UN COM

Project acronym: UNICOM
Project full title: Up-scaling the global univocal identification of medicines in the context of Digital Single Market strategy
Call identifier: H2020-SC1-DTH-2019

D4.10 Croatia: Progress report on refactoring or new build of national IT systems, migration of national data, and data interfaces to EMA's SPOR

Version:	1.0
Status:	Final
Dissemination Level[1]:	PU
Due date of deliverable:	31.01.2021
Actual submission date:	31.01.2021
Work Package:	WP4: IDMP implementation at National Drug Agencies
Lead partner for this deliverable:	HALMED
Partner(s) contributing:	-
Deliverable type[2]:	R

Main author(s):

Sanja Grčić Plečko	HALMED
Dubravka Sudić	HALMED

Resource consumption estimate:	Person months
HALMED	1,0

Revision history

Version	Date	Changes made	Author(s)
0.1	10.12.2020	First draft	Sanja Grčić Plečko (HALMED)
0.2	22.12.2020	Version for internal WP4 review	Sanja Grčić Plečko (HALMED)
0.3	13.01.2021	Revisions based on reviewer's feedback	Maja Fatiga (HALMED)
0.4	22.01.2021	Review	Sanja Grčić Plečko (HALMED)
0.5	23.01.2021	Version sent to WP lead and coordinator	Sanja Grčić Plečko (HALMED)
1.0	29.01.2021	Document review and submission	EMP

Statement of originality

This deliverable contains original unpublished work except where clearly indicated otherwise. Acknowledgement of previously published material and of the work of others has been made through appropriate citation, quotation or both.

Deliverable abstract

HALMED undertook the task of refactoring data model and making all necessary changes in UI in its core business application (NRL-PKL-PhV) in order to be able to use SPOR referential lists and to ensure reliable exchange of medicinal product information in compliance with ISO IDMP standards and cross interoperability.

As first steps, we started to conduct workshops with key business users to understand business processes and the set of data that they rely on, and to better apprehend gaps concerning existing IT system and ISO IDMP data model.

So far, we converted the connection from formerly used EUTCT referential lists to RMS lists and we add new RMS lists. The process of introducing new RMS lists is ongoing work, starting with workshops with key business users, prioritizing the lists to be introduced, preparing User Requirements Specification (URS) and Functional Requirements Specification (FRS), implementing required changes in database and in UI, followed by IQ/OQ/PQ testing and deployment on production environment. In parallel, we are working on cleansing and mapping data and if needed, migration of legacy data.

Besides introduction of new RMS lists, by using OMS API, internal organization IDs and internal location IDs are being linked with OMS Org and OMS Loc IDs.

Keywords: HALMED, NRL-PKL-PhV, ISO IDMP, SPOR, RMS, OMS

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

List of abbreviations

Abbreviation	Complete form
API	An API can be defined in various ways; the definitions below form a good start for this: 1. "It is a set of routines, protocols, and tools for building software applications." 2. "It expresses a software component in terms of its operations, inputs, outputs, and underlying types." If we take the second definition, on SPOR API[3]: - *Software component* is system hosted by EMA - *Operations* – create, read, update, and delete - *Inputs -* Search terms, documents, metadata attributes - *Outputs -* Documents, metadata attributes - *Underlying types -* Lists, Terms, Translations, Change Requests, Documents, user defined Tags, Subscriptions, Organisations, Locations
DAIS	Document Archive Information System
DB	Database
DoA	Description of the Action
eAF	Electronic Application Form
EUTCT	European Union Telematics Controlled Terms
FHIR	Fast Healthcare Interoperability Resources
FRS	Functional Requirements Specification
HALMED	Agencija za lijekove i medicinske proizvode
IDMP	Identification of Medicinal Products
IG	Installation Guide
IQ/OQ/PQ	Installation Qualification /Operational Qualification / Performance Qualification
MRP/DCP	Mutual Recognition Procedure/Decentralised Procedure
MP	Medicinal Product
MPID	Medicinal Product Identification
NCA	National Competent Authority
NRL-PKL-PhV	HALMED's IT system for core business processes: Nacionalni registar lijekova (National medicine registry) for MA processes – Provjera kakvoće lijekova (Medicine quality control) LIMS in OMCL – and PhV for Pharmacovigilance processes
OMCL	Official Medicines Control Laboratory

---

[3] Definition taken from document: SPOR API v2 Specification

OMS	Organisation Management Services
PhPID	Pharmaceutical Product Identification
PMS	Product Management Services
RDM	Reference Data Model
RMM	Risk Minimization Measures
RMS	Referentials Management Services
SMS	Substance Management Services
SPOR	EMA service delivering quality data management services for substances, products, organisations and referentials (SPOR) to power EU regulatory activities. The four SPOR data management services are: SMS, PMS. OMS, RMS
UI	User Interface
URS	User Requirements Specification
WP	Work package

1   Executive summary

This document describes HALMED's plan and the first year execution of Task 4.11: „Progressing ISO IDMP implementation at HALMED in Croatia. Lead: HALMED".

In the paragraph "HALMED Task", current NRL-PKL-PhV system is briefly described and short task execution plan with the risk mitigation plan is provided.

From the early stages of NRL-PKL-PhV system development until recently, fourteen EUTCT lists have been used as our referential lists and those were synchronized on daily basis. In some of those lists was, until recently, allowed to add user-defined terms and before transition to RMS lists, we are conducting data cleansing. Depending on the current referential list usage, we detected four different scenarios and implementation steps for each of them. So far, we converted the connection from formerly used EUTCT referential lists to RMS lists and we add new RMS lists. The process of introducing new RMS lists is ongoing work, starting with workshops with key business users, prioritizing the lists to be introduced, preparing User Requirements Specification (URS) and Functional Requirements Specification (FRS), implementing required changes in database and in UI, followed by IQ/OQ/PQ testing and deployment on production environment. In parallel, we are working on cleansing and mapping data and if needed, migration of legacy data.

Besides introduction of new RMS lists, by using OMS API, internal organization IDs and internal location IDs are being linked with OMS Org and OMS Loc IDs.

In 2010 HALMED decided to build their own medicinal products database on the data model described in RDM 3.0 model (Reference data model published by EMA), that was confirmed as good practice at that time. Due to the simplification of RDM data model vs. ISO IDMP data model, packaged products were not properly described, Manufactured item is missing and in our data model descriptive text fields have been used. From the beginning of Task 4.11 execution, we conducted workshops with key business users to understand business processes and the set of data that they rely on. The result of those workshops is better understanding of gaps concerning existing IT system, ISO IDMP data model and business needs. Even more, implementation of new business process in HALMED for calculation of maximal medicinal product price shown that there are shortages in data model that are making impossible to describe packages properly so they could be compared with medicinal products from referent countries.

Comparing the currently used medicinal product data model with ISO IDMP and business needs analysed so far, three important refactoring areas were detected:

- ► Packaged Medicinal Product: Manufactured Item should be introduced in data model
- ► Pharmaceutical product needs some adjustments
- ► Ingredients: first phase of data model reconstruction is implemented and further analysis should be conducted after introduction of Manufactured Item.

The plan for M13-M24 is to:

- ► Continue data cleansing and data mapping
- ► Deploy the NRL-PKL-PhV version 2 (mainly concerning the UI changes, introduction of new RMS lists and first phase of "Ingredients" data model refactoring) to production environment.
- ► Continue prioritizing the introduction of new RMS lists and deploy to production those in the testing phase
- ► Continue conducting workshops and discussions with key business users to define business processes and data sets needed
- ► Participate in eMedicines project (and prepare User Requirements Specification for integration services for exchange MP data with National MP database)
- ► NRL-PKL-PhV upgrade/reconstruction User Requirements Specification preparation for public tender and conduct public procurement.

2   HALMED: Task 4.11

Task 4.11: Progressing ISO IDMP implementation at HALMED in Croatia. Lead: HALMED (M1-M48)

HALMED will undertake project management and organisation tasks to understand impact of implementing ISO IDMP standard on business processes within the institution and understand gaps with regards to existing IT system and data model. Further activities will include migration of legacy data towards IDMP as well as setting/maintaining OMS, RMS and SMS connection with EMA service. In addition, HALMED plans to contribute to the definition of common rules on how to standardise data according to IDMP.

2.1   About HALMED

Agency for Medicinal Products and Medical Devices of Croatia (HALMED) is the Croatian national competent authority that provides services pertaining to medicinal products, medical devices, homeopathic medicinal products and veterinary medicinal products in accordance with the primary and secondary legislation of the Republic of Croatia.

