Towards a Medication Core Data Set for the Medical Informatics Initiative (MII): Initial Mapping Experience between the German Procedure Classification (OPS) and the Identification of Medicinal Products (IDMP)

Susanne ZABKA [a], Danny AMMON [b], Thomas GANSLANDT [c], Jan GEWEHR [d], Christian HAVERKAMP [e], Saskia KIEFER [a], Heinrich LAUTENBACHER [f], Matthias LÖBE [g], Sylvia THUN [h] and Martin BOEKER [a 1]

[a] *Institute for Medical Biometry and Medical Informatics, University of Freiburg, Freiburg, Germany*

[b] *Data Integration Center, Institute of Medical Statistics, Computer and Data Sciences & IT Department, Jena University Hospital, Jena, Germany*

[c] *Heinrich-Lanz-Center for Digital Health, University Medicine Mannheim, Germany*

[d] *Research IT, University Medical Center Hamburg-Eppendorf, Hamburg, Germany*

[e] *Staff Unit IT-Processes, Faculty of Medicine and Medical Center, University of Freiburg, Freiburg, Germany*

[f] *Staff Unit Research Support, Department IT, University Hospital of Tuebingen, Tuebingen, Germany*

[g] *Institute for Medical Informatics, Statistics and Epidemiology (IMISE), Leipzig University, Leipzig, Germany*

[h] *Berlin Institute of Health (BIH), Berlin, Germany*

Abstract. Documentation of medication processes is among the most difficult tasks associated with digital clinical documentation. Despite its great potential medical impact, it has not been consistently adopted in German university hospitals, with one of the reasons being the lack of a comprehensive information model with sound terminological support. With the Identification of Medicinal Products (IDMP), several international authorities have recently provided a comprehensive set of standards for the formal description of drugs, mainly for regulatory purposes. In this paper, we describe the approach of the German Medical Informatics Initiative (MII) towards the modelling of a medication core dataset using IDMP. Three different process models with minimal datasets for medication were defined: summative documentation of episodes, point-wise documentation, and medication plans (snapshot documentation). As a feasibility

[1] Corresponding Author: Susanne Zabka, Institute for Medical Biometry and Medical Informatics, University of Freiburg, Faculty of Medicine, Stefan-Meier-Str. 26, 79104 Freiburg i. Br., Germany; E-mail: susanne.zabka@imbi.uni-freiburg.de.

study evaluating how standard terminologies can be used for a minimal data set of hospital medication data, a mapping between IDMP terminologies and the medication chapter of the German Procedure Classification "OPS" (Operationen- und Prozedurenschlüssel) was developed. About 1700 OPS classes, representing about 160 highly reimbursement relevant drugs, were mapped onto different axes of IDMP (substances, optionally: routes of administration and units) using several coding systems with different scopes, to analyze their coverage and particular advantages. A mapping was possible for almost all OPS codes. For the substances, it is necessary to distinguish between the common substance name and the active ingredient, as these may be different for a drug. This "lightweight" mapping approach demonstrates the basic feasibility of using IDMP for medication documentation.

Keywords. Identification of Medicinal Products (IDMP), medication data, German Medical Informatics Initiative, data standards, terminology, standards mapping

1. Introduction

Electronic documentation of medication processes is among the most difficult tasks associated with digital clinical documentation. Despite its great potential medical impact e.g. for patient safety, it has not been consistently adopted in German university hospitals. Besides complex and divergent medical processes, the lack of a comprehensive information model with sound terminological support has hindered the development of interoperable documentation systems in this domain. A first step in 2016 was the introduction of the right to receive a structured medication plan for insured patients who are using at least three prescribed drugs at the same time. With the Identification of Medicinal Products (IDMP), several international authorities, e.g. the European Medicines Agency (EMA), the Food and Drug Administration (FDA), and the International Organisation for Standardisation (ISO), have recently provided a comprehensive set of standards for the formal description of drugs and other medicinal products mainly for regulatory purposes.

In this paper, we describe the approach of the German Medical Informatics Initiative (MII) towards the modelling of a medication core dataset based on IDMP and a feasibility study evaluating how standard terminologies can be used for hospital medication data using a minimum data set available in all German hospitals.

