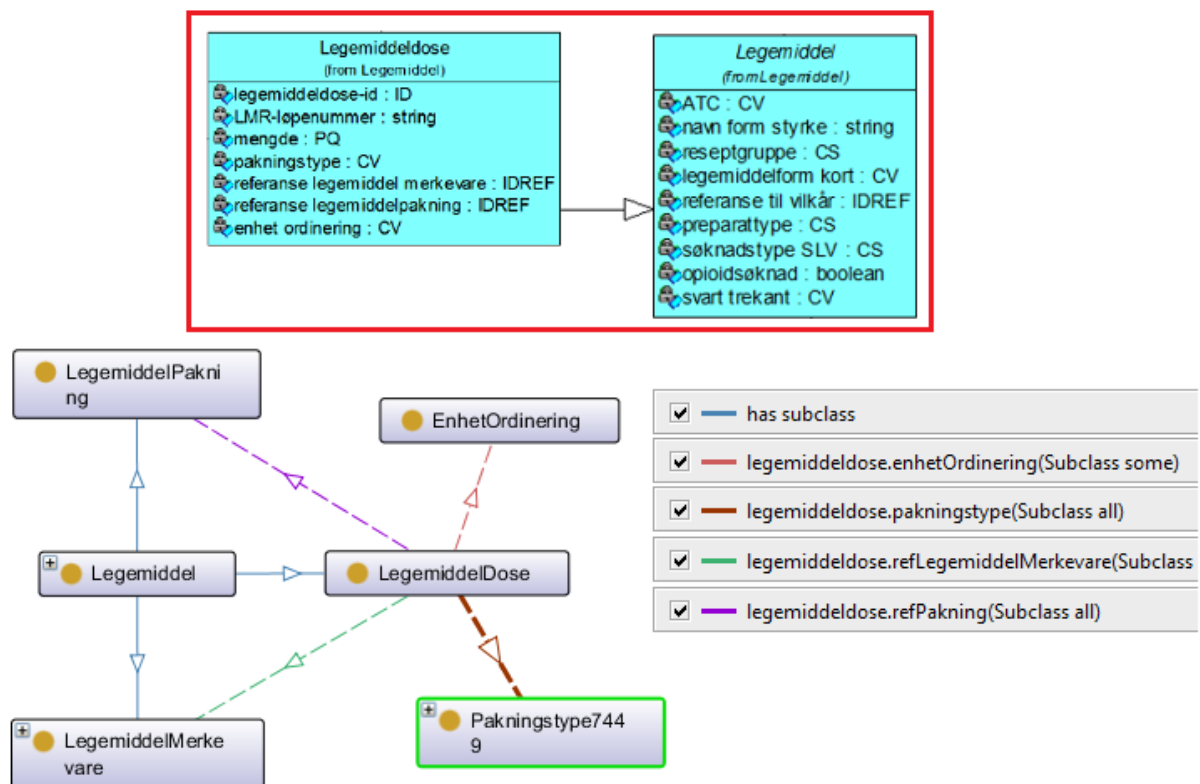
Property	Domain	Range	Short Explanation
<i>legemiddelpakning.id</i>	LegemiddelPakning	<i>xsd:string</i>	Unique ID for the packaging
<i>legemiddelpakning.ikkeKonservering</i>	LegemiddelPakning	<i>xsd:boolean</i>	A Boolean if packaging include some preservative
<i>legemiddelpakning.oppbevaring</i>	LegemiddelPakning	<i>xsd:string</i>	Used to describe recommended temperature
<i>legemiddelpakning.varenr</i>	LegemiddelPakning	<i>xsd:integer</i>	Unique item number.
<i>pakningsinformasjon.antall</i>	Pakningsinformasjon	<i>xsd:integer</i>	Used to describe total number of items in packaging.
<i>pakningsinformasjon.mengde</i>	Pakningsinformasjon	<i>xsd:decimal</i>	Used to describe amount/quantity per item.
<i>pakningsinformasjon.pakningsStr</i>	Pakningsinformasjon	<i>xsd:integer</i>	Used to describe Size of the package in terms of quantity (antall * mengde)
<i>pakningsinformasjon.enhetPakning</i>	Pakningsinformasjon	EnhetForPakning7452	Used to describe unit of packaging such as gram, and centimeter.

<i>pakningsinformasjon.paknings Type</i>	Pakningsinformasjon	Pakningstype7449	Used to describe the type of packaging such as box, and glass.
<i>pakningsinformasjon.refLegemiddelMerkevare</i>	Pakningsinformasjon	LegemiddelMerkevare	Reference to the branded medicine which this packaging belongs to.

Table 3.6 Properties for class *LegemiddelPakning*

3.12 Mapping of class **LegemiddelDose**

The class **LegemiddelDose** contains all the information related to dosage quantity of a branded medicine (**LegemiddelMerkevare**). This catalogue/source helps in determining the dosage of a particular medicine that can be prescribed. It inherits all the properties from the parent class **Legemiddel**. The figure below shows the mapping of class **LegemiddelDose** to FEST ontology and its corresponding UML structure defined by Norwegian Medicine Agency.

Figure 3.18 Mapping of class *LegemiddelDose*

In the figure above, classes **EnhetOrdinerer** and **Pakningstype7449** are coding systems defined under the parent class **Kodeverk**. Every instance of class **LegemiddelDose** has association with instances of these classes for the description of packaging type and dosage. There are direct references from class **LegemiddelDose** to the class **LegemiddelPakning** and **LegemiddelMerkevare**. These references are mapped using object properties

Legemiddeldose.refLegemiddelPakning

Legemiddeldose.refLegemiddelMerkevare

respectively. The conditions we have imposed on the class **LegemiddelDose** are shown in the figure below:

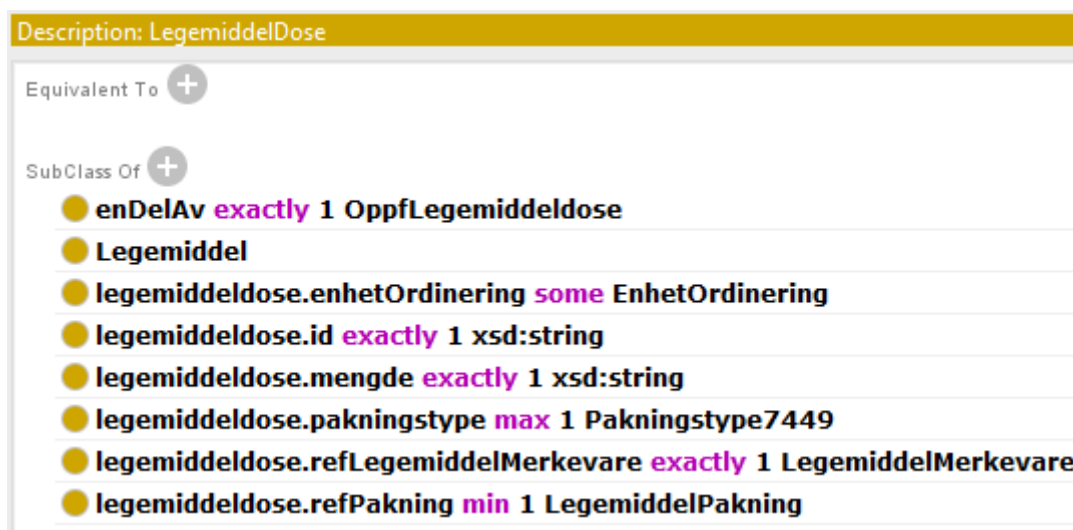


Figure 3.19 Cardinality restrictions on class *LegemiddelDose*

The figure highlights that any instance of class **LegemiddelDose** have exactly 1 reference to a brand, and minimum 1 reference to a packaging. The cardinality for the *unit of dosage*, mapped as *legemiddeldose.enhetOrdinering* in the figure above, is not restrictive because a dosage can have different units leading to same dosage quantity such as 2 drops, 1 ml, and 1 capsule. A detailed description of the properties associated with class **LegemiddelDose** is shown in the table below:

Property	Domain	Range	Short Explanation
<i>legemiddeldose.id</i>	LegemiddelDose	<i>xsd:integer</i>	A unique ID for identification.
<i>legemiddeldose.mengde</i>	LegemiddelDose	<i>xsd:integer</i>	Same as in packaging
<i>legemiddeldose.enhetOrdinering</i>	LegemiddelDose	EnhetOrdinering	Used to identify unit of dose i.e. capsule, drop etc.
<i>legemiddeldose.pakningstype</i>	LegemiddelDose	Pakningstype7449	Same as used for describing type of packaging
<i>legemiddeldose.refPakning</i>	LegemiddelDose	LegemiddelPakning	Reference to all packaging which belong to this dose.
<i>legemiddeldose.refLegemiddelMerkevare</i>	LegemiddelDose	LegemiddelMerkevare	Reference to branded medicines belonging to this dose.

Table 3.7 Properties for class LegemiddelDose

3.13 Mapping of class Diagnose

The class **Diagnose** is mainly used to support the practitioner during prescription process, giving him information about medicines that are relevant in certain conditions. Practitioners are generally not able to memorize all the medicines that can be prescribed, in this situation class **Diagnose** is used to give them available choices related to certain diagnoses. The UML model defined in FEST is shown in the figure below along with the corresponding mapping of class **Diagnose** in the ontology:

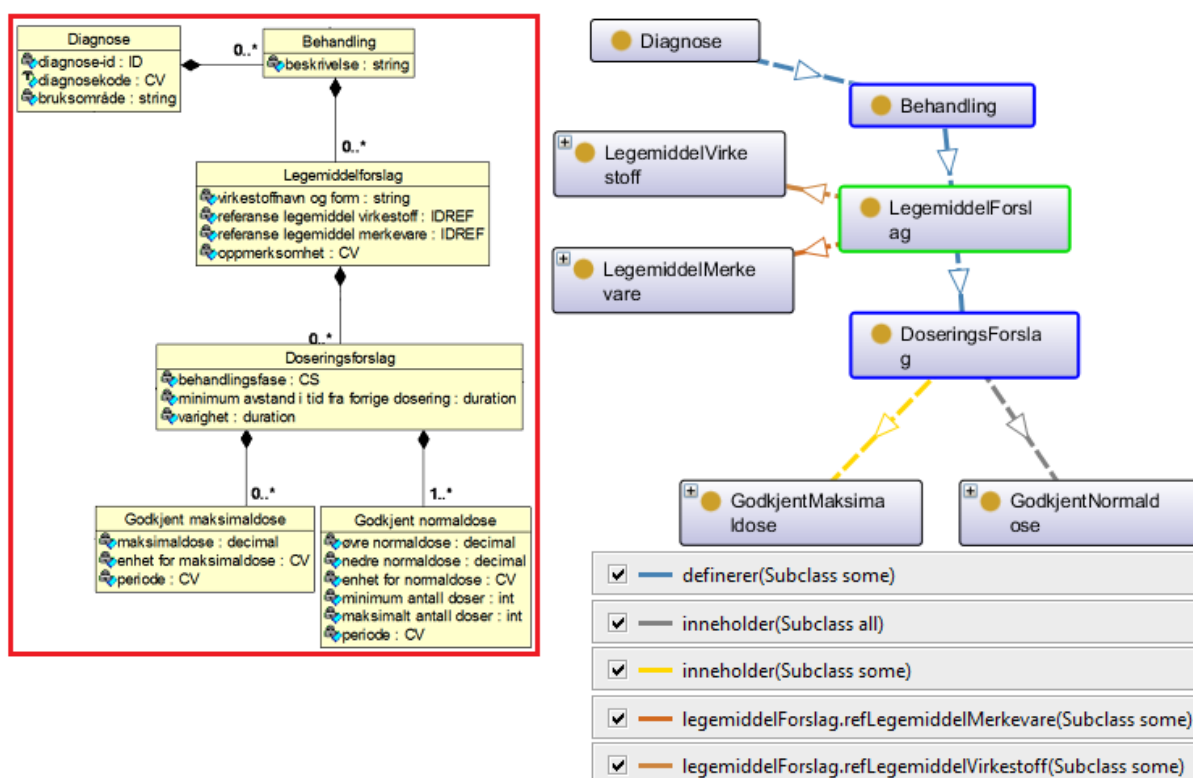


Figure 3.20 Mapping of class Diagnose

As used to store information about possible alternatives for a diagnose, the structure of mapping is defined as **Diagnose** --> **Behandling** --> **LegemiddelForslag** --> **Doseringsforslag** ==> **GodkjentMaksimaldose**, **GodkjentNormaldose** through the properties shown in the figure above. The class **LegemiddelForslag** has a direct reference to class **LegemiddelMerkevare** and **LegemiddelVirkestoff**, and is mapped through the properties *LegemiddelForslag.refLegemiddelMerkevare* and *LegemiddelForslag.refLegemiddelVirkestoff* respectively. These mappings are used to identify the brand and packaging of proposed medicine in a particular diagnose. The property restrictions defined on the class **Diagnose** are shown in the figure below:

The image shows three panels of class cardinality restrictions. Each panel has a yellow header with the class name and a 'SubClass Of' section with a plus icon. The restrictions are listed as follows:

- Diagnose:**
 - definerer **some** Behandling
 - diagnose.bruksomrade **max 1** xsd:string
 - diagnose.diagnosekode **exactly 1** xsd:string
 - diagnose.id **exactly 1** xsd:string
 - enDelAv **only** OppfDiagnose
- Behandling:**
 - behandling.beskrivelse **max 1** xsd:string
 - definerer **some** LegemiddelForslag
- LegemiddelForslag:**
 - definerer **some** DoseringsForslag
 - legemiddelForslag.oppmerksomhet **some** xsd:string
 - legemiddelForslag.refLegemiddelMerkevare **some** LegemiddelMerkeva
 - legemiddelForslag.refLegemiddelVirkestoff **some** LegemiddelVirkestoff
 - legemiddelForslag.virkestoffNavnForm **exactly 1** xsd:string

Figure 3.21 Cardinality restrictions on class Diagnose

Every instance of class Diagnose can have more than 1 treatment suggestion (Behandling) because different patients may require a different treatment based on his health record. This is achieved by defining **Diagnose** *definerer* **some** **Behandling** on the class **Diagnose** as shown in the figure 3.17. Similarly, a particular treatment may also include several medicine recommendations, and this is achieved by defining **Behandling** *definerer* **some** **LegemiddelForslag** on the class **Behandling**. Furthermore, a recommended medicine may also have several dosage possibilities in terms of quantity, severity, etc. This is achieved by defining **LegemiddelForslag** *definerer* **some** **DoseringsForslag** on the class **LegemiddelForslag**. A direct reference from the class **LegemiddelForslag** is also mapped through the properties shown in figure 3.17. A detailed description of class properties associated with class Diagnose is shown in the table below:

Property	Domain	Range	Short Explanation
<i>diagnose.id</i>	Diagnose	<i>xsd:string</i>	Unique ID used for the identification
<i>diagnose.diagnosekode</i>	Diagnose	<i>xsd:string</i>	Used to identify code for a particular diagnose.

<i>diagnose.bruksomrade</i>	Diagnose	<i>xsd:string</i>	Used to describe which area is treatment used for. i.e. heat stroke, fever etc.
<i>behandling.beskrivelse</i>	Behandling	<i>xsd:string</i>	Used to describe treatment in simple text.
<i>legemiddelForslag.oppmerksomhet</i>	LegemiddelForslag	<i>xsd:string</i>	Used to describe conditions of treatment doctor should consider such as lever failure, and low dose in start.
<i>legemiddelForslag.virkestoffNavnForm</i>	LegemiddelForslag	<i>xsd:string</i>	Used for text description of name and form of substance recommended in treatment.
<i>LegemiddelForslag.refLegemiddelMerkevare</i>	LegemiddelForslag	LegemiddelMerkevare	If reference to actual drug/substance is not present, then a reference to branded medicine is given.
<i>LegemiddelForslag.refLegemiddelVirkestoff</i>	LegemiddelForslag	LegemiddelVirkestoff	Reference to actual drug/substance that can be prescribed under this dose.
<i>doseringsforslag.behandlingsfase</i>	DoseringsForslag	<i>xsd:string</i>	Used to describe the treatment phase of dosage recommendation i.e. start phase, according to requirement etc.
<i>doseringsforslag.varighet</i>	DoseringsForslag	<i>xsd:string</i>	Used to describe the duration of treatment in terms of days, weeks or months.

Table 3.8 Properties for class Diagnose

3.14 Mapping of class VarselfraSLV

The class VarselfraSLV is mainly used by Norwegian Medicines Agency to send important notifications and warnings about drugs, brands, interactions etc. to different stakeholders which are using FEST database. An ontological version of this class, along with class **Kodeverk**, has been implemented as an ontology [3], and the data is published over the web. We have used a different approach while mapping this class to our FEST ontology, because we are also mapping this class to the other catalogues and classes in our ontology. The UML structure of **VarselfraSLV** and its corresponding mapping to our ontology is shown in the figure below:

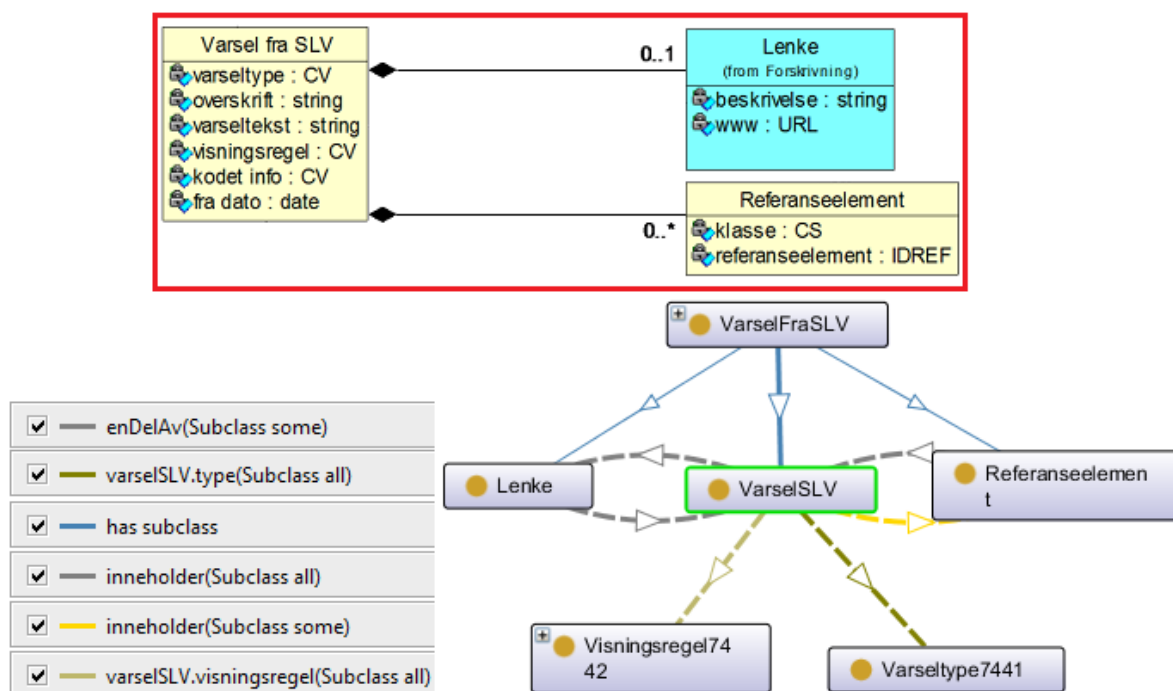


Figure 3.22 Mapping of class Varsel fra SLV

We defined a main class **VarselFraSLV** to contain all the three classes **VarselSLV**, **Lenke**, and **Referanseelement**. The main class **VarselFraSLV** doesn't have any attributes to inherit and works as a container for three classes. The classes **Visningsregel7442** and **Varseltype7441** are coding systems defined under the main class **Kodeverk**, and are used to capture information related to viewing authority and warning type respectively. Every instance of class **VarselSLV** is connected to an instance of reference element and link. The restrictions on the class **VarselSLV** are shown in the figure below:

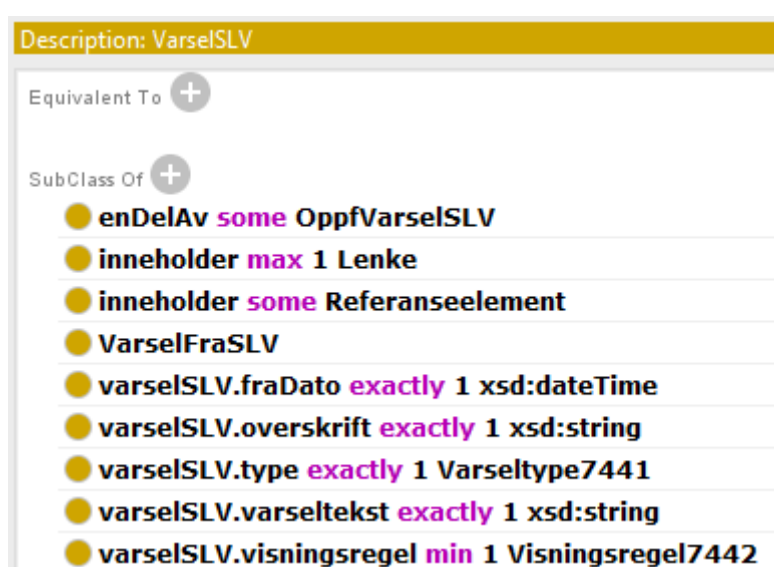


Figure 3.23 Cardinality restrictions on class VarselSLV

Every instance of class **VarselSLV** can only belong to one type of warning, therefore it is mapped with the property *VarselSLV.type* **exactly 1 Varseltype7441**. Any warning should also be viewable by at least one stakeholder, otherwise any warning is meaningless, this mapping is achieved by the property *VarselSLV.visningsregel* **min 1 Visningsregel7442**. A detailed description of the properties associated with class **VarselSLV** and its associated classes is shown in the table below:

Property	Domain	Range	Short Explanation
<i>varselSLV.overskrift</i>	VarselSLV	<i>xsd:string</i>	Used to describe heading of the warning/notification.
<i>varselSLV.varseltekst</i>	VarselSLV	<i>xsd:string</i>	Used to describe the notification/warning in detail.
<i>varselSLV.fraDato</i>	VarselSLV	<i>xsd:dateTime</i>	Use to describe the date/time from which the notification is effective.
<i>varselSLV.type</i>	VarselSLV	Varseltype7441	Used to describe type of notification/warning such as Safety notice, general notice, and shipment failure.
<i>varselSLV.visningsregel</i>	VarselSLV	Visningsregel7442	Used to describe which stakeholder should see the notification.
<i>lenke.beskrivelse</i>	Lenke	<i>xsd:string</i>	Used to describe the purpose of link.
<i>lenke.URL</i>	Lenke	<i>xsd:string</i>	Used to capture actual URL link.