The Agency was established on October 1st 2003 as a legal successor to the Croatian Institute of Medicines Control and the Croatian Institute of Immunobiological Preparations Control, albeit with a considerably broader scope of work.
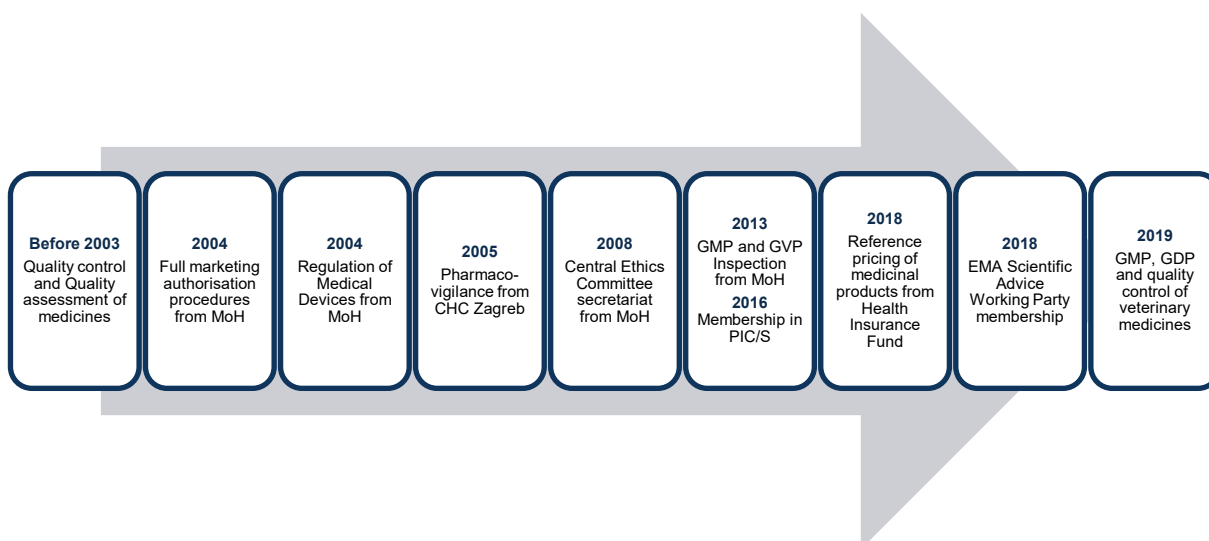

Figure 1. HALMED timeline

With 230 employees, HALMED has offices on three locations and its own IT infrastructure is located in two separate data centres: primary location is within the Agency facilities and secondary location is in rental facilities.

Additional information:
- 7.550 medicinal products in database (5.964 authorised nationally (2.463 active) and 1.586 through MRP/DCP procedures (1.313 active)).
- 8.422 organizations in local repository.

Three employees of Marketing Authorisation Division dedicated solely to the development, improvements and support to the end-users of HALMED's Registry of Medicines and they act as a link between business end-users and IT. Regular monthly meetings are organized between heads of IT and Medicines Authorisation Department.

HALMED's IT team consists of eleven employees, supported by external contractors and service providers. For core business processes, tailor made applications are used. Business experts are very much engaged in all data model and processes' analysis workshops, majority of departments and divisions dedicated business experts that are assigned on custom application development projects.

2.2 HALMED's current system

NRL-PKL-PhV consists of three applications that share not only user interface, but also same database, same referential lists that are daily synchronized with SPOR lists and EUTCT substance list and same administration tools. NRL-PKL-PhV is a custom developed system for core business processes:

► Case tracking for marketing authorization procedures
  ► tracking of all procedural phases,
  ► tracking of deadlines and tasks completed by assessors
  ► supporting the Committee for Medicinal Products processes
  ► business reporting
► Performing pharmacovigilance tasks (Risk Minimization Measures (RMM) and Referral procedures)
► Inspectorate activities related to planning and executing medicinal products sampling
► Quality control of medicinal products (Human and Veterinary) in the official medicines control laboratory (OMCL)
  ► Filing incoming samples, sample analysis and analysis task assignment
  ► Reagent management and management of standards
  ► Reporting of results and filing outgoing documents

Agency staff prepared user specifications and an architecture model in 2010. The first modules were deployed in production environment in 2011. What we learned: in IT system development process, internal business experts' engagement is crucial for success of system development.
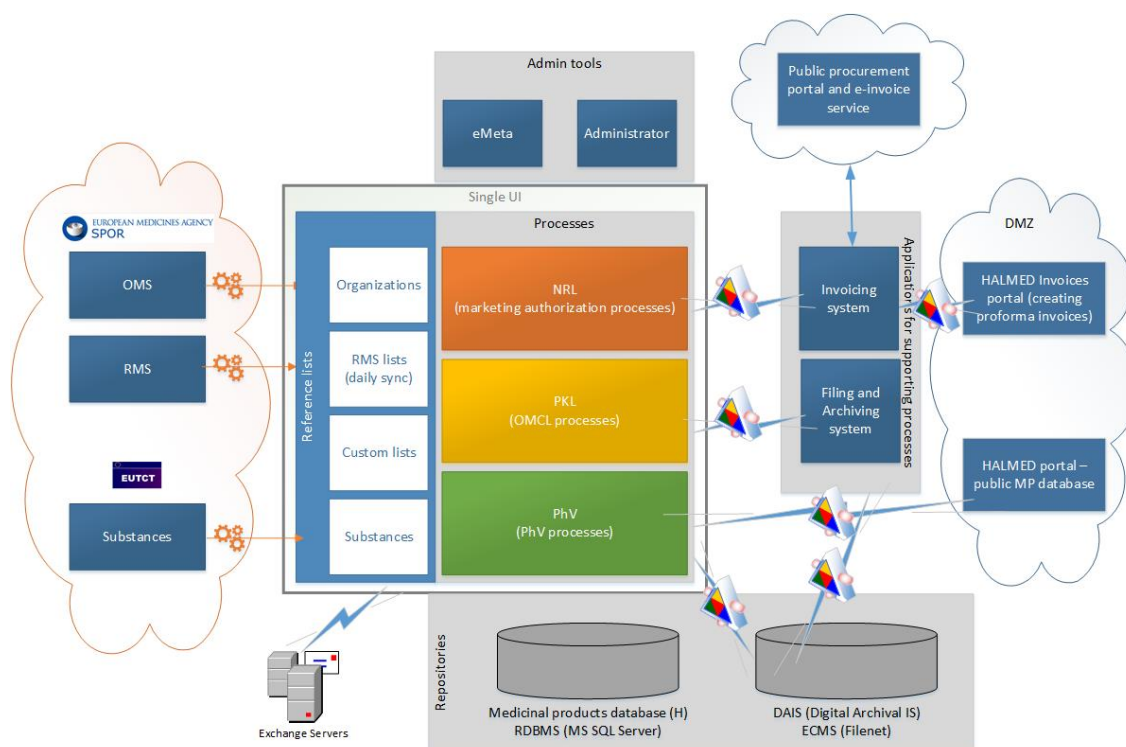
Figure 2. NRL-PKL-PhV system

Although Agency IT systems have been developed and upgraded in phases over the years, they are all interconnected with the services for data exchange and process tasks automation. Medicines data model that we use in NRL was implemented in other Agency IT systems, that are using medicines data in their processes, as well. The systems' design enables users to carry out all steps required for a process via only one application.

System is connected with DAIS (Enterprise Content Management System built on IBM Filenet), through web-services. This enables users to work with electronic documentation directly from the NRL-PKL-PhV system. According to Croatian legislation, Agency is still obligated to receive documentation in paper form, so incoming documents in paper form are digitized, enriched with metadata, stored on DAIS and accessed directly through NRL-PKL-PhV system. Through web-services, the system is also connected

with the other Agency systems such as the filing system (Centrix), Archival Management System (Pismohrana) and invoicing system, so users can complete all their tasks from one application.

2.3   Dependencies and relationships

HALMED IT system is not connected to the national eHealth system (yet), therefore the process of referential lists replacement and introduction of new SPOR lists is less complex.

Decision was made on national level to create National Medicinal Product Database (EU funded project eMedicines), so that nationally relevant data could be stored (for e.g. MP availability on Croatian market, the highest allowed MP price, etc.). On that project, HALMED cooperates with Ministry of health and Croatian Health Insurance Fund. HALMED and Croatian Health Insurance Fund will develop web services to send data (for which they are responsible) from their internal systems to National Medicinal Products Database.

Development of National Medicines Database, as the foundation for e-services is dependent on:

► SPOR deliverables
► UNICOM (WP1, WP2, WP3) project deliverables
► Services (OMS, SMS, PMS) that will enable synchronization of data for medicinal products authorized through centralized procedures.

2.4   Risks and mitigations

In the following table risks perceived in execution of Task 4.11 and overall UNICOM project risks[4] are listed. Risks are reviewed, assessed, analysed, and updated regularly. In risk list for Task 4.11, as well as in the Risk Register, risks are scored on a 3-level scale for their likelihood and potential impact; and a risk level will be assigned according to the table presented following Figure:

Figure 3. Risk scoring[5]

Risk management strategies include four options:

► 1) Avoid – taking action that will eliminate the threat/risk
► 2) Transfer – delegating or transferring risk to third-party (that is taking over the risk ownership)
► 3) Reduce/Mitigate – taking action that will reduce the likelihood or impact of a threat
► 4) Accept – risk is accepted and reaction plan is prepared.