2. Background

The Medical Informatics Initiative (MII) was launched by the German Federal Ministry of Education and Research (BMBF), with the goal of developing infrastructure for the integration of clinical data from patient care and medical research in Germany. Four consortia consisting of university hospitals and other institutions communicate and collaborate under the guidance of the national steering committee. This includes the consistent use of international standards to ensure interoperability [1], [2] and maintaining a core data set in each university hospital as a minimum requirement for patient data [3]. For medication in the hospital, these data can be collected by all inpatient care facilities based on the codes for medications eligible for supplemental reimbursement [4]. The German procedure classification OPS (Operationen- und

Prozedurenschlüssel) is the official classification system in the German health system for the reimbursement of surgeries and other medical interventions [5]. OPS is an adaptation of the World Health Organisation (WHO) International Classification of Procedures in Medicine (ICPM) [5], developed and maintained by the DIMDI (German Institute of Medical Documentation and Information). The OPS list consists of alphanumeric codes assigned to each intervention. It includes a section on medication (chapter 6) with more than 1600 codes representing about 160 highly reimbursement-relevant drugs. These codes have different levels of granularity, but in most cases they stand for the application of a defined amount of a drug, for example:

Code 6-006.bf: "*Parenteral application of 50 mg up to 75 mg Brentuximabvedotin*"

The OPS codes are mandatory in all hospitals in Germany and are essential in order to determine the DRG (diagnosis related groups) code and therefore for billing. They can be used to extract information about the active substance applied to a patient in a certain episode (period of hospitalisation) in a standardized way.

2.1. Information models for medication

In the United States, **RxNorm** [6] is an information model for medication already in existence for several decades and which is often cited as a standard drug terminology [25]. It is a tool for supporting semantic interoperation between drug terminologies and pharmacy knowledge base systems. The National Library of Medicine (NLM) produces RxNorm and provides it via the UMLS Terminology Services [26].
Term types are used to indicate generic and branded drug names at different levels of specificity, and relationships link concepts which contain the same ingredient or dose form. In addition to normalized names and relationships, attributes like unique identifiers are associated with a concept, for example, unique ingredient identifiers (UNIIs) or national drug codes (NDCs) [26].

2.2. The international standard for the Identification of Medicinal Products (IDMP)

While RxNorm is an information model specific to the US, ISO IDMP came from a need to standardise the definition of medicinal product information globally, initially in the context of pharmacovigilance activities, and later expanded to regulatory activities and healthcare practices such as the prescription and dispensation of medicines [6]. To ensure wide interoperability across global regulatory and healthcare communities, these standards were developed and published under the auspices of the ISO (International Organization for Standardization), with input from the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), Health Level Seven (HL7) and other international stakeholders and experts [6].

The ISO IDMP comprises five separate standards published in 2012 which establish definitions and concepts, and describe data elements and their structural relationships to uniquely identify and exchange information on:

- substances (ISO 11238);
- pharmaceutical dose forms, units of presentation, routes of administration and packaging (ISO 11239);
- units of measurement (ISO 11240);

- regulated pharmaceutical product information (ISO 11616);
- regulated medicinal product information (ISO 11615).

These standards cover the following aspects of describing a medicinal product for human use: medicinal product name, ingredient substances, pharmaceutical product (route of administration, strength), marketing authorization, clinical particulars, packaging and manufacturing [6], [7].

In the EU, the European Medicines Agency (EMA) is implementing the IDMP standards in a phased program based on the four domains of master data in pharmaceutical regulatory processes: substance, product, organisation and referential (SPOR) master data [7]. Of these, the Referentials Management Service was launched in June 2017 to supply master data to the electronic application forms [10], [11] and contains over a hundred lists of controlled vocabularies to describe attributes of products, e.g. lists of dosage forms, units of measurement and routes of administration. These include the lists of standard terms of the European Directorate for the Quality of Medicines and HealthCare (EDQM) of the Council of Europe, corresponding to ISO 11239 and ISO 11240 [9]. For the substances, it was decided to use and adapt G-SRS (a global substance registration system developed by the FDA in collaboration with several European experts) as a basis and adapt it to European requirements (EU-SRS) [8].