Table 3.9 Properties for class *VarselSLV*

3.15 Mapping of class **Kodeverk**

The catalogue **Kodeverk** represents all the coding systems currently utilized by FEST database. These coding systems are maintained by Norwegian directorate of eHealth. An ontology to represent the **Kodeverk** catalogue is also developed by FEST management, but in our mapping we used a different approach from that ontology to maintain the coherence between the structure of our ontology. The figure below shows the mapping between catalogue **Kodeverk** to our FEST ontology:

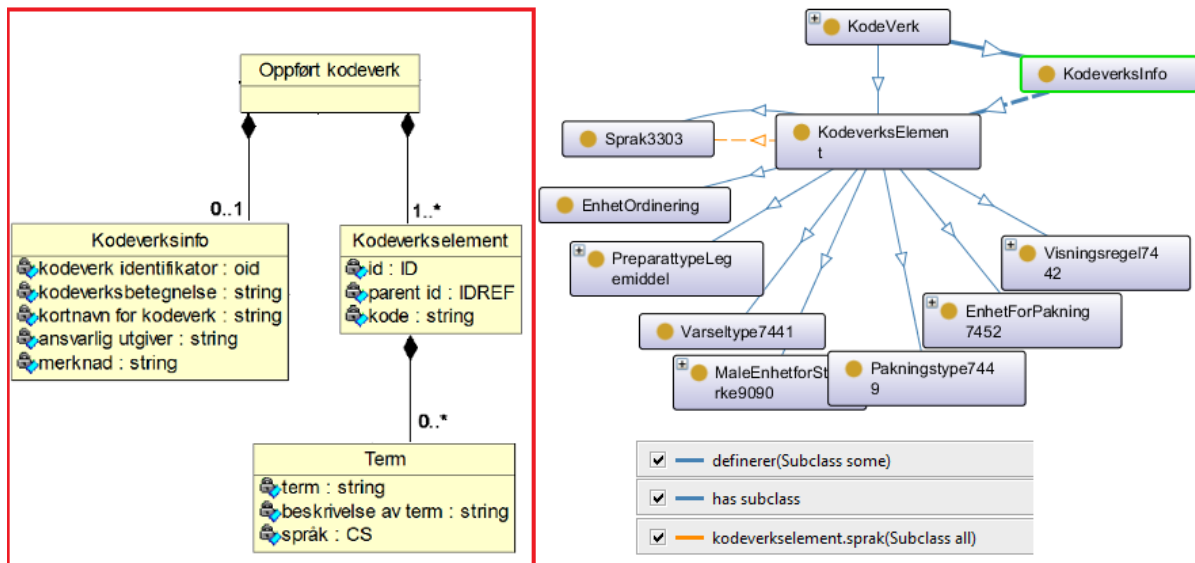


Figure 3.24 Mapping of class Kodeverk

We have used a slight different approach while mapping the class **Kodeverk** by defining a main class **Kodeverk** having the subclasses **KodeverksInfo** and **KodeverksElement** which are also visible in the UML structure. Any instance of class **KodeverksElement** is defined by an instance of class **KodeverksInfo**, and the mapping is accomplished using the property *definerer*. We can observe the class **Term** in UML structure, but in our approach we have mapped these attributes by using data properties and extending the notation of **KodeverksElement**. Different property assertions on the class **KodeverksInfo** and **KodeverksElement** are shown in the figure below:

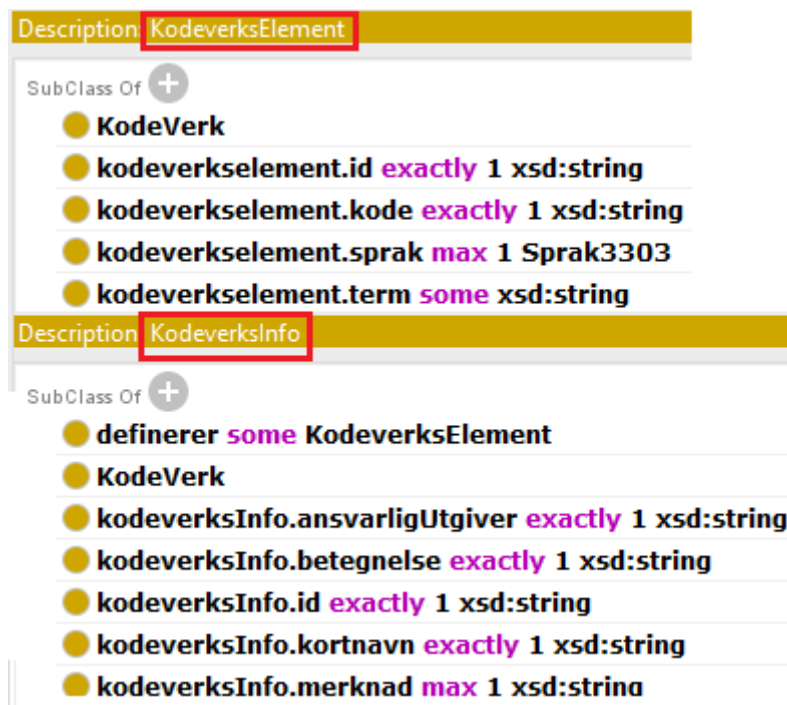


Figure 3.25 Cardinality restrictions on class Kodeverk

This class does not have reference to any other class, but other classes such as **LegemiddelVirkestoff**, and **LegemiddelMerkevare** use this class to refer to certain elements defined under different coding systems. A coding system **Varseltype7441** will have different instances to represent different type of warnings, and all those warning instances may also have further attributes that are shown in the figure 3.25. Different properties associated with class **Kodeverk** are summarized in the table below:

Property	Domain	Range	Short Explanation
<i>kodeverksInfo.id</i>	KodeverksInfo	<i>xsd:string</i>	A unique ID for identification of coding system.
<i>kodeverksInfo.merknad</i>	KodeverksInfo	<i>xsd:string</i>	Used to insert comments to a particular coding system.
<i>kodeverksInfo.kortnavn</i>	KodeverksInfo	<i>xsd:string</i>	Short name of coding system.
<i>kodeverksInfo.betegnelse</i>	KodeverksInfo	<i>xsd:string</i>	Used to describe actual specification of coding system
<i>kodeverksInfo.ansvarligUtgiver</i>	KodeverksInfo	<i>xsd:string</i>	Used to describe responsible publisher of coding system.
<i>kodeverkselement.id</i>	KodeverksElement	<i>xsd:string</i>	A unique ID Used to identify an coding element inside FEST ontology.
<i>kodeverkselement.kode</i>	KodeverksElement	<i>xsd:string</i>	Used to describe actual code of element given by the publisher.
<i>kodeverkselement.term</i>	KodeverksElement	<i>xsd:string</i>	Name or term of the element given by publisher of coding system.
<i>kodeverkselement.sprak</i>	KodeverksElement	Sprak3303	Used to specify which language is element defined in.

Table 3.10 Properties for class *Kodeverk*

3.16 Mapping of class **Interaksjon**

Catalogue **Interaksjon** is of great importance, as we propose a use case to generate implicit data from the existing data for safe medication. We have also proposed in thesis to represent Interaction mechanisms by integrating FEST Ontology (particularly **Interaksjon** class) with

DINTO ontology. The figure below shows the mapping of Interaction catalogue to our ontology:

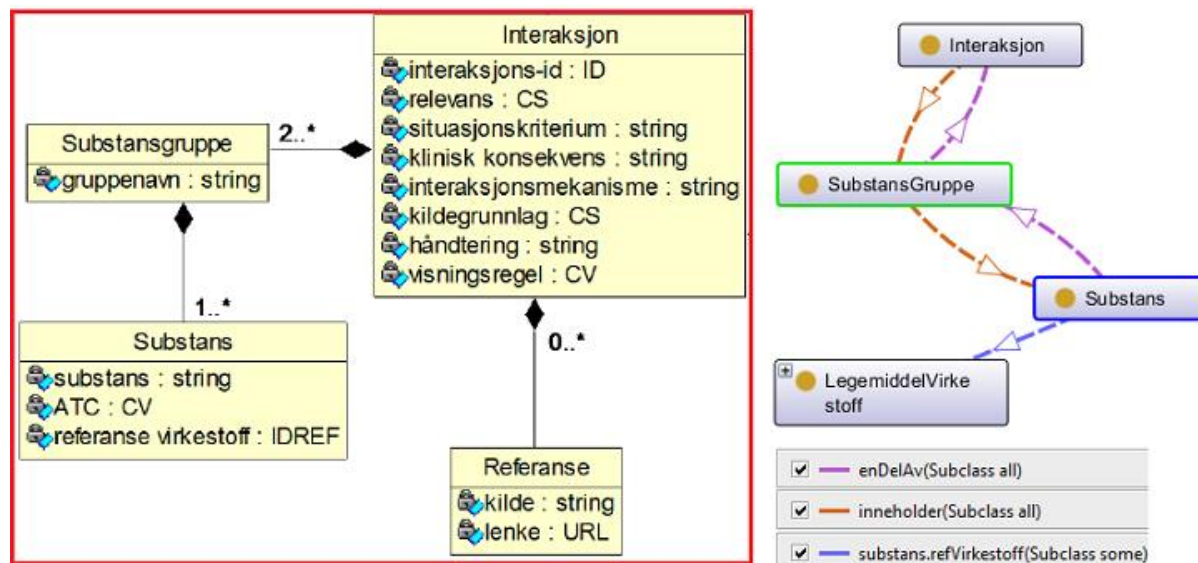


Figure 3.26 Mapping of *Interaksjon*

Most of the attributes of catalogue **Interaksjon** are represented as data properties with range as string. The class **Interaksjon** contains **Substansgruppe** and **Substans** class, and are mapped through object property *inneholder*, which is used as a condition in the class structure of **Interaksjon**. Figure below shows the cardinality restrictions along with other property conditions that we have mapped from the FEST to the class **Interaksjon**:

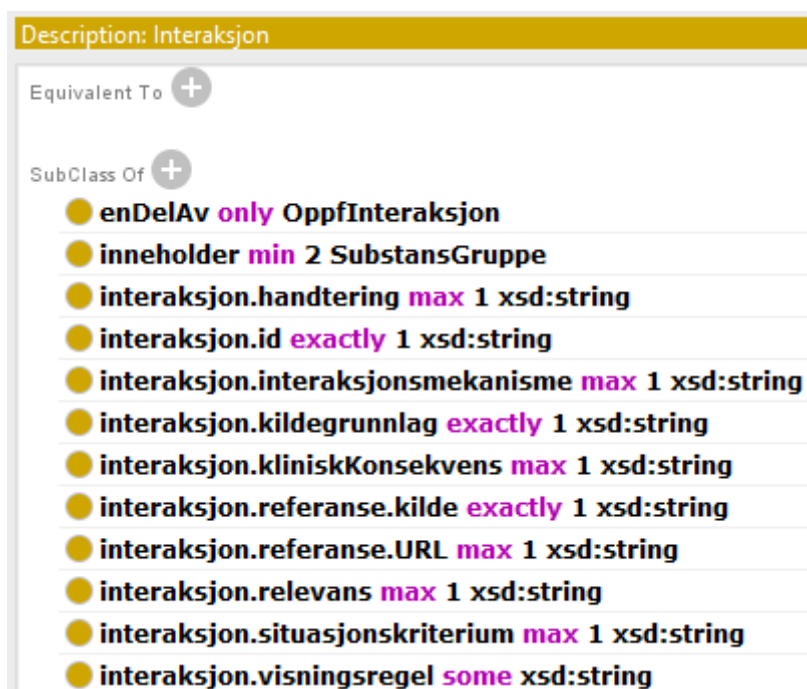


Figure 3.27 Cardinality restrictions on class *Interaksjon*

We also mapped the **Referanse** class from the UML as an object property by extending property notation as *interaksjon.referanse.kilde* and *interaksjon.referanse.URL*. These properties are used to capture the source from where the information about the drug interaction is taken. Every **Interaksjon** instance will include 2 or more substance groups, and every substance group will have minimum 1 substance instance. Suppose there are two substance groups A and B. Group A have 1 substance, and group B has 3 substances in it, this entails that the 1 substance from group A will have an interaction with all the three substances of group B. Every substance have a direct reference to class **typeVirkestoff** which is identified further using ATC coding system. The properties such as *relevans*, *kildegrunnlag*, and *visningsregel* are mapped as data properties which could also have been mapped as object properties, as described in section 3.3, by defining their corresponding coding system in the class **Kodeverk**.