Table 1. Risk mitigation on UNICOM WP4 and Task 4.11

Risk	Likelihood	Impact	Risk level	Date of appearance	Mitigation
Unforeseen events, such as epidemics, limiting travelling and switching focus of	Likely	Major	High	M5-?	Switching to teleworking, substituting face-to-face meetings with teleconferences and webinars. Active utilisation of SharePoint potential

---

[4] Risks copied from document „UNICOM_D11.1 Project management plan_20200529.pdf"

[5] From document „UNICOM_D11.1 Project management plan_20200529.pdf"

Risk	Likelihood	Impact	Risk level	Date of appearance	Mitigation
Consortium Members towards national priorities, causing delays in overall work			High		Task 4.11 (HALMED): Aligning workshop timeline with key business experts with their other assignments well in advance and with flexibility of rescheduling.
Development not progressing as expected	Possible	Major	High	M5-M48	Assessment and prioritisation of requirements and resources. Regular coordination (at least twice-a-week) with vendor that is developing system and implementation of agile software development methodologies on their side.
Complexity higher than expected	Possible	Major	High	M6-M48	Assessment and prioritisation of requirements and resources. Regular coordination (at least twice-a-week) with vendor that is developing system and implementation of agile software development methodologies on their side.
Low availability of IDMP and NCA/EMA experts	Possible	Major	High	M5-M48	Intensive collaboration with consortium partners and, if needed, with external experts to clarify relevant topics
Data migration towards IDMP delayed or scope must be reduced	Likely	Moderate	High	M1-M48	Adapt the scope of IDMP data migration to a minimum which is defined by the needs of the data consumers
Due to national prioritisations and internal dependencies implementation of national tasks slows down or benefits from more financial resources	Possible	Moderate	Medium	M1-M48	Contribution monitoring of progress and consumption at NCA level. Possible reallocation of funding between tasks (NCA's) to mitigate risk and enhance progress where possible
ISO IDMP identifiers needed for the univocal identification of medicinal products that depend on EMA publication and maintenance are not available	Likely	Major	High	M1-M48	Find replacement for these identifiers through direct collaboration with Drug NCAs of countries involved; substitute with MP data of repository piloted in WP9

Risk	Likelihood	Impact	Risk level	Date of appearance	Mitigation
Different work packages are not aligned or progress at different paces thus affecting the outcome of WP4	Possible	Moderate	Medium	M1-M48	Increase alignment efforts between work packages. Regular - monthly - review meetings of timetable and progress
Key partner or expert(s) leave the project (e.g. contract termination, longer illness, force majeure)	Possible	Major	High	M1-M48	Adequate structures for knowledge transfer will be implemented; reallocation of responsibilities, hiring of new experts as appropriate.
Short deadlines and parallel assignments/tasks execution	Possible	Major	High	M1-M48	Regular reassessment of all Task 4.11 activities and communicate and coordinate plan with all involved, including key business experts and users needed on project, vendor engaged on software development and system engineering team. Regular coordination meetings with other project managers so resource conflicts or other resource constraints could be avoided or mitigated as occur.
On software development vendor side: parallel system development sprints with the urgent and unpredictable bug solving requests	Possible	Moderate	Medium	M1-M48	Assessment and prioritisation of requirements and resources. Regular coordination (at least twice-a-week) with vendor that is developing system and implementation of agile software development methodologies on their side.
Key business experts could be unavailable for business or private reasons	Likely	Major	High	M1-M48	Adequate alternate should stand in for the unavailable business expert. Mitigation: define member stand-ins in advance, ensure knowledge transfer and responsibilities hand-over. Moreover, all activities that need business experts' engagement and workshops with business experts should be planned and communicated well in advance.

Risk	Likelihood	Impact	Risk level	Date of appearance	Mitigation
Developed functionalities does not suite the need expressed in User Requirement Specification.	Possible	Moderate	Medium	M1-M48	Engagement of all team members (IT and business representatives) on workshops with vendor's business analysts and development team representatives in order to prepare detailed Functional Requirements Specification.
Dependability of NRL-PKL-PhV system on other integrated IT systems in HALMED	Possible	Major	High	M1-M48	Regular coordination meetings with other project managers so resource conflicts or other resource constraints could be avoided or mitigated as occur

2.5 Task 4.11 Timeframe & Milestones

Table 2. Task 4.11 timeframe and deliverables

#	Task	Deliverable	Due month	Status
1.	HALMED kick-off meeting	UNICOM introduced to HALMED team; WP4 and WP8 team members defined	M1	done
2.	WP4 kick-off meeting	WP4 introductory workshop	M2	done
3.	Introductory workshop with software vendor on ISO IDMP	Vendor's team familiar with ISO IDMP and gaps vs IDMP in local DB data model, detected during workshops with key business experts	M2	done
4.	UNICOM kick-off meeting	UNICOM introductory workshop	M3	done
5.	NRL-PKL-PhV version 2 implementation	IQ, OQ, PQ testing on testing environment Deployment on production environment	M4-M15	In progress: testing & bug fixing
6.	Workshops with key business experts: SPOR RMS lists introduction prioritization	Business priorities agreed and set URS prepared for introduction of new SPOR RMS lists	M1-M48	Ongoing

#	Task	Deliverable	Due month	Status
7.	Introducing new RMS list: "Variation Classification"	Development of all FRS specified functionalities in application and introduction of new RMS list IQ, OQ, PQ testing on testing environment Deployment on production environment	M5-M15	In progress: testing, bug fixing
8.	Introducing new RMS list: "Anatomical Therapeutic Chemical classification system – Human"	Development of all FRS specified functionalities in application and introduction of new RMS list IQ, OQ, PQ testing on testing environment Deployment on production environment	M5-M15	In progress: testing, bug fixing
9.	Introduction of localized term versioning on referential lists (that are synchronized with SPOR RMS list)	Development of new functionalities: ► data versioning in the list ► notifications to users about the changes made in lists ► enabling search by old and new term IQ, OQ, PQ testing on testing environment Deployment on production environment	M5-M15	In progress: testing and bug fixing
10.	Data cleansing: Variation Classification list related data	Analysing and mapping values in internal variation classification referential list with EMA RMS Variation Classification list	M6-M16	In progress
11.	Data cleansing: Packaging	Analysing and Mapping values in internal referential list with EMA RMS list Packaging	M8-M20	In progress
12.	Data cleansing: Routes and Methods of Administration	Analysing and Mapping values in internal referential list with EMA RMS list Routes and Methods of Administration	M8-M18	In progress
13.	Data cleansing: ATC classification system – Human	Analysing and Mapping values in internal referential list with EMA RMS list ATC classification system – Human	M8-M18	In progress
14.	Data cleansing: Substances	Analysing and correcting/replacing values in internal MP database with EMA SMS (EUTCT Substance list)	M9-M21	In progress
15.	Data cleansing: Organizations repository	Analysing and data cleansing in internal Organizations repository, linking with OMS records	M11-M24	In progress

#	Task	Deliverable	Due month	Status
16.	New version of integrated filing system implementation (Centrix 2)	Implemented renewed integration services IQ, OQ, PQ testing on testing and production environment	M10-M12	Done
17.	New version of integrated ECM platform implementation (DAIS – Filenet platform)	IQ, OQ, PQ testing on testing and production environment	M14-M17	Not started
18.	Get acquainted with project communication and results dissemination plan	PR team familiar with UNICOM communication and dissemination plan	M7	Done
19.	NRL-PKL-PhV data model – gap analysis vs ISO IDMP	Analysis results document that will be foundation for FRS preparation for data model reconstruction and UI adaptation.	M9-M15	In progress
20.	Learning, familiarizing with FHIR and EU IDMP Implementation guide v2	HALMED IT team familiar with FHIR and EU IDMP IG v2	M8-M15	In progress
21.	Workshops with software vendor on FHIR and ISO IDMP	Vendor's team familiar with FHIR Implementation plan for SMS integration in place Test with UPD	M14-M20	Not started
22.	Workshops with key business experts: discussions about MA and medicines data in different use scenarios (national procedures)	Gaps in local DB data model vs IDMP detected during workshops with key business experts. Proposed set of medicinal products data for reviewed scenarios.	M2-M6	done
23.	Workshops with key business experts: discussions about MA and medicines data in different use scenarios (MRP/DCP)	Gaps in local DB data model vs IDMP detected during workshops with key business experts. Proposed set of medicinal products data for reviewed scenarios.	M8-M14	In progress
24.	Workshops with key business experts: discussions about medicinal products data in different use scenarios (Pharmacovigilance)	Gaps in local DB data model vs IDMP detected during workshops with key business experts. Proposed set of medicinal products data for reviewed scenarios.	M13-M16	Not started
25.	Workshops with key business experts: discussions about medicinal products data in different use scenarios (OMCL)	Gaps in local DB data model vs IDMP detected during workshops with key business experts. Proposed set of medicinal products data for reviewed scenarios.	M14-M17	Not started
26.	Workshops with key business experts: review of proposed medicinal products data set (based on findings from MA Division, PhV and OMCL	Gaps in local DB data model vs IDMP detected during workshops with key business experts.	M17-M19	Not started

