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Gap Analysis about Existing and New standards and Profiles

This is a draft working document. Only the approved document as published on the www.unicom-project.eu website will be the deliverable from the UNICOM project.

Summary

Identification of Medicinal Products (IDMP) standards uniquely identify and describe medicinal products for the consistent documentation, coding and exchange of product information between global regulators, manufacturers, suppliers and distributors and others. Complying to IDMP standards supports the regulatory domain to facilitate pharmaceutical development and registration, life cycle management of medicinal products, pharmacovigilance and risk management. They are also applied to clinical needs for prescriptions, dispensing, medicinal product comparisons and much more.

Yet, divergent and inconsistent approaches to IDMP implementations are a major risk. Implementations by the European Medicines Agency (EMA), EU's national competent authorities (NCAs), marketing authorisation holders (MAHs) and clinical health experts have been conducted mostly "in silos."

To drive an efficient, uniform set of IDMP implementation practices, the UNICOM Work Package 1 (WP-1) team has mapped stakeholders' needs to existing standardised artefacts, within five implementation domains—from development and production to utilisation and outcome assessment. To do this, the WP-1 held seven interactive sessions that focused on IDMP and other related standards in regulatory and clinical use cases. WP-1 collected additional stakeholder input and consulted with the "community of expertise" for a thorough analysis. The result was the identification of gaps that will help determine the required future actions by the respective standard development organisations (SDOs), individually or by collaboration.

This document is to be shared with the relevant Standard Development Organisations (SDO), so that they can immediately take action to evaluate, validate, propose solutions or changes to their standards, or reject the propositions with justifications for their decision. Their feedback to UNICOM's WP-1 will be valued, documented and shared appropriately with the other Work Packages (WPs).

Change log

Date	What	Who	Version #
12.6.2020	Initial version. Methodology	Hay	1
30.6.2020	Update interactive sessions	Team	2
3.7.2020	Introduction, etc	Team	3
7.7.2020	Standards (chap 3, annex 9)	Team	4
13.7.2020	Updates chap 4	Team	5
14.7.2020	Update chap 5, annexes	Team	6
20.7.2020	Preparation chap 6	Team	7
27.7.2020	Chap 6 updates	Team	8
28.7.2020	Chap 6 update	Team	9
29.7.2020	Chap 6 finalisation	Team	10
31.7.2020	Overall review	Hay	11
31.8.2020	Update after UNICOM internal review	Hay	12

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1 Scope and objectives

1.1 Purpose

The purpose of this document is to provide evidence about various standards and their respective process cycles, including potential "disconnects" observed in the markets. Gaps that are identified here are not exhaustive; rather, they correspond to the level of information and knowledge assembled by the UNICOM WP-1 at the time of writing this report. The report focuses on the IDMP suite of standards as well as considers all other relevant standards beyond IDMP.

Even though this gap analysis was documented in July 2020, it will be updated as additional insights emerge from IDMP implementations, especially from the EMA Substance, Product, Organisation, Referentials (SPOR) implementation.

This document is intended for all stakeholders involved in IDMP implementations with special emphasis on experts in SDOs.

Throughout the document, abbreviations are used for brevity and ease of reading. A list of the abbreviations and their meanings can be found in Chapter 8 (Annex).

1.2 Background

Part of the European Agencies, the EMA is charged with the scientific evaluation and supervision of medicines for the benefit of public and animal health in the EU.

UNICOM is a four-year project that has been established by the European Commission as part of its Horizon 2020 programme. UNICOM aims to address the needs of stakeholders who are implementing IDMP standards and related technologies in regulated business and clinical environments. The project was commissioned to drive consistencies across IDMP implementations and, as a result, increase the adoption of IDMP.

In 2012, the initial version of IDMP was jointly developed by standards development organisations—CEN TC251, ISO TC215 and HL7 International. In 2016 and 2017, IDMP was revised by CEN TC251 and ISO TC215, with the current IDMP standards and implementation guide finalised in 2018.

The vast, complex and diverse nature of IDMP—its data structure and data content—along with how it can be implemented and used across multiple environments is illustrated by the number of UNICOM work packages. Eight work packages alone are dedicated to the "how-tos" of

EMA and NCAs are pursuing HL7 Fast Healthcare Interoperability Resources (FHIR) standard-based implementation approaches that need to be aligned among themselves, with clinical initiatives and large-scale projects, as well as will the approach pursued by CEN TC251, ISO TC215 and specific HL7 WGs such as HL7 Biomedical Research and Regulation, HL7 Patient Care and HL7 Pharmacy. Lack of consistency among all these initiatives is an area addressed by the analysis conducted here. This UNICOM deliverable aims to identify gaps in standards specifications, understanding, or awareness, and proposes concrete steps to bridge them.

One important challenge is to keep implementers and SDOs aligned. Furthermore, the health IT industry is not fully aware of IDMP-related standards and how to leverage these standards

in their solutions for the benefit of users, clinicians and patients. Therefore, this document highlights the various process cycles—from standards development to implementations—related to pharmacovigilance, marketing authorisation, clinical and supply chain. It considers their interdependencies and classifies the gaps within these process cycles.

1.3 Work package 1

The UNICOM project has been separated into different "work packages." With SDO involvement, stakeholder needs will be identified within each work package.

Work package 1 (WP-1) is focused on the universal use of IDMP and its related strategies and technologies. To date, WP-1 team members have mapped stakeholder needs to existing standardised artefacts that are currently available, identifying the gaps between the needs and artefacts. This gap analysis (See Chapter 6)—the first deliverable of WP-1—will help determine the actions to be taken within the multiple work packages.

It's important to note that this gap analysis document will be updated along with the UNICOM project, as IDMP standards and other standards are implemented and insights uncovered —evolving over time to become even more useful for stakeholders.

Value of logical models

The purpose of the IDMP logical model is to shift IDMP's current data architecture to one that is agnostic so that implementers can easily "plug" IDMP into any system for automatic connectivity. With an IDMP logical model and, for example, an ePrescription logical model, implementations can be achieved more easily and

In another deliverable, WP-1 aims to explain the relationship between IDMP and other standards. It will provide a European community of expertise forum that addresses the application and maintenance of IDMP and related standards—providing a "one-stop" source for standards-related questions about gaps, interpretations and interrelationships. In short, WP-1 intends to create a sustainable community of expertise on IDMP standards via a "university" of educational opportunities—well beyond the lifetime of the UNICOM project.

1.4 Implementation efforts

Part of the complexity of the IDMP suite of standards stems from the fact that the trade and use of medicinal products are highly regulated. A substantial percentage of healthcare expenditure is consumed by medicinal products, between 6% and 27% in Organisation for Economic Co-operation and Development (OECD) countries. Moreover, medicinal products can harm, can be highly addictive and can cause severe side effects. This is all the more reason to have a very strong regulatory field including to conduct a surveillance on the effects, positive or negative, of medicinal products, making sure that money is spent on safe and effective medicinal products.

The next step is to make sure that medicinal products are used safely and effectively by the patients who need them and the doctors who prescribe them. Ultimately, the supply chain—from manufacturing medicinal products to the patients who take them—needs to be controlled, as well. There are three, very different fields of application that all need to relate in some way to the same medicinal product—hence, the crucial need for proper identification across these application areas.

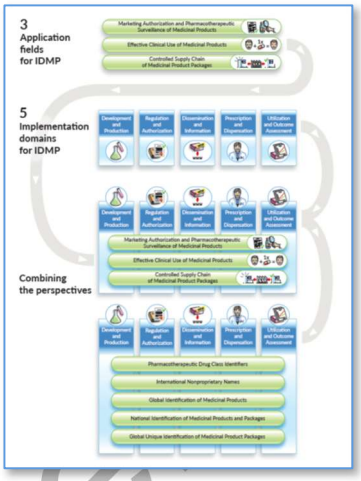


Figure 1: Structuring application fields and domains

Throughout these applications, different implementation domains can be identified that have their own established ways of doing business and solving problems. Gaining agreement on a single set of standards across these implementation domains is not easy, but given the objective of safe and effective medication, the need is obvious.

With simplicity in mind, the WP-1 team distinguishes five implementation domains, ranging from research and development in the labs of the pharmaceutical industry to the actual utilisation and outcome assessment in the daily lives of patients. Another implementation domain is focused on the regulatory area of dissemination and information—ensuring that clinicians are aware and educated about the availability and suitability of medicinal products for their patients and, of course, the clinicians and pharmacists involved in prescribing and dispensing medications to patients.

From global to local, from class of medication to the individual packaged product, there is a need to link the data used across the application fields and implementation domains. That's where the different types of identification come into play. As each type of identification currently has its own life cycle, the task is to ensure that a step forward in the life cycle of one identifier is properly propagated across the life cycles of the other identifiers, taking the relevant related changes in medicinal product data with them across all boundaries. That's the landscape being navigating—making sure medicinal products are uniquely identified for regulatory, clinical and logistical purposes.

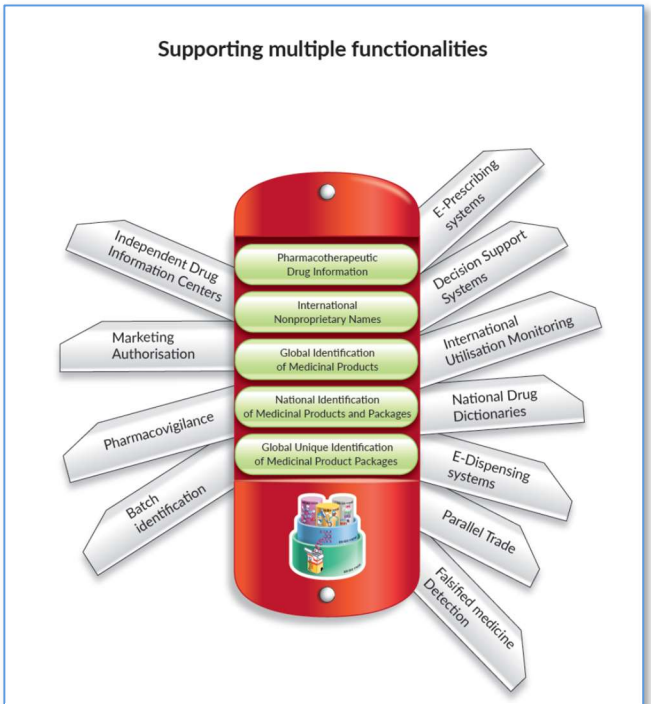


Figure 2: IDMP supports multiple functionalities

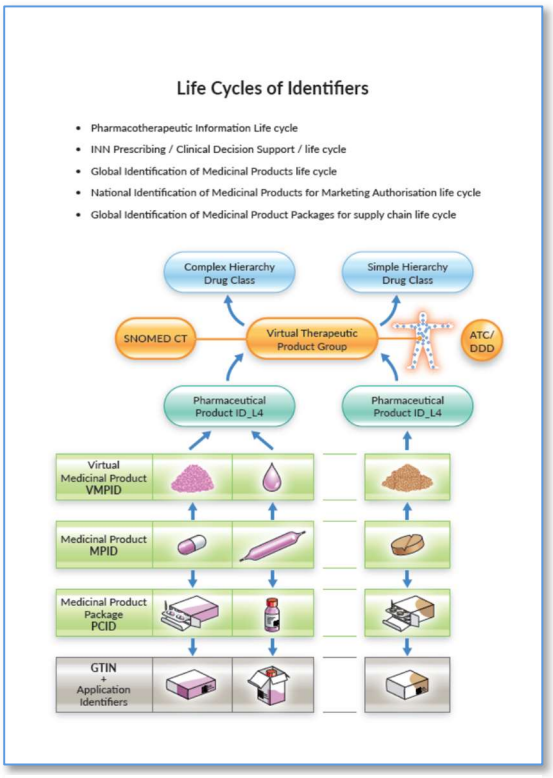


Figure 3: Life cycle of identifiers

2 Methodology

The approach taken to collect information for the gap analysis was primarily from the interactive sessions conducted with various SDO experts. This gap analysis document will be updated throughout its lifetime as new learnings and information become available from implementers and participants, from other UNICOM work packages and from community of expertise meetings. (See Chapter 5.2).

2.1 Collecting input

This report highlights identified gaps discovered during IDMP implementations and adoption. As a primary source of information, a three-day workshop in Brussels was planned. Yet, in March 2020, it was evident that the COVID-19 pandemic would prevent participants from attending the meeting.

In response, a series of virtual, interactive sessions were conducted throughout the month of April. Each session was moderated, with ample time allocated for questions and discussion. The session discussions were summarised by the moderator. These summaries in table format are included in Chapter 10 (Annex).

The WP-1 team provided implementers with an opportunity to submit their questions and comments in order to develop interactive sessions organised by domains, so that discussions could be useful, and exchanges structured. Each session focused on specific areas where IDMP and related standards provide support (or should provide support). In addition, use cases were defined to appropriately steer discussions to recognise linkages between the selected domains.

2.2 Use cases

Following is the initial list of five use cases referenced during the interactive sessions; others may be added as UNICOM work efforts progress. The interactive discussions focused on these use cases within a framework of regulatory and clinical domains. Initially, IDMP was developed to address regulatory needs, yet in a later phase, it was extended to the clinical domain. As a result, the use cases address both.

The **ePrescription** use case supports the process that involves the electronic exchange of patient prescription and/or dispense information across one or more geographical borders and locations (e.g., intercontinental, cross-border). The use case supports the patient pick up of an initial or refill prescription at a licensed or approved retail pharmacy location. Stakeholders include the patient, healthcare provider, pharmacist and retail pharmacy.

The **clinical processes** use case supports patient treatment and care processes that leverage the International Patient Summary (IPS), medication lists and more. It involves making relevant medical information available to caregivers who need it, when and where they need it—across a myriad of health systems that cross local, regional and national jurisdictional borders. Stakeholders include the patient, healthcare provider, pharmacist and retail pharmacy. It further includes clinical decision support systems, which are used by the prescriber and dispenser.

The **adverse events** (AEs) use case is defined as follows: Any untoward medical occurrence in a patient or clinical investigation subject who is administered a pharmaceutical product and

who does not necessarily have to have a causal relationship with this treatment[1]. The use case supports the identification, assessment and reporting of AEs. AE assessment can be supported based on patient observations (e.g., physical exam or laboratory results) or aided by automated tools such as a clinical decision support system or bedside scanning. Stakeholders include the patient, risk/incident manager, jurisdictional registries (local, regional, national) for critical incident reporting, surveillance authorities for controlled substances, prescription and restricted drug usage, and pharmaceutical manufacturers.

The **medication errors** use case involves an unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient[2]. The use case includes the identification, assessment and reporting of medication errors (actual or near miss). Like AEs, medication errors can be assessed based on patient observations (e.g., physical exam or laboratory results) or aided by automated tools such as a clinical decision support system or bedside scanning. Stakeholders include the patient, risk/Incident manager, jurisdictional registries (local, regional, national) for critical incident reporting, prescription and restricted drug usage, and pharmaceutical manufacturers.

The **supply chain management** use case covers multiple scenarios such as: (1) Identification and management of a product recall due to contamination/falsification or other safety-related issue; (2) drug shortages due to increased demand (e.g., pandemic, flu) or limited manufacturing supply. Stakeholders include the patient, pharmaceutical manufacturer, authorised distributor or relabeler, regulatory/competent authority, healthcare provider, retail or hospital pharmacy, and hospital risk/incident manager.

2.3 Workshops and presenters

Following are the workshops, topics of discussion and presenters:

1. IDMP and HL7 FHIR, April 9
    - Chris Kravogel, HCI Solutions Ltd
    - Hugh Glover, Blue Wave Informatics
2. Dose forms, April 21
    - Chris Jarvis, EDQM
3. EU serialisation – Falsified Medicines Directive, April 22
    - Jean-Gonzague Fontaine, GSK
    - Laure Pontis, GS1 Global Office
4. Medicinal product identification, IDMP, SNOMED & MedDRA, April 23
    - Lise Stevens, Iperion
    - Jane Millar and Monica Harry, SNOMED International
5. IDMP & Individual Case Safety Report (ICSR), April 24
    - Lise Stevens, Iperion
    - Anja Van Haren, CBG-MEB

[1] EU Good Clinical Practice Guideline: https://ec.europa.eu/health//sites/health/files/files/eudralex/vol-10/3cc1aen_en.pdf

[2] https://www.ema.europa.eu/en/human-regulatory/post-authorisation/pharmacovigilance/medication-errors

6. IDMP, ePrescription and dispensing, April 27
    - Giorgio Cangioli, HL7 Italy
    - Robert vander Stichele, i~HD, University of Gent
7. Pharmaceutical product identification, April 28
    - Leonora Grandia, Z-Index

2.4 Future plans

Alongside of this gap analysis and the source of information put in place, WP-1 has started to organise publicly open, community of expertise webinars, where SDO experts and implementation experts meet to discuss defined subjects and also start an open discussion on their fervent points. The first community of expertise forum took place on 1 July 2020 and will be followed in September (and following months) with subjects such as the pharmaceutical product identifier (PhPID), substances, gap analysis (this deliverable) and IDMP and COVID-19.

Because of the close relationship between UNICOM WP-1 and SDOs, the plan is to socialise our findings from this gap analysis to trigger and support standards development or maintenance, at ISO TC 215, WG-6 (pharmacy and medicines business), HL7 International (several working groups), IHE International (pharmacy domain) and more.

3 Standards status review

ISO standards correspond to the needs expressed by ISO's national mirror bodies as well as by the technical committee's liaison organisation. So, IDMP has been developed over the years in response to an expressed demand initially by International Council on Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)[3] and seconded by the EMA as well as by the US Food and Drug Administration (FDA). The IDMP standards were published first in 2012 and have been revised since then.

Today, HL7 International provides different types of HL7 standards relevant to the scope of the UNICOM project: informative[4], standards for trial use, (STU)[5] and normative. It includes only universal non-retired standards and has a hierarchical structure with base standards on the first level and other products (e.g., implementation guides, profiles) added as children.

IHE International has developed integrated profiles that assemble various standards to answer specific user needs. In the IHE pharmacy domain, several IHE profiles are already available and can be selected for deployment at the local, regional, national and cross-border levels; they mostly address clinical and supply chain domains. IHE distinguishes content profiles such as the prescription profile (PRE), from workflow profiles such as the integration of the prescription, the validation of the medication and the dispensation in the out-patient sector.

SNOMED International is a global organisation, supporting the international edition of SNOMED CT and derivative products such as reference sets (e.g., Global Patient Set) and maps (e.g., SNOMED CT to ICD-10). SNOMED CT modelling is based on description logic, thus supporting detailed analytics for different purposes such as research, decision support, public health and more. The SNOMED CT drug model was recently updated to provide consistency for national drug models and is aligned with IDMP, where appropriate. To enable the development and maintenance of these products, there is an extensive set of tools, which are open source and, in many cases, are used by member countries to manage national extensions of the International edition in support of translations and content, which only has national relevance. SNOMED International works with different stakeholder groups, including other SDOs, to facilitate semantic interoperability for those that are implementing standards as part of electronic health record (EHR) solutions, thus ensuring consistency and reliability over time.

[3] International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), https://ich.org

[4] An *Informative* document is "the product of a Work Group that is not currently deemed normative, but nonetheless is intended for general publication." [HL7 GOM]

[5] A *Standard for Trial Use* (STU) is a standard "released for use to refine and enhance its content through demonstrations of interoperability" before becoming normative. Known in the past as "Draft Standard for Trial Use (DSTU)", the DSTU term has been recently discontinued because HL7 no longer produces "Draft" Standards. [HL7 GOM]

4 Workshop results and suggesting gaps

As mentioned earlier, this gap analysis document is intended to be an evolving document that will be updated with new observations and findings as they emerge from the community of expertise forums as well as UNICOM WP efforts that address the identified gaps. For an overview on these discussions, refer to Chapter 10.

As noted earlier, a deliverable of WP-1 includes the requirements associated with the IDMP logical model. While currently not in UNICOM's scope, there is a need to formulate other logical models—such as an ePrescription logical model—so that the data requirements of, in this case, the ePrescription can be easily "connected to" or fulfilled with the data provided by the IDMP logical model.

4.1 Dose forms

- Chris Jarvis, EDQM

4.1.1 Introduction

The purpose of this chapter is to present the EN ISO 11239 IDMP standard and its companion Technical Specification, based on experiences from the European Directorate for the Quality of Medicines & HealthCare (EDQM) and the interactive session held in April 2020.

EDQM had been chosen by ICH stakeholders as the reference maintenance organisation for pharmaceutical dose forms and other referentials. The adoption of this IDMP standard has been difficult, at times.

- EMA has implemented the EN ISO 11239 standard in its SPOR programme—in the area of "referentials." By doing this, EMA has brought in some different concepts, recognising that the source for PhPID calculation—with a worldwide perspective—remains the EDQM Standard Terms.
- NCAs are in the process of implementing the standard in their own processes and are facing backward compatibility issues, because the granularity of terminologies varies frequently from EDQM.
- The US FDA has shared its implementation difficulties, which are similar to those of the NCAs.

4.1.2 Discussion questions and gaps

There is a need to access the EDQM Standard Terms to find and use their unique identifiers. For that purpose, the EDQM platform is publicly available, free of charge, and APIs can be used to implement automated ways for updating processes.

There is a shared need to organise a grouping function for EDQM Standard Terms for:

- Regulatory purposes that correspond to the needs expressed by NCAs (See above.)
- The World Health Organization (WHO) in its pharmacovigilance activities
- Clinical purposes that are needed to support prescription and additional clinical processes

In the clinical space, there is a need to organise an effort to link EDQM Standard Terms and SNOMED. An investigation is further needed on how to map EDQM Standard Terms with defined daily dose (DDD) concepts that are required by users.

4.1.3 Use cases

For clinical IT, pharmaceutical dose forms are important for prescribing processes, calculating the DDD, pharmacoepidemiology, public health (surveillance of antibiotic consumption by European Surveillance of Antimicrobial Consumption or ESAC and more.