The table below summarizes the properties associated with class **Interaksjon**:

Property	Domain	Range	Short Explanation
<i>interaksjon.id</i>	Interaksjon	<i>xsd:string</i>	A unique ID to identify an interaction inside FEST.
<i>interaksjon.forklaring</i>	Interaksjon	<i>xsd:string</i>	a replacement for “ <i>interaksjon.mekanisme</i> ” to describe the cause of interaction in textual form.
<i>interaksjon.handtering</i>	Interaksjon	<i>xsd:string</i>	Used to specify information about handling suggestions for interaction.
<i>interaksjon.kildegrunnlag</i>	Interaksjon	<i>xsd:string</i>	Used to specify the source of how interaction was discovered.
<i>interaksjon.kliniskKonsekvens</i>	Interaksjon	<i>xsd:string</i>	Used to specify clinical consequences of interaction.
<i>interaksjon.relevans</i>	Interaksjon	<i>xsd:string</i>	Used to specify recommended actions.
<i>interaksjon.situasjonskriterium</i>	Interaksjon	<i>xsd:string</i>	Used to specify when an interaction should be handled.
<i>interaksjon.referanse.kilde</i>	Interaksjon	<i>xsd:string</i>	Reference to the source on interaction discovery

<i>interaksjon.referanse.URL</i>	Interaksjon	<i>xsd:string</i>	Link/URL to the source.
<i>interaksjon.visningsregel</i>	Interaksjon	Visningsregel7442	Used to specify stakeholder who should see this interaction.
<i>interaksjon.mekanisme</i>	Interaksjon	DDI_Mekanisme	Used to integrate with drug interaction mechanisms.
<i>substansGruppe.navn</i>	SubstansGruppe	<i>xsd:string</i>	Used to describe name of the substance group.
<i>substans.ATC</i>	Substans	ATC	Used to identify substance using ATC code defined in coding system.
<i>substans.navn</i>	Substans	<i>xsd:string</i>	Used to specify name of the substance as in coding system.
<i>substans.refVirkestoff</i>	Substans	LegemiddelVirkestoff	Used to refer to actual medicine(s) that contains this Substans.

Table 3.11 Properties for class *Interaksjon*

3.17 Mapping of FEST ontology for Drug interaction mechanisms

Drug Interaction mechanism describe the process and means by which a particular drug interaction is provoked. These mechanisms can help in classification of interactions on the basis of procedure which can be valuable in identifying and scrutinizing the similar characteristics between interactions. Two drugs can generate undesired results If they are prescribed simultaneously. Drug interaction mechanisms are generally divided in two types, Pharmacodynamic and Pharmacokinetic mechanisms. Former refers to an interaction where two drugs add up together to give an additive or adverse side effects. While latter indicates an interaction where one of the drug affects the efficiency of the other drug. As presented in an article by Philip Hansten and John Horn, Pharmacokinetic interactions may have further classifications such as Inhibition of Absorption, Enzyme Inhibition Increasing Risk of Toxicity, Enzyme Inhibitors Resulting in Reduced Drug Effect, Enzyme Induction Resulting in Reduced Drug Effect, Enzyme Induction Resulting in Toxic Metabolites, and Altered Renal Elimination [31]. While Pharmacodynamic interactions may also be further classified into Additive Pharmacodynamic Effects, and Antagonistic Pharmacodynamic Effects [31]. We are

not concerned with the biological effects of these mechanisms, but instead, we present a method for the classification of drug interactions in our ontology.

As we argued about the benefits of representing FEST data as an ontology and how it can be combined with existing ontologies to develop more advanced support systems. We integrated the drug interaction mechanism structure from DINTO ontology with our FEST ontology by using the existing attribute in FEST database that is *interaksjon.mekanisme*. This particular attribute is currently used to accept data as a string by which merely states about the cause of particular interaction. For example, one of the interaction in FEST database points towards the mechanism of interaction by stating that “substance A increases the metabolism of substance B” which is recorded under the property *interaksjon.mekanisme*. In contrast to that, We have used similar method as represented in DINTO ontology, for the representation of interaction mechanisms, and have integrated it into FEST ontology that will result not only in a more sophisticated classification of interaction mechanism, but also in identifying the mechanisms which can incur similar interactions. The figure below shows the class structure of Interaction mechanism:

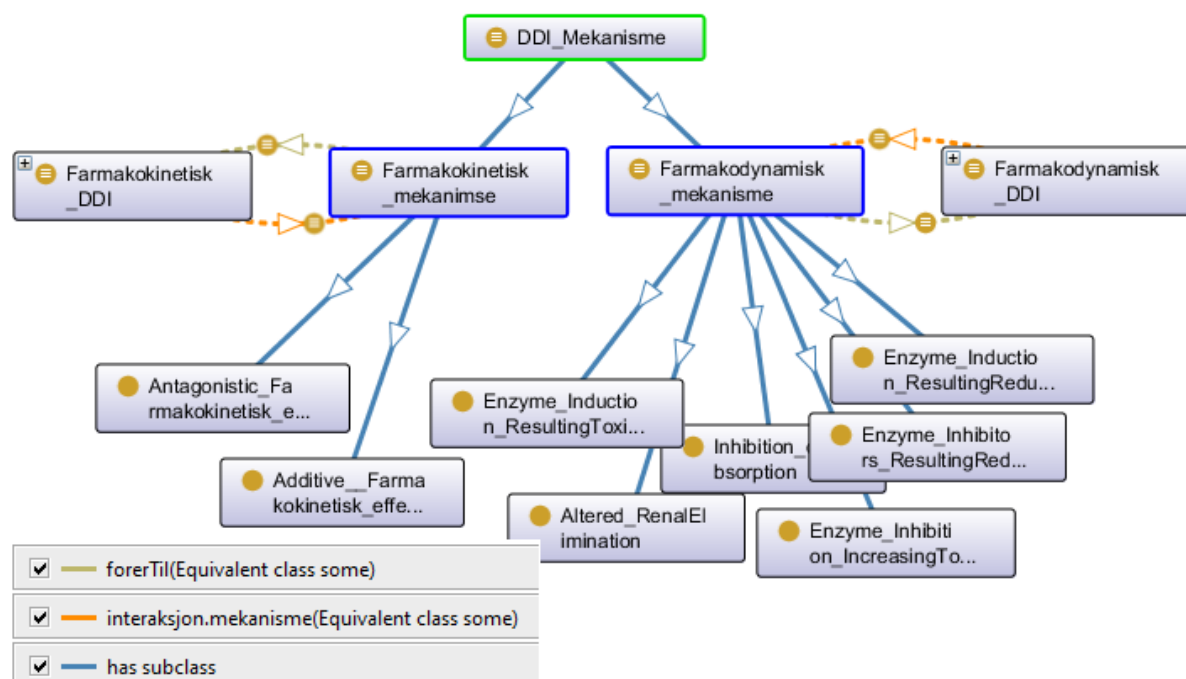


Figure 3.28 class hierarchy for Interaction Mechanisms

In this thesis, we are not concerned about the biological or clinical rules and effects of these mechanisms, therefore subclasses of Pharmacodynamic and Pharmacokinetic doesn't have any rules or restrictions on them. We can, in future, use these classes to define proper conditions for a particular mechanism, and all the interaction in FEST database can be classified under

these classes. We also have **Farmakokinetisk_Interaksjon** and **Farmakodynamisk_Interaksjon** defined as subclasses of **Interaksjon**. The mechanism defined above will result in these interactions. The figure below represents the conditions that should be fulfilled in order to be classified as an Pharmacodynamic or Pharmacokinetic interaction:

The image shows two panels, each representing a class definition. The top panel is for **Farmakodynamisk_Interaksjon**. Its description is `Farmakodynamisk_Interaksjon`. Below the description, it lists 'Equivalent To' conditions: **Interaksjon** and `and (inneholder some Gruppe_1)`, `and (inneholder some Gruppe_2)`, and `and (interaksjon.mekanisme some Farmakodynamisk_mekanisme)`. The bottom panel is for **Farmakokinetisk_Interaksjon**. Its description is `Farmakokinetisk_Interaksjon`. Below the description, it lists 'Equivalent To' conditions: **Interaksjon** and `and (inneholder some Gruppe_3)`, `and (inneholder some Gruppe_4)`, and `and (interaksjon.mekanisme some Farmakokinetisk_mekanisme)`.

Figure 3.29 Well defined conditions for interaction classification

We will again emphasize that the conditions might not be biological correct, but the actual representation with accurate conditions will be similar to the figure 3.29. If an interaction has instances of group 1 and group 2, and mechanism behind it is Pharmacodynamic, then that interaction can be classified as an Pharmacodynamic interaction. Similar conditions are imposed on Pharmacokinetic interaction. We took in consideration the existing information connected with the `interaksjon.mekanisme` in FEST, and that is now represented by using another string defined as *interaksjon.forklaring*.

4 RESULTS

In this chapter, we will describe the different results we can achieve using SPARQL queries. We have used SPARQL plugin for protégé to demonstrate the execution of queries. A SPARQL endpoint such as Fuseki can also be used for the same purpose. These results will also help in further understanding the mapping between different classes that we have described in chapter 3. It is to be noted that we have not imported all the instances from FEST database, as this would be another project. Instead, we have mapped a limited amount of instances from different classes to demonstrate different use cases such as drug interactions, and interaction mechanisms.

4.1 SPARQL queries on LegemiddelVirkestoff

The class LegemiddelVirkestoff, as described earlier, is used to identify all the medicines that can be prescribed in Norway. If we simply want to retrieve all the medicines that can be prescribed, we can use a simple query shown in the figure below:

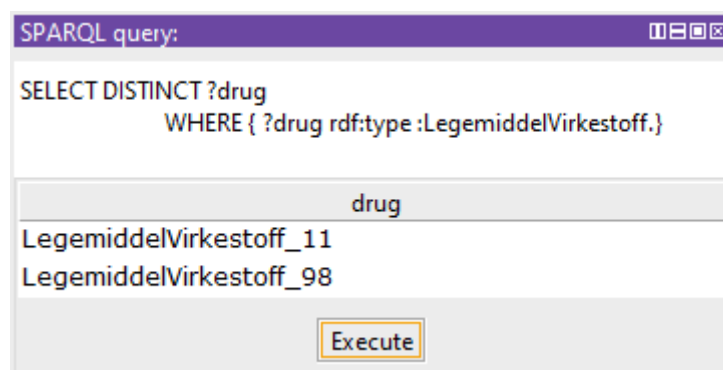


Figure 4.1 query result for instances of LegemiddelVirkestoff

This will fetch us all the drugs that are of type **Legemiddel**, or in other terms, all the instances that belong to Legemiddel class. At the moment, for the purpose of demonstration, we have only two instances of class LegemiddelVirkestoff which are also shown in the RDF graph in the figure below:

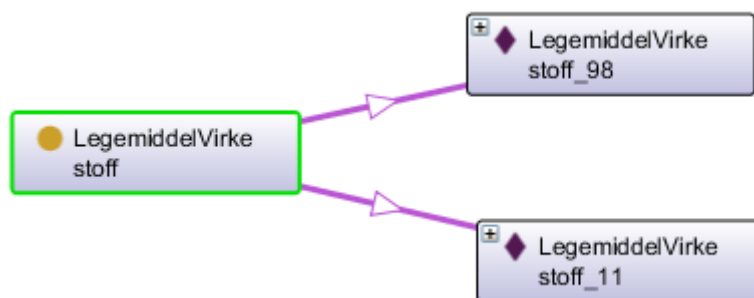


Figure 4.2 RDF graph for instances of Legemiddel

We can fetch the details of a particular drug (instance of **Legemiddel**) such as ATC code, name, and reference to other classes by using a simple query shown in the figure below along with the corresponding results:

SPARQL query:

```
SELECT DISTINCT ?attributes ?value
WHERE { :LegemiddelVirkestoff_11 ?attributes ?value }
```

attributes	value
legemiddel.ATC	J02AC01
legemiddel.navnFormStyrke	"Flukonazol Kaps 100 mg"@
legemiddelVirkestoff.refLegemiddelMerkevare	ID_9A108EFF-697B-4049-B89F-C3037D751F70
legemiddelVirkestoff.refLegemiddelMerkevare	ID_8A1AEFCC-C5F5-4218-8AB1-648085204D38
legemiddelVirkestoff.refPakning	ID_812C23DE-BA32-473E-8341-03F9890CD686
legemiddelVirkestoff.refPakning	ID_0B46FCF8-1247-4851-BD35-8F69BE106646
rdf:type	owl:NamedIndividual
rdf:type	LegemiddelVirkestoff

Execute

Figure 4.3 query result for a particular instance of Legemiddel

The instance **LegemiddelVirkestoff_11** have two references to LegemiddelMerkevare (marked as blue), and two references to the instances of class **LegemiddelPakning** (marked as green), as shown in the figure 4.3. This implies, that the drug **LegemiddelVirkestoff_11** is available in two different packages, and two different brand names. The drug itself is identified by the ATC code “J02AC01”. Please refer to figure and for the specifications of referred instances. The same results as in figure 4.3 are shown as an RDF graph in the figure below:

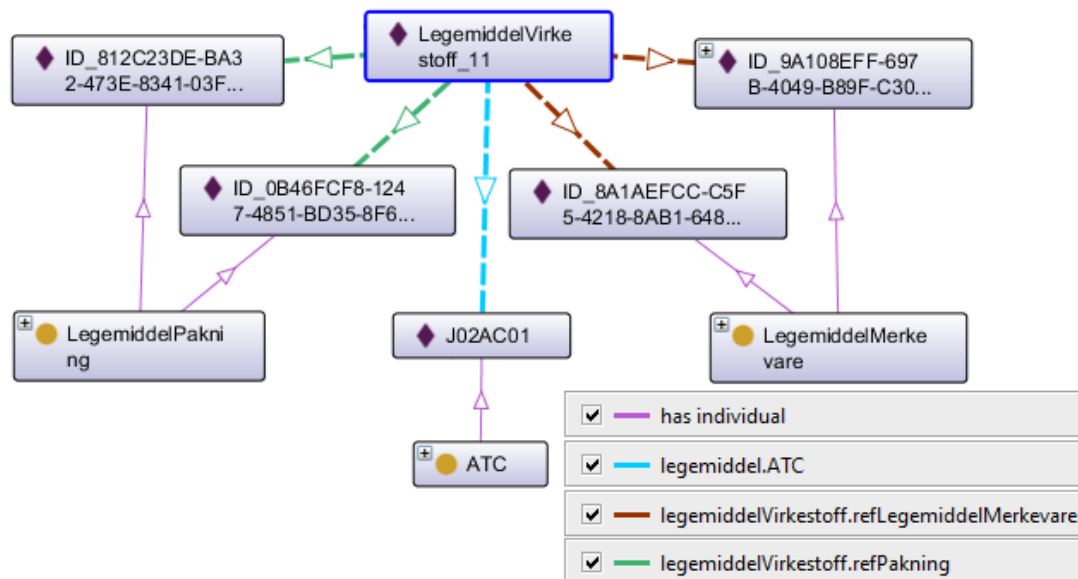


Figure 4.4 RDF graph for Legemiddel instance

The referred instances belong to class **LegemiddelPakning** and **LegemiddelMerkevare**. We can also notice that **LegemiddelVirkestoff_11** is identified using **J2AC01** which is defined under the ATC coding system in class **ATC**.

4.2 SPARQL queries for LegemiddelMerkevare

An instance of class **LegemiddelMerkevare** describes a particular brand of the medicine. As shown in the figure 4.3, one medicine can be available in the market having different brand names. All the instances of class **LegemiddelMerkevare** can be accessed using a query similar to the query shown in figure 4.1, and only difference would be to replace **:LegemiddelVirkestoff** with **:LegemiddelMerkevare**. To retrieve all the information related to a particular brand we can use the following query:

SPARQL query:	
<pre>SELECT DISTINCT ?attributes ?value WHERE { :ID_A2BAA17E-231F-4891-B704-4FB83DD8A737 ?attributes ?value} ORDER BY ASC(?attributes)</pre>	
attributes	value
legemiddel.ATC	J02AC02
legemiddel.legemiddelformKort	Kapsel
legemiddel.navnFormStyrke	"Sporanox Kaps 100 mg"@
legemiddel.preparattype	Legemiddel
legemiddel.reseptgruppe	"C"@
legemiddel.typeSoknadSlv	"1"
legemiddelMerkevare.id	"ID_A2BAA17E-231F-4891-B704-4FB83DD8A737"
legemiddelMerkevare.legemiddelformLang	"Kapsel, hard"@
legemiddelMerkevare.produktInfo.produsent	"Janssen-Cilag AS"@
legemiddelMerkevare.produktInfo.varselTrekant	"false"
legemiddelMerkevare.varenavn	"Sporanox"@
rdf:type	owl:NamedIndividual

Figure 4.5 Query result for an instance of LegemiddelMerkevare

The instance of LegemiddelMerkevare with ID “ID_A2BAA17E-231F-4891-B704-4FB83DD8A737”, as shown in the figure above, is the same instance that is being referred in figure 4.3 by **LegemiddelVirkestoff_11** instance. The drug Itrakonazol (**LegemiddelVirkestoff_11**) is available under the brand shown in figure above, and is produced by Janssen-Cilag AS. An RDF graph of the result is shown in the figure below:

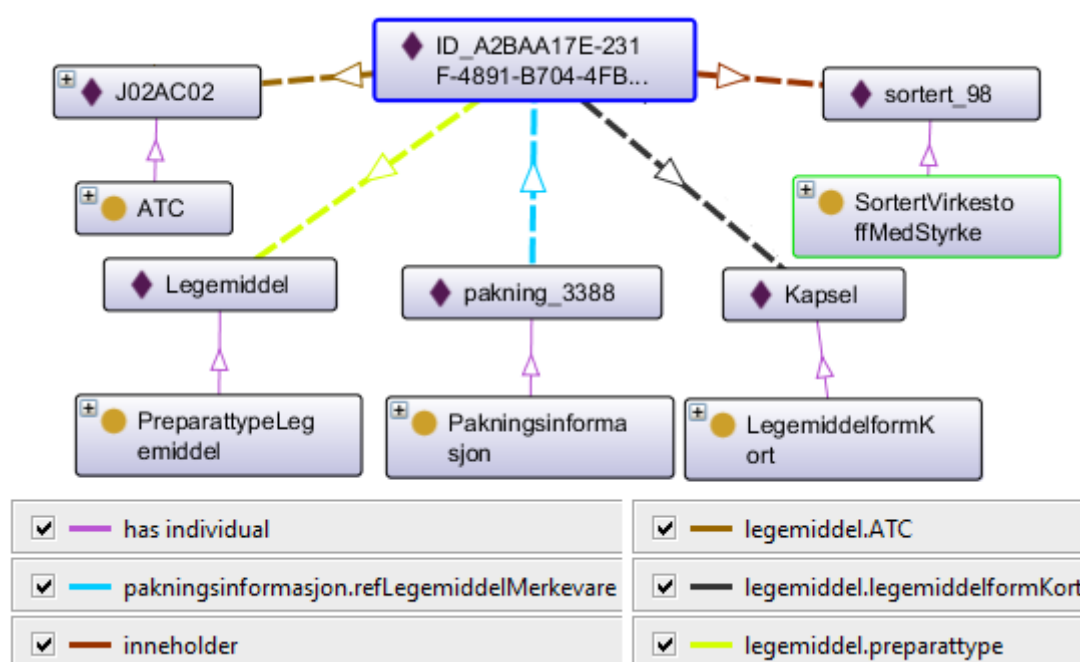
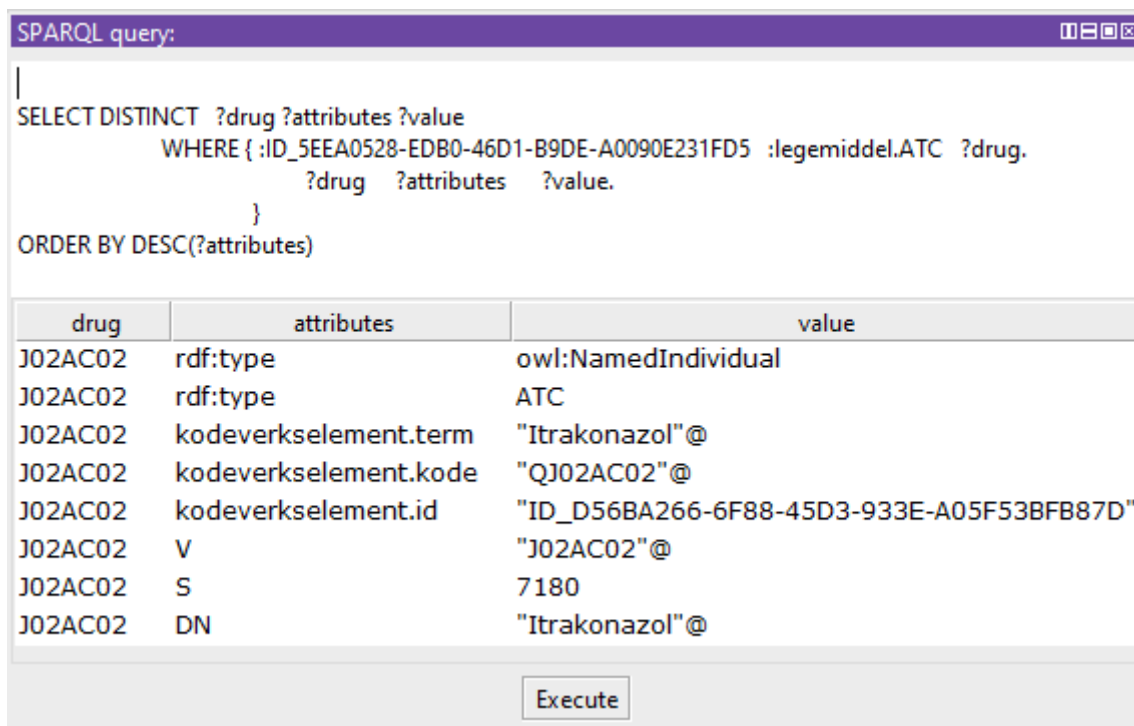


Figure 4.6 RDF graph LegemiddelMerkevare instance

The graph shows the reference to different instances that we have also retrieved using the query in figure 4.5. The instances Legemiddel, pakning_3388, and Kapsel, as shown in the figure above, belong to the corresponding coding systems, which are mainly defined in the class **Kodeverk**.

4.3 SPARQL queries for LegemiddelPakning

Similar to the queries shown in section 4.2 and 4.3, we can also retrieve the information related to a particular instance of class **LegemiddelPakning**. We can also retrieve the information about the actual drug or substance which is being represented by a particular packaging. The figure below shows the SPARQL query to get such information:



The screenshot shows a SPARQL query window with the following query:

```
SELECT DISTINCT ?drug ?attributes ?value
WHERE { :ID_5EEA0528-EDB0-46D1-B9DE-A0090E231FD5 :legemiddel.ATC ?drug.
?drug ?attributes ?value.
}
ORDER BY DESC(?attributes)
```

The results are displayed in a table with three columns: drug, attributes, and value.

drug	attributes	value
J02AC02	rdf:type	owl:NamedIndividual
J02AC02	rdf:type	ATC
J02AC02	kodeverkselement.term	"Itrakonazol"@
J02AC02	kodeverkselement.kode	"QJ02AC02"@
J02AC02	kodeverkselement.id	"ID_D56BA266-6F88-45D3-933E-A05F53BFB87D"
J02AC02	V	"J02AC02"@
J02AC02	S	7180
J02AC02	DN	"Itrakonazol"@

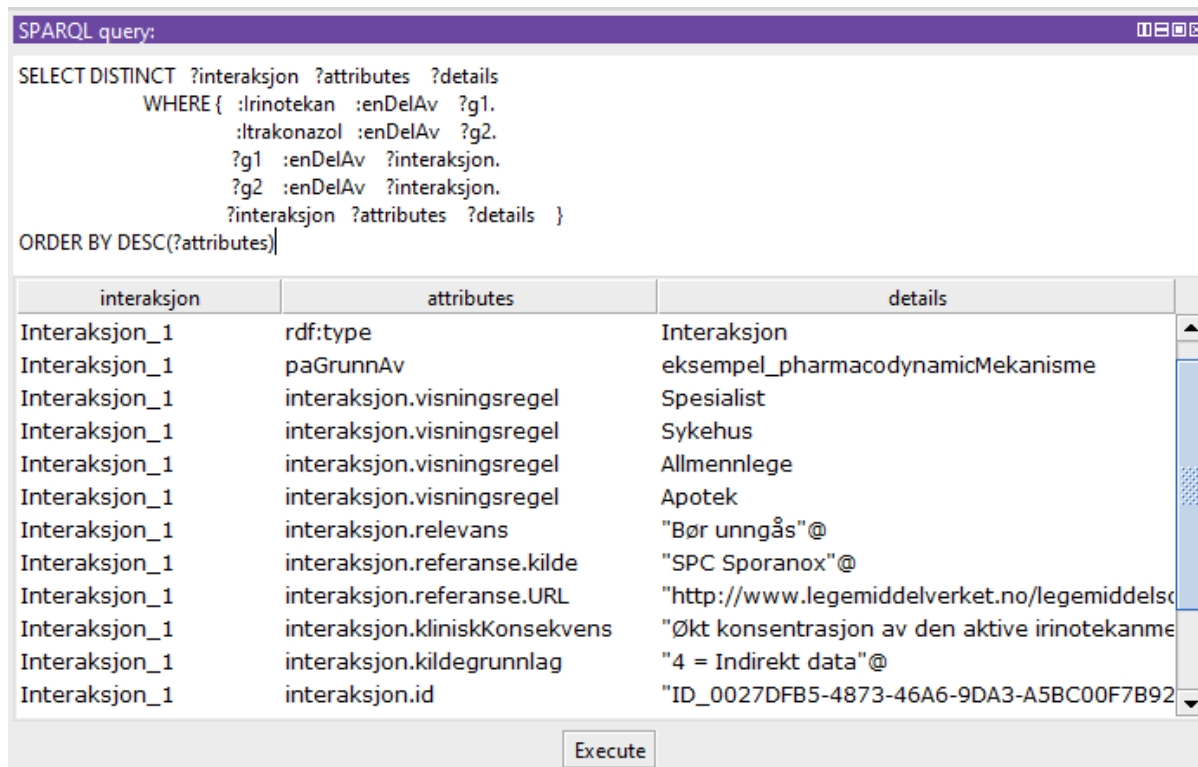
An "Execute" button is visible at the bottom of the interface.