While IDMP has its origin mainly in the regulatory context, the implementation of the standard models and terminology will be also extremely useful for modelling medication processes in the hospital context.

2.3. Standard vocabularies in the pharmaceutical context

The IDMP ISO standards provide a conceptual framework including definitions, data elements and structures as well as examples of vocabularies or identifiers, but do not specify which terminology has to be used in each case. Therefore, some existing vocabularies are described in the following table:

Table 1. Overview of vocabularies and coding systems used in the pharmaceutical context

Vocabulary or coding system (abbreviation, meaning, format)	**Details**
INN (*International Nonproprietary Name*) generic name (common name according to the IDMP nomenclature) of a drug substance	Each INN is a unique, globally recognized public name assigned to pharmaceutical substances or active pharmaceutical ingredients by The World Health Organisation (WHO) [13]. Modified INNs can be used to describe salts, esters etc. of the same active substance (for example, epinephrine has an INN, but pharmaceutically manufactured drugs contain epinephrine hydrochloride or epinephrine hydrogentartrate).
ASK numbers (*ASK: Arzneistoffkatalog*, German drug substances catalogue) Unique number for substances used in drugs (Germany), ISO 11238	The German Institute of Medical Documentation and Information (DIMDI) publishes the drug substances catalogue ASK which is used in a drug information system managed and updated by the German drug regulatory authorities [14]. The substances are listed with different nomenclatures and are identified by a unique ASK number.
CAS registry number *(CAS: Chemical Abstracts Service)* Unique number for chemical	The Chemical Abstracts Service (CAS) Chemical Registry System, operating since 1965, uniquely identifies chemical substances on the basis of molecular structure [15].

Vocabulary or coding system (abbreviation, meaning, format)	Details
substances, ISO 11238	
UNII *(Unique Ingredient Identifier)* Unique alphanumeric code for substances used in drugs, ISO 11238	UNIIs are generated by the US Substance Registration System and are part of the RxNorm described above [16]. The GINAS (Global Ingredient Archival System) project now establishes a global information system for pharmaceutical ingredients, called G-SRS (global substance registration system). It provides a common identifier for all of the substances used in medicinal products, utilizing a consistent definition of substances globally, including active substances under clinical investigation, consistent with the ISO 11238 standard [17].
ATC code *(Anatomical Therapeutic Chemical)* Alphanumeric code for the pharmacological, therapeutic and chemical properties of a substance or substance combination used in a drug	In the ATC classification system provided by the WHO, active substances are classified into a hierarchy with five different levels with anatomical/pharmacological groups at the highest level, further divided into chemical, pharmacological or therapeutic subgroups and the chemical substance on the 5th level [18]. In Germany, the DIMDI publishes the annually updated official version of the German Anatomical Therapeutic Chemical (ATC) classification [19] which is also available as an Excel file compiled by the scientific institute of a health insurance company [20].
EDQM Standard Terms (*European Directorate for the Quality of Medicines and Health Care)* standard vocabulary and associated code for the pharmaceutical dosage forms, routes and/or methods of administration and others, mainly in the context of drug registration, ISO 11239	The European Directorate for the Quality of Medicines and Health Care (EDQM) is a directorate of the Council of Europe ensuring the quality and safety of medicines. They offer a standard terms database with over 900 terms in 34 world languages, to be used in European marketing authorisation applications as standard vocabulary for the pharmaceutical dosage forms, routes and/or methods of administration, units of presentation, and containers, closures and delivery devices [22].
UCUM codes *(Unified Code for Units of Measure*) code and description for units of measure, ISO 11240	Code system intended to be able to construct all units of measures contemporarily used in international science, engineering, and business [24].

3. Methods

The Interoperability Working Group of the National Steering Committee of the MII created an inter-disciplinary taskforce to define a core module for medication documentation, intended for the interoperable exchange/analysis of medication data throughout German university hospitals. All decisions are reached by consensus among the four participating consortia. The levels of documentation of the medication process in the clinical setting were analysed with regard to their timing and associated data. Based on this, different process models with minimal datasets and suitable options for their terminological representation were developed.