#	Task	Deliverable	Due month	Status
	workshops) in scenarios of calculating maximal wholesales medicinal product prices	Finalized set of medicinal products data that will be recorded in NRL-PKL-PhV system.		
27.	Changes in data model related to capturing Substances data (Pharmaceutical product reconstruction) and implementation of necessary changes in UI – phase I	FRS prepared Data model reconstruction and development of all FRS specified functionalities in application. IQ, OQ, PQ testing on testing environment Deployment on production environment	M6-M20	In progress: testing and bug fixing
28.	eMedicines project (National medicinal products database) - Integration services for exchanging medicinal products data from NRL database	FRS prepared Development of all FRS specified functionalities in application and introduction of new RMS list IQ, OQ, PQ testing on testing environment Deployment on production environment	M12-M29	In progress
29.	NRL-PKL-PhV upgrade/reconstruction User Requirements Specification preparation for public tender	URS prepared	M20-M23	Not started
30.	Public tender for NRL-PKL-PhV data model reconstruction, database refactoring and UI upgrade	Public tender processed	M23-M26	Not started
31.	Changes in data model related to capturing Manufactured Item and additional fields in Packaged Medicinal Product, plus implementation of necessary changes in UI	FRS prepared Data model reconstruction and development of all FRS specified functionalities in application. IQ, OQ, PQ testing on testing environment Deployment on production environment	M26-M36	Not started
32.	Changes in data model related to Pharmaceutical product reconstruction and implementation of necessary changes in UI	FRS prepared Data model reconstruction and development of all FRS specified functionalities in application. IQ, OQ, PQ testing on testing environment Deployment on production environment	M28-M38	Not started
33.	Changes in data model related to capturing Substances data (Pharmaceutical product reconstruction) and implementation of necessary	FRS prepared Data model reconstruction and development of all FRS specified functionalities in application.	M30-M40	Not started

#	Task	Deliverable	Due month	Status
	changes in UI – phase II (connection with Packaged Medicinal Product)	IQ, OQ, PQ testing on testing environment Deployment on production environment		
34.	Upgrade NRL-PKL-PhV UI and Organizations repository in order to enable Validation team to easily (and directly from application) compare local and OMS data during the process of validating incoming MAH's documents.	FRS prepared Development of all FRS specified functionalities in application and introduction of new RMS list IQ, OQ, PQ testing on testing environment Deployment on production environment	M32-M40	Not started
35.	eAF integration with NRL-PKL-PhV system	FRS prepared Development of all FRS specified functionalities in application and introduction of new RMS list IQ, OQ, PQ testing on testing environment Deployment on production environment	M33-M41	Not started
36.	Synchronization with SMS	FRS prepared Development of all FRS specified functionalities in application and introduction of new RMS list IQ, OQ, PQ testing on testing environment Deployment on production environment	M34-M42	Not started
37.	Task 4.11 closure	All UNICOM Task 4.11 Documentation updated and finalized.	M42-M48	Not started

3 HALMED Deliverables

3.1 SPOR API usage

3.1.1 RMS

From the early stages of NRL system development until recently, following EUTCT lists have been used as our referential lists and syncronized on daily basis:

► Substance (still in usage) (Tvari)
► Country (Države)
► Dosage Form Category (Grupe farmaceutskih oblika)
► Dosage Form (Farmaceutski Oblici)
► Units of Measurement (Jedinice mjere)
► Route of Administration (Put primjene)
► Authorisation Status (Registracijski status lijeka)
► Marketing Status (Status lijeka na tržištu)
► Ingredient Role (Vrste sastojaka)
► Container (Vrste pakiranja)
► Supply (Mjesto izdavanja)
► Legal Status for the Supply (Način propisivanja)
► Special Precaution for Storage (Uvjeti čuvanja)
► Quantity Operator (Quantity operatori)

Until recently, it was allowed to add user-defined terms, because of UI limitations (for e.g. in cases when three routes of administration should be added in only one field, users were forced to add user-defined route of administration).

During the planning of transition to RMS lists, we detected four different scenarios and in following table are listed implementation steps for each of them, with examples of RMS lists already implemented in our system:

Table 3. Scenarios for RMS lists implementation

Scenario	Implementation process	RMS lists already implemented
Existing EUTCT lists with no custom-added terms	► Detecting corresponding RMS list ► Updating NRL referential list – changes in database and UI (adding fields in database and columns in UI for RMS and NRL (local) term versions) ► Establishing daily (automatic) one-way synchronization (download) with corresponding RMS list ► Term versioning and notifying users about new versions of terms, so that new term version could be used in regulatory activity that is changing product information documents. Old and new term versions are searchable.	► Country ► Language ► Legal Status for the Supply ► Quantity Operator ► Regulatory Entitlement Status ► Ingredient Role
NRL referential list connected with EUTCT list, but with some additional user-added terms	► Data cleansing, disabling the possibility to add custom terms in EUTCT list, deactivating custom-added terms that are not used (or shouldn't be used) ► Detecting corresponding RMS list ► Analysing and implementing changes needed in UI and database (if needed, adding fields in database and columns in UI for RMS IDs and RMS and NRL (local) term versions)	► Pharmaceutical Dose Form, Combined term, Combined Pharmaceutical Dose Form, Combination Package ► Dosage Form Category ► Units of Measurement ► Supply

| Scenario	Implementation process	RMS lists already implemented
	► Establishing daily (automatic) synchronization with corresponding RMS list ► Term versioning and notifying users about new versions of terms, so that new term version could be used in regulatory activity that is changing product information documents. Old and new term versions are searchable.	► Routes and Methods of Administration ► Marketing Status ► Special Precaution for Storage ► Packaging
Existing custom lists	► Business analysis for referential list prioritization ► Detecting corresponding RMS list ► Before connecting to new RMS list, perform data quality analysis and data cleansing ► Creating new NRL referential list for downloaded RMS referential list, adapting NRL functionalities, UI and database structure if needed ► Download RMS list and mapping terms from custom list with terms from RMS list and deactivating redundant terms (no mapping tools are used) ► Establishing daily (automatic) one-way synchronization (download) with corresponding RMS list ► Term versioning and notifying users about new versions of terms, so that new term version could be used in regulatory activity that is changing product information documents. Old and new term versions are searchable.	► Anatomical Therapeutic Chemical classification system – Human ► Variation Classification
Currently no lists are used (new list implementation needed)	► Business analysis for referential list prioritization ► Creating new NRL referential list for downloaded RMS referential list, adapting NRL functionalities, UI and database structure if needed (for e.g. for packaging description significant changes in data model should be implemented so Manufactured item could be described) ► Establishing daily (automatic) one-way synchronization (download) with corresponding RMS list ► Term versioning and notifying users about new versions of terms, so that new term version could be used in regulatory activity that is changing product information documents. Old and new term versions are searchable.	► Domain ► Units of Presentation ► Container Category
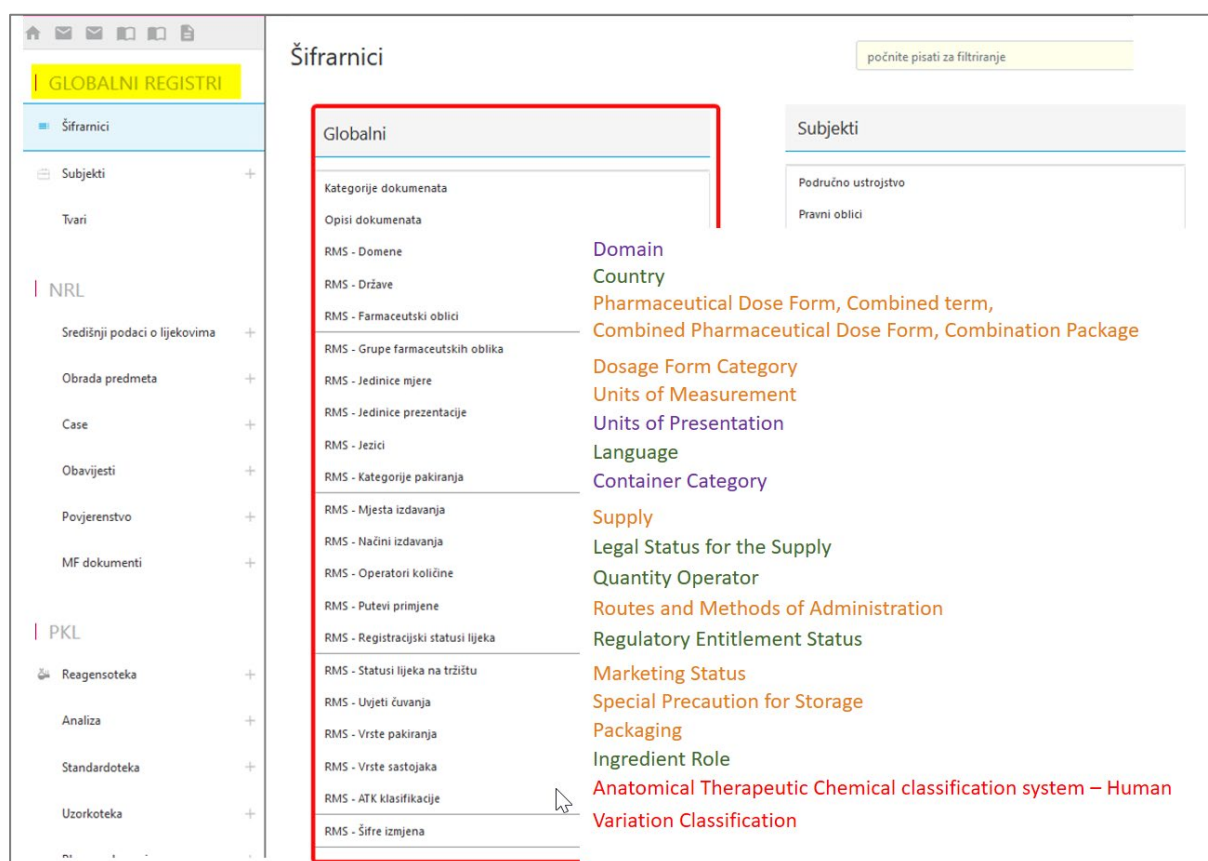
Figure 4. RMS lists already in use in NRL-PKL-PhV system

Localized term versioning

With introduction of RMS lists, SPOR and NRL term versions are stored (separately). On all opened applications and MPs that have old term, it is not changing before regulatory activity that is changing product information documents. In order to announce a term change to business users, an e-mail notification is sent with details about new term version from NRL, emphasizing term change on status bar and in the field where it appears in user interface. Besides, in the search engine, both old and new term version, are searchable.