Figure 4.7 Query result for retrieving drug information through Packaging

The query shown above identifies all the ATC codes associated with the instance of LegemiddelPakning, shown as ?drug. Because only one instance of ATC code is associated, which is J02AC02, the information for only that code is retrieved. The value of “S” denotes the coding system under which the instance “J02AC02” is defined. And “7180” denotes the coding system for ATC classifications. We can also check through class LegemiddelMerkevarer or LegemiddelPakning about the potential drug-drug interaction. This is not explicitly stated in the FEST database that a particular brand may lead to some interaction, but using SPARQL queries we can generate that result. An example of a similar query is shown in the section.

4.4 SPARQL queries for Drug Interactions

To check for an interaction between two drugs we can retrieve information from the class **Interaksjon**. All the interactions are listed under this class as instances, and we can check for an interaction between two specific drugs by using the query shown in figure below:



SPARQL query:

```
SELECT DISTINCT ?interaksjon ?attributes ?details
WHERE {
  :Irinotekan :enDelAv ?g1.
  :Itrakonazol :enDelAv ?g2.
  ?g1 :enDelAv ?interaksjon.
  ?g2 :enDelAv ?interaksjon.
  ?interaksjon ?attributes ?details }
ORDER BY DESC(?attributes)
```

interaksjon	attributes	details
Interaksjon_1	rdf:type	Interaksjon
Interaksjon_1	paGrunnAv	eksempel_pharmacodynamicMekanisme
Interaksjon_1	interaksjon.visningsregel	Spesialist
Interaksjon_1	interaksjon.visningsregel	Sykehus
Interaksjon_1	interaksjon.visningsregel	Allmennlege
Interaksjon_1	interaksjon.visningsregel	Apotek
Interaksjon_1	interaksjon.relevans	"Bør unngås"@
Interaksjon_1	interaksjon.referanse.kilde	"SPC Sporanox"@
Interaksjon_1	interaksjon.referanse.URL	"http://www.legemiddelverket.no/legemiddelse"
Interaksjon_1	interaksjon.kliniskKonsekvens	"Økt konsentrasjon av den aktive irinotekanme"
Interaksjon_1	interaksjon.kildegrunnlag	"4 = Indirekt data"@
Interaksjon_1	interaksjon.id	"ID_0027DFB5-4873-46A6-9DA3-A5BC00F7B92"

Execute

Figure 4.8 Query for checking drug-drug interaction

The substances Irinotekan and Itrakonazol belong to two different substance groups, and both of those Substans groups, when combined, lead to a potential drug interaction. The query shown in the figure above also shows all the details of the particular interaction such as reference, consequences and relevant precaution. It can also be seen in the figure above that there is a particular mechanism (*eksempel_pharmacodynamicMekanisme*) which has triggered this interaction. We have used the FEST property *Interaksjon.mekanisme* to map this information which is not defined in FEST database. More information about drug mechanism is given in the section . We can combine and customize this query with previous queries to generate results about whether a particular brand may lead to an interaction.

A substance group may include more than one medicines which means that all those medicines will have a reaction with the other group. The query below shows an example of such a scenario:

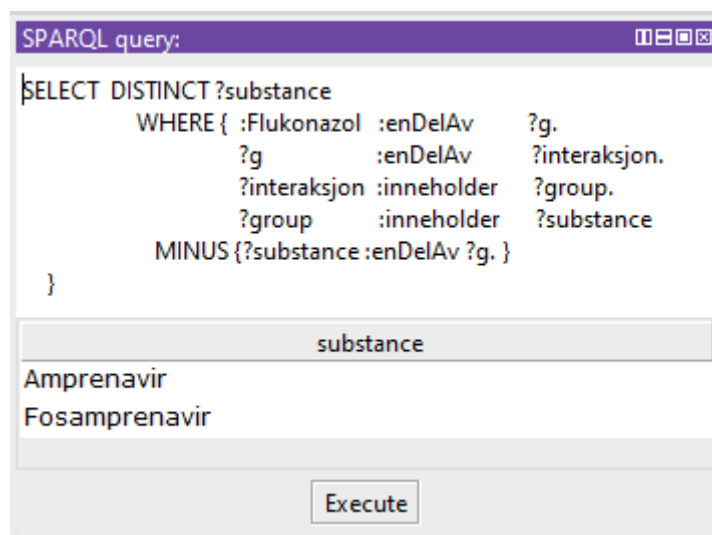


Figure 4.9 query result for checking all the potential interactions

We first retrieved the group of Flukonazol, and then checked whether that group has interaction with other groups. In case of true statement, we checked further for all the groups that particular interaction belongs to. Then we retrieved the information about specific substances of the second group. We used MINUS in this query to exclude the instances of first group. The result in figure 4.9 shows that the drug Flukonazol have an interaction with both Amprenavir and Fosamprenavir, which are instances of the same group. By Combining and customizing the query shown in figure 4.8 with this query, we can further retrieve the information of the interaction itself. The figure shown the RDF graph of the case presented above and confirms the query results too:

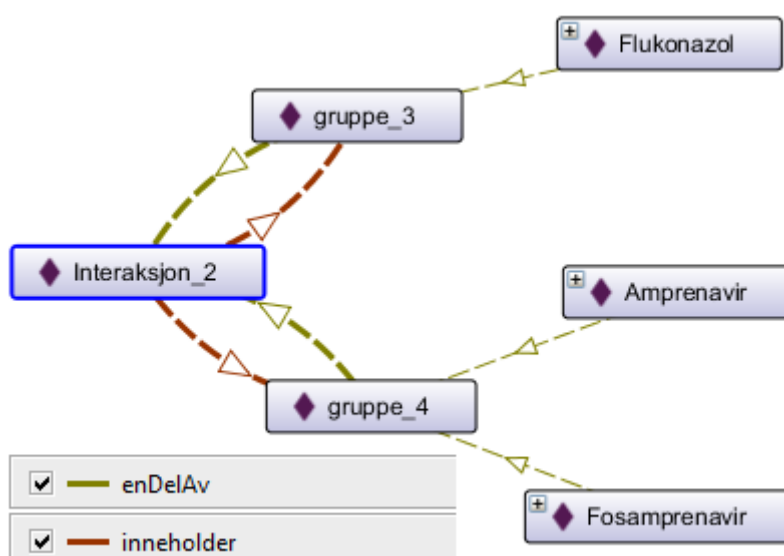


Figure 4.10 RDF graph for drug interaction

4.5 Query results for Drug Interaction Mechanisms

In section we have described the methodology for the classification of interaction mechanisms. Now, if there is an interaction which satisfies the necessary conditions for the classification, then that interaction should be classified correctly. The figure below shows the results of reasoner which classifies *Interaksjon_1* instance as Pharmacodynamic interaction.

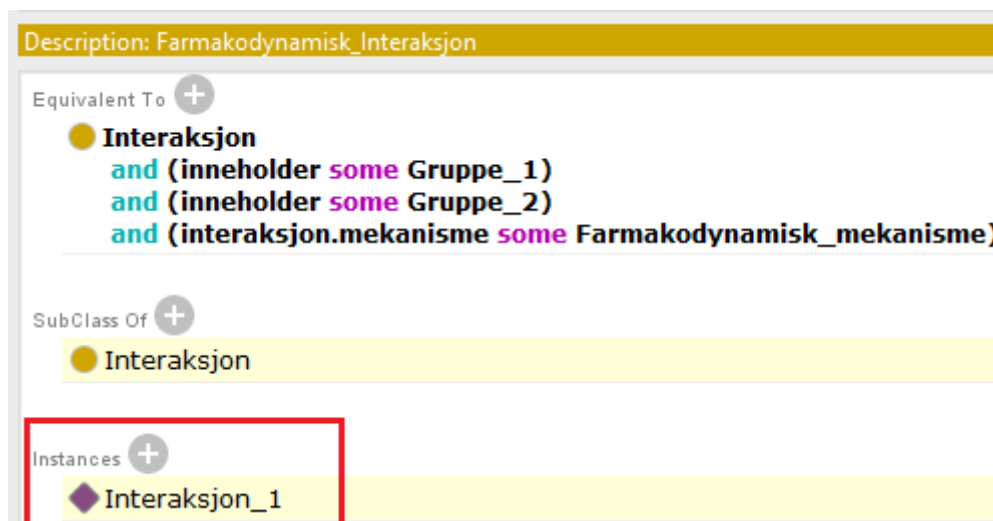
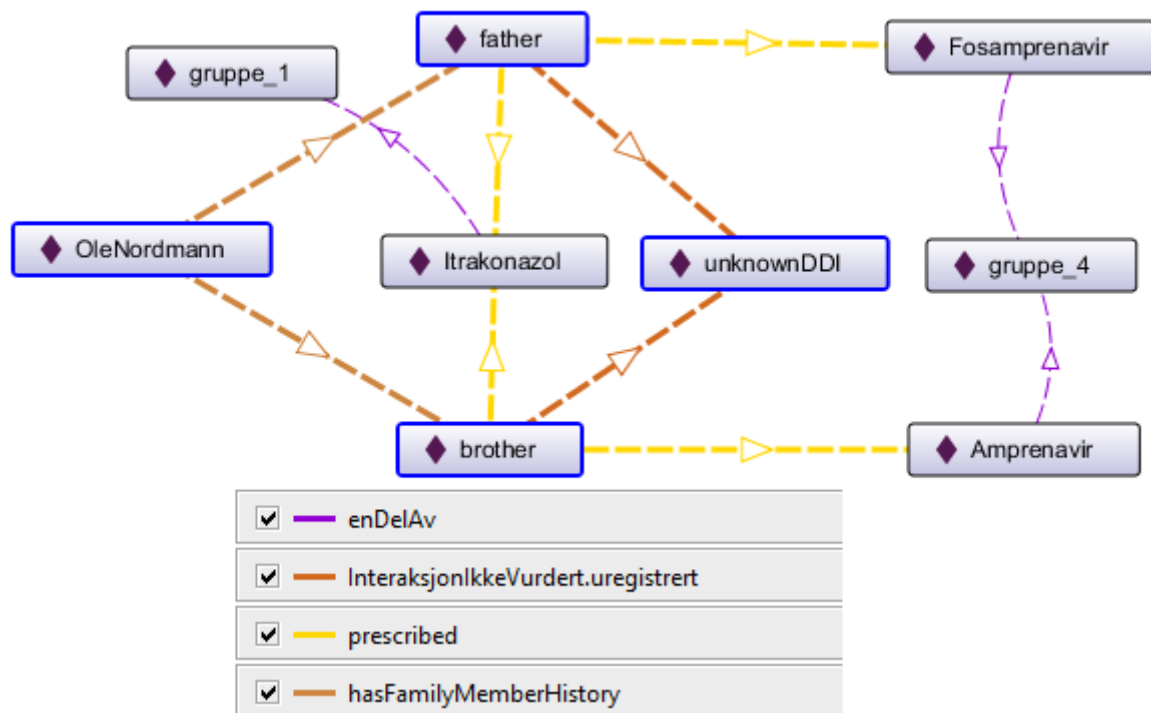