To investigate the feasibility of a formal representation of a medication process, a mapping between IDMP terminologies and the German Procedure Classification (OPS), chapter 6 (medication) was developed. The OPS codes related to medication were selected for the first study as they are mandatory for billing and thus available at each

hospital. They were downloaded from the DIMDI homepage [5] into a Microsoft Excel table. For each OPS expression, the substance name, the information related to the dosage form or administration route and to the amount and unit of substance was extracted manually. These expressions were mapped to the standard terminologies (c.f. figure 1) and added to the Excel table.

Component of the OPS-code	**OPS-Code**	**[application]**	**[minimum amount]**	**[maximum amount]**	**[unit]**	**Active substance**	**[additional active sub-stance(s)]**	**[Additional information]**
Example	*6-006.bf*	*Parenteral application*	*of 50 […]*	*up to 75*	*Mg*	*Brentuximab vedotin*		
Mapping:	↓	↓	↓	↓	↓	↓	↓	↓
Mapping to (if possible):	N/A	EDQM stan-dard terms: **Route of ad-ministration** and/or **intended site** and/or **application method**	Number	Number	**UCUM**	**WHO INN** and **ASK number** and **CAS number** and **UNII code** and **ATC code**	**WHO INN** and **ASK number** and **CAS number** and **UNII code** and **ATC code**	N/A

Figure 1: Mapping of OPS-codes to the following standard terminologies:

- OPS: Operationen- und Prozedurenschlüssel (German procedure classification) [5]
- EDQM: European Directorate for the Quality of Medicines, standard terms for: Intended Site [27], Administration Method [27] and Routes and Methods of Administration [28]
- UCUM: Unified Code for Units of Measure [24]
- WHO INN: World Health Organisation International Nonproprietary Name [13]
- ASK number: Arzneistoffkatalog (German drug substances catalogue) number [14]
- CAS number: Chemical Abstracts Service number taken from [14] and partly from [16]
- UNII code: Unique Ingredient Identifiers code [16]
- ATC code: Anatomical Therapeutic Chemical code [20],

N/A: not applicable, in brackets []: expression not part of all OPS codes

4. Results

The MII defined a core data set for the representation of clinical medication processes. To represent the different approaches and capabilities of sites with regard to structured medication documentation, three “levels” of documentation were defined: summative documentation of episodes, point-wise documentation, and snapshot documentation (medication plans, discharge medication). The levels differ in their references to time and in the comprehensiveness of their data sets.

The **summative documentation of episodes** describes the medication applied to a patient during a hospital stay. This includes the substance, the start and end date of the medication episode and optionally the product, the amount of substance and dosing information.

The **point-wise documentation** describes the medication applied at a given point in time and includes information about the substance, the application time (or start and end time), the dosage and optionally also the drug product and route of administration.

The **snapshot documentation** describes medication plans or the discharge medication with the drug name, the dosing scheme and strength and optionally the substance.

4.1. Mapping of OPS codes

For the summative documentation of episodes, the OPS codes available at all German hospitals can be used to extract the medication data for all reimbursement relevant drugs. A mapping table was created representing all 1630 medication-related OPS codes. The list downloaded from the official site contains 1668 rows as several OPS codes were listed with two or more meanings or with different expressions for the same drug.

The following table 1 is an example of a complete set of mapping information for one OPS code.

Table 2: Example for the mapping of an OPS code *6-006.bf* to different standard terminologies. Abbreviations: OPS: Operationen- und Prozedurenschlüssel (German procedure classification), EDQM: European Directorate for the Quality of Medicines, UCUM: Unified Code for Units of Measure, WHO INN: World Health Organisation International Nonproprietary Name, ASK: Arzneistoffkatalog (German drug substances catalogue), CAS: Chemical Abstracts Service, UNII: Unique Ingredient Identifiers, ATC: Anatomical Therapeutic Chemical, N/A: not applicable