The examination of standards for pharmaceutical dose forms was discussed in the context of use cases: ePrescription, clinical processes, adverse events, medication errors and supply chain. (See Chapter 10)

4.2 IDMP and HL7 FHIR

- Chris Kravogel, HCI Solutions Ltd
- Hugh Glover, Blue Wave Informatics

4.2.1 Introduction

The purpose of this chapter is to present the IDMP landscape and its underlying standardisation needs. It will also provide insight into what and how HL7 FHIR meets these needs.

EMA and NCAs are in the process of implementing IDMP in a set of registries that is called the SPOR programme. These registries are critical in realising processes in both clinical and regulatory workflows. EMA recently released for consultation within the SPOR task force the second iteration of the EU IDMP Implementation Guide Version 2 (EU IG v2). Already EMA is implementing the use of FHIR as the data standard for Information exchange.

These are steps in a larger plan to use FHIR messages in the marketing authorisation and pharmacovigilance workflows as part of the communication among regulatory bodies, and between regulatory bodies and marketing authorisation holders.

In the areas of eHealth and clinical IT, FHIR resources are going to be used extensively, and FHIR resources are expected to coexist with CDA-based implementations or implementations based on other versions of HL7 standards (see Figure 4 illustrating FHIR resources and working groups).

4.2.2 Discussion questions and gaps

A mapping between IDMP (data model according to HL7 v3) and FHIR resources should be part of the EU IDMP Implementation Guide Version 2 and refers back to the HL7 v3 IDMP data model. Such a mapping requires maintenance and governance that need to be examined and improved upon, including where specifically to find accurate information. More importantly, there are IDMP-related FHIR resources—some fit for clinical use cases, others for regulatory and others for pharmacovigilance. They are hosted by different work

groups, namely, HL7 Patient Care, HL7 Pharmacy, HL7 Biomedical and Regulatory (BR&R WG).

Additionally, the Mobile Health WG of HL7 is working on projects related to the use of FHIR in mHealth, where alignment with IDMP is not clear. There has been no clarity on mHealth apps for AE reporting using IDMP and FHIR.

As a reference for any IDMP implementation, an implementation guide should be based on a standards-agnostic logical model at a detailed level of granularity that can cover both clinical, pharmacovigilance and regulatory use cases. The EU IDMP Implementation Guide Version 2 builds on regulatory resources shown as supplementary (Figure 4) presented by Hugh Glover's presentation during the April 9 interactive session, *IDMP and HL7 FHIR*.

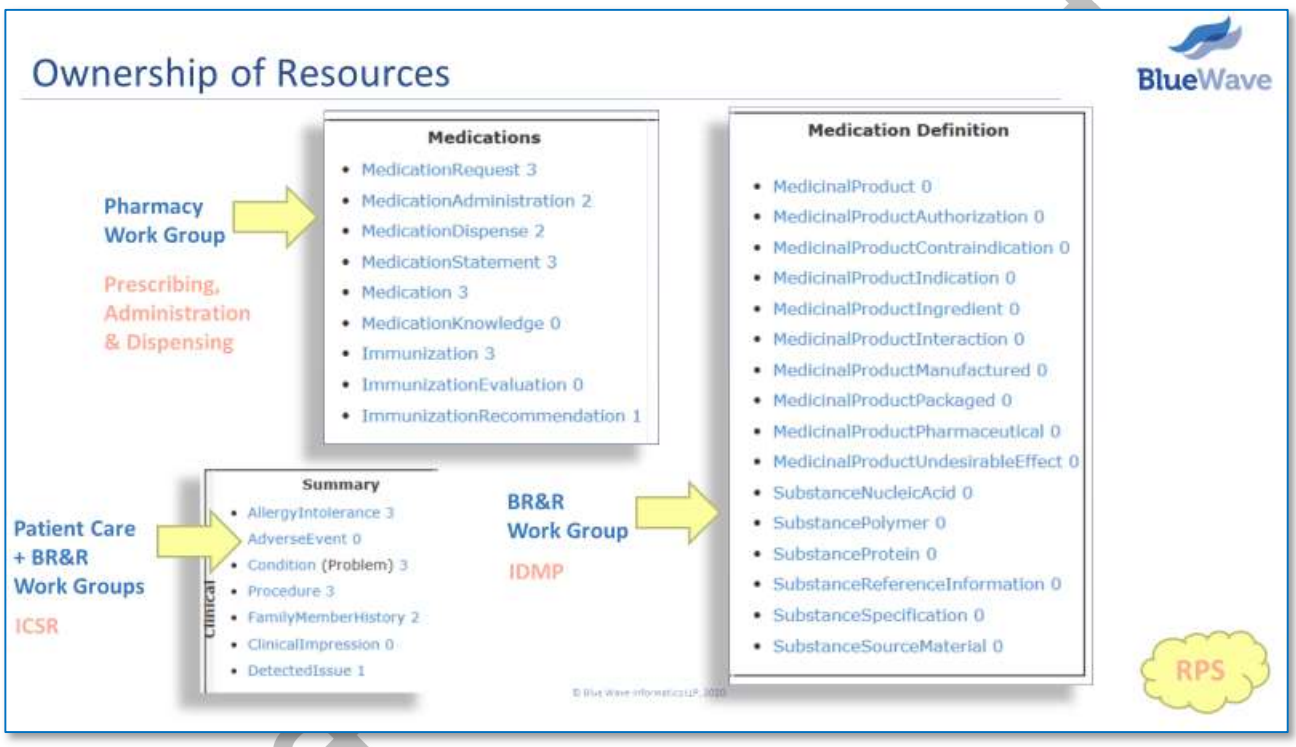


Figure 4 FHIR Ownership of resources

As IDMP and SPOR are used in clinical and patient empowering use cases, the importance of this overarching logical information model will grow.

The session refers to five use cases; however, WP- 8 has already recognised several additional use cases that make use of the IDMP data model, or just IDMP-compliant identifiers. As the number of domains covered by IDMP increase, the imperative for an overarching logical data model becomes stronger in the quest for alignment and consistency.

4.2.3 Use cases

The interactive discussion centred on an IDMP and FHIR maintenance document and a one-to-one cross reference table with IDMP and FHIR definitions, which is part of the EU IDMP Implementation Guide Version 2, version 2 currently under consultation. It is yet unclear how change management and maintenance of this IG will proceed. The group explored the question: "Can FHIR be used as a database standard?" and any mobile apps using FHIR in the space of IDMP. These are rather general and high-level questions that need to be scoped in order to be answered succinctly.

A synthesis of the discussions can be found in Chapter 10 (Annex).

4.3 EU serialisation – Falsified Medicines Directive

- Jean-Gonzague Fontaine, GSK vaccine
- Laure Pontis, GS1 Global Office

4.3.1 Introduction

The purpose of this chapter is to uncover master data needs for regulatory purposes (IDMP, EMA, NCA) and for fighting counterfeit medicinal products according the European Falsified Medicines Directive (FMD) regulation. It illustrates the similarities and differences between regulatory data and supply chain data (in particular regarding identification), as well as how the supply chain uses serialisation in the fight against falsified pharmaceuticals.

Stakeholders understand how medicinal product packages are identified in the market's supply chain and how traceability is processed with unique pharmaceutical identifiers and attributes like the lot/batch and serial numbers. There is a need to better understand how the data carrier identifier (DCID) such as GS1 Global Trade Item Number® (GTIN®) is linked to the package identifier (PCID), marketing authorisation and the medicinal product identifier (MPID).

The European FMD regulation requires that the verification process is supported by a limited number of master data. UNICOM stakeholders understand the current and future data flow between IDMP (SPOR) and FMD's European Medicines Verification System (EMVS).

Specific questions were raised about parallel trade and repackaging. (See Chapter 5.2)

Regarding prescription, dispensation and patient summaries, there is a need to know exactly what has been administered to the patient, using automatic identification and data capture (AIDC) scanned at points of care and captured in electronic health records.

4.3.2 Discussion questions and gaps

The discussion focused on the unique identification of medicinal products—whether a single identifier like the GTIN corresponds to more than one marketing authorisation and/or PCID, from a different NCA.

Also considered was the frequency during which an identifier changes along the medicinal product life cycle and whether it supports registries such as immunisation registries and international patient summaries. Furthermore, how does the identifier support the cross-border prescription process, in the dispense record and in case of a non-substitutable medicine.

The identified gaps include the need for documenting:

- How the medicinal product's unique identifier (DCID/GTIN) supports the prescription process
- If and how the DCID/GTIN supports registries
- How the DCID/GTIN is or can be linked to the latest patient instructions (e.g., for patient instructions)
- How "unique numbers" that comply with the FMD are handled with parallel imports

4.3.3 Use cases

Most of the discussion during this session focused on master data and how to appropriately link SPOR and EMVS. The vision was outlined that some master data could be imported from SPOR to EMVS, with the master and transaction data managed by EMVS only.

There are two EU requirements—one leading to SPOR and another to EMVS—which are fed through different channels. There is a need to secure alignment when data concepts are the same in the two requirement areas. How this will be achieved must be researched.

An identified gap is the need for documentation regarding the traceability challenge for multi-country packaging—the same DCID/GTIN, linked to different marketing authorisations and/or PCIDs.

Another documentation gap is when FMD parallel-traded medicinal products have to be decommissioned by the parallel trader and re-serialised (and re-identified) before entering the target market.

4.4 Medicinal product identification, IDMP, SNOMED CT & MedDRA

- Lise Stevens, Iperion
- Jane Millar and Monica Harry, SNOMED International

4.4.1 Introduction

The purpose of this chapter is to present how the need for terminologies is addressed, in particular with SNOMED CT, and how SNOMED CT can be bridged with IDMP concepts. The interactive session focused on better understanding how the two terminology systems could work together, with a collaborative effort to create linkages that expand the use of IDMP in regulatory and clinical environments.

IDMP, which incorporates EDQM's terminologies and the Unified Code for Units of Measure (UCUM) units of measurement, appears fit for purpose in the regulatory space, including AE reporting. However, SNOMED CT is already extensively used in clinical environments.

4.4.2 Discussion questions and gaps

The interactive session centred on gaining a greater understanding of SNOMED CT and its relationship with IDMP. For example, a mapping between SNOMED CT and IDMP was discussed.

The session revealed a demand for more information about what SNOMED CT provides and how that is linked to IDMP and MedDRA. SNOMED International has documented the SNOMED CT specification for an international model and national extensions, and their impact on interoperability/prescription.

There is a need to document why IDMP and SNOMED CT are important in cross-border processes, how they both support interoperability on an international level, how the linkage of both is planned and how this will be provided.

4.4.3 Use cases

SNOMED CT has a logical model that has been applied to pharmacy-related content that provides the ability to define specific elements of any product.

SNOMED CT has provided a free set for the HL7 International Patient Summary that is supplemented by EU-required additional content. This content is also part of the Global Patient Set provided free by SNOMED International for global use. SNOMED International is also prepared to support the sharing of cross-border information.

An examination of the use of SNOMED CT and IDMP in use cases associated with ePrescription, clinical purposes, adverse effects, medication errors, and supply chain can be found in Chapter 10 (Annex).

4.5 IDMP and Individual Case Safety Report

- Lise Stevens, Iperion
- Anja Van Haren, CBG-MEB

4.5.1 Introduction

The purpose of this April 2020 interactive session was to present the regulatory requirements for adverse event reporting, and how these requirements are linked to IDMP and other standards. It included considerations about the capture of adverse events in clinical environments. An individual case safety report (ICSR) is a process and messaging defined in a normative way by EN/ISO/HL7 27953 ICSRs in pharmacovigilance: Part 1 - Framework for adverse event reporting and Part 2 - Human pharmaceutical reporting requirements for ICSR.

4.5.2 Discussion questions and gaps

Questions explored during this session included regulatory requirements for IDMP, MedDRA and SNOMED CT in the regulatory and clinical domains. Other areas of discussion evolved around identifiers and their process cycles.

The discussion revealed that adverse events and medication errors have differences that should be documented differently in clinical or regulatory domains. There is further a need to better present the three different terminology standards—MedDRA, SNOMED CT and EDQM Standard Terms— to a wider audience: how they are useful in different processes, how they relate to each other and what roles they play or should play in IDMP implementations.

There is no general agreement on which terminology (SNOMED CT or MedDRA) should be used for clinical processes. It's expected that regulators would use MedDRA since it is used in the Summary of Product Characteristics (SmPCs) and in the ICSRs (by regulation). MedDRA helps regulators in their own processes for monitoring products and identifying new signals.

In contrast, the clinical domain would most likely prefer SNOMED CT. This difference in preference is a matter of different implementations. The gap: Provide clarity in the clinical domain, explain linkages and their improvement perspectives.

Where necessary, the clinical area could use parts from the IDMP-model for its own purposes even before regulators have implemented these parts. Therefore, it is important to identify the key aspects of an IDMP implementation that should rely on regulators, NCAs and EMA (e.g., composition of the medicinal product) and which aspects are relevant for separate implementations in clinical environments (e.g. standard terms, units of measurement).

4.5.3 Use cases

Use cases include the regulatory domain (AE reporting) as well as clinical domain specifics such as prescription, medication lists, IPS and supply chain (e.g., in case of shortages) and those processes in the clinical domain where the physical product identification is required to avoid medication errors.

There is certainly a strong need to enable clinician information that is captured to be leveraged automatically to generate adverse event reporting.

4.6 IDMP, ePrescription and eDispense

- Giorgio Cangioli, HL7 Italy
- Robert Vander Stichele, i~HD, University of Gent

4.6.1 Introduction

The purpose of this chapter is to discuss the adoption of the IDMP-related standards in cross-border ePrescription and eDispense scenarios. (Cross-border ePrescription and eDispensing is a subject covered in WP-5.)

To improve patient safety and healthcare for all, UNICOM promotes the standardised identification of medicinal products, to allow for the sharing of accurate clinical information and prescriptions between European member states.

4.6.2 Discussion questions and gaps

The interactive session introduced past experiences and current known aspects of cross-border ePrescriptions.

The epSOS project tried to be strict when defining medications and defining it exactly at the point of prescription, but in reality, flexibility was quickly introduced in the way products can be identified across borders—very strict product identification does not allow for cross-border identification or correspondence.

From an ePrescription-dispense perspective, the need stated is to describe "what needs to be dispensed" in a standard, flexible enough way to have something dispensed in the variety of realities that exist among European countries.

In a prescription, there are several ways the product is prescribed—with more or less granularity. The more precise the prescription is written, the easier it is for the pharmacist to find the product without having to decide among options or the less likely that the pharmacist has a corresponding product.

The information associated with a dispense is no longer flexible. The product is described as an actual package. During eDispensing, information is captured exactly as what has been handed to the patient—detailed identification information as well as the batch/lot and serial numbers.

There are several terminologies, but none provide an adequate level of granularity for all scenarios. In epSOS, Anatomical Therapeutic Chemical Classification (ATC) was used, because it was available in various countries, even if it was not conceived for the identification of products. International Non-Proprietary Name (INN) was not accepted, because it is vocabulary

and not a coded system. However, using ATC for some products hides the biological composition of the medicinal product.

How can IDMP contribute to accurate, cross-border flow of prescriptions and medication lists in patient summaries? How can IDMP contribute to accurate cross-border application of national clinical decision support systems or pharmaceutical audits? For some of the use cases, the IDMP identifiers, that have been designed for specific purposes, seem to either be too specific (e.g., eP/eD; PS) or do not have enough detail (e.g., DSS).

The discussion provided some direction to be investigated:

- Provide a list of items and attributes identified in IDMP. Include product data and prescription data and keep mapping with ATC.
- Do not include text as is. Even substances should be coded.
- Besides identifiers (including the pharmaceutical product identifier), analyse the impact of identified attributes for cross-border ePrescription and eDispensing. For example, some excipients were considered as relevant to express allergies. ATC is difficult to use in order to achieve biosimilar substitution since the same ATC can have different substances identified.

Consider the challenge of making the technical definition and relation between products across different concept levels.

4.6.3 Use cases

In the future, ePrescription will be included in the continuity of care use case as well as the medication list (medication profile). Other use cases were analysed in the openMedicine European project[6].

The prescription is not an isolated act: It is part of patient's medication treatment in various events such as ePrescription in a foreign country, in acute care, in chronic diseases and more.

Applying the new paradigm shift means that the prescriber in country B may have to understand the medication list of country A, not just the prescription they are shown. For example, in the scenario, the decision in country B is not what to dispense, but what to prescribe. For this reason, they need to provide continuity to the patient's medication record.

There is a two-level decision—by the prescriber and by the pharmacist. It is highly recommended to include as much information available when sending the prescription to the pharmacy. When the prescriber uses a medicinal product database it doesn't require extra work from the prescriber. The quality of the prescription is definitely determined by integration in the clinical process.

Use case construction should consider clinical storylines—this is what will happen in reality. Prescription dispense and clinical decision support should benefit from unambiguous identification and what IDMP will mean for actual patient safety.

Finland and Estonia have been exchanging prescriptions, and several issues have been identified that can provide experience and lessons learned. ePrescription is today a service (not a pilot) used cross- border and represents thousands of prescriptions.

[6] See : https://ec.europa.eu/digital-single-market/en/news/openmedicine-project-how-get-correct-medication-abroad

4.7 Pharmaceutical product Identification

- Leonora Grandia, Z-Index

4.7.1 Introduction

The PhPID plays a central role for IDMP implementations, since it provides the means to link medicinal products marketed in various jurisdictions and, in turn, enables adverse events management and tracking. As for the other IDMP concepts, PhPID has been designed to meet the primary objectives of the regulation of medicines and pharmacovigilance; however, several assessments (including the openMedicine project) have recognised the potential added value of the PhPID for other cases of use.

This chapter addresses the creation and maintenance processes of PhPIDs, and the adoption of PhPIDs in different domains and cases of use.

The interactive session provided the initial foundation for the gap analysis.

4.7.2 Discussion questions and gaps

Questions and issues during the interactive session can be grouped in these main categories:

- General comments
- How PhPIDs are created and maintained (regulation of medicines domain)
- PhPID fit for purpose (general or domain specific)

General comments

The PhPID appears to be straightforward until an organisation is faced with using it in an implementation.

Regulation of medicines domain

Generation and maintenance

- The discussion examined a number of topics about the generation and maintenance of PhPIDs, that need clear and urgent clarification. For example, this includes the links with substances and strength levels; availability and harmonisation of the data used as input; organisational processes including business rules; and others as summarised below.

Substances

- The global identification system for substances is not yet available for practical usage (input for PhPID calculation). (Several "depend on" issues. See dedicated topic).
- There is a need for a global maintenance organisation for substances that understands which goal and principle a substance identifier is defined for. This is an organisational issue. It depends also on a new work item that intends to define a minimum set of fields to be used to distinguish substances. This is needed for stable substance identification. (SDO issue)
- It has been highlighted that there is a need of more precise business rules for identifying substances when manufactured items are combined for forming one PhPID. There are cases when the active substance is not the same (e.g., Shingrix). There are similar questions for dissolved salts.

Strengths

Some of the issues related to strengths are related to the kind of substance to be considered.

The PhPID identifies a substance at the most granular level for clinical use (including salt and ester, if relevant). It is at this level that strength needs to be defined.

- The basis of strength is not always the active moiety. These differ often, especially for older products.
- For liquid, specifications distinguish between the presentation and concentration strengths and indicate that a PhPID should be generated to represent a strength concentration per unit volume. This is called the pharmaceutical product concept code (PPCC) and is intended to be an abstract PhPID. It is not clear, however, if it is a distinct, additional PhPID.
- EDQM defines pharmaceutical dose forms.
- For different cases, it is useful to refer to the presentation or to concentration strengths. How can this be taken in account?
- For manufactured items and pharmaceutical products, it was suggested, as a key task within UNICOM, to disambiguate the three active ingredient roles and the strengths that relate to them, including:
    - The strength of the active ingredient substance as it is present at the most detailed level of granularity available (i.e., including modifiers and solvation)
    - The "basis of strength substance" –the substance that is used for the strength description of the product (usually the clinically relevant strength). This may be a moiety substance or a substance with modification. It may be the same as the precise ingredient substance. It may not be the strength of the active moiety that provides the pharmacological action.

Analyse how this consideration impacts the PhPID and how the three types of strength should be chosen to deliver the "value" for the PhPID calculation.

Administrable dose form

- The common global identification system for the administrable dose form is not yet agreed upon and available. (input for PhPID calculation). (several “depends on” issues, see the dedicated section).
- Forms can be transformed in an administrable Dose Form. It does not contain an explicit separate list of administrable dose forms. When a transformation occurs, the expression of strength changes, and it must be clear which expression will be used for the PhPID.

Organisational processes and business rules

- Different organisations may describe differently the same thing. A different PhPID could be, therefore, generated. Enforce clear rules for the creation of the PhPID and/or a single organisation for PhPID generation.
- While a PhPID can be issued regionally, its purpose is to provide global identification. This raises the question of a maintenance or governance organisation. This is not in scope for UNICOM nor the SDOs but needs to be addressed since it is a critical prerequisite for an IDMP implementation. The WHO Uppsala Monitoring Centre (UMC) or SNOMED International may provide this support. There are conversations in place between SNOMED International and WHO UMC for follow-up.

- The limitations of having a central maintenance organisation needs further investigation (e.g., sharing information about not yet public substances).
- For combination products, rules need to be made with regard to the order of substances and strengths.

Exceptionally, medicinal products contain more than three active substances. Is it still possible in that case to create a PhPID and present all these numbers to the Hash Function?

PhPID usage

Generic

Even assuming an "ideal" PhPID calculation, the PhPID might still be too specific or too generic based on the purpose of use. For example, "users" could not care about the volume of the ampoule (presentation strength) or the kind of salts. On the contrary, they might be interested to know if a product contains sugar or not, or which kind of inhalator is used.

PhPID has been designed for regulatory and pharmacovigilance purposes. Should ISO explore how to use, extend or integrate these concepts beyond pharmacovigilance? Or, should other organisations take care of it (e.g., SNOMED International)? In both cases, a clear identification of gaps is needed.

Prescription / dispensation

Some concerns have risen about the specificity of PhPID. A prescriber may be more interested in the active moiety rather than the specific salt. Similar considerations can be made for the dose forms or presentation strengths. This may also have an impact on the cross-border dispensation process. All of the above cases are where the substitution rules are very restrictive.