Figure 4.11 Reasoner result for classification of Interaction

The instance *Interaksjon_1* includes some medicines from group 1, and some medicines from group 2, and is also caused by an instance of *Farmakodynamisk_mekanisme*, therefore it has been classified correctly under the category of Pharmacodynamic interaction. For the details of *Interaksjon_1* please refer to

4.6 Query results for drug interaction in context with patient's family member history

We created a class structure and integrated it with FEST ontology to generate implicit data about possible drug-drug interaction by examining the data related to patient and his family member history. In the FEST database there is a class **InteraksjonIkkeVurdert**, which we have used to integrate FEST ontology with the case specified. Any interaction which is not currently stated in FEST database will be defined under this class. If two or more family members of a patient were prescribed a combination of medicines, and their journal have a record that they showed some unwanted side effects, but those medicines were not expected to generate any side effects. In this case, the patient should be examined before giving same combination of drugs as there may be case of genetical reaction to those drugs. This case has been presented in presented in our research paper. The figure below shows the RDF graph of the scenario described above:



We used the SPARQL CONSTRUCT query to generate implicit triples about unknown DDI's by examining the existing data. For example, suppose that father of Ole Nordmann, having a heart disease, was prescribed a combination of drugs Itrakonazol and Fosamprenavir; and his brother, having similar disease, was also prescribed Itrakonazol and Amprenavir. Both Amprenavir and Fosamprenavir belong to same substance group in FEST. Their patient history exhibit that both of them suffered from some side effects, possibly a DDI. But this DDI is not explicitly stated in the database nor the drugs were supposed to exhibit a reaction. A hypothetical diagnose can be linked to such a situation that genes of the concerned persons may have a possible reaction to this combination of drugs. We can check this whole scenario by constructing a SPARQL query, and in response, Ole Nordmann can be prevented from taking the same combination as he is inheriting the same genes. A possible warning can be generated for the practitioner responsible for treating Ole, and he may further order some more clinical tests. The figure below shoes the SPARQL query result to construct an explicit triple.

SPARQL query:

```

CONSTRUCT { :OleNordmann :InteraksjonIkkeVurdert.uregistrert :HypotheticalDDI.
             :hypotheticalDDI rdf:type :InteraksjonIkkeVurdert}

WHERE { { :OleNordmann :hasFamilyMemberHistory :father.
          :father      :prescribed :ltrakonazol;
          :father      :prescribed :Fosamprenavir;
          :father      :InteraksjonIkkeVurdert.uregistrert :unknownDDI. }
        { :OleNordmann :hasFamilyMemberHistory :brother.
          :brother     :prescribed :ltrakonazol;
          :brother     :prescribed :Amprenavir;
          :brother     :InteraksjonIkkeVurdert.uregistrert :unknownDDI. }

```

Subject	Predicate	Object
OleNordmann	InteraksjonIkkeVurdert.uregistrert	HypotheticalDDI
hypotheticalDDI	rdf:type	InteraksjonIkkeVurdert

Execute

Figure 4.12 query result for hypothetical DDI

We used the class **InteraksjonIkkeVurdert** to classify the potential unknown interaction. It should be noted that the scenario presented above may be biological incorrect i.e. the medicines involved in the case are only used for the demonstration purpose. Similarly, If we have all the medicines in our FEST ontology, we can integrate the patient and his history with those medicines to generate such results. This will help in providing better and safe medication prescription.

5 Discussion and Conclusion

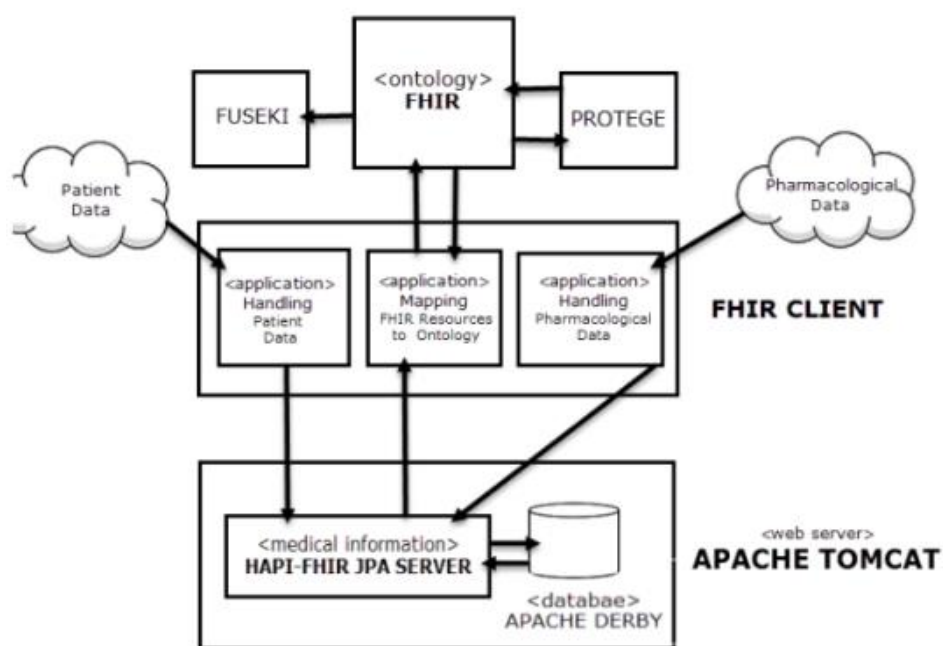
This thesis is in a way continuation of the paper that we have submitted. We developed an ontological model of FEST and demonstrated the integration of ontology with different concepts for drug interaction reasoning. One of our goals was to demonstrate semantic interoperability. HL7 is also complying to the same idea and have started implementing ontological representation for FHIR specifications in RDF format. The mapping between FEST XML and FEST ontology is mostly one-to-one, and concepts such as attributes, and class names were mapped using similar notation in most of the cases. Another goal was to generate information about potential drug-drug interactions that are not explicitly declared in FEST database. We demonstrated one use case of such a scenario by generating possible drug interaction based on family history of the patient. This use case has also been submitted in **paper**. We also presented a possible method to classify drug interactions which are listed in FEST, based on different mechanisms such as Pharmacodynamic and Pharmacokinetic interactions.

5.1 Future work

To illustrate the future work, one of the most interesting aspect is that Norwegian Medicine Agency (Statens legemiddelverk), being responsible for FEST, is also working on the similar project which is to represent FEST as open and linked data [2]. We had a discussion with Aleksander Skøyeneie, advisor at Legemiddelverket, and he briefed that they do not have an ontological model of FEST at the moment and have only implemented two catalogues as ontology. Furthermore, he stated that they would be interested in having a presentation if we are able to develop an ontological model and present a demonstration. We hope that we will be able to present the thesis work to Legemiddelverket and continue working in this direction as this may directly help Norwegian healthcare systems. In addition to this, one of the student who also worked on the paper, have shown interest in developing an API based on Java and Jena libraries to import and map all the data instances automatically from FEST XML database to the FEST ontology that we have developed.

On the other hand, the ontology that we have developed can be integrated with other ontologies such as FHIR ontology and SNOMED CT for semantic interoperability. FHIR specifications, developed by HL7, are used to exchange clinical information across different systems. Information related to drugs, patient's history, and family medical history is represented by FHIR resources [32]. By integrating FEST ontology with FHIR ontology, we can import clinical data from any system utilizing FHIR, and generate implicit data based on user defined

rules. The figure below shows the architecture overview of our paper, and the scenario described above can clearly fit in this case.



The pharmacological data in the figure above is can be imported from FEST ontology.

SNOMED CT is a nomenclature used to provide standard vocabulary for clinical terms [11]. In the current FEST database, drugs and substances are identified by ATC coding system. We can integrate FEST ontology with SNOMED ontology to identify drugs based on two different coding systems. We can also combine the pharmacological drug data used in Norway with the data from other sources based on SNOMED. In this way we can generate inferred data about drug usage in Norwegian systems compared with other systems from the world. The other systems will also be able to utilize the pharmacological drug data used in Norway, which will mutually help in better and safe medication. This is just an example use case, and once integrated, there may be several possibilities.

A use case that we have presented to classify drug interactions according to different mechanisms may also be extended. A more detailed and biologically correct definition of interaction mechanisms in the class hierarchy will result in more effective classification of drug interactions.

Certainly, there are some shortcomings or concerns that should be addressed before implementing the solution discussed in this thesis in real world. The data instances we have used for the demonstration purpose are imported manually from the FEST XML database, and

preferably this should have been done automatically. However, in the first phase of the thesis, we tried to implement it automatically by using some existing XML to RDF/OWL parsing tools such as JXML2OWL API⁸, Ontmalizer⁹, and TopBraid composer¹⁰, which are. None of the tools provided a meaningful or ordered output structure of data. Because one of the point of interest was to demonstrate drug interaction inferencing based on family history, and working on automatic mapping of whole FEST database would then mean more focus on XML parsing techniques rather than drug interactions and their mechanisms. After discussing the implementation possibilities with supervisors, we decided to develop the ontology and import some of the data manually for the purpose of demonstration.

Another shortcoming, or we will rather say “limitation”, is the fact some of the resources of FEST are not mapped in this thesis. We decided to exclude the mapping of Refusjon, Vilkår, and Byttegruppe catalogues. However, a complete system (API, web application etc.) based on FEST ontology should also have these catalogues. The reason for the exclusion of these catalogues is that they are not much related with the drugs directly. Although these catalogues are excluded, we can map them by the same methodology that we have discussed in chapter 3.

⁸ <http://jxml2owl.projects.semwebcentral.org/jxml2owlapi/>

⁹ <https://github.com/srdc/ontmalizer>

¹⁰ <http://www.topquadrant.com/tools/ide-topbraid-composer-maestro-edition/>

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7 APPENDICES

7.1 APPENDIX A : Glossary

Merkevare	Branded product
Kodeverk	Kodeverk
Handelsvarer	Commodities
Enhet for dosering	Dosage unit
DoseringsForslag	Dosage suggestion
GodkjentMaksimaldose	Approved max dosage
GodkjentNormaldose	Approved Normal dosage
Interaksjon	Interaction
KodeVerk	Coding system
Varsel fra SLV	Notification from Statens Legemiddelverk
Pakningsstørrelse	Package size
Paknigstype	Package type
LegemiddelMerkevare	Branded medicine
LegemiddelPakning	Medicine Packaging
LegemiddelVirkestoff	Medicine substance
LegemiddelForslag	Medicine suggestion
Pakningsinformasjon	Packaging Information
Referanseelement	Reference Element
Lenke	Link
Legemiddeldose	Medicine dosage
Forskrivning	Prescription
Preparattype	Product type
Substans	Substance
Substansgruppe	Substance groups
Byttegruppe	Substitution group
Diagnose	Diagnosis