Uredi	ID	Naziv	Šifra (RMS)	Naziv (RMS)	↓ NRL verzija	Vrijedi od	Aktivno	Primjenjivo	SPOR verzija	SPOR status
		Q	Q	Q	Q	Q	(Svi) ▼	(Svi) ▼	Q	Q
✏	1269	Otopina za injekciju u ulošku za dozator	100000167461	Solution for injection in dose-dis...	2	19. 08. 2019.	✓	✓	31	CURRENT
✏	1268	Otopina za injekciju u napunjenom inj...	100000166823	Solution for injection in pre-fille...	2	19. 08. 2019.	✓	✓	35	CURRENT
✏	1267	Mast za oko u jednodoznom spremniku	100000136322	Eye ointment in single-dose con...	2	19. 08. 2019.	✓	✓	33	CURRENT
✏	1266	Kapi za oko, suspenzija u jednodozno...	100000136321	Eye drops, suspension in single-...	2	19. 08. 2019.	✓	✓	34	CURRENT
✏	1265	Kapi za oko, otopina s produljenim osl...	100000136320	Eye drops, prolonged-release so...	2	19. 08. 2019.	✓	✓	34	CURRENT
✏	1264	Prašak, otapalo i matrica za implantaci...	100000143552	Powder, solvent and matrix for i...	2	19. 08. 2019.	✓	✓	33	CURRENT
✏	1263	Prašak i otapalo za suspenziju za endo...	100000143546	Endotracheopulmonary instillati...	2	19. 08. 2019.	✓	✓	32	CURRENT
✏	1262	Prašak i otapalo za dentalni cement	100000143502	Powder and solution for dental ...	2	19. 08. 2019.	✓	✓	33	CURRENT
✏	1261		100000136907	Solution for dispersion for injecti...	2	13. 01. 2017.	☐	☐	3	NULLIFIED
✏	1260	Suspenzija i otapalo za suspenziju za i...	100000125777	Suspension and solvent for susp...	2	19. 08. 2019.	☐	☐	34	NON_CURRENT
✏	1259	Kapi za nos, prašak i otapalo za otopinu	100000125747	Nasal drops, powder and solven...	2	19. 08. 2019.	✓	✓	38	CURRENT

Figure 5. Referential list in NRL-PKL-PhV system with localized and SPOR version recorded

Farmaceutski oblici

Promijenjen je zapis: 100000073673		
Naziv kolone	**Stara vrijednost**	**Nova vrijednost**
Version	0	17
DosageFormCategoryID	11	[NULL]
ValidFrom	2019-08-30 06:01:37.463	2019-08-19 08:41:22.900
Name_HR	grgljača	Otopina za grgljanje
Promijenjen je zapis: 200000010731		
Naziv kolone	**Stara vrijednost**	**Nova vrijednost**
Name_EN	Oral powder in capsules for opening	Oral powder in single-dose container
ValidFrom	2020-03-18 16:05:45.957	2020-04-21 11:15:41.947
SporStatusID	PROVISIONAL	CURRENT
Version	1	2

Figure 6. Localized term versioning – e-mail notifications

On all opened applications and medicinal products that have old term, term is not changing before regulatory activities that are changing product information documents. Changed terms are indicated on status bar:

Figure 7. New term indicated on status bar

Old terms are indicated with red letters where they appear in UI and in drop down lists. In marketing authorization application for new medicinal product, only new terms will be listed on all lists:

Figure 8. Indication of old term version in use

3.1.2   OMS

HALMED is using own Organizations repository for more business processes, for medicinal products and medical devices and in different IT systems. Currently, by using OMS API internal organization IDs and location IDs are linked with OMS Org and Loc IDs. This is done because internal Organizations repository data quality assessments have shown that internal data is of higher quality level than data in OMS repository.

Figure 9. Linking organizations in internal repository with OMS Org IDs and Loc IDs

Organizations repository contains Croatian or English organization names, locations and location purposes (for example headquarter, manufacturing address, billing address, etc.). HALMED already implemented Organizations versioning.

Organizations data was impaired with bug on synchronization routines and internal, custom developed tool NRL Administrator is used for data cleansing.

Plan is to upgrade UI and Organizations repository in order to enable Validation team to easily (and directly from application) compare local and OMS data during the process of validating incoming MAH's documents.

3.1.3 SMS

Currently we are in the process of data cleansing while 0,3% terms (175 out of 61.308) were custom added:

► 36 already deactivated (replaced with EUTCT terms)
► 139 still active – will be replaced with EUTCT terms during regulatory activities that are changing product information documents

HALMED IT team just recently started to explore SMS API on https://spor-uat.portal.azure-api.net/docs/services.

3.1.4 PMS

HALMED is responsible only for human medicinal products, but we have just become responsible for some processes that are based on veterinary products:

► performing quality control of veterinary products in OMCL
► granting authorisation to manufacturers and wholesalers of veterinary products
► GMP and GDP inspection

Currently HALMED team is analysing concepts of storing data for veterinary products in the same database with human medicinal products.

HALMED IT team just started to participate on UPD calls, received access to UPD Informal UAT of data repository and API and consider this as a great learning and good preparation for PMS API.

3.2 Data Model - Gap Analysis

In 2010 HALMED decided to build own medicinal products database on the data model described in RDM 3.0 model (Reference data model published by EMA), that was confirmed as good practice at that time. Due to the simplification of RDM data model vs. ISO IDMP data model (or vs. data model according to at that time relevant standard CEN ENV 12610 Medical Informatics - Medicinal Product Identification), packaged products were not properly described, Manufactured item is missing and in our data model descriptive text fields were used.

Implementation of new business process in HALMED for calculation of maximal medicinal product wholesale price visibly show that there are shortages in data model that make it impossible to describe packages properly so they could be compared with medicinal products from referent countries. For example, in HALMED medicinal products database, following data is missing:

► Container type (single use / multi-use)
► Unit of presentation
► Number of containers in package
► Quantity of pharmaceutical form in container
► Number of units of presentation in package

Comparing the currently used medicinal product data model with ISO IDMP, three important refactoring areas were detected:
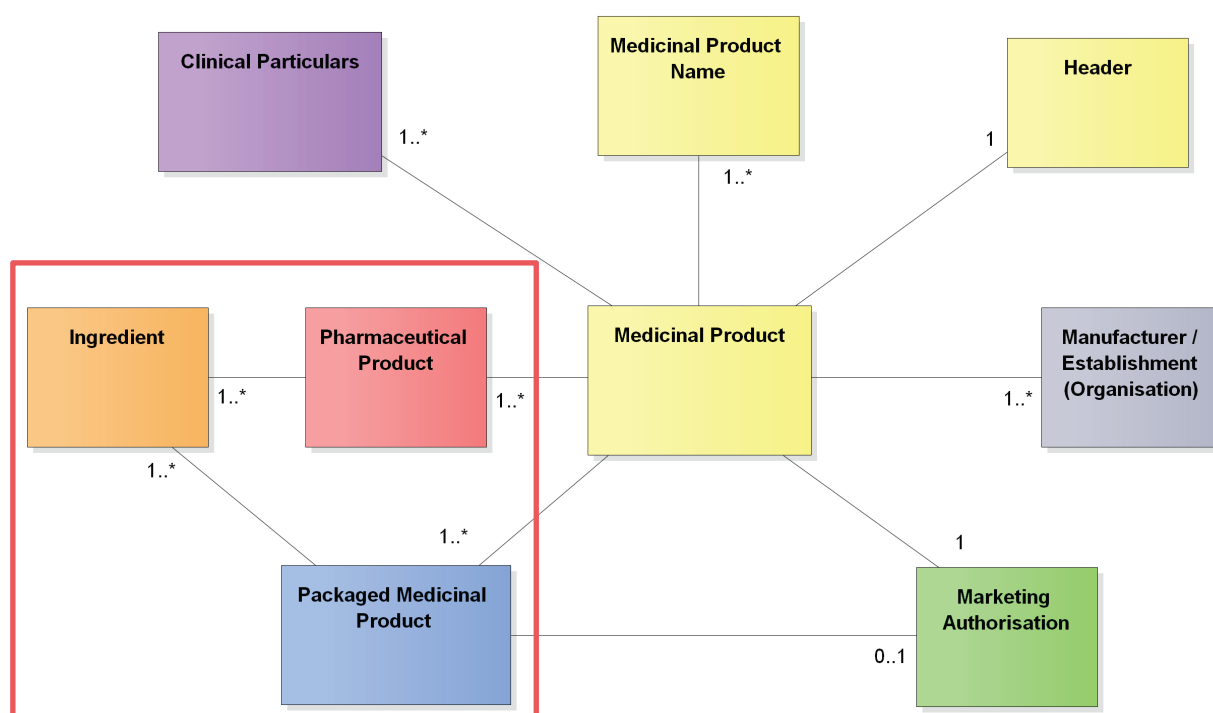
Figure 10. IDMP partial logical model -UML representation from EN ISO 11615