As the standards recognise a role for a special kind of PhPID, the PPCC is "necessary to support ePrescribing and eDispensing activities in cases where what is prescribed is simply a given strength concentration per unit volume." Could this concept be further extended to be more generic the substance and the dose form?

It should be clear whether these higher levels of abstraction (e.g., an INN prescription) should be addressed with PhPIDs or with another mechanism mapped to the more detailed PhPID.

Adverse events

It has been suggested to split this use case at least in two parts: the reporting for pharmacovigilance (ICRS) that a PhPID is designed for and the support for clinicians (knowledge base) for the identification of possible reactions associated to the usage of specific drugs. In the latter case, the general considerations made above apply. This second case will be included in the clinical purposes use case in Chapter 10.

Clinical purposes

In some specific situation, more detailed information on the medicinal product may be needed—e.g. to identify the presence of excipients the patient could be allergic to), using a prescription-decision supporting system. It is impossible to integrate this information in the PhPID, but it should be possible to generate this by mapping the PhPID to well-structured National Product Dictionaries.

It might be impossible to integrate this information into the PhPID, but it should be possible to generate this by mapping the PhPID to the well-structured National Product Dictionaries.

4.7.3 Use cases

The use cases are summarised in Chapter 10 (Annex).

5 Additional inputs

5.1 UNICOM work package

Some inputs were provided by Work Package experts, which are summarised below:

- One area of input regarding IDMP changes is the manufactured item. The suggestion is to make it its own "identification class" since this would make implementations easier with many PCIDs relating back to one manufactured item. This would also make mapping to other terminologies (that have something like this class, which many do like SNOMED CT) much easier.
- A second area pertains to the substance strength and reference strength. The contributor commented that although the current conceptual model and any logical or physical implementation of it can support all that is needed, it is not the simplest way to do so. It would probably be better to slightly remodel the ingredient/substance/strength section (§9.7, EN ISO 11616) to be explicit about active ingredient roles and types and how these relate to strength. A proposal is scheduled to be shared with WP-1.
- PhPID calculation is another area to address. The contributor says there is a need for a single source of truth that will determine the sequence of information used to calculate the PhPID. In the meantime, UNICOM has decided to use a small set of substances to calculate the PhPIDs and other identifiers (e.g., MPID) for a limited number of substances. If the PhPID is available, other identification generation can also be accurately made. UNICOM has selected six substances from which PhPIDs have been calculated that correspond to a few thousand medicinal product packages (PCIDs) in Europe (pilot product list).
- Regarding the medicinal product identifier (MPID), the pilot product list will reveal the need for a better shared understanding about to how to implement and use MPIDs in healthcare domains. The way to use the MPID is not sufficiently described with the needed details.
- There is a need for clarification between MedDRA and SNOMED CT terminologies in that European regulators and authorities are expecting to have translations in all EU languages. MedDRA provides these translations, but SNOMED CT's number of translations is limited to what the member countries decide. (SNOMED CT is currently available in US English, UK English, Spanish, Danish, Swedish and more.) This is critical since MedDRA is mandated in the regulatory domain, while SNOMED CT is the preferred terminology in the clinical space. Which of these should be captured into SPOR/IDMP—both or only one—and which one?
- The need to dispose of translated terms for the development of the electronic leaflet (ePL) and prescription will be documented in UNICOM.
- Noting that the ISO TC215 Work Group 6 NWIP will start working on "clinical particulars," this raises the question about how this effort fits with the above mentioned MedDRA and SNOMED work effort, which already exists.
- WHODrug Global is a global drug dictionary for medical product information used to identify drug-related problems in clinical trials and pharmacovigilance. WHODrug Global is maintained by the Uppsala Monitoring Centre—the WHO Collaborating Centre for International Drug Monitoring. It is not known if its current data architecture is compatible with IDMP.

5.2 Community of expertise

An open, virtual "community of expertise" meeting was held on 1 July 2020. The dialogue complemented one of the interactive session's discussion about the cross-border movement of medicinal product packages in the fight against counterfeits via the FMD regulation.

This first community of expertise meeting was open to experts from UNICOM as well as those outside the consortium. As an initial meeting, improvements were noted for future bi-monthly meetings, starting in September.

The introduction was followed by a moderated Q&A session, which helped promote the need to bridge the regulatory domain to the supply chain and clinical domains.

- The combination of IDMP's PCID and DCID requires additional and explicit explanation for the user community so that NCAs and industry can reach a common understanding about the value of these distinct identification keys.
- The speaker presented cross-border pharmaceutical practices, including inter-market transactions and parallel distribution processes.
- Questions about medicinal package identification included the use of GS1 Global Trade Item Numbers (GTINs) in parallel distribution and the need to generate new GTINs if the size of the package changes or if an importer re-packages the medicinal product.
- What about parallel distribution from an OTC country where a product does not require a prescription and may not be serialised, to an RX country where it is? With this status change in the new country, the medicinal product would require a new GTIN with a serial number.
- Regarding a cross-border medicinal product, the local language of the country where it is being parallel imported must be included on the product's package, triggering a new GTIN.
- The governance and assignment processes for PCID and GTIN are different, and the assigning authorities are different. If that is true, how would they be "mixed"? The PCID is a regulatory representation of an authorised pack with a regulatory life cycle. The GTIN provides a supply chain identification of a pack with a supply chain life cycle. Either can change without the other changing—they are completely independent of each other. The IDMP provides reconciliation between the regulatory and supply chain life cycles without the need for complex mapping.
- Are their reasons for not including GTINs in the SPOR? The GTIN, which is assigned by the manufacturer, and the National Trade Item Number (NTIN), assigned by the regulatory agency, are both unique global identifiers. They are part of the IDMP data model, named "data carrier identifier."
- This complex system permits parallel trade, despite the possibilities of breaches in the protection against falsification. A main principle in the EU is to provide for the free movement of goods yet, at the same time, to protect against the falsification of medicines. It is recognised that the fight against falsification includes additional features to serialisation, which do not impact directly or indirectly IDMP.
- What if somebody puts falsified medicines into parallel trade boxes, and uses the "correct" medicines in another market? How is this detected? The unique identifier comprised of the GTIN and serial number, can be verified only once in the European

Medicines Verification System (EMVS) and should enable detection of such a situation.

5.3 EU IDMP Implementation Guide Version 2 consultation

On 10 July 2020, the EMA opened a restricted consultation on its IDMP implementation guide Version 2, including a selection of chapters from this considerable artwork.

We acknowledge this major document that is aimed to be used for the regulatory implementations of IDMP by NCAs and the pharmaceutical industry. It will be inspirational for applications in other domains and especially for the implementation of National Medicinal Product Dictionaries (UNICOM WP-9).

The SDOs from the UNICOM WP-1 were invited to contribute to this consultation process, which will close at the end of August (because EMA requests its consulted stakeholders to consolidate their feedbacks by groups—UNICOM WP-1 being allocated to the "industry" group).

The considerable documents have been reviewed but do not allow WP-1 to express specific comments in this short time frame.

Consequently, analysing the EMA documents requires heavy and skilled resources—a task involving a large number of experts from the SDO communities. After a preliminary read of the EU IDMP Implementation Guide Version 2, it appears that several gaps collected in the present document, correspond to challenges noticed by the experts having prepared the EU IDMP Implementation Guide Version 2.

6 Analysis of identified gaps

The outcomes from discussions during the interactive sessions (See Chapter 4) combined with additional inputs (See Chapter 5) have provided a wealth of information from which to identify and analyse current gaps in the IDMP implementation. This chapter has not the ambition to deliver an ultimate, complete, list of gaps: it corresponds to what has been collected in the first months of the UNICOM project. This document will be updated; it will include later comments and gaps, and information regarding their resolution, by the SDOs.

The gaps have been categorised using five implementation "pillars" according the Chapter 1.4 landscape where IDMP standards and related standards respond to the needs of users. Clearly, some of the gaps are allocated to one pillar, while they are transversal.

These domains or pillars are the following:

- Development and production: the domain where industry researches, manufactures and exchanges with competent authorities
- Regulation and Authorisation: the domain where competent authorities evaluate, capture and authorise the marketing of medicinal products, including post-market surveillance
- Dissemination and Information: the domain where information about medicinal products is managed, enriched and distributed to users such as prescribers
- Prescription and Dispensation: the domain where users decide about the use of medicinal products
- Utilisation and Outcome Assessment: the domain that includes utilisation of consumption data in the widest sense, which includes supply chain

Following is the summary of the identified gaps, a short analysis of them and additional indicators for the handling of the gaps. The chapter is targeted to standards developers.

6.1 Development and production

This domain involves mainly the research organisations and pharmaceutical companies and their interactions with other domains as depicted in Chapter 1.4.

6.1.1 Manufactured item

Problem: This concept does not exist in the current model. (See Chapter 5.1)

Background: The manufactured item concept is quite complicated and causes issues with IDMP implementation, affecting the many PCIDs that relate back to the one manufactured item. This would also make mapping to other terminologies (that have something like this class, which many do, e.g. SNOMED CT) much easier.

Impact considerations: By addressing this issue, it could make IDMP implementation and mapping to other terminologies much easier. There is a risk, since some implementations are already advanced, and that addition might be disruptive.

Proposed next step: Consider making the manufactured item its own "identification class."

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status

6.1.1	Manufactured item	CEN/ISO		

6.1.2 Administrable dose form

Problem: EDQM does not have an explicit list of administrable dose forms. (See Chapter 4.7.2.)

Background: Information about dose forms is missing in EDQM's Standard Terms. It only notes that the pharmaceutical dose form is subject to transformation but doesn't specify the result of this transformation. The dose forms they use are not instrumental in separating medicinal from systemic effect.

Impact considerations: Common global identification system for administrable dose form is an input for PhPID calculation. When a transformation occurs, the expression of strength changes, and it must be clear which expression will be used for the PhPID.

Proposed next step: Confirm that EDQM will add "administrative dose form" in the revision. Include this gap in the 11239 / 20440 revision.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.1.2	Administrable dose form to be added	CEN/ISO & EDQM		

6.1.3 Substances and strength

Problem: Global maintenance organisation for substances with more precise business rules for identifying substances when manufactured items are combined to form one PhPID. In other words, a global substance identification is needed.

The level of granularity for the active substance (salts and esters, if relevant), and the roles of the ingredients (active ingredient, adjuvants and clinically relevant excipient) roles and the strengths that relate to them are not clear. This includes the strength of the active ingredient substance as it is present at the most detailed level of granularity available and the "basis of strength substance"—the substance that is used for the strength description of the product. (See Chapter 4.7.2. and Chapter 12)

Background: There is space for interpretation, which negatively impacts PhPID accuracy.

Impact consideration: This is a crucial gap, if not addressed timely it opens risks for inconsistent implementations. Concepts are available, we need consensus on which concept is the "right" one.

Proposed next step: Analyse how this consideration impacts the PhPID and how the three types of strength should be chosen to deliver "value" for the PhPID calculation. Conduct the standard interpretation in the course of UNICOM pilot product list. Integrate into the documentation.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.1.3.1	Substances & strength	WHO-UMC & SNOMED International	December 2020	
6.1.3.2	Substance / governance			

6.1.4 IDMP and official medicinal product labelling

Problem: A new European standard for *Electronic Product Information* (ePI) is prepared by EMA and HMAs to support medical product labelling and specifically Summary of Product Characteristics (SmPC) and Patient Information Leaflets (PIL)[7]. This future standard needs to be aligned with IDMP master data. On an NCA point of view, these data shall be made available in their national language and include a link (URL) to the most recent version. (See 5.1.)

Background: There are major projects on ePI in Europe and other regions. Gravitate Health is a new IMI project that specifically references UNICOM and IDMP and will pilot the creation and update of ePIs in the upstream, and the downstream dissemination. Clarifying for Europe in coordination with other regions, what should be sourced in IDMP master data (SPOR) is important to streamline the project efforts and encourage their convergence.

Impact consideration: This requirement is partially in UNICOM's scope (since it includes IDMP master data) and corresponds to a real need. Today Patient Information Leaflets and SmPC are offered in the local languages but not sourced from the IDMP master data. This has implications for pharmacovigilance and consistencies in reporting drug to drug interactions.

Proposed next step: UNICOM WP-3 and WP-4 to provide a description of the current situation regarding ePI (SmPC and ePIL) and their structure/content compared to IDMP. Before any translation the logical data model for ePI is needed. Identify the ePI data to be sourced from IDMP with input from WP-3 and WP-4. WP8 and WP9 to share information and findings.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.1.4.1	ePI / SmPC, description of IDMP sources	WP-3 or WP-4		
6.1.4.2	Pilot list of medicinal products to be shared and joint demonstrators to be explored	WP-8, WP-9	UNICOM Y4	

[7] https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-draft-key-principles_en.pdf

6.1.5 DCID and parallel distribution

Problem: Better understand and document how the data carrier identifier (DCID/GTIN) is handled with parallel imports, and its impact on the PCID, marketing authorisation and MPIDs, since they have different process cycles. Document the traceability challenge for multi-country packaging—the same DCID/GTIN, linked to different marketing authorisations and/or PCID. (See Chapters 4.3.1, 4.3.2 and 4.3.3)

Background: Medicinal product packages are produced to be marketed in a single country that corresponds to a single series of MPID and PCID as well as a DCID. If a product is parallel traded into another country, it will require another PCID, and because of language requirements, a new DCID will be assigned by the parallel importer. Multi-country packages show one single DCID linked to multiple PCIDs (one per country).

Impact consideration: Traceability in the supply chain should always link to regulatory information (PCID, marketing authorisation). Gaining clarity for this requirement will help stakeholders to implement IDMP in their respective jurisdictions.

Proposed next step: Develop a process description for the different cycles. See 6.5.3.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.1.5	DCID & parallel distribution process description	GS1	December 2020	

6.2 Regulation and authorisation

This domain involves mainly the NCAs as well as the EMA and their interactions with other domains as depicted in Chapter 1.4.

6.2.1 Substances and strength

Problem: For the identification of substances in a product to be globally unequivocal, there are a few gaps. A substance and its strength can be defined in different levels of granularity, and this flexibility can lead to ambiguity. There is a need to clarify substance strength and reference strength and which are used when calculating a PhPID. A global identification system (and underlying processes, and custodian organisation) for substances, strength and roles is needed. See Chapter 12 for more detailed description and examples.

Background: "Substance" can refer to different levels of granularity. Regardless of any possible variability in regulatory processes, it is important to clearly identify the different substance levels and then chose the right level that will be used to identify products. The substance level is important when defining the strength of the precise active ingredient versus that of the moiety.

Also, the substances can have different roles in a product. Usually the active ingredient or ingredients are the ones for which the strength is specified. It is, therefore, imperative that this strength is unequivocally specified, in the most detailed level of granularity.

Finally, all these different levels must be related in a common model upon which the different processes can rely.

Impact consideration: Most of these gaps are for clarification, additional guidance and the improved implementation of standards and regulations. Such guidance should be triggered by the UNICOM project, and implementation support should follow the UNICOM goals to ensure it meets its ultimate purpose—not only on the regulatory and authorisation phases, but throughout the entire life cycles described in this document. Changes to IDMP will likely be adopted and reflected in downstream standards, semantic or technical. It should be documented if this raises a backward compatibility issue.

Also, criteria should be established to define stewardship processes and the custodian organisation.

Proposed next steps: Consider clarifying or slightly remodelling the ingredient/substance/strength section (§9.7, EN ISO 11616) to be explicit about the active ingredient roles and types and how these relate to strength. (See 5.1.). Specifically consider the new attribute, Reference Strength Type.

Clarify the three active ingredients' roles and the strengths that relate to them. This includes the strength of the active ingredient as it is present at the most detailed level of granularity and the "basis of strength substance"— the substance that is used for the strength description of the product. (See 4.7.2.)

Define a maintenance process with clear business rules for distinguishing and identifying substances. Define a custodian organisation for the identification of the substances.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.2.1.1	Disambiguate ingredient / substance / strength(s) and levels; add Reference Strength to IDMP models and impacted standards and terminologies	CEN/ISO		
6.2.1.2	Specify global rules for which roles and granularity of substances to be used when identifying a product	CEN/ISO		
6.2.1.3	Define processes for stewardship and custodianship of substance and	all		

	strength identifiers			
6.2.1.4	Identify custodian organisation			
6.2.1.5	Ensure adoption throughout other SDOs and stakeholders	all		

6.2.2 PhPID calculation and governance

Problem: The different levels of substance specification defined above (See 6.2.1) will cause issues in calculating PhPID. The PhPID will be different for the same substance specified at different levels. Without this, the PhPID cannot really fulfil its purpose of being a global identifier that can be used in different scenarios.

Background: PhPID calculation needs to be addressed with a single source of truth that will precisely determine the sequence of data used to calculate the PhPID. While PhPIDs can be issued regionally, its purpose is to provide global identification, which brings up the need for a precise algorithm and a maintenance/governance organisation.

Impact consideration: This change will require SDOs and/or experts to participate in a common definition. To make sure no ambiguity is left, any definition should be validated against real data: For example, use the UNICOM example substances to validate the clarity of the PhPID calculation rule.

Proposed next step: Analyse how this (See 6.2.1) consideration impacts the PhPID calculation and how the three types of strength should be chosen to deliver the "value" for the PhPID calculation. Define PhPID calculation rule with the necessary precision (removing the ambiguities) and mandate a maintenance/governance organisation. This is not in the present scope for UNICOM nor the SDOs, but needs to be addressed since it is a critical prerequisite for any IDMP implementation. The WHO UMC and/or SNOMED International may provide the international leverage needed for this. (See 4.7.2 and 5.1.). The pilot product list, developed by a joint expert group in UNICOM, is to be used immediately as a source of experience and to be communicated strongly through UNICOM and abroad.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.2.2.1	PhPID calculation & governance processes	Piloted during UNICOM to gather experience	June 2021	
6.2.2.2	Use UNICOM pilot product list to validate PhPID calculation	Piloted during UNICOM to gather experience	June 2021	
6.2.2.3	PhPID assigning and managing authority/ies	Piloted during UNICOM to gather experience	June 2021	

6.2.3 Manufactured Item class

Definition from ISO 11616: "Qualitative and quantitative composition of a product as contained in the packaging of the medicinal product as put on the market or investigational medicinal product as used in a clinical trial."

Problem: In implementation, the concept of "manufactured item" in IDMP is pivotal. For example, there can be several packaged items referring to one manufactured item. This is important for the SDO since most terminologies do have a concept similar to the manufactured item. However, this is not an identified class in the IDMP conceptual model, which creates complexity and ambiguity in implementation.

Background: When first designing IDMP models, the notion of the manufactured item was present, but it was not considered as a class of its own. It did not have a specified identifier.

Impact consideration: Having the manufactured item as a class with its own identifier would allow linking it to other terminologies and, thus, facilitate implementations of regulatory, clinical and supply chain systems. This would require changes in IDMP, which would propagate to downstream designs. Given the implementation complexity, this would be a welcomed change.

Proposed next step: Add manufactured Item class to ISO IDMP 11615 (and related standards where applicable). Analyse impact on backward compatibility.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.2.3.1	Add manufactured item class and attributes	ISO	ASAP	
6.2.3.2	Evaluate impact and implement new manufactured item class/identifier	HL7, IHE		
6.2.3.2	Link manufactured item identifier to standard terminologies	SNOMED International		

6.2.4 MPID and PCID generation

Problem: Unlike PhPIDs, which are calculated, the MPIDs and PCIDs are generated and assigned, and they typically have local governance. The way to generate MPIDs and PCIDs is not sufficiently described with the needed details. There are expected issues that will be uncovered as part of the pilot product list (See 5.1). The deliberate and necessarily flexibility when assigning MPIDs or PCIDs will impact also the identification processes.

Background: As identified in the openMedicine project, the rules for assigning a new MPID are not strict. This flexibility is considered intentional because it supports variance in the national regulatory processes. But even if this flexibility may be maintained, the impact of that in identification must be considered. The rules for defining MPIDs can be defined in parallel with those for defining PhPID, but this should be done in strict articulation.

Impact consideration: The process for MPID generation should be clarified, especially the governance rules that describe what is fixed universally, what depends on country regulations and what is left for implementers (and how any ambiguity is resolved). Changing the MPIDs can be either a strictly technical or semantic change, which requires some standards to change or may be determining the need for readiness by the national regulators. Whatever solutions can emerge from this, it must take into account the impact on regulations in all member states.

Proposed next step: Verify, using examples, what is the impact of the MPID assignment rules and find whether the variance is needed. Find ways to address this variance, either by confirming that the impact is only technical (and incorporating this impact in UNICOM guidance) or by raising the need for changes or readiness in the member states' regulatory processes and catalogues. Document the process and rules, clearly identifying the fixed parameters and variable options.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.2.4.1	Describe MPID governance -what is fixed and what is variable	ISO	During PhPID analysis	
6.2.4.2	MPID implementation options	CEN/ISO (Lead), others as needed		

6.2.5 Logical models

Problem: The IDMP family of standards defines a data model focused on the regulatory needs for identification products, starting with marketing authorisation and looking at pharmacovigilance. Between these activities, there is a range of diverse domains (identified in this document), which have their own data needs. IDMP is not intended to replace all those models, but there is little awareness of the real impact of IDMP in the data models of the other processes.

Background: The IDMP logical model requirements is a WP-1 deliverable. IDMP extensively details some of the data models, but there is still a need for creation of one logical model to facilitate IDMP implementation with FHIR in the regulatory domain and by other processes such as ePrescription (which as well shall benefit of its own logical model). More generally, any implementation guide should be based on a standards agnostic logical model at a detailed level of granularity that can cover several domains or use cases. (See Chapter 4.2.2.).

Impact consideration: Starting with logical models is not uncommon in health IT standards but is not available in several instances used today (e.g., ISO, HL7, IHE). In this space, the

IDMP logical model is a priority to support the development of other logical models and boost implementations.

Several working groups (IHE Pharmacy, CEN TC251) have started to publish their information and data needs in the form of data models.