7.2 APPENDIX B Code

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<Class IRI="#Antagonistic_Farmakokinetisk_effekt"/>
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<SubClassOf>
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<Class IRI="#M30Fest"/>
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<Class IRI="#KodeverksInfo"/>
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<NamedIndividual IRI="#ID_5EEA0528-EDB0-46D1-B9DE-A0090E231FD5"/>
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<DataProperty IRI="#legemiddel.reseptgruppe"/>
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<DataProperty IRI="#legemiddel.typeSoknadSlv"/>
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<DataProperty IRI="#legemiddelMerkevare.produktInfo.producent"/>
<NamedIndividual IRI="#ID_A2BAA17E-231F-4891-B704-4FB83DD8A737"/>
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<NamedIndividual IRI="#ID_A997E9FE-7622-4C1B-B626-FCACE5235B1A"/>
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<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Itrakonazol</Literal>
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<DataProperty IRI="#interaksjon.forklaring"/>
<NamedIndividual IRI="#Interaksjon_1"/>
<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Hemmet metabolisme av irinotkan til inaktiv metabolitt via CYP3A4. Dette fører til shunting av metabolismen til den aktive metabolitten SN-38.</Literal>
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<DataProperty IRI="#interaksjon.handtering"/>
<NamedIndividual IRI="#Interaksjon_1"/>
<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Dosetilpasning: Produsenten av itrakonazol og noen produsenter av irinotekan kontraindiserer kombinasjonen på grunn av irinotekans smale terapeutiske bredde. På grunn av lang halveringstid for itrakonazol kan interaksjonen vedvare i 1-2 uker etter avsluttet behandling med itrakonazol. Hvis midlene likevel må kombineres, kan irinotekandosen forsøksvis reduseres til halvparten av vanlig dose.
Monitorering: Pasienten må følges opp med tanke på bivirkninger og mangelfull effekt av irinotekan og dosen justeres ytterligere etter dette.</Literal>
</DataPropertyAssertion>
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<DataProperty IRI="#interaksjon.id"/>
<NamedIndividual IRI="#Interaksjon_1"/>
<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">ID_0027DFB5-4873-46A6-9DA3-A5BC00F7B92D</Literal>

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</DataPropertyAssertion>
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<DataProperty IRI="#interaksjon.kliniskKonsekvens"/>
<NamedIndividual IRI="#Interaksjon_1"/>
<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Økt konsentrasjon av den aktive irinotekanmetabolitten
SN-38 (100 % basert på data med den kraftige hemmeren ketokonazol) med risiko for alvorlige toksiske effekter.</Literal>
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<DataProperty IRI="#interaksjon.referanse.URL"/>
<NamedIndividual IRI="#Interaksjon_1"/>
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ns#PlainLiteral">http://www.legemiddelverket.no/legemiddelsok</Literal>
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<DataProperty IRI="#interaksjon.referanse.kilde"/>
<NamedIndividual IRI="#Interaksjon_1"/>
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<DataProperty IRI="#interaksjon.relevans"/>
<NamedIndividual IRI="#Interaksjon_1"/>
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<NamedIndividual IRI="#Interaksjon_2"/>
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CYP3A4.</Literal>
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<NamedIndividual IRI="#Interaksjon_2"/>
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<NamedIndividual IRI="#Interaksjon_2"/>
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</DataPropertyAssertion>
<DataPropertyAssertion>
<DataProperty IRI="#interaksjon.relevans"/>
<NamedIndividual IRI="#Interaksjon_2"/>
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<NamedIndividual IRI="#J02AC01"/>
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27E426BC48D3</Literal>
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Methodology (WHOCC)</Literal>
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<AnnotationProperty abbreviatedIRI="rdfs:comment"/>
<IRI#KodeverksElement</IRI>
<Literal xml:lang="no" datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Element i et kodeverk</Literal>
```



```

</AnnotationAssertion>
<AnnotationAssertion>
<AnnotationProperty abbreviatedIRI="rdfs:label"/>
<IRI>#KodeverksElement</IRI>
<Literal xml:lang="no" datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Element</Literal>
</AnnotationAssertion>
<AnnotationAssertion>
<AnnotationProperty abbreviatedIRI="rdfs:comment"/>
<IRI>#KodeverksInfo</IRI>
<Literal xml:lang="no" datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Et kodeverk</Literal>
</AnnotationAssertion>
<AnnotationAssertion>
<AnnotationProperty abbreviatedIRI="rdfs:label"/>
<IRI>#KodeverksInfo</IRI>
<Literal xml:lang="no" datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Kodeverk</Literal>
</AnnotationAssertion>
<AnnotationAssertion>
<AnnotationProperty abbreviatedIRI="rdfs:comment"/>
<IRI>#VarselSLV</IRI>
<Literal xml:lang="no" datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Varsel fra SLV har som hensikt å gi forskriver, utleverer og bruker viktig informasjon knyttet til legemidler. Varsel fra SLV inneholder informasjon med en gitt gyldighetsperiode. Informasjonen er knyttet til spesifikke hendelser og kategoriseres i ulike typer.</Literal>
</AnnotationAssertion>
<AnnotationAssertion>
<AnnotationProperty abbreviatedIRI="rdfs:label"/>
<IRI>#VarselSLV</IRI>
<Literal xml:lang="no" datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Varsel fra SLV</Literal>
</AnnotationAssertion>
<AnnotationAssertion>
<AnnotationProperty abbreviatedIRI="rdfs:label"/>
<IRI>#definerer</IRI>
<Literal xml:lang="no" datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Definerer element</Literal>
</AnnotationAssertion>
<AnnotationAssertion>
<AnnotationProperty abbreviatedIRI="rdfs:label"/>
<IRI>#definert_i</IRI>
<Literal xml:lang="no" datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">I kodeverk</Literal>
</AnnotationAssertion>

```

```

<AnnotationAssertion>
<AnnotationProperty abbreviatedIRI="rdfs:comment"/>
<IRI>#doseringsforslag.behandlingsfase</IRI>
<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Kodeverk: 7473 Behandlingsfase
1 Startdose
2 Vedlikeholdsdose
3 Nedtrappingsdose
4 Kur
5 Ved behov</Literal>
</AnnotationAssertion>
<AnnotationAssertion>
<AnnotationProperty abbreviatedIRI="rdfs:comment"/>
<IRI>#enkeltoppforingFEST.status</IRI>
<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">A = Aktiv (Active)
U = Utgått (Inactive)</Literal>
</AnnotationAssertion>
<AnnotationAssertion>
<AnnotationProperty abbreviatedIRI="rdfs:label"/>
<IRI>#gjelder_fra</IRI>
<Literal xml:lang="no" datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Gjelder fra</Literal>
</AnnotationAssertion>
<AnnotationAssertion>
<AnnotationProperty abbreviatedIRI="rdfs:comment"/>
<IRI>#gjelder_til</IRI>
<Literal xml:lang="no" datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Datoen varselet gjelder til.</Literal>
</AnnotationAssertion>
<AnnotationAssertion>
<AnnotationProperty abbreviatedIRI="rdfs:label"/>
<IRI>#gjelder_til</IRI>
<Literal xml:lang="no" datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Gjelder til</Literal>
</AnnotationAssertion>
<AnnotationAssertion>
<AnnotationProperty abbreviatedIRI="rdfs:comment"/>
<IRI>#interaksjon.kildegrunnlag</IRI>
<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">1 = Interaksjonsstudier (Interaction Studies)
2 = Kasusrapporter (Case Studies)
3 = Interaksjonsstudier og kasusrapporter (Interaction and Case studies)
4 = Indirekte data (Indirect data)

```

NOTE: Can also be implemented as Objects of class Kodeverk with 7485 "Kildegrunnlag for interaksjoner"</Literal>

</AnnotationAssertion>

<AnnotationAssertion>

<AnnotationProperty abbreviatedIRI="rdfs:comment"/>

<IRI>#interaksjon.relevans</IRI>

<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Classification of interactions

1 = Bør unngås (Should be avoided)

2 = Forholdsregler bør tas (Precaution should be taken)

3 = Ingen tiltak nødvendig (No action needed)

NOTE: it can also be implemented by using Objects of class Kodeverk

with code "7483 Relevans for interaksjoner"</Literal>

</AnnotationAssertion>

<AnnotationAssertion>

<AnnotationProperty abbreviatedIRI="rdfs:comment"/>

<IRI>#legemiddel.reseptgruppe</IRI>

<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Use following notation:

A = Reseptgruppe A

B = Reseptgruppe B

C = Reseptgruppe C

CF = Reseptgruppe CF

F = Reseptgruppe F

K = Kosttilskudd (Supplements)

NOTE: it can also be implemented by using Object of class KodeverksElement with code "7421 Reseptgruppe"</Literal>

</AnnotationAssertion>

<AnnotationAssertion>

<AnnotationProperty abbreviatedIRI="rdfs:comment"/>

<IRI>#legemiddel.typeSoknadSlv</IRI>

<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Forklaring kodeverk:

1 = Skal ikke søkes: Alle legemidler som er godkjent fra Legemiddelverket eller er NAF-preparat/magistrell fra Apotekforeningen/fremstilt på sykehusapotek vil være merket med denne verdien.

2 = Søknad vurderes av apotek: Brukes for uregistrerte legemidler (Preparattype = Krever godkj. fritak) der apotek må vurdere om det kan brukes notifisering eller om søknad må sendes til Legemiddelverket.

3 = Må søkes: Brukes for uregistrerte legemidler (Preparattype = Krever godkj. fritak) der reseptformidler skal sende som søknad direkte til Legemiddelverket.

Kodeverk: 7422 Søknadstype

1 = Skal ikke søkes

2 = Søknad vurderes av apotek

3 = Må søkes</Literal>

</AnnotationAssertion>

<AnnotationAssertion>

<AnnotationProperty abbreviatedIRI="rdfs:comment"/>

<IRI>#legemiddelMerkevare.smak</IRI>

<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Not used too much in FEST.</Literal>

</AnnotationAssertion>

<AnnotationAssertion>

<AnnotationProperty abbreviatedIRI="rdfs:comment"/>

<IRI>#legemiddelpakning.oppbevaring</IRI>

<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Preservance Temperature

R = Rom (Room) 15-25 grader

K = Kaldt (Cold) 2-8 grader

D = Frys (Freeze) -18 grader</Literal>

</AnnotationAssertion>

<AnnotationAssertion>

<AnnotationProperty abbreviatedIRI="rdfs:comment"/>

<IRI>#lenke.beskrivelse</IRI>

<Literal xml:lang="no" datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Beskrivelse av et varsels eksterne lenke.</Literal>

</AnnotationAssertion>

<AnnotationAssertion>

<AnnotationProperty abbreviatedIRI="rdfs:label"/>

<IRI>#lenke.beskrivelse</IRI>

<Literal xml:lang="no" datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Beskrivelse av ekstern lenke</Literal>

</AnnotationAssertion>

<AnnotationAssertion>

<AnnotationProperty abbreviatedIRI="rdfs:comment"/>

<IRI>#m30Fest.hentetDato</IRI>

<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Was used to specify the time of download. In our case, every query (optionally) can utilize this variable to specify the last update date and time.</Literal>

</AnnotationAssertion>

<AnnotationAssertion>

<AnnotationProperty abbreviatedIRI="rdfs:comment"/>

```
<IRI>#substans.refVirkestoff</IRI>
```

```
<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">IDREF. Used when ATC code for a substance is not found.</Literal>
```

```
</AnnotationAssertion>
```

```
<AnnotationAssertion>
```

```
<AnnotationProperty abbreviatedIRI="rdfs:comment"/>
```

```
<IRI>#varselSLV.type</IRI>
```

```
<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Hvilken type et varsel er av. Varsel fra SLV er kategorisert i ulike typer: et eksempel på en type er &quot;sikkerhetsinformasjon&quot;. Et slikt Varsel fra SLV vil inneholde informasjon om viktige sikkerhetsoppdateringer og nye alvorlige bivirkninger. Et annet eksempel er &quot;leveringssvikt&quot;. Dette vil inneholde informasjon om forsyningssvikt av viktige legemidler eller avregistrering av mye brukte legemidler. Typene er definert i kodeverket Varseltype.</Literal>
```

```
</AnnotationAssertion>
```

```
<AnnotationAssertion>
```

```
<AnnotationProperty abbreviatedIRI="rdfs:comment"/>
```

```
<IRI>#virkestoffMedStyrke.styrkeoperator</IRI>
```

```
<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">I = Intervall (interval)
```

```
L = Lik (same)
```

```
M = Mindre enn (lower/less than)
```

```
S = Større enn (larger/greater than)</Literal>
```

```
</AnnotationAssertion>
```

```
<AnnotationAssertion>
```

```
<AnnotationProperty abbreviatedIRI="rdfs:label"/>
```

```
<IRI>https://fest.legemiddelverket.no/f5/ontologi/kodeverk#Varseltype</IRI>
```

```
<Literal datatypeIRI="http://www.w3.org/1999/02/22-rdf-syntax-ns#PlainLiteral">Varseltype</Literal>
```

```
</AnnotationAssertion>
```

```
</Ontology>
```