► Packaged Medicinal Product: Manufactured Item should be introduced in data model
► Pharmaceutical product needs some adjustments
► Ingredients – first phase of ingredients data model reconstruction implemented on test environment.

3.2.1   Packaged Medicinal Product gap analysis

Current data model: Packaging

Currently only one text field is used to describe package (without possibility to record inner packaging or devices for combo examples). Additional packaging data is captured separately (mostly in text fields), but on the process data set and not as part of packaging data set. For example, during OMCL (Official Medicines Control Laboratory) processes of sampling or analysing medicinal products and some of those fields are not required – for example:

- ► Batch identifier
- ► Expiration date
- ► Shelf life
► We are generating Package ID
► RMS lists used:
  - ► Packaging
  - ► Container Category
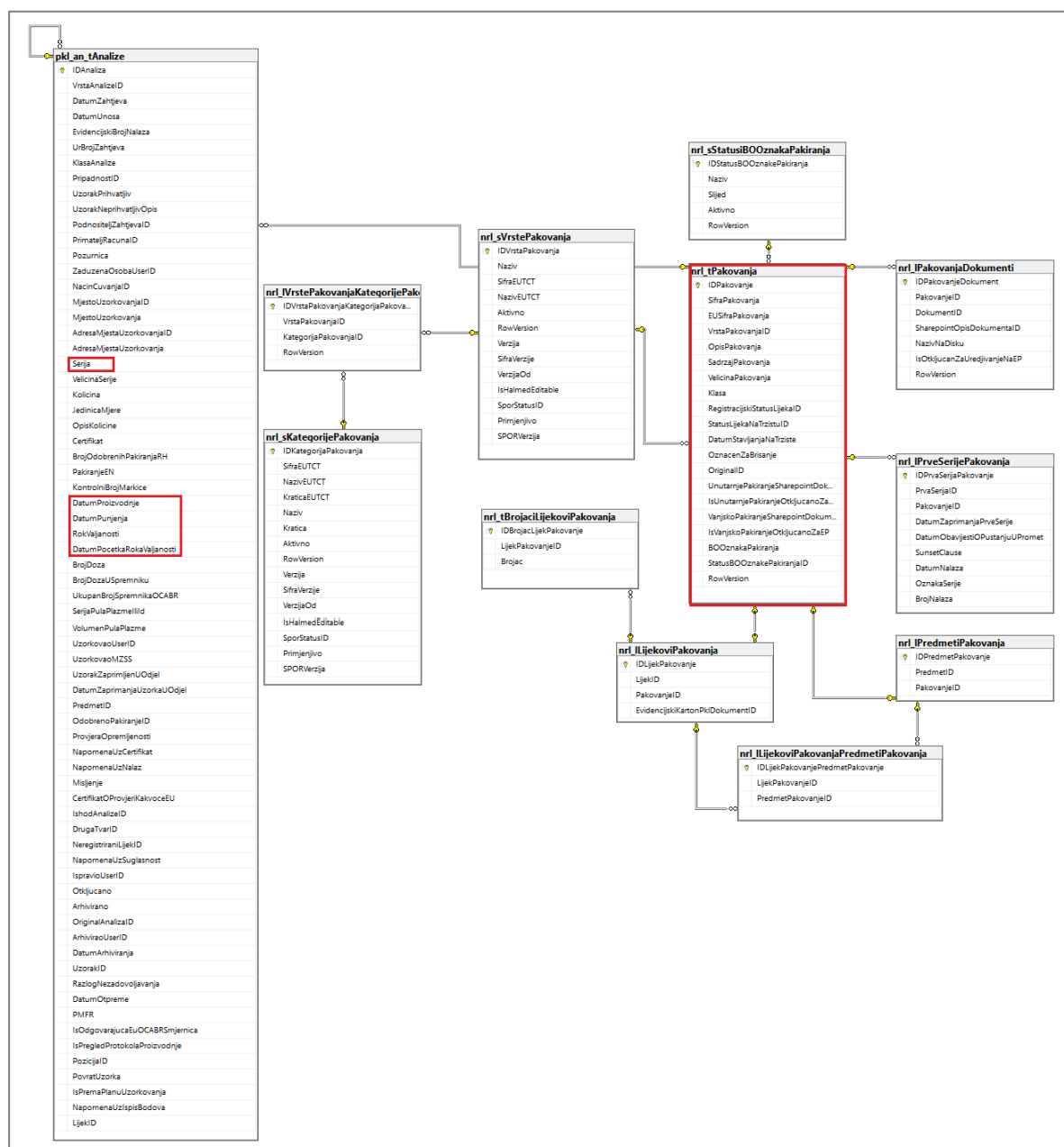 - ► Regulatory Entitlement Status
  - ► Marketing Status

Figure 11. Current data model with fields describing packaging

In current data model, it is not possible to properly describe complex packages, for example:

► with more packaged products inside box
► with more manufactured items inside packaged product
► with administration device (applicator)

Furthermore, it is not possible to record Device data, administrable product dose and there is no possibility to describe Manufactured item in current data model.
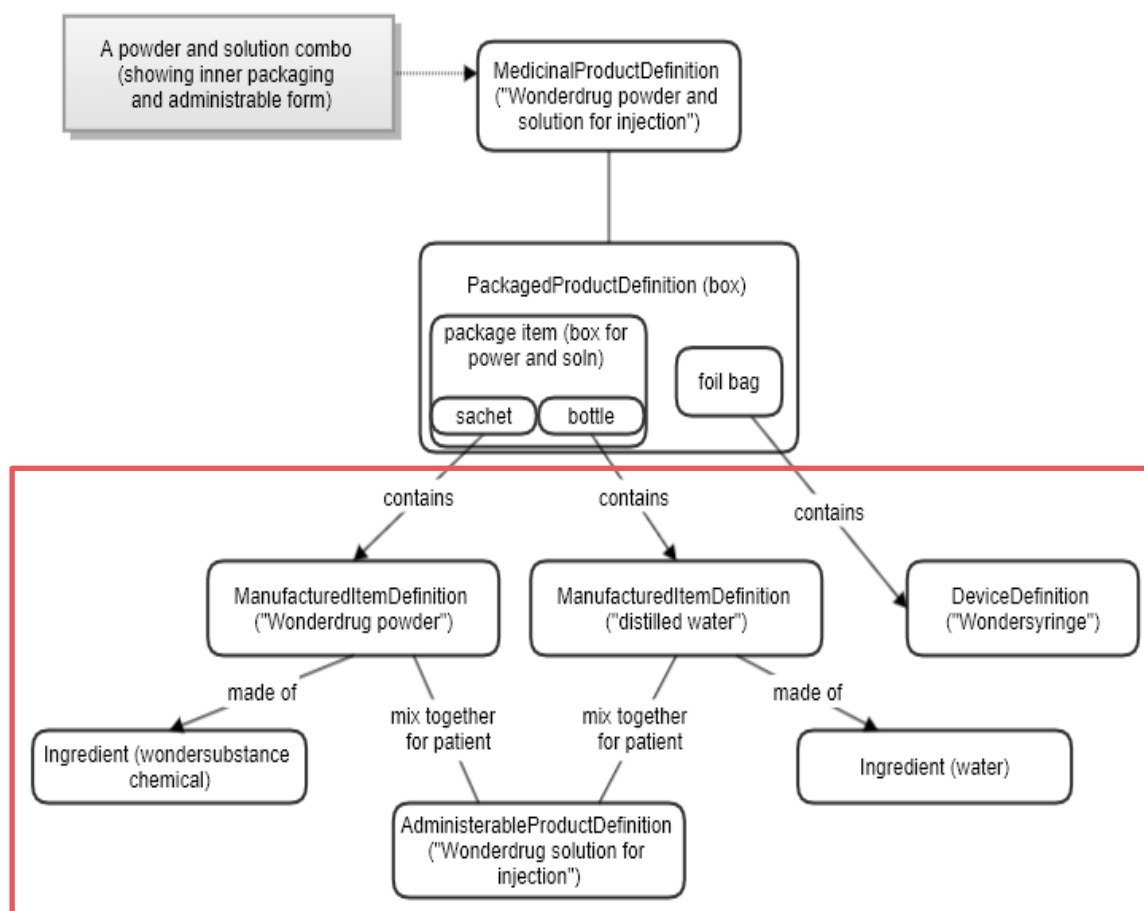
Figure 12. Complex packaging described[6]