Proposed next step:

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.2.4.1	Logical model for IDMP	CEN/ISO		

6.2.6 EDQM Standard Terms

Problem: The granularity of the concepts and their coded value sets (e.g., administration routes) are a key problem in IDMP. The required granularity varies frequently in national regulatory processes. Adoption of a global value set of EDQM Standard Terms (e.g., pharmaceutical dose forms, route of administration) is a critical challenge. EDQM Standard Terms are used in the calculation of a PhPID.

Background: EDQM provides a set of reference values of different granularities. It does not provide a kind of aggregated value set, which would facilitate IDMP implementations where the full EDQM Standard Terms cannot be used.

Impact consideration: As long as the appropriate EDQM Standard Terms value has not been agreed on, this gap is a barrier to IDMP implementations.

Proposed next steps: Define a simplified value set to be provided by EDQM, sustained by a transparent ontology and used across IDMP implementations.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.2.6	Define a simpler, aggregated, value set for pharmaceutical dose forms	CEN/ISO		Revision of EN ISO 11239 and CEN ISO TS 20440 started

6.2.7 IDMP and FHIR

Problem: With IDMP as a data model and FHIR as a technical standard, their alignment is not complete. IDMP support has been taken up by HL7 working groups (WGs), but the results are still in progress. IDMP-related FHIR resources are hosted by different regulatory agencies and HL7 working groups, namely HL7 Patient Care, HL7 Pharmacy, HL7 Biomedical and Regulatory (BR&R WG). (See 4.2.2). As a consequence, there are gaps in describing how these different resources can be used to meet the real-life use cases.

This requires improved maintenance and governance, including where specifically to find accurate information. When a member state regulatory authority, medicinal product dictionary provider or clinical software vendor needs to become IDMP compatible, there is no

clear guidance on what this means. Education and dissemination are still only starting and for implementers, FHIR and IDMP are not at all related, or they are reduced to a few identifiers like PhPID.

Background: The FHIR resources are in progress, and they will most likely go through some harmonisation and validation. From the regulatory side, mapping is needed between IDMP and FHIR resources is part of the EU IDMP Implementation Guide Version 2, referring back to the HL7 v3 IDMP data model. There is an ongoing effort to share medicinal product catalogues (dictionaries) in FHIR, but this is still being developed.

Impact consideration: Aligning FHIR to IDMP means aligning the base resources, producing some guidance and implementation support. This will be an effort from several groups, and most likely will need to be orchestrated by a set of common use cases that show, end-to-end, how the different resources play a part in the overall data exchange. It is expected that several SDOs will need to contribute. And, the alignment will need to be visible to all stakeholders—the authorities, providers of medicinal product dictionaries, system vendors and the implementer community. This requires awareness and dissemination.

Proposed next steps: The WG-1 team suggests covering the gaps in HL7 by using the same materials designed in UNICOM, since they provide a real-life, end-to-end set of products and use cases. Concretely, the life cycle of a product—from regulatory submission to its use in the supply chain, to clinical ordering and dispensing, and to pharmacovigilance—should be considered in a collaborative effort by HL7 FHIR WGs and the relevant SDO involved in UNICOM, which should demonstrate the maturity and consistence of the standards throughout their life cycle. In addition, the different users should be more aware so that they can provide useful feedback and promote the rapid adoption of the standards, specifically the adoption of the IDMP concepts.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.2.7.1	IDMP & FHIR alignment – cross-workgroup use cases and requirements definition	HL7 on behalf of UNICOM	End 2021	
6.2.7.2	IDMP & FHIR alignment – resource harmonisation	HL7 WGs	End 2021	
6.2.7.3	Training & awareness	?	June 2021	

6.3 Dissemination and information

This domain involves mainly the public and commercial providers of structured drug information, including tools for process and decision support, and their interactions with other domains as depicted in Chapter 1.4.

6.3.1 DCID, dispense and clinical processes

Problem: Documentation is missing on how the medicinal product's unique identifier (DCID/GTIN) supports the prescription and dispensation processes, if and how it supports registries and how it can be linked to the latest patient instructions (ePL) or SmPC. (See 4.3.2.)

Background: AIDC is used in dispensing processes. Verifying that the right product is given to the right patient requires a kind of a mapping with the prescription. It further enables populating registries and electronic patient records. The DCID/GTIN information links to master data that should be available at any time. See 6.5.3.

Impact consideration: It is crucial that there is a thorough understanding of these processes for proper implementations of prescription or dispensing systems, as well as populating information into registries or patient records. A message must be sent back to the prescriber, detailing what has been dispensed / administered. Include the feedback in the workflow.

Proposed next step: Investigate to what degrees CEN/ISO TS 16791 and CEN/ISO TS 19256 might fill this gap. Ensure the adoption of a feedback message.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.3.1.1	DCID, dispense, clinical processes, medicinal product dictionary	CEN/ISO	June 2021	
6.3.1.2	Feedback message	IHE - all		

6.3.2 MedDRA, SNOMED CT and EDQM Standard Terms

Problem: Present the three different terminology standards—MedDRA, SNOMED CT and EDQM Standard Terms— to a wider audience. Include how they are useful in different processes, how they relate to each other, and what roles they play or should play in IDMP implementation. (See 4.5.2 and 5.1.)

Background: The three terminologies are developed and used in very distinct domains: MedDRA in the regulated reporting of adverse events, SNOMED CT in the clinical domain, and EDQM in the domain of regulated market authorisation. How and where they are (to be) used in relation to an IDMP implementation is not clearly identified, which means that the required relationships are still uncertain. Maps from MedDRA to SNOMED CT and vice versa have been developed for a priority set of MedDRA concepts, identified outside of UNICOM for defined use cases (e.g., WEB RADR 2 project).

Impact consideration: Without proper guidance, implementers of IDMP might make choices around the use of these terminologies that are inappropriate and lead to inconsistent use

across implementations. Also, without a proper understanding of the required linkage between these terminologies, changes in one terminology may lead to undesirable consequences for their particular use within IDMP or in relation to (their mapping to) other terminologies.

Proposed next step: Develop guidance on the appropriate use of MedDRA, SNOMED CT, and EDQM Standard Terms within IDMP implementation. Engage with implementers and users to further understand the requirements for additional content and mapping between the terminologies. The recently started ISO project on "IDMP / clinical particulars" is intended to clarify the available terminologies and their use. Develop collaboration between WP-1, MedDRA and EDQM.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.3.2.1	MedDRA, SNOMED CT, EDQM	MedDRA MSSO, SNOMED International, EDQM	December 2020?? (tbc)	
6.3.2.2	"clinical particular"	ISO	December 2022	
6.3.2.3	Integrate MedDRA & EDQM to WP-1	WP-1	asap	

6.3.3 MedDRA and SNOMED CT translations

Problem: SNOMED CT translations do not fully cover the regulatory requirement in adverse event reporting for translations in all EU languages. Since MedDRA is mandated in the regulatory domain, it will provide all required translations. (See 4.5.2 and 5.1.)

Background: Given that SNOMED CT is the preferred terminology in the clinical domain, one would hope to be able to satisfy the regulatory requirements through the use of SNOMED CT, rather than forcing the implementation of MedDRA in the clinical domain. SNOMED International releases SNOMED CT International Edition in US English, UK English and Spanish. Other translations are undertaken by member countries, in some cases full translations and others specific content areas. (Sometimes a large users community takes on the translation task.) Where a language is used in more than one country, members will work together on the translation. SNOMED CT is used to capture clinical care and in some non-English speaking countries, their clinical records remain in English.

Impact consideration: If no perspective is provided on how to fulfil the regulatory translation requirement when using SNOMED CT, there is a risk that implementers will search for another solution, leading to non-standard approaches.

Proposed next step: Provide an overview of the availability of the translations of SNOMED CT required terms. Identify whether and how the mapping from MedDRA to SNOMED CT and vice versa can fulfil the regulatory translation expectations**.**

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.3.3	Evaluation of existing solutions / translations	MedDRA MSSO, SNOMED International		

6.3.4 SNOMED CT and cross-border healthcare

Problem: Document why IDMP and SNOMED CT are important in cross-border healthcare processes, how they both support interoperability on an international level, how the linkage of both is planned and how this will be provided. (See 4.4.2. and 9.1.3, 9.2.3 and 9.3.3)

Background: Current cross-border initiatives in the EU include the IPS and ePrescription/eDispensation use cases. Both scenarios carry important clinical information concerning the medication of the patient. In the European eHealth Digital Services Infrastructure (DSI), they rely on the Master Value Sets Catalogue (MVC) and its related Central Terminology Services (CTS) to provide translation into the local language and healthcare practice. For medication, the MVC currently makes use of ATC-codes for translation/transformation purposes. It is not clear what the added value of IDMP and SNOMED CT could be in relation to the MVC/CTS and the information structures needed for cross-border care. The fact that SNOMED International has made available the Global Patient Set free for use, which includes the required data for the IPS as developed by CEN and HL7, could be an important driver for implementation.

Impact consideration: If IDMP and SNOMED CT are not considered as logical components of cross-border care, the added value of adopting these global standards in a local healthcare system will be diminished substantially.

Proposed next step: Provide the rationale for SNOMED CT as a reference terminology in cross-border processes, and work with the cross-border initiatives to test the rationale and further develop the requirements for proper deployment in their eHealth services.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.3.4	SNOMED CT & cross-border processes	SNOMED International	June 2021	

6.3.5 EDQM Standard Terms

Problem: The granularity of the concepts and their coded value sets (e.g., administration routes) are a key problem in IDMP. The required granularity varies frequently in national clinical processes and especially in prescription and other processes, so it is not possible to expect one single granularity and set of codes meeting all the needs.

For UNICOM, identifying a product (and possibly even defining the PhPIDs) requires navigating concepts and their codes at different levels.

For example, the “administrable dose form” may or may not be related to the “pharmaceutical dose form” or to a more generic “dose form”—depending on the process that requires the data element. Within a precise concept like “the administrable dose form”,

there are levels like "oral use," "oromucosal use" and "sublingual use," which may or may not be equivalent. For any deterministic method of finding of equivalents or near-equivalents, it is important their relationship is clear.

Not only NCAs are facing backward compatibility issues with implementing IDMP, but are conducting clinical implementations as well. The granularity of terminologies may vary from EDQM Standard Terms, and between NCA and clinical implementations. This need also applies to the WHO in its pharmacovigilance activities. (See 4.1.2.).

Background: See 6.2.5

Impact consideration: See 6.2.5

Proposed next steps: See 6.2.5

6.3.6 Logical models

Problem: The IDMP family of standards defines a data model focused on the regulatory needs for identification products. Between these activities, there is a range of diverse domains (identified in this document), which have their own data needs. IDMP is not intended to replace all those models, but there is little awareness of the real impact of IDMP in the data models of the other processes.

Background: A WP-1 deliverable is the IDMP logical model requirements. IDMP extensively details some of the data models, but there is still a need for creation of other logical models—such as an ePrescription logical model—so that the data requirements of, in this case, the ePrescription can be easily "connected" or fulfilled with the data accessed through the IDMP logical model. (See Chapter 4.2.2.).

Impact consideration: Starting with logical models is not uncommon in health IT standards, but they are not available in several instances used today (i.e., ISO, HL7, IHE). Lacking logical models increases implementation and interoperability difficulties.

Several working groups (e.g., IHE Pharmacy, CEN TC251) have started to publish their information and data needs in the form of logical data models.

Proposed next step:

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.3.6.1	Logical models for ePrescription	CEN/ISO/HL7		
6.3.6.2	Logical models for Patient Summary	CEN/ISO/HL7		Available (need to incorporate IDMP)
6.3.6.3	Map/ adopt Logical models in ePrescription exchange standards (IHE)	IHE		
6.3.6.4	Logical models for Adverse Event Reporting	CEN/ISO? IHE/HL7?		

6.3.6.5	Logical models for Supply	IHE		In progress

6.3.7 IDMP and data exchange

Problem: IDMP presents a model for data structures and key concepts in identification, but it is not a data exchange technical standard. For IDMP data to be used, there is an obvious need to exchange product attributes (product master data) at the different granularity levels in all areas—regulatory but also AE reporting, supply chain and more. Today, the compatibility between IDMP and the different data exchange mechanisms is not known.

For product master data synchronisation, there is hardly implementation guidance by HL7 and IHE that supports the range of actors.

Another gap is that the IDMP model, attributes and identifiers should be supported by the clinical data exchange standards (e.g., ePrescription profiles, FHIR medication resources and others). This is an implementation gap. For example, it's not known how to include IDMP in the ePrescription. What attributes are needed in an ePrescription to enable cross-border dispense? Do those attributes replace the current ones? Is the cross-border a superset of the national prescription, or a different document altogether?

Background: This gap has been identified by the SDOs (IHE and HL7) – during the openMedicine project, the need for a technical way to exchange data became evident, and the need to exchange IHE profiles to support IDMP. There are some resources in FHIR to address the exchange of product master data in regulatory environment, and there are other resources for the exchange in more clinical settings. IHE standards support one product identifier and a few attributes, which will not be sufficient to support UNICOM needs.

Impact consideration: This will require new IHE profiles to be developed, and HL7 standards to be refined and mapped.

Proposed next steps: Conduct technical analysis of the gaps (using the logical models described in 6.3.6 and the development of the technical standards or extensions.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.3.7.1	New profile: IHE Product Catalog Profile(s) and Implementation Guidance	IHE	TBD: when is the beginning of testing?	
6.3.7.2	Profile updates: ePrescription, eDispense – update to align to IDMP and meet UNICOM needs	HL7 & IHE	TBD: when is the beginning of testing?	

6.4 Prescription and dispensation

This domain involves mainly the clinical professionals prescribing medication and the pharmacies dispensing them safely and securely. Their interactions with other domains are relevant, as depicted in Chapter 1.4.

6.4.1 eDispensing

Problem: During eDispensing, it is important to capture exactly what has been handed to the patient—detailed identification information as well as the batch/lot and serial numbers. No terminology (ATC, INN) provides an adequate level of granularity for all scenarios. The prescriber typically does not know what exactly has been dispensed. A dispense record message is missing.

Background: Depending of the country regulations, ePrescription services can vary with the authorities conveyed to pharmacists and the regulation regarding generics. This makes it difficult to track medicines, track adverse event, and manage effectively the supply chain of medicinal products. See 6.5.3

Impact consideration: Patient safety is highly vulnerable.

Proposed next step: Streamlining consistent implementation of IDMP can help bridge this gap.

Provide a list of items and attributes identified in IDMP; include product data and prescription data to added in the existing messages. Analyse identifiers (including the PhPID, DCID and its attributes), and the impact of identified attributes for the cross-border ePrescription and eDispensing. (See 4.6.2)

Create a logical model for eDispensation (CEN/ISO TS 19293).

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.4.1.1	eDispensing related items and attributes in IDMP	CEN/ISO/HL7/IHE	UNICOM Y2	
6.4.1.2	IDMP logical model for eDispensing	ISO (include in ISO TS 19293)	UNICOM Y3	

6.4.2 Adverse events and medication errors

Adverse events (AE)

Definition: An adverse event is an untoward medical occurrence in a patient or clinical investigation subject who is administered a pharmaceutical product and who does not necessarily have to have a causal relationship with this treatment. For example, this is when the right medicinal product is given to the right patient, but has an unintended, potentially harmful effect to the patient.

Problem: How to process an AE has been thoroughly documented, yet AEs can be linked to different processes when submitted by a doctor, nurse, pharmacist or patient. (See 4.5.2)

Background: The processes of documenting adverse events has not been adequately analysed, although the process is well described in legislations. There are three different terminology standards used in clinical and regulatory domains—MedDRA, SNOMED CT and EDQM Standard Terms.

Impact consideration: The lack of detailed process and structured data that bridge regulatory, clinical and consumer environments results in a lack of information in post-AE investigations. Moreover, patient safety is compromised as critical information does not find its way back to regulatory bodies.

Proposed next step: Identify the IDMP elements and attributes that are used in the documentation of adverse events. Analyse the relevant workflows and when medicinal product identifiers are used, clarify how the contributing IDMP elements and attributes are used. Develop logical models for information used in AE processes.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.4.2.1	IDMP logical data model AEs	ISO/CEN	UNICOM Y3	
6.4.2.2	AEs processes, structured data and value sets	ISO/CEN/IHE/HL7/SNOMED INTERNATIONAL	UNICOM Y3	

Medication errors

Definition: A medication error involves an unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient. In short, it is when the wrong medication is given to the wrong patient or for example when the patient forgets to take a medication, takes it too often, etc.

Problem: There is a lack of understanding about process for documenting medication errors. Medication errors are not well documented or even not documented at all.

Background: The processes of documenting medication errors has not been adequately analysed. SNODMED CT is primarily used in clinical environments, but that seems not sufficient to get standardised documentation files.

Impact consideration: The lack of detailed process and structured data that bridge clinical and consumer environments results in a lack of information in error investigations. Moreover, patient safety is compromised as critical information does not find its way back to patient electronic health records.

Proposed next step: Identify the elements and attributes of IDMP that are used in the documentation of medication errors. Analyse the relevant workflows and when medication identifiers are used, clarify how the contributing IDMP elements and attributes are captured. Develop logical models for information used in medication error processes.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.4.2.3	IDMP logical data model medication errors	ISO/CEN	UNICOM Y3	
6.4.2.4	medication error processes, structured data and value sets	ISO/CEN/IHE/HL7/SNOMED INTERNATIONAL	UNICOM Y3	

6.4.3 mHealth apps

Problem: Gain clarity on mHealth apps for adverse event reporting using IDMP and FHIR. (See 4.2.2). At the moment, it is not at all clear what is the added value of using IDMP in mHealth Apps for citizen-led adverse event reporting. This gap links back to Chapter 6.3 and to the previous gap. Furthermore, it is not clear how IDMP compatible identifiers can add value to patient-facing apps that provide information to patients.

Background: Today most patient facing mHealth apps providing information to patients on specific medicinal products are not using IDMP. This is partly due to the lack of clarity on the added value of IDMP, or for that matter, how to use IDMP and what is relevant. In other words, there is lack of awareness and lack of tools that would streamline the use of IDMP in mHealth. This applies also to HL7 FHIR-based APIs, which typically use other identifiers. The problem becomes harder when apps address virtually the same medicinal product sold under a different name in the different parts of the work (under different marketing authorisation). Moreover, the lack of structured data in electronic product information makes it difficult to fully check interactions and dependencies. Make use of AIDC technologies to capture DCID/GTIN for accessing information through mHealth app.

Impact consideration: The suboptimal identification of medicinal products in mHealth apps has adverse impact on the quality and comprehensiveness of information collected from the patients via mHealth apps. The low awareness on how to use IDMP in mHealth apps perpetuates a difficult situation.

Proposed next step: Create logical models on using IDMP to record AEs on mHealth Apps. Raise awareness and provide guidance on how to use HL7 FHIR to record IDMP-related information as part of AE reporting via mHealth apps. Raise awareness on the value of IDMP in mHealth apps that relate to management of medication lists and more broadly identify medicinal products. Clarify the relevant parts of IDMP in mHealth apps addressing specific use cases. Issue recommendations on the use of IDMP to countries developing mHealth apps—how to use identifiers of medicinal products for the quality of the app.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.4.3.1	Guidance on the use of IDMP on mHealth apps	ISO/CEN/HL7 consult WP-8	Unicom Y4	

6.4.3.2	Logical model using IDMP to record AE	CEN/ISO & HL7 Consult WP-8		

6.4.4 Regulatory and clinical domains

Problem: Identify and describe the key aspects of an IDMP implementation in the clinical domain that should rely on regulators like NCAs and EMA (e.g., composition of the medicinal product) and which aspects are relevant for separate implementations in clinical environments (e.g., standard terms, units of measurement). (See 4.5.2)

Background: IDMP was originally developed for the regulatory domain. The main use cases are marketing authorisation-related processes (e.g., initial, update) and pharmacovigilance (e.g., adverse events, medication errors). Currently, the main regulatory processes are converging with implementations of IDMP; however, the gap between the clinical and regulatory domains remains wide.

Impact consideration: The gap between the regulatory use of IDMP and the implementation of IDMP in the clinical domain does not allow for realising the benefits of connecting the two worlds, improving clinical trial management and collecting information from the patient—securely, safely and with trust.

Proposed next step: Analyse processes that bridge information between regulatory and clinical domains. Explain added value provided by IDMP elements and identifiers, and raise awareness on the benefits for emerging domains like AI, where structured data can improve quality and trust in the algorithms.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.4.4.1	Bridging Regulatory & clinical domains –quality and maturity considerations	ISO/CEN/HL7/SNOMED International WP-9	UNICOM Y4	
6.4.4.2	Use of IDMP to improve trust in AI through structured data	All WP-9		

6.4.5 PhPID and patient

Problem: The patient or the prescriber may need to identify the presence of excipients the patient could be allergic to. Using a clinical decision support system may warn the prescriber before the prescription is issued or, more generically, when it is relevant to describe some therapeutic characteristics rather than the composition of that particular product. This information is not integrated in the PhPID, but it should be possible to generate this by mapping the PhPID to well-structured National Product Dictionaries. (See 4.7.2)

Background: This specific gap relates to the ability of retrieving those substances included in the medicinal product through the national MPID and/or medicinal product dictionary, and/or the clinical decision support system.

Impact consideration: Solving this gap is contributing to patient safety, but might be beyond UNICOM's initial scope.

Proposed next step:

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.4.5	PhPID & patient safety	WP-8, T8.3		

6.5 Utilisation and outcome assessment

This domain involves mainly the patients themselves and the organisations that assess the use of medication and their (un)intended outcomes. The interactions with other domains are highly relevant, as depicted in Chapter 1.4.

6.5.1 IDMP in regulatory pharmacovigilance

ICSR from clinical practice

Problem: Sometimes, adverse drug reactions may occur from production errors, affecting isolated batches of medicinal product packages or criminal tampering with medication in the distribution. Such occurrences might be reported through the traditional pharmacovigilance system and in the ICSR along with other ADR reports, without recognising the different nature of these issues.