	OPS-Code	**[application]**	**[minimum amount]**	**[maximum amount]**	**[unit]**	**Active substance**	**[Active substance]**
Mapping example:	*6-006.bf*	*Parenteral application*	*of 50 […]*	*up to 75*	*mg*	*Brentuximabvedotin *)*	*N/A*
Mapped to Code: *value*		**EDQM Intended Site Code:** *ISI – 0033* **Term:** *Parenteral* **EDQM Routes and Methods of Administration Code:** *20045000 **)* **Term:** *Intravenous use **)* **EDQM Administration Method: Code:** *AME-0009 **)* **Term:** *Infusion **)*	Number: *50*	Number: *75*	**UCUM Code:** *mg* **Description:** *milligram*	**WHO INN:** *Brentuximab vedotin *)* **ASK number:** *39958* **CAS number:** *914088-09-8* **UNII code:** *7XL5ISS668* ***ATC code:*** *L01XC12*	*N/A*

*) The substance name has a different spelling in WHO INN, ASK and ATC.
**) In this case, only the "intended site" could be derived from the expression used in the OPS code. The values for the "route of administration" and "administration method" were looked up in registration information

The mapping of the active substances was possible for almost all OPS codes and is described in more detail in the next chapter.

The mapping of additional information included in many of the OPS codes was optional according to the requirements in the data set for the summative documentation of episodes. The following mapping was performed:

- **Amount of drug:** For all OPS code expressions containing a unit, the mapping to a UCUM code was possible. The corresponding UCUM codes and UCUM descriptions, as well as the minimum and maximum amount of drug

as listed in the OPS codes, were added to the table. The units used in the table are gram, milligram, microgram, international unit and Giga-Becquerel.

- **Application or Route of administration:** OPS codes often contain expressions like "parental application of…" or "oral application of …" for drug administration. In these cases a mapping to the long established lists of EDQM standard terms for the "routes and methods of administration" was intended. However, a unique mapping of the application form is difficult in many cases, as the expressions in the OPS codes are rather unspecific and the data model used for the EDQM standards terms is much more specific. Here, the EDQM terminology distinguishes between terms for "Intended Site", "Administration Method" and "Routes and Methods of Administration". As an example, the expression "parental application", which can be found in many OPS codes, would be coded with the EDQM terminology "intended site"= "parenteral", whereas the EDQM application method and EDQM routes and methods of administration are not clearly defined. In most cases, the expression in the OPS code could be clearly mapped to the EDQM "intended site" (e.g. "parenteral", "oral"), but sometimes it corresponded to the EQDM „Routes and Methods of Administration" (e.g. "intrathecal application" or "implantation").
- **Information related to the drug product:** The OPS codes contain almost no information about the dosage form of the drug product, therefore no mapping was performed.

4.2. Mapping of the active substance

Three OPS codes could not be mapped as they are not related to a unique substance. The remaining 1627 OPS codes comprise 155 drugs with one active substance and seven drugs with combinations of two or more active substances. Altogether 166 individual substances, including those substances that were only included as a component of the combination drugs, were mapped to the WHO INN name, the German ASK number, the UNII number and the CAS number. For the combination products, this mapping was performed for each individual substance.

ATC codes are assigned to combination products as well, therefore the mapping contains the ATC codes for 162 substances or substance combinations.

During the mapping procedure we encountered several instances of different numbers for the substance and its derivatives due to the fact that the substance's common name (e.g. INN name) is not always identical to the drug's active ingredient, which may be a salt or other preparation (e.g. INN name „Doxorubicin" with active ingredient „Doxorubicin hydrochloride", or INN "liposomal Irinotecan" with active ingredient "Irinotecanhydrochlorid trihydrate"). This difference between the active ingredient, which is only listed in the registration information, and the "commonly used" INN expression, is usually not obvious from the OPS list or the drug name.

The mapping was adapted to both include codes for the substance´s common name and for the derivatives representing the active ingredient of the drug, if applicable.

Table 3 summarizes the kinds of mappings and the number of codes found.