Example: for capturing data of Packaged Medicinal Product (Canesten 3 combi 200 mg tablete za rodnicu i 10 mg/g krema) only two text fields are used – package description (for final document export) and Package content:

Figure 13. Capturing Packaged medicinal product data in current system

---

[6] Source: http://build.fhir.org/medication-definition-module.html

Transition strategy

In the following figure the fields in red rectangles are those that we have to introduce in our model and in yellow are those that would need some reconstruction:
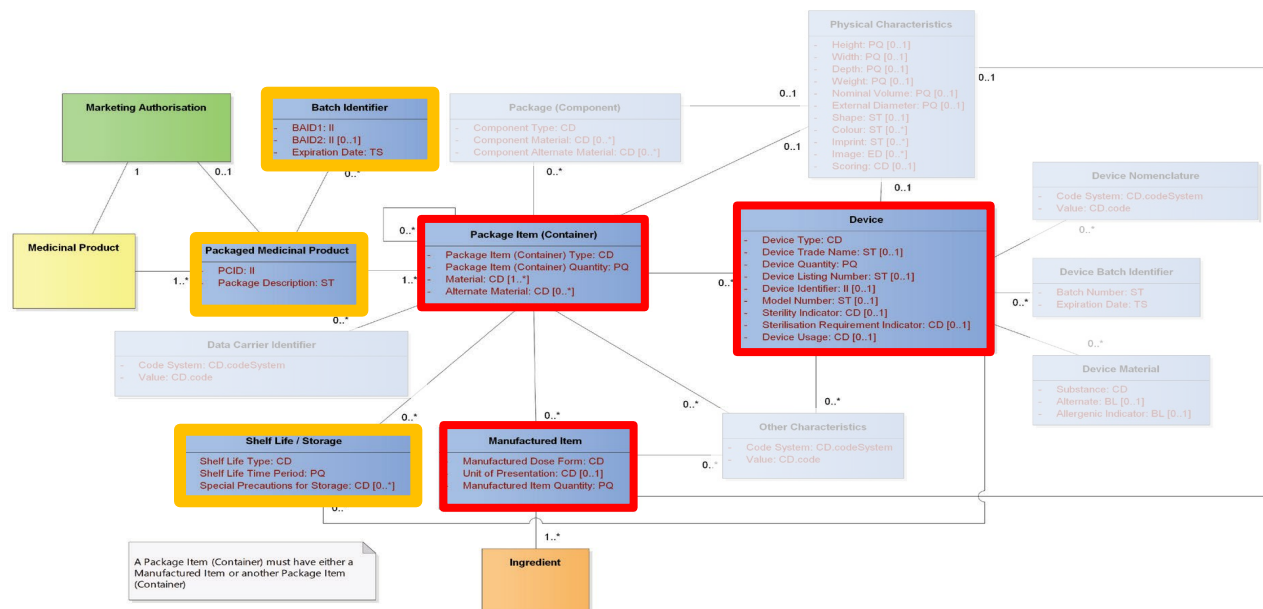

Figure 14. Refactoring Packaged Medicinal Product prioritization[7]

Besides adding new tables and establishing new relations in the database, following tasks should be performed:

► Adding structure and fields in data model:
   ► Manufactured Item
   ► Package Item (Container)
   ► Device
► UI reconstruction (tab „Packaging"):
   ► enable input of more Packaged Medicinal Products
   ► enable input of more Package Items
   ► enable input of Devices
   ► enable input of Manufactured Items
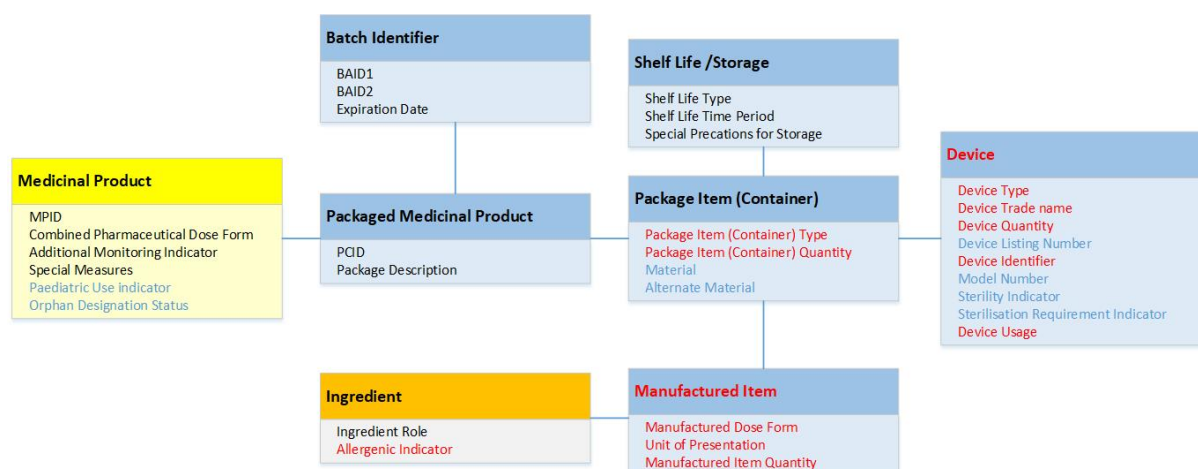► Data cleansing and data migration (challenge: extracting data from package description text field)

Figure 15. Packaged Medicinal Product Data model refactoring

---

[7] Source: ISO 11615 (Packaged Medicinal Product section detailed description diagram)

3.2.2   Pharmaceutical Product

Current data model: Pharmaceutical Product

For Pharmaceutical Product, we are already capturing all the data and some adjustments are needed:
► Reorganizing data structure
► Adding field for PhPID
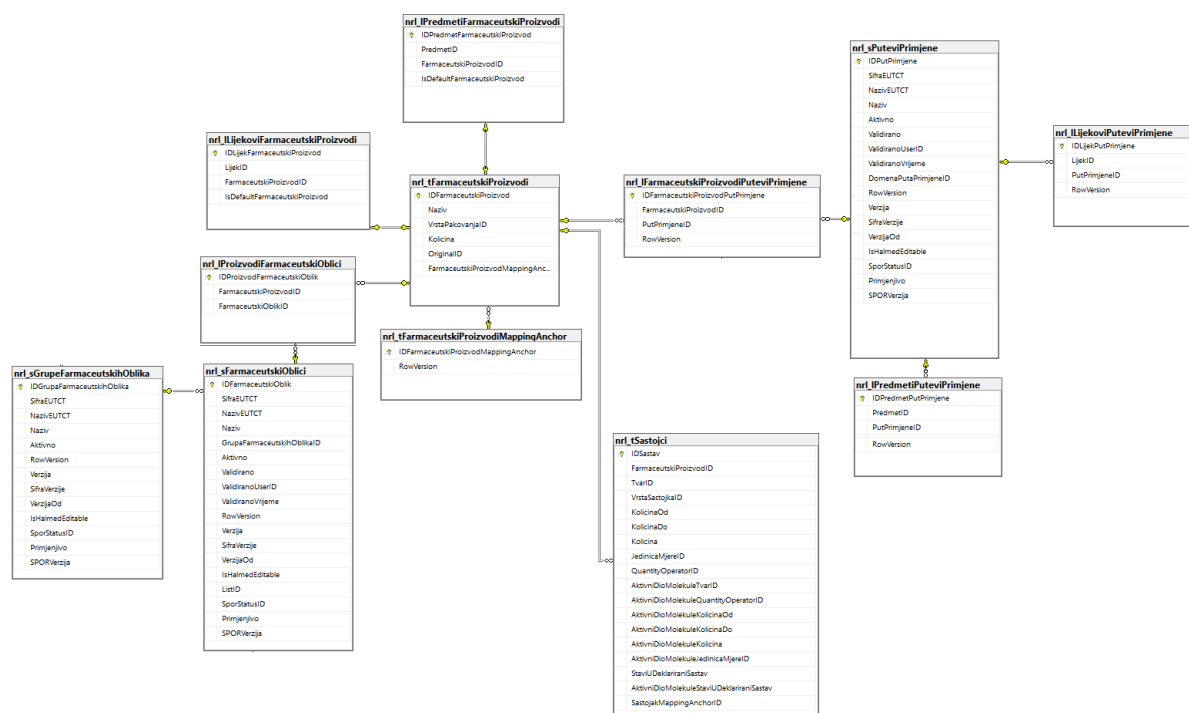► Adding Administrable Dose Form