Background: Adding the possibility of entering the DCIN/GTIN and production identification (preferably with appropriate 2D code technology) to the ICSR could facilitate the tracing of production or dispensing problems. In case registers exist that link the DCIN/GTIN code to the IDMP identifiers (PCID, MPID, PhPID), this could further facilitate electronic reporting of adverse events.

Impact consideration: This implies no change or implementation measure for IDMP. It is for the ICSR standard to consider whether they want to take this action. UNICOM and GS1 should consider together the idea of a national portfolio of identifiers. There is no impact on the current deliverables.

Proposed next steps:

- Check the format of the ICSR for the existence of fields for GTIN and production identification.
- Create and maintain national portfolios of Identifiers (PhPID, MPID, PCID, DCID) and attributes.

#of gap	Description	Addressee /SDO	Expected timeline/ needed by	Status
6.5.1	GTIN & production identification in ICSR	GS1, ISO, ICH, WP-8	End 2021	Proposal

6.5.2 IDMP in clinical research

Drug utilisation research

IDMP and drug classification

Problem : IDMP is focused on standardising global identification of medicinal product packages. The relationship with the global identifier (PhPID_L4) and higher levels of therapeutic classification has not been established, yet.

There is the relationship with the multi-axis hierarchy of SNOMED-CT, with the 5-level taxonomy of the World Health Organization ATC and the DDD methodology. There is the relationship with a number of variable classifications of therapeutic drug classes, as used in various textbooks and drug information websites (e.g., BNF, Vidal, CBIP, Farmacotherapeutiisch Kompas and others).

Background: This endeavour will need cooperation between drug utilisation researchers, clinical pharmacologists, medical informaticians and medical educators.The link between IDMP PhPID-L4 and ATC/DDD will be very important for cross-national comparison of drug utilisation, and will assist national researchers in the first steps of calculating the number of DDD per medicinal product package. The link with SNOMED CT will be important for integration in the clinical EHR software. The development of a link between PhPID-L4 and a simple drug classification is instrumental to the UNICOM deliverables from WP-8.1 (drug classification) and WP-8.3 (IDMP and patient-facing apps).

It might be necessary to provide an intermediate level of abstraction for the concept of INN prescription, between the PhPID_L4 and the hierarchy of pharmacotherapeutic drug classes. The grouping of PhPID_L4s with the same ATC/DDD code and units could be helpful in this respect. This would also be instrumental to clarifying the concept of substitution

Impact Consideration: The resolution of this gap will strengthen the relationship with WHO (UMC and Oslo), and with the SNOMED International. It will facilitate and expedite deliverables of WP-8, if completed by 2021.

Proposed next steps:

- Formalise collaboration with WHO in the UNICOM product pilot list, with global PhPID-L4 and link to ATC/DDD in scope, and the link to SNOMED CT substances.
- Expedite UNICOM T8.1.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.5.2.1.1	Link IDMP/drug classification	I-HD, SNOMED	12/2021	Proposal

IDMP and PCID pack size

Problem: IDMP identifies units of presentation and pack size. However, units of presentation is a limited term, which may not support all variations of transformation of the pharmaceutical dose form to administrable dose form and of administration instructions (e.g.,

ophthalmic preparation in gel or in ml/drops). Moreover, the implications of the product description for the structured signature (the second line of any prescription, with instructions to patients on how to take the medication), has not been in scope of the implementation studies.

Background: The new ISO 17251 under revision on structured dosing instructions, and the ontology of EDQM for dosing forms and units of presentation, needs to corroborate for new fields of application. This is ultimately important for individual stock management (alerts when prescriptions need to be renewed) and for calculation of the medication possession rate (the number of days between refills and expected treatment days, based on individual posology) for clinical follow-up and research on patient adherence to therapy.

Implementation consideration: This item will need a coordinated action in WG6 of ISO for quick resolution and consistency between several ISO standards.

Proposed next steps:

- Inform the ISO group on structured dosing information (ISO TS 17251).
- Analyse units of pack size and dosing instructions in a number of national drug dictionaries.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.5.2.1.2	IDMP and Pack size	Logical model IDMP/e-prescription	12/2021	PROPOSAL

IDMP and reimbursement regulation

Problem: Reimbursement rules have become of the utmost importance in healthcare management and in the implementation of Health Technology Assessment recommendations. It is crucial that efforts to integrate reimbursement regulation (often complex legislation and procedural rules) into EHR systems, with tight integration to the Medicinal Product Dictionaries and IDMP.

Background: Medicinal Product Dictionaries not only have to implement the flow of information of the NCA for marketing authorisation, but also the health Insurance regulation with regard to pharmacotherapy, with global PhPID_L4, but also national PCIDs in a pivotal role.

Implementation consideration: This is not really in scope of UNICOM, but in a number of participating countries this integration of marketing authorisation and reimbursement regulation has been implemented. It would be instrumental to other European countries to be provided with some examples of successful dual implementation with integration of IDMP.

Proposed next steps:

- Identify the countries with successful dual implementation within UNICOM (based on T9.1).
- Study the impact of integration of IDMP with reimbursement information.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.5.2.1.3	IDMP and Reimbursment Regulation	Ehealth Partners UNICOM	2022	PROPOSAL

IDMP and ontology of dosage forms

Problem: For some scientific applications, higher levels of abstraction of dosage forms are needed than those currently described by EDQM. For the determination of polypharmacy (defined as five or more chronic medications with systemic action taken by one patient), an aggregation of dosage forms with or without systemic action is needed. Different oral forms (tablets, capsules, solutions) leading to the same dose might need to be aggregated.

Impact considerations: While this item is not crucial for the successful finalisation of the project, it might greatly contribute to its clinical relevance. It is synergistic.

Proposed next steps:

- Better coordination with EDQM within WP-1 (as EDQM can be considered as an SDO).

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.5.2.1.4	IDMP and dosage forms	EDQM	8/2021	PROPOSAL

IDMP and quantification of import/export/utilisation

Problem: The ESAC project has clearly demonstrated that national drug utilisation data can be biased by parallel export (leading to an over-estimation of local consumption, if taken into account for national consumption) and by parallel import (leading to under-estimation, if not taken into account).

Background: While precautions have been made to safeguard parallel import/export from falsification, steps need to be taken to understand the dynamics of parallel import/export in different origins and target countries, and their impact on national statistics. This issue could also be linked to the international ordering of medicinal products, not available in the country. (See proposals of the Irish Pharmacist Association.)

Impact considerations: While not critical for the further development of IDMP in UNICOM, progress in this matter will be perceived as an achievement of the UNICOM project.

Proposed next steps:

- Identify PhPID-L4 for which parallel trade is of substantial volume.
- Develop a case study in a cluster of origin/target countries.
- Develop a case study with the Irish National Pharmacy Association.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.5.2.1.5	IDMP and Import/export	GS1, EFPIA	2022	PROPOSAL

Pharmaco-epidemiology

IDMP and common data models in big data projects

Problem: As real-world data in healthcare is really growing, many networks are emerging that collect data from data marts in healthcare facilities or operating with distributed analytics sent to local data marts. Most of these systems work with a common data model. Examples include the European Health Data & Evidence Network (EHDEN) that implements a OMOP data model in the EU; the Observational Health data Sciences and Informatics (OHDSI) programme that is a multi-stakeholder scientific collaborative doing large-scale analysis of health data; the National Patient-Centered Clinical Research Network (PCORnet); Sentinel used by the US FDA for medical product monitoring; and the MIMIC Critical Care Database. Representation of drug identification and dosing information in these common data models is often rudimentary and might improve considerably with the global adoption of PhPID.

Background: Awareness of IDMP among the leaders of these international and national data networks is limited.

Implementation consideration: This is a crucial issue in the dissemination of IDMP in data handling systems.

Proposed next steps : Establish communication between T8.2 and international health data networks.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.5.2.2.1	IDMP and common data models	ISPE, UNICOM	2021	PROPOSAL

IDMP and structuring of diagnoses

Problem: Measuring exposure to medicine is related to the recording of the diagnosis for which the medication has been prescribed. Medications have approved lists of indications, which may vary by jurisdiction and by company). Standardisation of relevant indications per PhPID_L4 with appropriate terminology binding to SNOMED CT, ICD, ICPC is lacking.

Background: An ISO group on clinical particulars is working on the issue of structured diagnoses (revision ISO 17251).

Implementation consideration: It is important to convince the experts involved in structuring diagnoses to consider IDMP as an important tool. Therefore, arriving at credible achievements within the timeframe of UNICOM is needed.

Proposed next steps: Create a liaison with the new working item on structured diagnoses in clinical particulars.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.5.2.2.2	IDMP and Diagnoses	WHO, SNOMED International	2023	PROPOSAL

IDMP and structuring of outcome information

Problem: Pharmaco-epidemiology studies the relationship between exposure and outcome (benefit or harm) in databases, using rigorous scientific methods.

Background: The assessment of outcome in databases is a crucial issue. Harm is traditionally measured in pharmacovigilance with MedDRA; however, only used in the regulatory domain. (SNOMED CT is the preferred terminology for the clinical domain). Outcomes as considered in clinical trials are dealt with within CDISC; however, only in the context of pharmaceutical research, not in clinical care. Standardisation of patient-relevant outcomes is under development with the International Consortium for Health Outcome Measurement (ICHOM).

Implementation Consideration: This is a long-term objective for UNICOM, to be developed for the follow-up of the project

Proposed next steps: Conduct a systematic review of standardisation efforts.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.5.2.2.3	IDMP and outcome	WHO, ICHOM, SNOMED International, ICD, MEDDRA	2023	PROPOSAL

IDMP and clinical trials

IDMP and CDISC

Problem: Clinical research in drug development is conducted on investigational medicinal products, awaiting marketing authorisation. Coordination of the identification in the transition of experimental to authorised medicinal product needs improvement. Registration of concomitant medication in international multi-centre trials can be burdensome.

Background: Cooperation between UNICOM and CDISC is not explicitly foreseen in the UNICOM description of action. Engage with regulators (e.g., EMA, US FDA) on this specific question.

Implementation Consideration: This is a long-term objective for supporting the impact of UNICOM.

Proposed next steps:

- Create a liaison with CDISC.
- Assess impact of co-medication documentation in clinical trials with WHO UMC.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.5.2.3.1	IDMP and Clinical trials.	CDISC	2023	PROPOSAL

6.5.3 Supply chain

IDMP and a portfolio of identifiers, including DCID/GTIN

Problem: Identifiers in the supply chain have different life cycles than identifiers in the regulatory process and prescription activities. A register linking these two life cycles can only be maintained at the national level.

Background: Incorporating PhPID, MPID, PCID and DCID/GTIN keys in a portfolio governed by the NCAs can assure this link. The presence of the PhPID can facilitate international cooperation, probably using semantic health principles and linked open data approaches.

Implementation consideration: Given the importance of such a portfolio for use cases operation in the second half of the project, workable portfolios should be established for a few exemplary countries, involved in cross-border ePrescription use cases.

Proposed next steps :

- Create such a portfolio for the UNICOM pilot product list.
- See as well 6.1.5.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.5.3.1	IDMP and portfolio of identifiers	UNICOM, GS1	12/2021	

DCID/GTIN and dispensing records

Problem: Securing that a medicinal product is not dispensed / administered to a patient in the case of recall (by batch) or withdrawal.

Background: Support prescription process with medicinal product's barcoded identifier (DCID/GTIN, on primary packaging), e.g., to link product's identifier (DCID/GTIN) and individual dispensing/nursing record. Fulfil the need to know exactly what has been administered to the patient, using AIDC scanned at points of care and captured in electronic health records.

Impact consideration: Patient safety can be negatively affected.

Proposed next step: Improve communication on the available ISO standard (CEN/ISO TS 19293).

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.5.3.2	DCID/GTIN and dispensing records	CEN/ISO		

DCID/GTIN and national registries

Problem: Traceability is a challenge for multi-country packaging, e.g., same DCID/GTIN linked to different marketing authorisations and PCID.

Background: Need to secure consistencies between medicinal product master data from the supply chain, including a verification system against falsification and regulatory master data such as SPOR.

Impact consideration: Inconsistencies are cost intensive for all stakeholders and increase the risk of product confusion.

Proposed next step: Develop a process map.

#of gap	Description	Addressee/SDO	Expected timeline/ needed by	Status
6.5.3.3	DCID/GTIN and national registries	EMVO		

7 Conclusion

The expansive number of entries in this gap analysis provides some insights about the development of standards and their subsequent implementations. It highlights the importance of standard development organisation collaboration such as the Joint Initiative Council (www.jointinitiativecouncil.org) and the need for better communication between SDOs and implementers in the sense of feedback loops.

The gaps reveal the challenges of making standards "work" in real-world use cases. Standards may (or may not) need to be adjusted based on these identified gaps that may occur along their normal life cycles of development, implementation and maintenance (revisions).

Regulatory and clinical domains are complex. As implementers have questions that need answers or face issues that require guidance, an ongoing community of expertise is needed for continuous knowledge sharing, support and standards improvements.

The identified gaps are simply the first steps of an ongoing journey of exploring the potential of the IDMP suite of standards—their development, implementation and use within global healthcare systems.

8 Abbreviations

ADR	Adverse Drug Reaction
ATC	Anatomical Therapeutic Chemical Classification
BAID	Medicinal Product Batch Identifier (BAID1 : outer packaging, BAID2: immediate packaging)
BRIDG	The Biomedical Research Integrated Domain Group Model
CDA	HL7's Clinical Data Architecture
CMC	Chemistry Manufacturing and Control
CV	Controlled Vocabulary
DCID	Data Carrier Identifier (e.g. GTIN)
EDQM	European Directorate for the Quality of Medicines & HealthCare
EEA	European Economic Area
EHDEN	European Health Data Evidence Network
EMA	European Medicines Agency
EP	Electronic Prescription
epSOS	European Patients Smart Open Services
ESAC	European Surveillance of Antibiotic Consumption
GTIN	Global Trade Item Number
HCP	Health Care Professional
IBAID	Investigational Medicinal Product Batch Identifier
ICH	International Council on Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICHOM	International Consortium for Health Outcome Measurement
ICPC	International Classification of Primary Care
ICSR	Individual Case Safety Report
ID	Identifier
IDMP	Identification of Medicinal Products
IMDRF	International Medical Devices Regulators' Forum
IMP	Investigational Medicinal Product
IMPID	Investigational Medicinal Product Identifier
INN	International Non-Proprietary Name
IPCID	Investigational Medicinal Product Package Identifier
IPS	International Patient Summary
MAH	Marketing Autorisation Holder
MMP	Multi-Market pack
MPID	Medicinal Product Identifier
NCA	National Competent Authority
NTIN	National Trade Item Number (a category of GTIN)
OHDSI	Observational Health Data Sciences and Informatics https://www.ohdsi.org/data-standardization/the-common-data-model/
OID	Object Identifier
OMG	Object Management Group
OMOP	Observational Medical Outcomes Partnership
PCID	Medicinal Product Package Identifier
PCORNET	National Patient-Centred Clinical Research Network
PhPID	Pharmaceutical Product Identifier

PhV	Pharmacovigilance
SKU	Stock Keeping Unit
SMP	Single-Market Pack
SNOMED CT	SNOMED Clinical Terms
SPC/SmPC	Summary of Product Characteristics
SPOR	Substance, Product, Organisation, Referentials
UDI	Unique Device Identification Code (IMDRF)
WHO	World Health Organization
WHO-DD	WHO Drug Dictionary
XEVMPD	Extended EudraVigilance Medicinal Product Dictionary

9 Annex: standards

9.1 Published standards

9.1.1 CEN/ISO standards

The CEN/ISO series of standards include the following standards (non-exclusive list):

- EN ISO 11240 – Identification of medicinal products — Data elements and structures for the unique identification and exchange of units of measurement – published 2012, and confirmed 2020.
- EN ISO 11239 - Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation, routes of administration and packaging (published 2012) and its companion CEN/ISO TS 20440 Identification of medicinal products — Implementation guide for ISO 11239 data elements and structures for the unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation, routes of administration and packaging (published 2016)
- EN ISO 11238 - Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated information on substances and its companion CEN/ISO TS 19844Identification of medicinal products (IDMP) — Implementation guidelines for ISO 11238 for data elements and structures for the unique identification and exchange of regulated information on substances, both published 2018
- EN ISO 11616 - Identification of medicinal products — Data elements and structures for unique identification and exchange of regulated pharmaceutical product information and its companion CEN/ISO TS Identification of medicinal products — Implementation guidelines for ISO 11616 data elements and structures for the unique identification and exchange of regulated pharmaceutical product information, both published 2017
- EN ISO 11615 - Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated medicinal product information and its companion CEN/ISO TS 20443 - Identification of medicinal products — Implementation guidelines for ISO 11615 data elements and structures for the unique identification and exchange of regulated medicinal product information, both published 2017
- CEN ISO/HL7 27953 - Individual case safety reports (ICSRs) in pharmacovigilance — Part 1: Framework for adverse event reporting and Part 2: Human pharmaceutical reporting requirements for ICSR, both published 2011 and confirmed
- EN ISO 17523 - Requirements for electronic prescriptions, published 2016
- CEN/ISO TS 19256 - Requirements for medicinal product dictionary systems for health care, published 2016
- CEN/ISO TS 16791 - Requirements for international machine-readable coding of medicinal product package identifiers, published 2014, new version to be published 2020
- CEN/ISO TS 19293 - Requirements for a record of a dispense of a medicinal product, published 2018
- ISO/TS 17251 - Business requirements for a syntax to exchange structured dose information for medicinal products

9.1.2 HL7 standards

The following list includes a non-exhaustive set of different types of HL7 publications (Informative[8], standard for trial use (STU)[9], or Normative) relevant for the scope of this project. It includes only universal non-retired standards and it has a hierarchical structure with base standards on the first level and other products (e.g. implementation guides, profiles) based on a specific base standard added as children.

- FHIR® R4 (HL7 Fast Healthcare Interoperability Resources, Release 4) (4.0.1) [Normative/STU]. This version includes the first FHIR normative resources. For the scope of this document the most relevant resources are those belonging to the 'Medications' (FHIR maturity levels[10] from 0 to 3) and 'Medication Definition' (FHIR maturity levels 0) categories.
    - HL7 FHIR® Profile: Pharmacy; Medication, Release 2 [STU]
    - HL7 FHIR® Implementation Guide: International Patient Summary, Release 1 [STU]
- CDA® Release 2 and CDA® R2.1 (HL7 Clinical Document Architecture, Release 2.1). [Normative]
    - HL7 CDA® R2 Implementation Guide: Pharmacy Templates, Release 1 [STU]
    - HL7 CDA® R2 Implementation Guide International Patient Summary, Release 1 [STU]
- HL7 Version 2 Product Suite (several versions still in use; latest published version is V2.9) [Normative]
- HL7 Version 3 Product Suite [Normative/STU]
    - HL7 Version 3 Standard: Common Product Model (CPM) CMETs, Release 4 [Normative]
    - HL7 Version 3 Standard: Structured Product Labeling Release 8 [Normative]
    - HL7 Version 3 Standard: Pharmacy CMETs [Normative]
    - HL7 Version 3 Standard: Pharmacy: Medication Dispense and Supply Event, R2 [Normative]
    - HL7 Version 3 Standard: Pharmacy; Medication Knowledge-Base Query, Release 1 [Normative]
    - HL7 Version 3 Standard: Pharmacy; Medication Order, Release 2 [Normative]
    - HL7 Version 3 Standard: Pharmacy; Medication Statement and Administration Event, Release 1 [Normative]
    - HL7 Version 3 Standard: Pharmacovigilance - Individual Case Safety Report, Part 1: The Framework for Adverse Event Reporting, R2 [Normative]
    - HL7 Version 3 Standard: Pharmacovigilance - Individual Case Safety Report, Part 2: Human Pharmaceutical Reporting Requirements for ICSR, R2 [Normative]
    - HL7 Version 3 Standard: Regulated Studies; Regulated Product Submissions (RPS), Release 2 [Normative]
- HL7 Electronic Health Record System Functional Model (EHR-S FM) Release 2.1 [Normative]; ISO/HL7 10781:2015(en) Health Informatics — HL7 Electronic Health

[8] An *Informative* document is "the product of a Work Group that is not currently deemed normative, but nonetheless is intended for general publication." [HL7 GOM]

[9] A *Standard for Trial Use* (STU) is a standard "released for use to refine and enhance its content through demonstrations of interoperability" before becoming normative. Known in the past as "Draft Standard for Trial Use (DSTU)", the DSTU term has been recently discontinued because HL7 no longer produces "Draft" Standards. [HL7 GOM]

[10] More details about the FHIR maturity level here https://www.hl7.org/fhir/versions.html#maturity

Records-System Functional Model, Release 2 (EHR FM). Not all the profiles listed below refer to the above-mentioned releases:

- HL7 EHR-System ePrescribing Functional Profile, Release 1 [Informative]
- HL7 EHRS-FM Release 2: Immunization Functional Profile, Release 1 [Normative]

- HL7 EHR-System Implementation Guide: Pharmacist/Pharmacy Provider Functional Profile for Community Practice, R1 [Informative]

9.1.3 Terminologies

Terminology standards deliver a *type of a content* rather than an architecture (e.g., IDMP or ePrescription). Because of this characteristic, terminologies—which are structured in a stable manner—are continuously evolving.

Following is a brief summary of the terminologies used or impacted by UNICOM.

SNOMED CT

SNOMED International is a multinational, Member-based, not-for-profit organization that owns, administers and develops SNOMED CT, the world's most comprehensive clinical terminology product. SNOMED International through its membership represents 28% of the world's populations, not including the large number of affiliate licenses in place.

SNOMED CT is a clinically validated, semantically rich vocabulary that enables users to share health information in an unambiguous manner within and across healthcare settings. SNOMED CT supports users in organizing, querying and analysing data, thus supporting interoperability across a broad range of settings and geographies.