Table 3. Summary of substance mapping

What	Number of	Comment

codes		
Substances / substance combinations used in OPS codes	162	3 OPS codes excluded as no clearly defined substance(s)
Of these: Products with one substance	155	
Of these: Combination products	7	mapped to > 1 substance
Overall number of individual substances	166	including those that are only part of combination
Mapping of 166 individual substances:		
Active ingredient different from common substance name	7	Of these: 1 active ingredient listed in OPS code: Abirateronacetat. For 6 drugs, the different active ingredient was only found in registration information. NOTE: The registration information was not checked in all cases, so there may be more examples.
Mapping to WHO INN	162	No INN: arsentrioxide, asparaginase, cholic acid, hemin
Mapping to ASK number	165	Missing: Crizotinib
Mapping to CAS number	165	No CAS: Pegaptanib (a nucleic acid) CAS numbers missing in ASK-list: 2 (Crizotinib and Eptotermin alfa), but found in G-SRS, some differences in G-SRS and ASK, some cases with > 1 CAS number
Mapping to UNII number (G-SRS)	165	No unambiguous mapping: 1 UNII code for dinutuximab and dinutuximab beta
Mapping of 162 substance/substance combinations (as listed in OPS) to ATC codes:		
Mapping to ATC codes	161	No ATC code for hemin
Of these: > 1 ATC code	5	
Of these: 1 ATC code for combination	7	

5. Summary and discussion

The mapping table is a useful tool to compare different terminologies for the coding of drugs based on the limited information available in the OPS codes. It also demonstrates the advantages and disadvantages of the terminologies used.

An important aspect to be considered in coding the individual substances is the distinction between "substance" in the sense of the generic name (WHO INN, "ingredient" in RxNorm terminology) as opposed to the "active ingredient", which may be a derivative of the substance in some cases (WHO modified INN, "precise ingredient" in RxNorm terminology [26]) . This difference may not be known to a non-expert and the active ingredient is usually not obvious from the common name routinely used. However, the active ingredient (or the code representing it) is listed in the registration information and in drug databases containing this information. For the retrieval of substances, possible solutions may either be to link the "related" substances and/or establish a convention to always use the number of the generic substance, accepting the inaccuracy at the chemical level.

None of the coding systems or terminologies used in this feasibility study could be used to unambiguously code each of the 166 individual substances (see table 3), however the coverage was above 99%. In addition, some inconsistencies related to the CAS numbers listed in the other substance lists were discovered.

The ATC codes have a different scope as they are mainly intended to identify the pharmaceutical and therapeutic area. Therefore they also provide identifiers for combination products. However, not all ATC codes are unique to a substance as these drugs are used for several indications. While the possibility of distinguishing between therapeutic areas may even be an advantage for retrieval, it would require the proper ATC code to be entered each time such a medication is given, which may be difficult in the clinical daily routine.

As the OPS codes do not contain sufficient information to allow an unambiguous mapping to the dosage form and even the route of administration cannot be mapped unambiguously to a common vocabulary, the presented mapping table only includes the EDQM terms as an example of how these terms would be applied to drug products.

The mapping in this list is specific to Germany, as it is based on German billing codes and the German drug catalog (ASK numbers). The OPS codes may evolve, therefore the mapping lists need to be checked and potentially adapted every year.

This mapping can only be used for the limited number of drugs included in the OPS codes. It is not feasible to perform the same mapping manually for all available drugs, therefore it will be necessary to check how the data model is structured in registration information systems like AMIS, commercial drug databases like ABDATA[2] or in the medication management solution of hospital information systems, and whether this can be used. In some hospital systems a specific coding of drugs may already be available, e.g. ATC.

6. Conclusion

The recent introduction of IDMP has provided a sound information model with strong terminological support. Although mainly intended for the description of drugs and other medicinal products in a regulatory context, the MII has adopted IDMP for the documentation of clinical medication processes.

The integrated use of IDMP standards combined with other terminologies and ontologies (e.g. SNOMED CT) in interoperable technical standards like HL7 FHIR enables a comprehensive description of medication processes and entities.

A “lightweight” approach based on a mapping between IDMP and the OPS demonstrated the basic feasibility of the approach presented here. The use of OPS codes has the advantage that all university hospital cases are already OPS-coded due to their role in the billing system for hospital stays. In future, however, a much more precise and comprehensive description of the medication processes will be necessary. An information model covering all three levels of the medication data set, and more formal specifications using the FHIR (Fast Healthcare Interoperability Resources) format are currently being developed within the framework of the Medical Informatics Initiative and will be successively introduced at the sites.

[2] https://abdata.de/datenangebot/abda-datenbank/

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