Figure 16. Current Data model - Pharmaceutical Product

Transition strategy

In red rectangles are those fields that have to be introduced in current data model and yellow are those that would need some reconstruction:
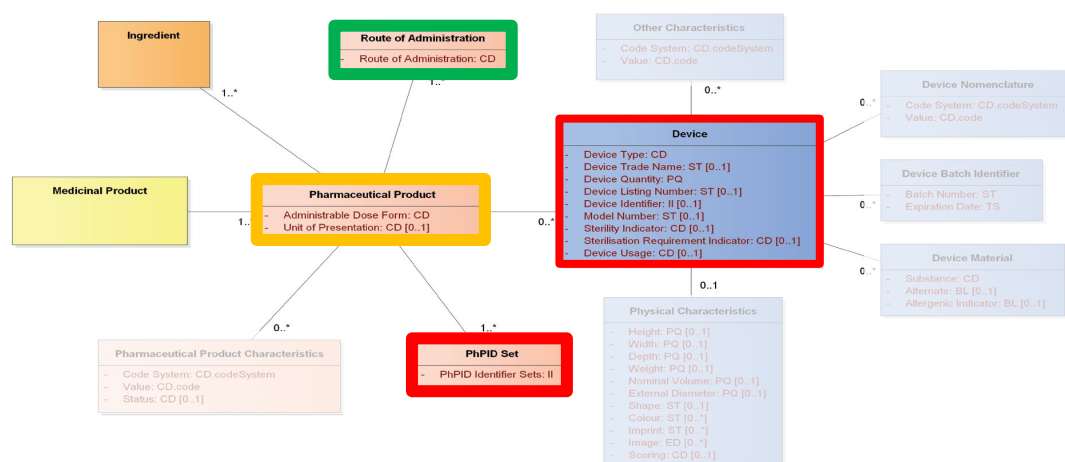

Figure 17. Refactoring Packaged Medicinal Product prioritization[8]

---

[8] Source: ISO 11615 (Pharmaceutical product and device section detailed description diagram

3.2.3   Ingredients

Current data model: Ingredients

For Ingredients, HALMED is in the process of first phase implementation that is prerequisite for properly capturing Pharmaceutical Product. In phase two, further analysis should be conducted for establishing relation with Packaged Medicinal Product.
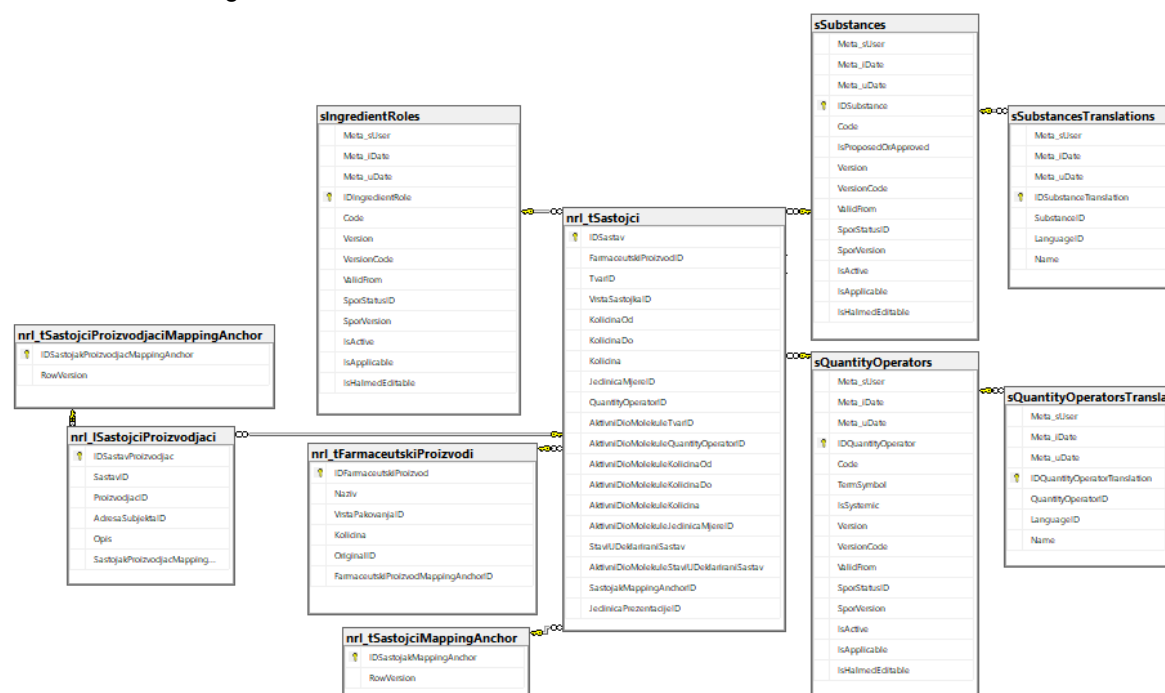

Figure 18. Current Data model - Ingredients

Transition strategy

In red rectangles are those fields that have to be introduced in current data model and yellow are those that would need some reconstruction:
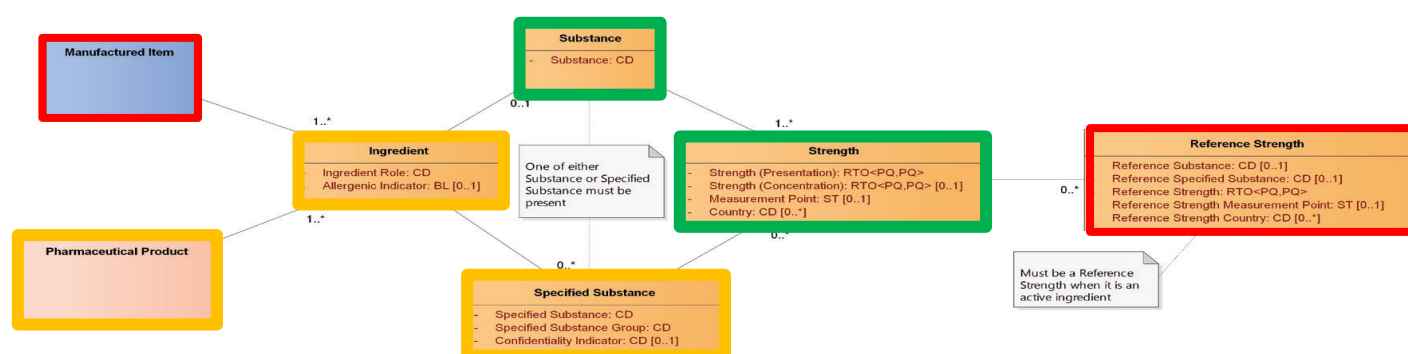

Figure 19. Refactoring Packaged Medicinal Product prioritization[9]

In the first phase of Ingredients data model reconstruction, we enabled capturing strength range as concentration (besides strength range as presentation) and referential list Units of presentation was added.
After the first phase of Ingredients data model reconstruction and the introduction of Manufactured Item, further analyses will be conducted to plan the representation of ingredients in Manufactured item.

---

[9] Source: ISO 11615 (Ingredients, substance and strength section detailed description diagram

4 Lessons learned and next steps

During the first year on executing Task 4.11, we have learned that:

- ► Internal business experts' engagement is crucial for success of system development.
- ► Database built on RDM 3.0 data model makes transition to IDMP data model easier than starting from scratch.
- ► Introduction of new processes related to calculation of maximum wholesale medicinal products' price, where medicinal products data should be compared for same products from different countries, helped us better understand ISO IDMP data model and to detect gaps in the internal system.
- ► It's never time to focus all your resources on developing new system – we found the way to continue working with the old one, with the new UI „skin" and continue gradually to refactor the code and database.
- ► Participation in the project of building National medicinal product database gives us an opportunity to foster SPOR and ISO IDMP data model on the National level.

Our plan for M13-M24 is to:

- ► Continue with data cleansing and data mapping.
- ► Deploy the NRL-PKL-PhV version 2 (mainly concerning the UI changes, introduction of new RMS lists and first phase of "Ingredients" data model refactoring) to production environment.
- ► Continue prioritizing the introduction of new RMS lists and deploy to production those in testing phase.
- ► Continue conducting workshops and discussions with key business users to define business processes and data sets needed.
- ► Participate in eMedicines project (and prepare URS for integration services for exchange MP data with National MP database).
- ► NRL-PKL-PhV upgrade/reconstruction User Requirements Specification preparation for public tender and conduct public procurement.

Our plan for M25-M48 is to:

- ► Continue with data cleansing and data mapping.
- ► Continue conducting workshops and discussions with key business users to prioritize implementation of SPOR RMS lists, clean internal referential list data and introduce new RMS lists.
- ► Implement changes in data model related to capturing Manufactured Item and additional fields in Packaged Medicinal Product, and implement necessary changes in user interface.
- ► Implement changes in data model related to Pharmaceutical product refactoring and implement necessary changes in user interface.
- ► Implement changes in data model related to capturing Substances data and implementation of necessary changes in UI (second phase of refactoring data model related to Substances data).
- ► Upgrade NRL-PKL-PhV and Organizations repository in order to enable Validation team to easily and directly from application compare local and OMS data during the process of validating incoming MAH's documents.
- ► eAF integration with NRL-PKL-PhV system.
- ► Establishing connection and daily synchronization with SMS.