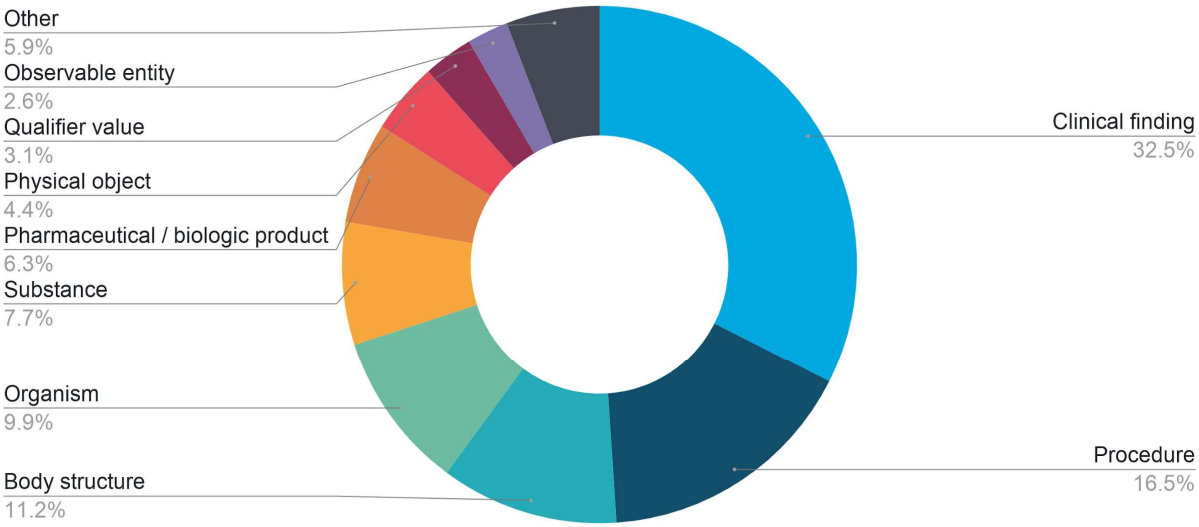
Intended for use in electronic health records, SNOMED CT's 350,000+ clinical concepts support the development of comprehensive high-quality clinical content in health records, providing a standardized way to represent clinical phrases captured by the clinician and to automatically interpret them.

Every concept represents a unique clinical meaning, which is referenced using a unique, numeric and machine-readable SNOMED CT identifier. This approach supports data interoperability across systems and over time, thus providing support longitudinal analysis. Each concept is supplied with a unique Fully Specified Name, which provides a human-readable unique description for each concept. Further descriptions are made available as synonyms, the number of which are specified by individual clinical use cases. The use of synonyms also provides a mechanism to supply translations to support implementations.

SNOMED CT scope of content coverage:

SNOMED CT is not just a coding system of diagnosis. It also covers other types of clinical findings like signs and symptoms. It includes tens of thousands of surgical, therapeutic and diagnostic procedures. It includes observables (for example heart rate), and also includes concepts representing body structures, organisms, substances, pharmaceutical products, physical objects, physical forces, specimens and many other types of information that may need to be recorded in or around the health record.

SNOMED CT descriptive statistics



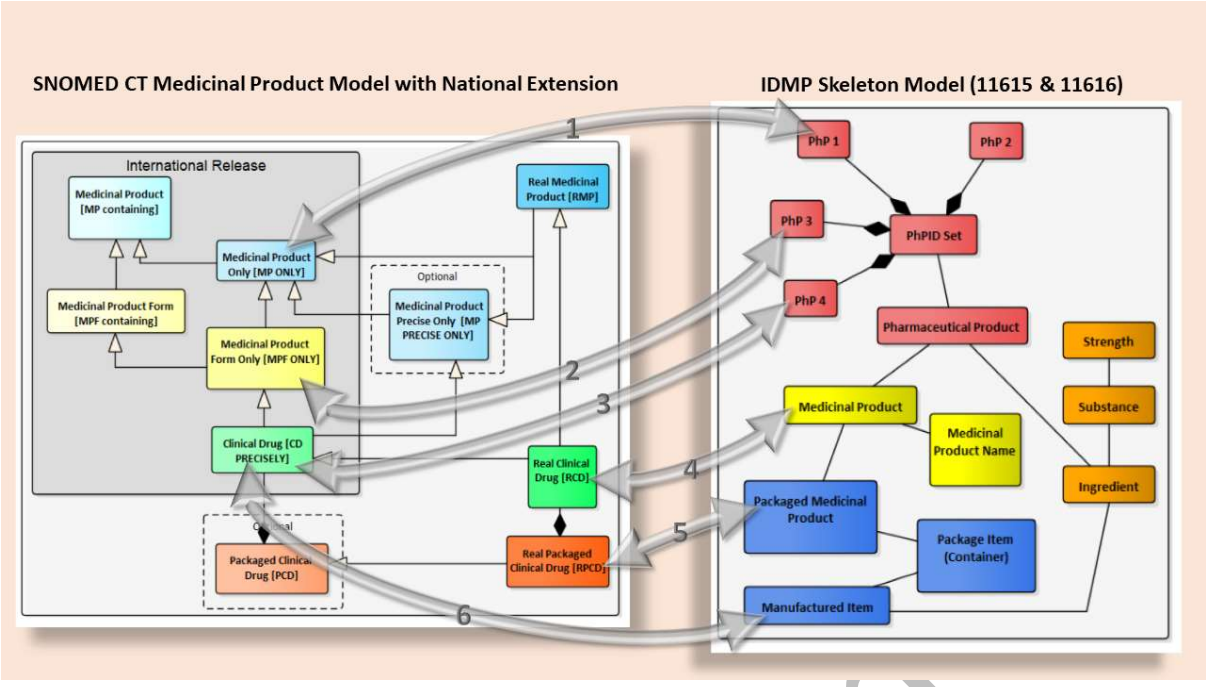
Working with other SDOs

SNOMED International works collaboratively with many other organizations who produce health informatics standards as well as professional bodies who can validate clinical content. The focus of all collaborative work is to support interoperability, avoid duplication of standards and provide solutions which ensure semantic meaning is maintained. Examples of key collaborations are with HL7 International, IHE and DICOM as well as clinical bodies such as the American Dental Association (ADA) and International Council of Nurses (ICN).

SNOMED CT support for the representation of drugs and alignment with the Identification of Medicinal Products (IDMP)

SNOMED International, in collaboration with its Member countries, has developed a logical model to represent the key components of a drug product. The model has a scope within the International Release to the generic level and is also supplied with an extensible logical model for detailed representation of drugs at a national level. The logical model has been developed to align with the IDMP and is documented accordingly. Information on this model is available to the UNICOM project.

Medicinal products are described in the International Edition of SNOMED CT in five different levels of abstraction. IDMP standards and the SNOMED CT Medicinal Product hierarchy are designed to support different domains with differing use cases; the former the regulatory domain, the latter the patient care domain. However, there is significant harmony and synergy between them, as demonstrated in the diagram following:



SNOMED CT in use

SNOMED CT has a role to play in care ecosystems that need information to flow effectively, efficiently, and accurately across all care settings, including hospital, family practice and social care, covering all specialty domains and disciplines and responding to requirements to support areas such genomics, precision medicine and clinical research. This can then support data collection activities and extends to in-depth data analysis. SNOMED CT supports a wide variety of care processes such as referrals, e-prescribing and medication management, and population health management, among others.

Product development and release process

SNOMED CT can be considered an ecosystem within which a number of releases are delivered to Members, affiliates and users globally throughout the course of the year. Although most clinical concepts are relevant in most countries, organizations and specialties, some concepts are relevant only to a particular environment.

Product releases

SNOMED International has a number of products that are released according to a predetermined and agreed upon schedule each year:

- The **SNOMED CT® International Edition** is released to Members and Affiliates in non-member countries on January 31 and July 31 each year after undergoing an extensive Member review and feedback process.
- **SNOMED CT Spanish Edition**: Contains the Spanish language version of the SNOMED CT® International Edition and is released in April and October following the SNOMED CT® International Edition release.
- **Member extensions**: A benefit of SNOMED International membership is the ability to create a SNOMED CT national extension to reflect local policy and priorities through structured terminology.

- **Global Patient Set**: The Global Patient Set (GPS) is a managed collection of existing SNOMED CT reference sets released by SNOMED International available at no cost and licensed under the Creative Commons Attribution 4.0 International License.

Responding to the global need for terminology – interim release

In March 2020, SNOMED International announced an interim release of the SNOMED CT International Edition outside of its customary release cycle to include updated COVID-19 content to support ongoing global efforts related to the pandemic. It also included that COVID-19 content in the free for use Global Patient Set (GPS) referenced above.

SNOMED CT derivative products

These products are derived from SNOMED CT® International Edition content and are maintained and distributed to Members and Affiliates in non-member countries by SNOMED International. Derivative products include:

- Clinical Reference sets such as HL7 International Patient Summary (available free for use), Nursing Activities and Health Issues and General Dentistry Diagnosis
- Maps provide a linkage between terminologies such as SNOMED CT to ICD-10 and ICD-O, SNOMED CT to GMDN, SNOMED CT to Orphanet and the two maps currently at Alpha release between SNOMED CT and MedDRA and vice versa. This supports interoperability and the movement of data.
- Free sets: A specific type of Derivative product, these contain only the SNOMED CT identifier (SCTID) and fully specified name (FSN) for each record in the refset, and so can be distributed to anyone with or without a license. These include DICOM standards content and IHE profile content sets.

Other terminologies

- ATC/DDD: The Anatomical Therapeutic Chemical (ATC) classification system and the Defined Daily Dose (DDD) as a measuring unit. Intended for drug utilization monitoring and research in order to improve quality of drug use. Maintained by WHO Collaborating Centre for Drug Statistics Methodology.
- ICD: International Classification of Diseases is a diagnostic classification standard for clinical and research purposes. Uses include health care statistics/disease burden, quality outcomes and mortality statistics. Maintained by the World Health Organization.
- INN: International Non-proprietary Names facilitate the identification of pharmaceutical substances or active pharmaceutical ingredients. Maintained by the World Health Organisation.

9.1.4 IHE standards

Integrated the Healthcare Enterprise (IHE) develops integration profiles that assemble various standards in order to answer specific user needs. It has been described in three ISO technical reports: ISO/TR 28380; Health informatics; IHE global standards adoption, part 1: processes, part 2: integration and content profiles, and part 3 deployment. In IHE pharmacy domains, several IHE profiles are already available and can be selected for deployment at the local, national/regional and cross-border levels. IHE distinguishes content profiles (such as the

prescription profile PRE) from workflow profiles such as the workflow that integrates the prescription, the validation of the medication and the dispensation in the ambulatory sector. IHE CMPD.

By design in IHE, these profiles are agnostic in term of medication identifiers. Any code can be used to identify a medicinal product. However, because the profiles are using "base standards" such as HL7 v2, CDAr2 and HL7 FHIR, a precise evaluation of needs has to be produced before updating the content and workflow profiles. The task is to better describe the medication in those "base standards" and, thereafter, in the profiles.

The main IHE profiles that are expected to require updates to accommodate the cross-border identification of products using IDMP are:

- MTP - Community Medication Treatment Plan records the planning of medication to a patient.
- PADV - Community Pharmaceutical Advice records a pharmaceutical advice;
- PRE - Community prescription.
- IHE DIS - Community Dispense – which records the dispensation of medication for a patient.
- IHE CMA - Community Medication Administration - records the administration of medication.
- PML – Pharmacy Medication List carries the full record or medication for the patient - planned, prescribed, dispensed or administered medication to patient, overlapping supporting the needs for Patient Medication Summary.
- CMPD – Community Medication Prescription and Dispense integrates the prescription, the validation of the medication and the dispense in the ambulatory sector.
- MMA - Mobile Medication Administration – a FHIR-based profile that allows registering administration of medication across different solutions – from traditional EHR systems to patient mobile applications.
- UBP – Uniform Barcode Processing – this profile allows the use of barcodes and identifiers in clinical or logistics workflows.

Anticipated changes include:

- For all of the profiles, notably PRE (community prescription), DIS (community dispense) and PML (pharmacy medication list), and by consequence all the others, the changes are in the identification and description of the product itself. Adding new identifiers or attributes and constraining terminologies will further improve cross-border interoperability.
- In some cases, like the PML (pharmacy medication list), the changes may be more substantial to accommodate the notion of Medication Summary where the PML profile provides a detailed list, the patient summary only uses a summary view, and this compatibility must be checked.
- In the workflow-related profiles (CMPD – community medication prescription and dispense and MMA – mobile medication administration), some changes may be expected to enable workflow continuity (e.g., status updates).
- For the FHIR profiles (currently only MMA - mobile medication administration and UBP – uniform barcode processing), the changes will be aligned to the base standard (FHIR), and will be taken up by the present and future IHE profiles, to produce a standard way to handle product identifiers and attributes.

- For MMA (mobile medication administration) and UBP (uniform barcode processing) specifically, the product can be identified via a barcode, which is typically an IDMP "data carrier identifier."
- It is assumed that IDMP will not be deployed within hospitals in the short term, so the hospital pharmacy profiles will not be impacted. If this assumption changes, the impact of the changes is similar in efforts as for the community profiles.

9.2 Standards currently in revision

9.2.1 CEN/ISO standards

The following standards are currently in revision process. Purpose of the revision is indicated for the sake of clarity:

- EN ISO 11239 - Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation, routes of administration and packaging (published 2012) and its companion CEN/ISO TS 20440 Identification of medicinal products — Implementation guide for ISO 11239 data elements and structures for the unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation, routes of administration and packaging.

  By fully respecting backward compatibilities, there is a need expressed by some regulators to dispose of a simplified way to implement this standard. This shall impact the calculation of PhPID, and there for facilitate IDMP adoption.

- CEN/ISO TS 19844 Identification of medicinal products (IDMP) — Implementation guidelines for ISO 11238 for data elements and structures for the unique identification and exchange of regulated information on substances.

  Adoption of global substance identification is facing difficulties, thus impacting PhPID calculation. The purpose of this revision is to add a new annex to the CEN ISO implementation guide, enabling unique identification of substances based on a simplified representation of these.

- EN ISO 11615 - Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated medicinal product information.

  Purpose of this revision is to add an annex with translations and synonyms, reviewed by the respective regulators, in a large series of languages. The core standard is not addressed by this revision.

- ISO/TS 17251 - Business requirements for a syntax to exchange structured dose information for medicinal products.

  Purpose of the revision is to adapt this technical specification to the latest IDMP standards.

9.2.2 HL7 standards

HL7 standards are subject to a continuous maintenance process and periodic revisions/re-affirmation. The following is a list of relevant standards in revision, or for the latter, under development. It does not include the normative standards that will be subject to re-affirmations.

- HL7 FHIR® R5 (http://build.fhir.org/). This version includes a substantive revision of the IDMP related resources under the "Medication Definition" category.
- HL7 FHIR® Profile: Pharmacy; Medication, Release 2 [STU]
- HL7 FHIR® Implementation Guide: International Patient Summary, Release 1 [STU]
- HL7 CDA® R2 Implementation Guide: Pharmacy Templates, Release 1 [STU]
- HL7 CDA® R2 Implementation Guide International Patient Summary, Release 1 [STU]
- FHIR Implementation Guide for ICSR Submissions [project under approval]

9.2.3 Terminologies

SNOMED CT

There is a requirement to be continually reviewing, maintaining and updating SNOMED CT since clinical terminologies need to be up to date whilst also supporting the use of historical data over time. Thus, it could be said that SNOMED CT is constantly in revision – from both a clinical content perspective as well as design and technical application perspective.

SNOMED International is committed to maintaining the quality of SNOMED CT. Extensive technical work is undertaken using a specifically designed set of open-source tooling, performing an extensive set of quality assurance processes, overseen by a dedicated technical team.

A dedicated team of SNOMED International clinical authors, with input from external collaborative editors, delivers the annual authoring plans and five-year roadmap that details specific developments as required by Members and other stakeholders. Through our current focused Quality Initiative, we adopt a greater focus on correcting structural anomalies as well as modification of content, resulting in a higher level of clinical accuracy. To widen the quality footprint, content quality assurance is also addressed through ongoing clinical review of current content and specification of requirements for new content, provided through our Clinical Reference and Project Groups. Specific work relevant to UNICOM is 1) Ongoing work on revision of substances, enabling a clear differentiation between Substances and Products, 2) Vaccines, differentiating and clarifying difference from immunization concepts and ensuring content is clinically relevant and 3) Work on clarifying terms related to allergies, poisoning and toxicity with relevant links to substances.

SNOMED International coordinates requests for additions or changes to SNOMED CT through its Members' National Release Centers (NRCs). Members' NRCs and other authorized users submit requests for additions or changes via the SNOMED CT Content Request Service (CRS). Requests that meet inclusion criteria for the International Release are addressed by SNOMED International staff. If a request is declined, a reason and explanation is provided to the requester, who may choose to appeal the decision to the Head of Terminology

The derivative products (maps, reference sets, free sets) are managed on an annual cycle. SNOMED International works with owners to manage existing content in the derivatives and add new content. In addition, we work with collaboration partners to ensure that any agreed content or artefacts are maintained and updated over time to reflect agreed use cases.

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9.2.4 IHE standards

The IHE Pharmacy profiles are relatively stable and current IHE Pharmacy efforts are to align with the base standards – HL7, GS1, ISO – to prepare the new generation of profiles.

9.3 Future standards

9.3.1 CEN/ISO standards

ISO TC 215, WG 6 is preparing:

- A standard as "IDMP logical model", which will be based on the requirements collected within the UNICOM project; it is planned to start this project as soon as the UNICOM deliverable will be available
- A standard on "Clinical particulars – Core principles for the harmonisation of indication terms and identifiers"" is in ballot as a new project during summer 2020.
- Standardisation of terms and mappings between internationally accessible standard vocabularies would enable efficient responses and comprehensive reporting and support a deeper and more consistent understanding of diseases.

9.3.2 HL7 standards

- HL7 FHIR Order Catalogue Implementation Guide (https://build.fhir.org/ig/HL7/fhir-order-catalog/) [on going project]
- HL7 FHIR IG Patient Medication List Guidance. Based on FHIR R5 [on going project]

9.3.3 Terminologies

SNOMED CT

The next evolution of SNOMED CT will benefit Members, governments and other stakeholders by allowing advanced technologies such as Artificial Intelligence, Natural Language Processing and Machine Learning to leverage SNOMED CT as a platform on which to develop new solutions for patient care.

As well as continuous maintenance and updating, new areas of content coverage are on the work plan including more extensive coverage of phenotypes to support genomics, feeding in to the need for precision medicine and some initial traditional medicine content. Of relevance to UNICOM is plans towards aligning dose forms in the clinical space with those supported by IDMP/EDQM along with other initiatives in ISO WG 6 which impact on the clinical domain such as Clinical Particulars.

Underpinning the need for content development and engaging with experts globally within member countries, clinical bodies and others, we are already exploring distributed editing which will facilitate the development of content outside the current processes that can then feed in to SNOMED CT International edition as required globally.

Within the scope of the organization's 2020-2025 strategy, evolving the SNOMED CT product is representative of positioning SNOMED CT's global terminology as a service delivering continuous releases, actioning the holistic vision for content categorization, and assessing and addressing gaps in current SNOMED CT content. This is in addition to any new/emerging

requirements that deliver interoperable solutions working with other organisations, projects and globally relevant initiatives.

Within the scope of the UNICOM standards group, we aim to support our Members and wider stakeholders so that they can implement the requirements by regulators for use of IDMP based on integration with the standards they are already committed to using in order to deliver regulatory requirements -- providing benefits at local, regional and national levels.

9.3.4 IHE standards

With the stable profiles in IHE Pharmacy (CDA profiles have evolved slightly, HL7 v2 profiles have not been challenged for changes), IHE Pharmacy works in 3 directions:

- Cover the entire spectrum of medication data exchange with reference standards-based specifications:
    - Clinical workflows (prescription, medication lists, dispense, adverse event reporting)
    - Supply and product tracking
    - Master Data Management (product catalogue)
- Incorporation of other standards to guarantee the continuum of interoperability – namely GS1 for the Supply Chain and Product Identification.
- Adoption of emerging standards like FHIR and IDMP when adequate

The first aspect is potentially influenced by (and influencing) UNICOM, because UNICOM requires data exchange beyond the Prescription/Dispense workflows – specifically supply, adverse event reporting, medication lists, and most clearly the Product Catalogue (also known as Formulary) which is evidently a core need for UNICOM.

Also, the incorporation of other standards like GS1 is related to UNICOM as it allows a proper identification of the products (for example via barcodes) not only in the supply chain but also in the clinical flows. For example, if a patient goes to the Emergency Department when visiting another country, taking with them the medication boxes that were dispensed in their home country, the barcode in the box can be essential in capturing the product identification in a way it can be converted to a concept that can be used in that country.

The adoption of FHIR and IDMP has also an impact: FHIR as a technical implementation mechanism and IDMP as a reference model for medicinal product information. Potentially also some terminologies would be defined which can influence the roadmap of IHE Pharmacy.

IHE Roadmap: IHE Supply of Products for Healthcare – this IHE White Paper and upcoming Profile describe the link between the clinical world and the logistics world.

Opportunity for cross-border identification: in the Supply workflows, which are commonly cross-border, a unique identifier is available (e.g. GTIN). IDMP is not expected to change the supply chain, but the crossover between clinical and logistics will face the challenge of adding additional identifiers to a product. This will include:

- Reviewing the role of the identifiers in the supply chain, and the interaction between the identifiers – for example the relation between GTIN and the IDMP concepts like PCID;
- Evaluate the impact of changing or adopting identifiers: GTIN and IDMP PCID are not necessarily equivalent or interchangeable – or even mappable, given the different granularities that are possible in the GTIN identifiers. In addition, as elicited in openMedicine D3.2, the assignment of a PCID does not follow the same rules in all

countries; the overlap between these concepts – GTIN and PCID – has to be well evaluated in the Supply profiles and the interaction between clinical and supply flows.
- Providing a continuous interoperability path from manufacturer to falsification detection, to clinical use and adverse event monitoring – using national identifiers, IDMP identifiers, or supply chain identifiers like the GTIN.

IHE Formulary: The IHE Pharmacy committee has approved the definition of Therapeutic Formulary standard interfaces – the need has been visible since the roll-out of the IHE HMW and CMPD profiles and is in the IHE roadmap. While at the time there was little concern about Product Master Data, and there were no standards in the clinical space, recently the appearance of ISO 19256 and IDMP, and the openMedicine effort, there has been a considerable push forward on the base standards.

IHE's role as a profiling organization is to use the existing standards to define interoperable, plug-and-play specifications for exchanging product master data. The IHE Formulary roadmap is targeted at providing a graph of product definitions, including national product concepts and codes, IDMP concepts, supply chain product identifiers.

Medication Record: Recently approved, this work item will provide a way to exchange a detailed list of the medication that the patient has been prescribed, dispensed, or taken. This could be an interesting source of data for the Medication Summary – but most importantly, it allows the continuous exchange of medication product information – an example scenario of the impact for this is that a patient can travel throughout the Union and at any time the patient's medication record will be fully up to date with not only a summary but also the details.

IDMP adoption for IHE Pharmacy will mean:

- Revise IHE Pharmacy content profiles (PRE, DIS, PML, PADV, CMA, MMA) and assign placeholders and concepts for the additional IDMP concepts, while retaining compatibility with the national and legacy product identifiers.
- Extend if needed the product specification attributes in IHE profiles or assigning the right terminology.
- IHE Formulary and Medication Record – to include IDMP

Finally, the FHIR adoption by IHE Pharmacy will introduce some new aspects in publication and specification that will allow the validation of IDMP and UNICOM – tighter integration with terminologies, better testing facilities, reusable Logical Data Models (which should align with those defined by UNICOM and IDMP). And most importantly, will consolidate the collaboration between IHE and other SDOs on these matters that has happened since the announcement of IDMP and the openMedicine project.

10 Annex: Table of remarks by workshop session

Dose forms	ePrescription	Clinical purposes (e.g. IPS, medication list)	Adverse events	Medication errors	Supply chain
Key discussion items	Appropriateness of EDQM Standard Terms questioned. Mapping issues considered: Standard Terms & SNOMED; DDD integrated into Standards Terms.	Standards Terms might be useful.	Not discussed	Not discussed	Not discussed
Identified gaps & actions	SNOMED is preferred for prescribing, and EDQM Standard Terms is preferred for regulatory submissions. Better document how Standard Terms, SNOMED and/or DDD complement each other. Clarify that Standard Terms should be preferred to SPOR identifiers for referentials in PhPID calculation, to achieve global uniqueness and interoperability. Investigate if characteristics can be made definitional and how they can be used to facilitate data exchange	idem	NA	NA	NA

ePrescription & eDispense	ePrescription	Clinical purposes (e.g. IPS, medication list)	Adverse events	Medication errors	Supply chain
Key discussion items	· Prescription – identifying the product cross-border depends on the granularity that the product is identified · Dispense information can be captured in exact form · Additional information are needed e.g. excipient · Besides product attributes, other information is needed e.g. indication	· Mapping in cross-border circumstances requires disposing of information such as clinical documents (patient summary), the prescription choice and the dispensation availabilities. · Each of these documents may imply different requirements for identifying products	Capturing ePrescription and eDispensing are crucial for adverse event documentation.	Medication errors term was questioned as too narrow.	Dispense is the last step of the process that is related to the supply chain, information should be captured to preserve traceability. Need to fulfil ePrescription in another country where shortage and/or branded medicine does not exist.
Identified gaps & actions	NA	A perspective of medical audit of prescribing quality or clinical decision support is needed.			

IDMP & individual Case Safety Report (ICSR)	ePrescription	Clinical purposes (e.g. IPS, medication list)	Adverse events	Medication errors	Supply chain
Key discussion items	ISO/HL7 ICSR message is not used for adverse event exchange between healthcare domain and pharmacovigilance centres, NCAs and MAHs. HL7 V3 ICSR message is quite complex and difficult to implement.	The clinical particulars from EN ISO 11615 are relevant as they can be used to inform clinicians of adverse events that are already mentioned in the SmPC/patient information leaflet.	ICSR can be used to exchange suspected adverse drug reactions in the context of medication errors.	ICSR is not adequate to support the exchange of medication errors since different information is needed.	IDMP can help to identify equivalent products in other jurisdictions when shortages occur.
Identified gaps & actions	It might be useful to have an easier to implement ICSR message. Perhaps this can even become an annex to the ISO/HL7 ICSR to make it more visible.		Adverse events need to be better documented related to the ICSR in clinical & regulatory areas. Better document MedDRA, SNOMED and IDMP—how they are useful in different processes and how they relate to each other.	Medication errors need to be better documented related to the ICSR in clinical & regulatory areas.	

PhPID	ePrescription	Clinical purposes (e.g. IPS, medication list)	Adverse events	Medication errors	Supply chain
Key discussion items	The potential value of PhPID for eP has been recognised, in particular for cross-jurisdiction ePrescribing, possibly in conjunction with other identifiers attributes. However more abstract 'PhPID' would be needed to better support this case.	PhPID may have a value, in particular for cross-jurisdiction situations. Depending on the specific cases however more specific or more generic 'PhPID' would be needed.	PhPID appears to be required to manage adverse events and reporting.	Not obvious how PhPID plays a role in medication errors.	PhPID and its various levels play a role when facing shortages (compare medicinal products) or in identifying counterfeits (supporting analysis and enable comparisons).
Identified gaps & actions	Investigate & document the appropriate PhPID level needed. Explore if and how more abstract 'PhPID' should be introduced (a set of PPCC (pharmaceutical product concept code)?) and what they actually need to represent. Evaluate who should be the SDO in charge of this action?	Explore if and how more abstract and more specific 'PhPID' should be introduced and what they actually need to represent. Evaluate who should be the SDO in charge of this action?	NA	NA	NA

IDMP & HL7 FHIR	ePrescription	Clinical purposes (e.g. IPS, medication list)	Adverse events	Medication errors	Supply chain
Key discussion items	IDMP and FHIR impact new eHealth implementations. IDMP impacts existing implementations such as CDA (e.g., CEF eHDSI). IDMP facilitating equivocal identification of medicines is relevant to any workflow or process that involves medicinal products.	Not discussed	FHIR might be the appropriate vehicle to document adverse events. Notification of adverse events (ICSR) between MAH, NCAs, EMA and WHO-UMC is processed with HL7 v3 messages (as prescribed by the ISO ICSR standards). There is an ongoing standardization project in progress on transitioning ICSR to FHIR. Communication of adverse events between care organisations and regulators / industry is flexible. There is a trend to use FHIR messages for that and aligning and exchanging practices across member states and EMA is critical	Not discussed	Not discussed
Identified gaps & actions	If eHealth included in use case, provide information on mobile apps making use of IDMP and FHIR.	NA	Highlight the need for governance of IDMP/ FHIR mapping How mHealth apps for adverse event reporting can use IDMP through FHIR	NA	NA

IDMP & FMD	ePrescription	Clinical purposes (e.g. IPS, medication list)	Adverse events	Medication errors	Supply chain
Key discussion items	In most of the countries, prescription by DCID/GTIN is not permitted except perhaps when a prescriber wants the patient to receive a specific medicinal product (no substitutions allowed)	Frequency during which an identifier changes during the medicine's life cycle; whether it supports registries such as immunisation and international patient summaries.	Documenting adverse events and which medicine was administered by capturing the DCID/GTIN, batch/lot and expiry (and serial number if available) encoded in the barcode, can improve data quality.	Verifying at the point of care that the right medicinal product is given to the right patient, requires primary packaging identification with a specific DCID (GTIN)	Master data and how to appropriately link SPOR and EMVS
Identified gaps & actions	Document how a medicine's identifier (DCID/GTIN) supports the prescription process	Document how the DCID/GTIN is or can be linked to the latest patient instructions	Document if and how the DCID/GTIN supports registries		Document traceability for multi-country packaging—the same medicine identifier, linked to different marketing authorisations. Document when FMD parallel-traded medicinal products must be decommissioned by parallel trader and re-serialised before entering target market.

IDMP, SNOMED CT, MedDRA	ePrescription	Clinical purposes (e.g. IPS, medication list)	Adverse events	Medication errors	Supply chain
Key discussion items	SNOMED CT and its national extensions are widely used to support the prescription process. SNOMED CT is translated in numerous languages.	SNOMED CT has a logical model that has been applied to pharmacy-related content, which provides the ability to define specific elements of any product. SNOMED CT has provided a free set for the HL7 International Patient Summary that is supplemented by EU required additional content. This content is also part of the Global Patient Set provided free by SNOMED International for global use. SNOMED International is also prepared to support the sharing of cross-border information.	Documenting adverse event by using MedDRA is mandatory in the space of regulation. To facilitate this process there are maps between SNOMED CT and MedDRA and MedDRA to SNOMED CT (available as an Alpha release for review). The key use case is to facilitate reporting from SNOMED CT enabled clinical records to regulation.	Documenting medication errors is less regulated than adverse event reporting. There is no benefit of using IDMP rather than SNOMED CT in these cases.	NA
Identified gaps & actions	Need to know more about what SNOMED CT provides, how that is linked to IDMP and MedDRA	Document why IDMP and SNOMED CT are important in cross-border processes and how they both support interoperability on a global level. Document how the linkage of IDMP and SNOMED CT is planned and how it will be provided.	NA		NA

11 Annex: Use cases

USE CASE EPRESCRIPTION

Descriptive Use Case Title	Electronic exchange of patient prescription and/or dispense information across one or more geographical borders/locations (e.g. intercontinental, cross-border).
Document Owner	
Version	0.1
Status	Draft
Date	26-07-2020

BRIEF DESCRIPTION

This use case supports electronic exchange of patient prescription and/or dispense information across one or more geographical borders/locations (e.g., intercontinental, cross-border). The use case supports patient pick up of an initial or refill prescription at a licensed or approved retail pharmacy location.

ACTORS

- Patient
- Pharmacist (dispenser)
- Healthcare provider (prescriber)

PRE-CONDITIONS

List any item, like technical system(s), organizational structures, legal agreements, agreed-upon procedures etc. that must be available/realised before the process can be implemented or adjusted (e.g. to IDMP).

This should include new/changed requirements to improve the IDMP suite of standards, terminologies, coding systems etc., gaps identified and others.

BASIC FLOW

The basic flow is the normal course of events, otherwise called the "happy path." Its steps cover the full scope of activities between the start and end points of the process. - Create a numbered list of each step.

1. Check patient ID
2. Get available prescription list (provide the list of available ePrescriptions to country of treatment)
3. Prepare the medicine to dispense
4. Send dispensed/to be dispensed medicine information to country of affiliation
5. Provide the medicine to the patient

ALTERNATE/EXCEPTION FLOWS

N/A

POST CONDITIONS

Post-conditions indicate what must be true of the state of the system after the steps of the use case are complete. These should be true for the basic flow and – where applicable - alternate flows. Alternate flows may have different post-conditions.

SUPPLEMENTAL REQUIREMENTS & INFORMATION

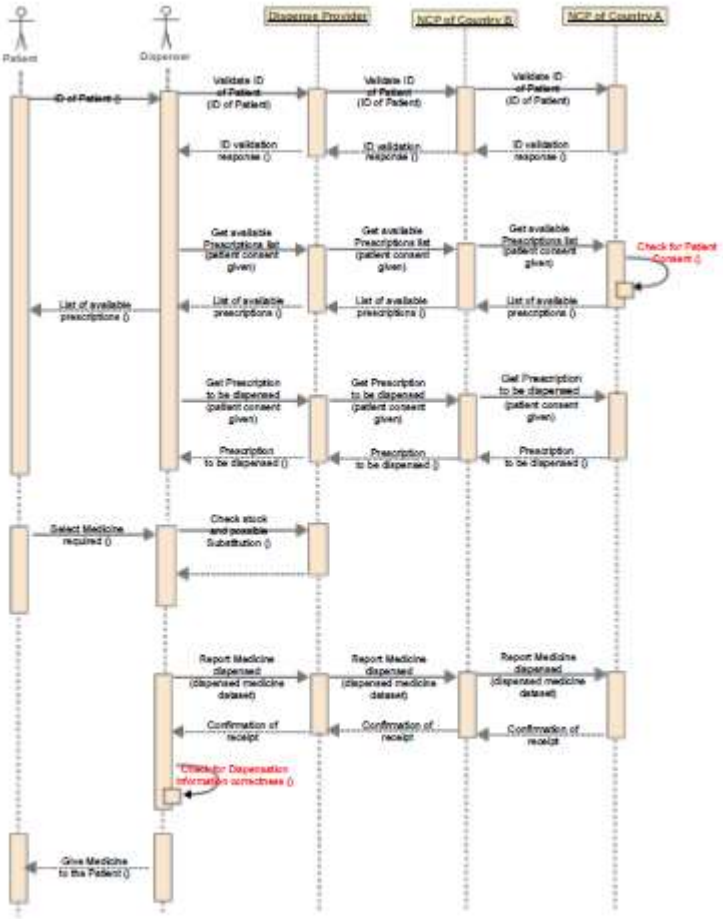
Applicable Data Standards:

- ISO IDMP (MPID/PhPID, PCID, DCID)
- GS1 GTIN
- [11]ESC/ESH practice guideline
- HL7 CDA (e.g., Pharmacy)
- HL7 SPL
- FHIR resources: MedicationRequest, Healthcare Service, MedicationDispense, Medication – Content, Immunization – Medication Definition (under development), Medication Knowledge
- ISO TS 17251 (Dose Syntax)

[11] The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH)

VISUAL MODEL

Example: eHDSI Sequence Diagram ePrescription



REVISION HISTORY

V.	Date	Author	Description	Status
01	26-07-2020	M. Klinkenberg	Adaption of IDMP Public Health Use Case Series to UNICOM Use Case Template	Initial draft

USE CASE CLINICAL PROCESSES

Descriptive Use Case Title	Patient treatment and care processes that requires relevant medical information used by caregivers, when and where they need it
Document Owner	
Version	0.1
Status	Draft
Date	26-07-2020

BRIEF DESCRIPTION

This use case supports patient treatment and care processes that leverage the International Patient Summary (IPS), medication lists and more. It involves making relevant medical information available to caregivers who need it, when and where they need it—across a myriad of health systems that cross local, regional and national jurisdictional borders.

ACTORS

- Patient
- Pharmacist (dispenser)
- Healthcare provider (prescriber)

PRE-CONDITIONS

The use case includes clinical decision support systems, which are used by the prescriber and dispenser.

BASIC FLOW

The basic flow is the normal course of events, otherwise called the "happy path." Its steps cover the full scope of activities between the start and end points of the process. - Create a numbered list of each step.

ALTERNATE/EXCEPTION FLOWS

N/A

POST CONDITIONS

Post-conditions indicate what must be true of the state of the system after the steps of the use case are complete. These should be true for the basic flow and – where applicable - alternate flows. Alternate flows may have different post-conditions.

SUPPLEMENTAL REQUIREMENTS & INFORMATION

Applicable Data Standards:

- TBC

VISUAL MODEL

TBC

REVISION HISTORY

V.	Date	Author	Description	Status

01	26-07-2020	M. Klinkenberg	Adaption of IDMP Public Health Use Case Series to UNICOM Use Case Template	Initial draft

USE CASE
ADVERSE EVENTS (ICSR)

Descriptive Use Case Title	Identification, assessment and reporting of adverse reactions to a medicinal product that occur in a single patient at a specific point of time
Document Owner	
Version	0.1
Status	Draft
Date	26-07-2020

BRIEF DESCRIPTION

This use case supports identification, assessment and reporting of adverse events (AE). AE are one or several suspected adverse reactions to a medicinal product that occur in a single patient at a specific point of time. The assessment of AE can be supported based upon patient observations (e.g., physical exam or laboratory results) or aided by automated tools such as clinical decision support.

The ICSR (Individual Case Safety Report) standard defines the format and content for the reporting of AE. The use case supports electronic exchange of ICSRs between regulators, pharmaceutical industry and clinical trial sponsors.

ACTORS

- Patient
- Healthcare provider
- ER department
- Clinical laboratory
- Hospital Risk/Incident Manager
- Jurisdictional registries (local, regional, national) for immunizations, prescription and restricted use drugs)
- Regulatory/Competent Authorities (including regional/national pharmacovigilance centers)
- WHO
- Pharmaceutical industry
- Clinical trial sponsors

PRE-CONDITIONS

List any item, like technical system(s), organizational structures, legal agreements, agreed-upon procedures etc. that must be available/realised before the process can be implemented or adjusted (e.g. to IDMP).

This should include new/changed requirements to improve the IDMP suite of standards, terminologies, coding systems etc., gaps identified and others.

BASIC FLOW

The basic flow is the normal course of events, otherwise called the “happy path.” Its steps cover the full scope of activities between the start and end points of the process. - Create a numbered list of each step.

6. Patient reports adverse reaction to healthcare provider (HP)
7. A. Healthcare provider reports adverse reaction to National Competent Authority (NCA) using ICSR form
8. NCA reports adverse reaction to European Medicines Agency (EMA)
9. EMA informs pharmaceutical industry of adverse reaction
10. EMA informs WHO of adverse reaction

Alternate/Exception Flows

N/A

Post Conditions

Post-conditions indicate what must be true of the state of the system after the steps of the use case are complete. These should be true for the basic flow and – where applicable - alternate flows. Alternate flows may have different post-conditions.

Supplemental Requirements & Information

Applicable Data Standards:

- ISO IDMP (MPID/PhPID, PCID, BAID, Clinical Particulars, Substance ID, Dose Forms, Routes of Administration, UCUM)
- HL7 CDA (e.g., Pharmacy, Laboratory)
- HL7 SPL
- FHIR resources: DetectedIssue, DiagnosticReport - Content, Allergy/Intolerance, Immunization Reaction, Adverse Event, Resource Observation Content, ResourceGuidance Response(?)
- LOINC
- SNOMED
- ICD 10
- ISO/HL7 ICSR
- ISO TS 22703 (Medications Safety Alerts)
- CEN ISO TS 22756 (Knowledge Base)
- ICH E2B(R3) Implementation guide
- MedDRA

Notification of adverse events (ICSR) between marketing authorisation holder, national competent authorities, EMA and WHO-UMC is processed with HL7 v3 messages (as prescribed by the ISO ICSR standards). Implicitly, means to communicate adverse events between care organisations and regulators / industry is flexible (may be FHIR, as noted above).

Visual Model

Where appropriate, a simple work-flow diagram may be used to visually depict the sequence of steps, and alternate and exception flows. Or a user interface mock-up may be used to

show a possible representation of user requirements in an interface). In some instances, a more formal UML diagram may be appropriate.

REVISION HISTORY

V.	Date	Author	Description	Status
01	26-07-2020	M. Klinkenberg	Adaption of IDMP Public Health Use Case Series to UNICOM Use Case Template	Initial Draft

USE CASE
MEDICATION ERRORS

Descriptive Use Case Title	Involves an unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient.
Document Owner	
Version	0.1
Status	Draft
Date	26-07-2020

BRIEF DESCRIPTION

The use case includes the identification, assessment and reporting of medication errors (actual or near miss). Like AEs, medication errors can be assessed based on patient observations (e.g., physical exam or laboratory results) or aided by automated tools such as clinical decision support or bedside scanning.

ACTORS

- Patient
- Doctors
- Nurses
- Pharmacist
- Healthcare provider
- ER department
- Pharmacy
- Hospital Risk/Incident Manager
- Jurisdictional registries (local, regional, national) for critical incident reporting, prescription and restricted drug usage
- Pharmaceutical manufacturers

PRE-CONDITIONS

List any item, like technical system(s), organizational structures, legal agreements, agreed-upon procedures etc. that must be available/realised before the process can be implemented or adjusted (e.g. to IDMP).

This should include new/changed requirements to improve the IDMP suite of standards, terminologies, coding systems etc., gaps identified and others.

BASIC FLOW

TBC

ALTERNATE/EXCEPTION FLOWS

N/A

POST CONDITIONS

Post-conditions indicate what must be true of the state of the system after the steps of the use case are complete. These should be true for the basic flow and – where applicable - alternate flows. Alternate flows may have different post-conditions.

Supplemental Requirements & Information

Applicable Data Standards:

TBC

Visual Model

Where appropriate, a simple work-flow diagram may be used to visually depict the sequence of steps, and alternate and exception flows. Or a user interface mock-up may be used to show a possible representation of user requirements in an interface). In some instances, a more formal UML diagram may be appropriate.

Revision History

V.	Date	Author	Description	Status
01	26-07-2020	M. Klinkenberg	Adaption of IDMP Public Health Use Case Series to UNICOM Use Case Template	Initial Draft

USE CASES
SUPPLY CHAIN MANAGEMENT

Descriptive Use Case Title	Multiple scenarios related to Supply Chain Management
Document Owner	
Version	0.1
Status	Draft
Date	26-07-2020

BRIEF DESCRIPTION

Supply Chain Management use cases cover multiple scenarios such as:
(1) identification and management of a product recall due to contamination/falsification or other safety-related issue;
(2) Drug shortages due to increased demand (e.g., pandemic flu) or limited manufacturing supply

ACTORS

- Drug manufacturer
- Authorized distributor or relabeler
- Regulatory/Competent Authority
- Healthcare professional
- Retail or hospital pharmacy
- Patient
- Hospital Risk Manager

PRE-CONDITIONS

List any item, like technical system(s), organizational structures, legal agreements, agreed-upon procedures etc. that must be available/realised before the process can be implemented or adjusted (e.g. to IDMP).

This should include new/changed requirements to improve the IDMP suite of standards, terminologies, coding systems etc., gaps identified and others.

BASIC FLOW – PRODUCT RECALL

11. Drug manufacturer reports quality defect to National Competent Authority (NCA)
12. NCA determines public health risk of the quality defect (risk classification) and decides on recall and relevant level (e.g. individual patient, pharmacy, distributor)
13. In case of recall, NCA informs the holder of the market authorisation
14. Holder of market authorisation informs relevant parties (e.g. pharmacies, healthcare professionals, patients) conform national procedure
15. NCA publishes recall
16. If necessary, NCA informs foreign NCA's

ALTERNATE/EXCEPTION FLOWS

N/A

POST CONDITIONS

Post-conditions indicate what must be true of the state of the system after the steps of the use case are complete. These should be true for the basic flow and – where applicable - alternate flows. Alternate flows may have different post-conditions.

SUPPLEMENTAL REQUIREMENTS & INFORMATION

Applicable Data Standards:

- ISO IDMP (MPID, PhPID, PCID, BAID)
- GS1 GTIN
- HL7 CDA
- FHIR resource: DetectedIssue
- CEN ISO TS 16791, Medication Definition (under development)
- ISO TS 22703

VISUAL MODEL

Where appropriate, a simple work-flow diagram may be used to visually depict the sequence of steps, and alternate and exception flows. Or a user interface mock-up may be used to show a possible representation of user requirements in an interface). In some instances, a more formal UML diagram may be appropriate.

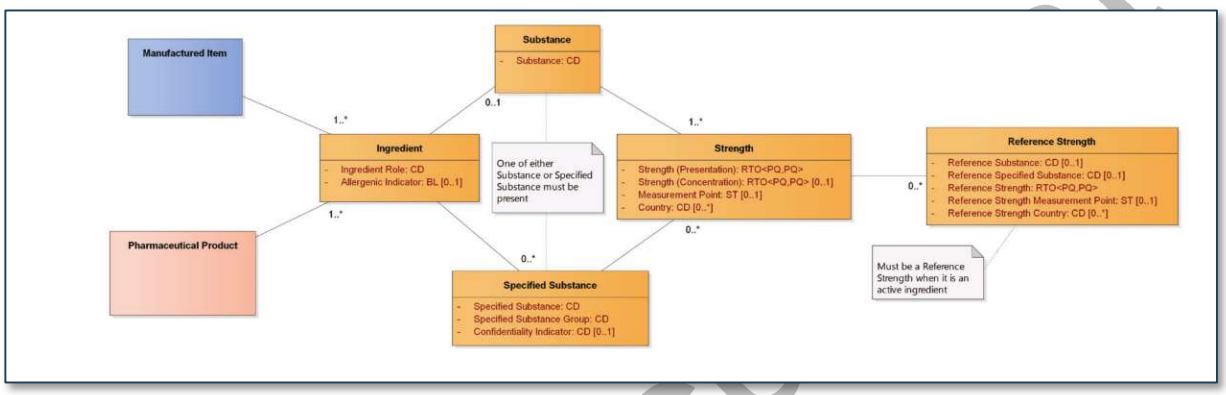
REVISION HISTORY

V.	Date	Author	Description	Status
01	26-07-2020	M. Klinkenberg	Adaption of IDMP Public Health Use Case Series to UNICOM Use Case Template	Initial draft

12 Substances and strength – Ingredient role and strength

Problem/Gap

The current conceptual model of ISO 11615 does not conveniently support the correct description of all the variations of ingredient role/strength that we find in medicinal products. There was an initial perception that this might be possible with the current model, but there would be some variation in how this is achieved and doing this correctly would require a significant amount of expertise. This would be an obstacle to UNICOM (and IDMP) goals of the unique identification of products.



The issue, here concentrating on therapeutically active ingredient, is that the strength of a medicinal product can be expressed differently depending on which substance the strength is referring to. Since strength has such a close relationship with dose quantity, this issue has a strong impact on both the regulatory domain and patient care.

When the strength refers to the precise active ingredient substance that is present in the manufactured item, at whatever granularity that is described (moiety, salt, other modification), the current model manages this fine. But this is not always the case.

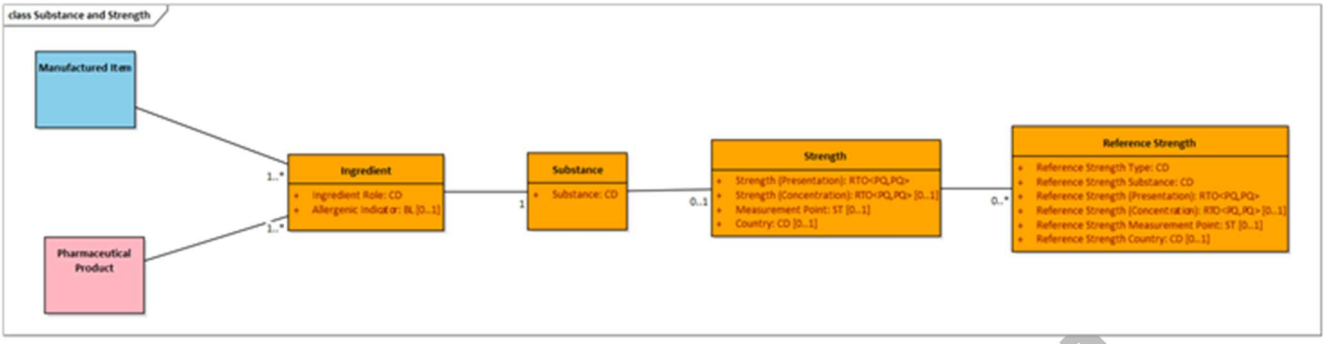
When the (clinically significant) strength refers to a basis of strength substance that is **not** precise active ingredient substance but is the active moiety of that substance, there is ambiguity in how to achieve this in the existing model and, therefore, implementations can differ.

Another pattern happens when the (clinically significant) strength refers to a basis of strength substance that is **neither** the precise active ingredient substance **nor** the active moiety of that substance but is a different substance, that may or may not be related in some way. Also here, the existing model could support this using the reference strength, but also there the ambiguity in how to achieve this would lead to inconsistencies. When there are true "alternative" strengths (as in the dexamethasone example following, there is no ability to reference what the reference strength type is (or if there is a strength expressed in different units).

Proposal: "Reference Strength Type"

The addition of a "Reference Strength Type" attribute on the Reference Strength class, as shown in the following model, allows all ingredient/strength combinations to be explicit, and particularly shows (See the Terlipressin example) how differently labelled products can have

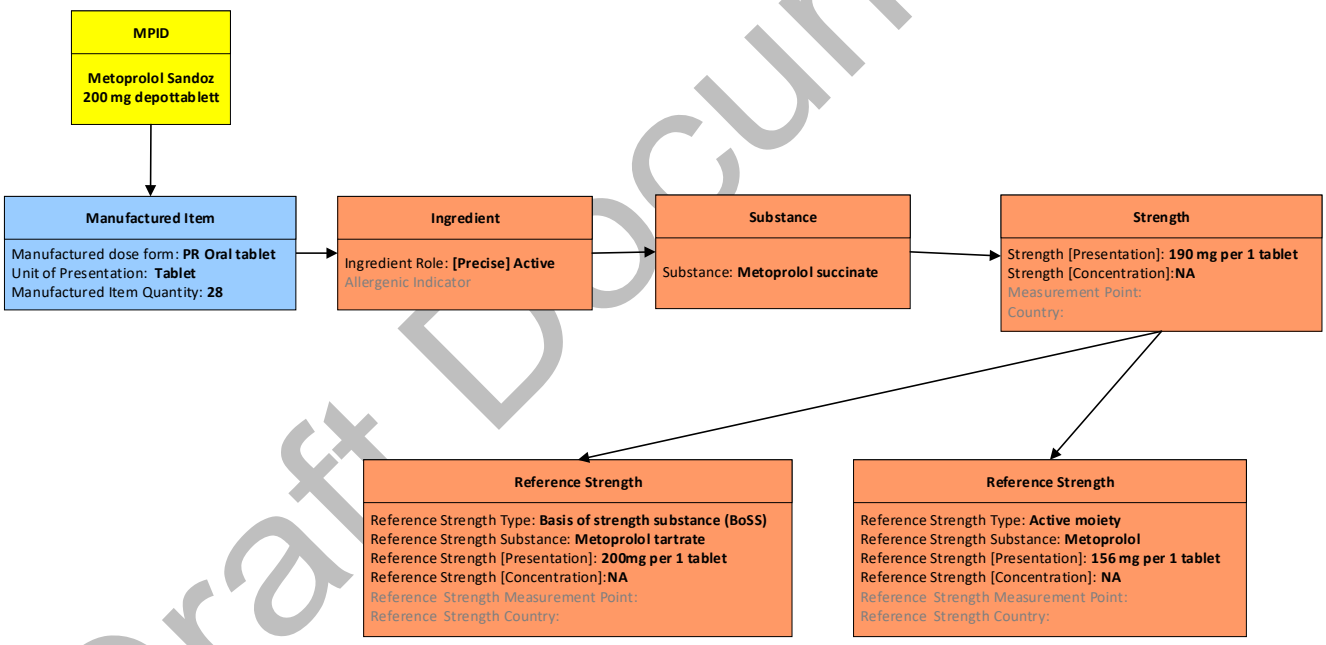
their various strengths expressed correctly and have the commonality needed for PhPIDs to be available.



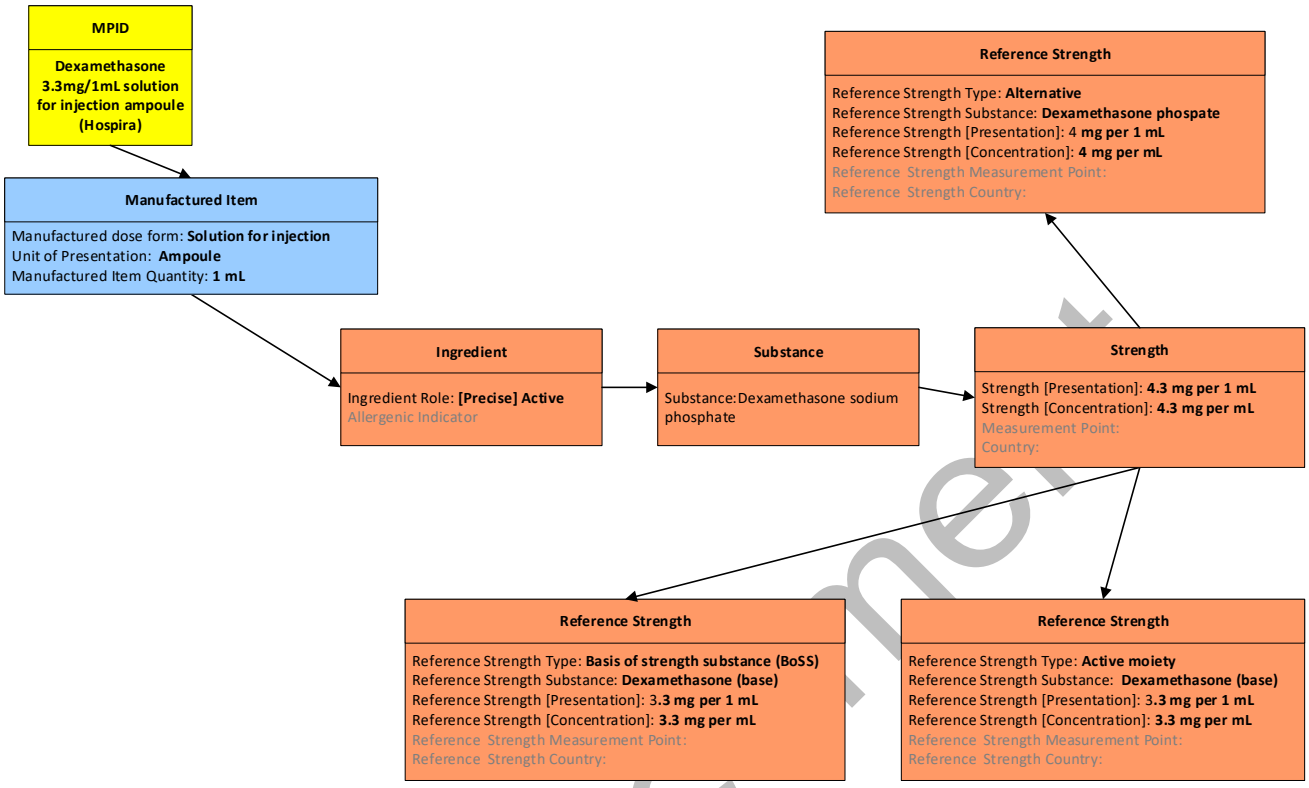
Demonstrative examples:

The following examples implement the proposal to demonstrate and validate its adequacy.

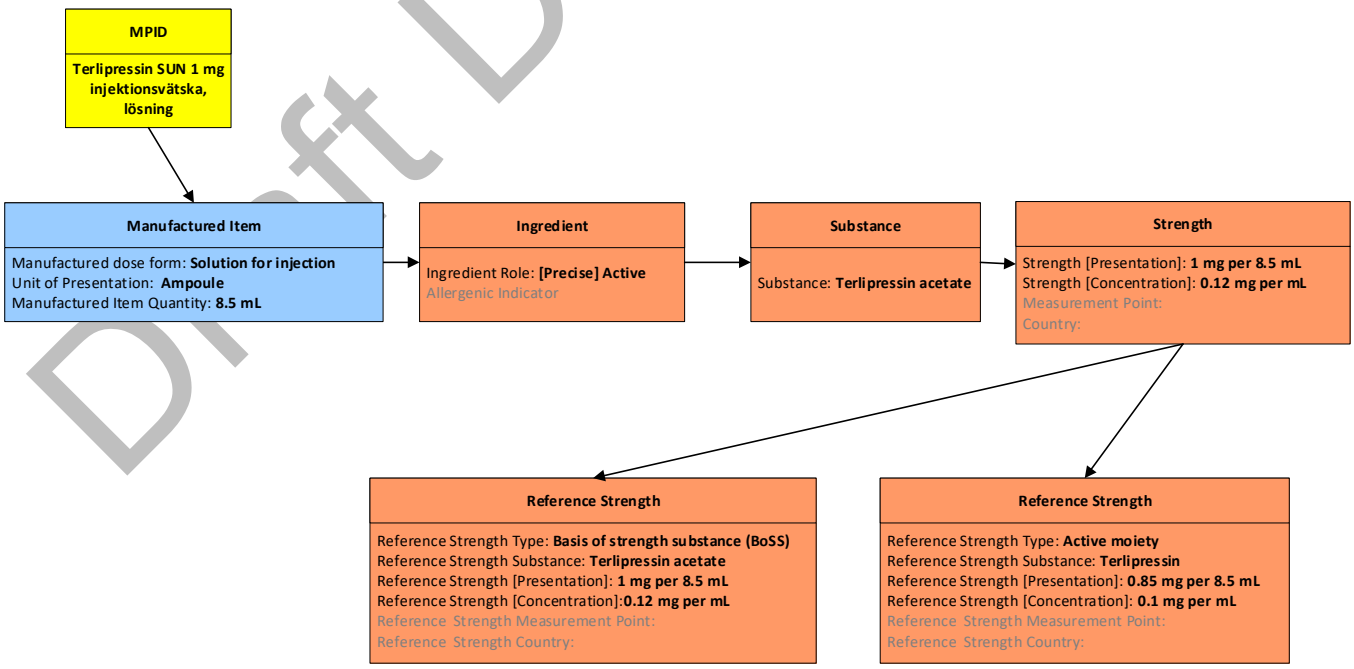
Metoprolol



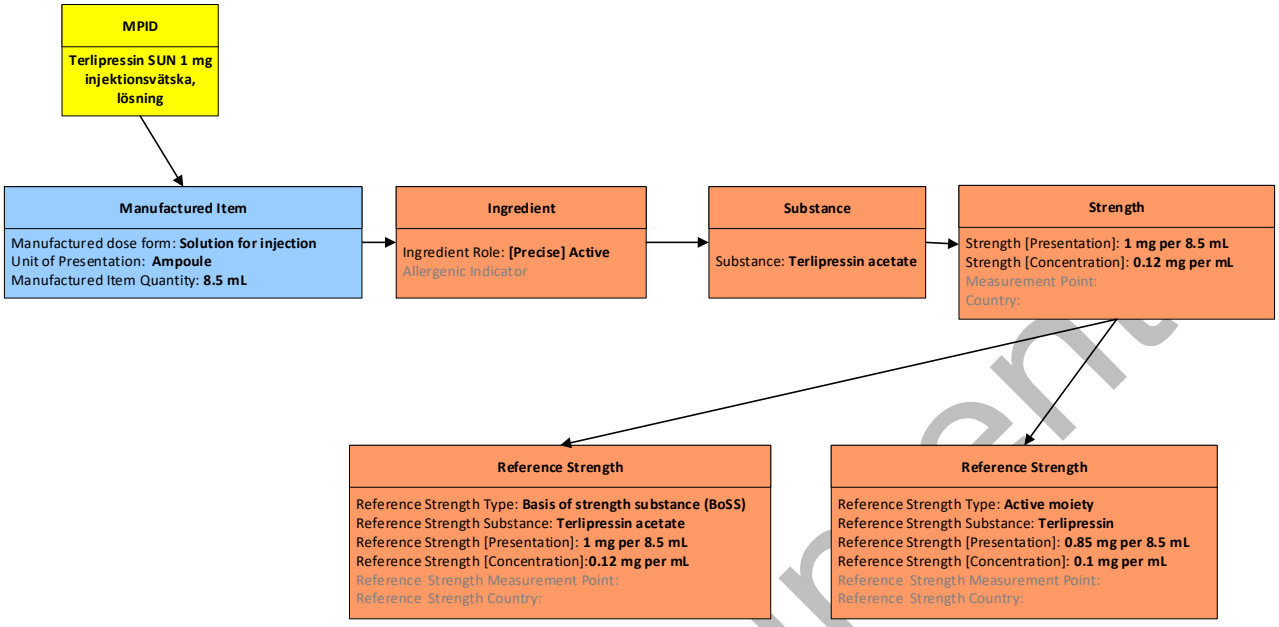
Dexamethasone



Terlipressin (SWE)



Terlipressin (UK)

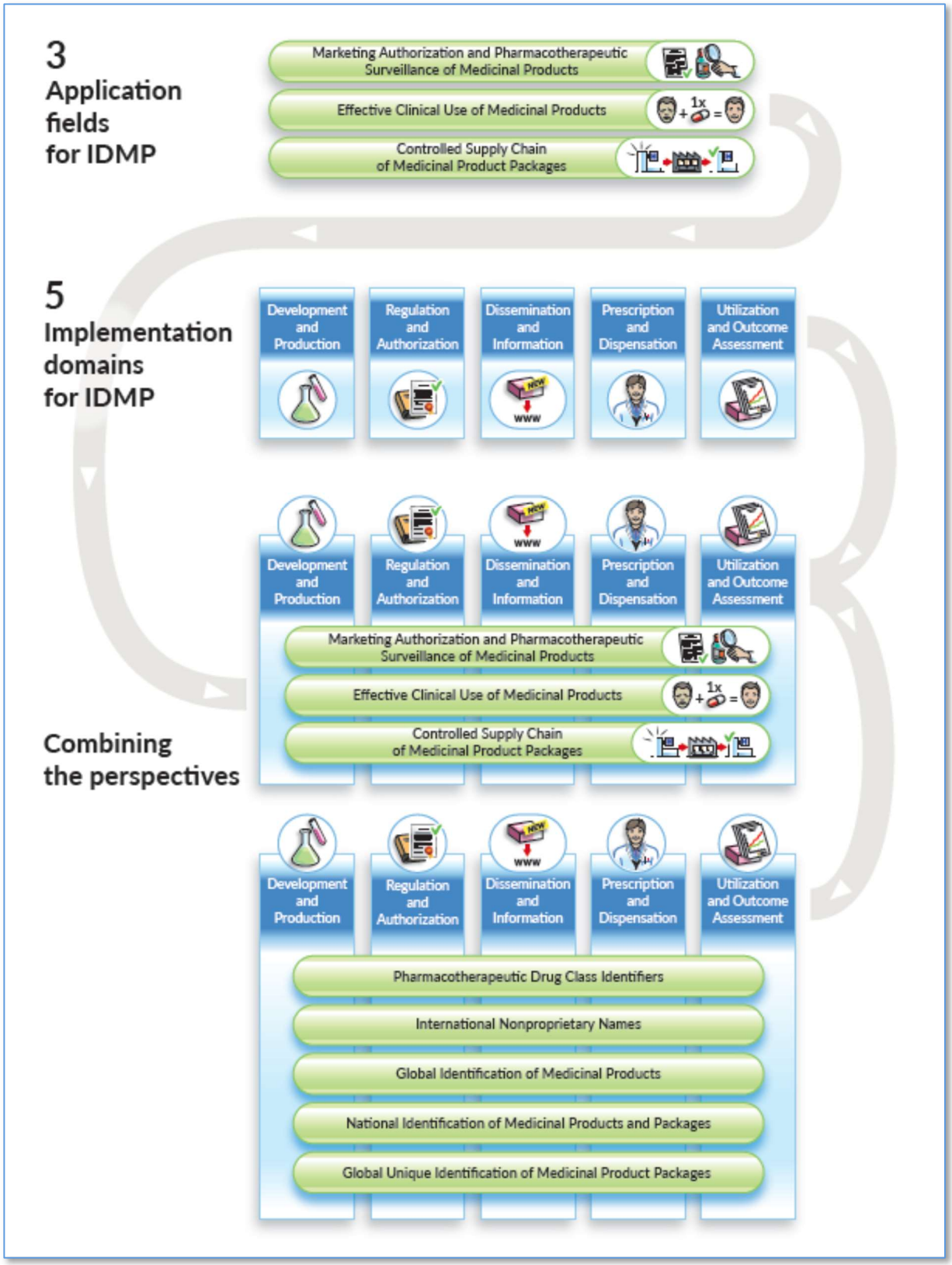


Conclusion

Having possibly different ways to express Reference Strength—and not explicitly capturing which of the different ways are being used—can lead to different approaches in implementation, which will result in different indications of strength for the exact same product. This will impact the product identification, namely the PhPID calculation.

To avoid the ambiguity of implementations in a crucial aspect such as the substance strength, it is recommended to add the attribute “Reference Strength Type” to the Reference Strength entity, and use a controlled value set to ensure the different type of reference strengths can be managed or at least identified.

13 Illustrations from § 1.4



Supporting multiple functionalities

Life Cycles of Identifiers

- Pharmacotherapeutic Information Life cycle
- INN Prescribing / Clinical Decision Support / life cycle
- Global Identification of Medicinal Products life cycle
- National Identification of Medicinal Products for Marketing Authorisation life cycle
- Global Identification of Medicinal Product Packages for supply chain life cycle