UNICOM

Up-scaling the global univocal identification of medicines

IDMP & FHIR for NCAs
Friday 10th of March 2023

Speakers: Noel Diamant (AGES), Gianluca Risi (AEMPS)
Work package lead: Georg Neuwirther (AGES)

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Do not use this information for decision making, but instead always refer to official documents, relevant regulations, regulatory guidelines and SPOR guidance material

Recording

► **This sessions will be recorded and made available after the training.**

Agenda

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➤ **Georg Neuwirther**
UNICOM WP3 Lead, Austrian Medicines Agency

➤ **Noel Diamant**
Product Co-Owner for DADI, Austrian Medicines Agency

➤ **Gianluca Risi**
Senior Software Engineer, AEMPS

1 **Introduction, Motivation**
10:00 – 10:20

➤ *Georg Neuwirther*
(AGES, Head of IT AGES Medical Market Surveillance)

2 **References – Where to start?**
10:20 – 10:25

➤ *Noel Diamant*
(AGES, Product Owner, Architect)

3 **Top 10 most wanted IDMP fields**
… and where to find them
10:25 – 10:45

➤ *Noel Diamant*

4 **Provenances –**
The list of changes in a variation
10:45 – 10:55

➤ *Noel Diamant*

5 minute break

5 **Basics - How to read FHIR and use XPath?**

11:00 – 11:15

➤ *Gianluca Risi (AEMPS, Senior Developer)*

6 **A guide to extracting information**
presented with a UNICOM reference implementation

11:15 – 11:50

➤ *Gianluca Risi, Noel Diamant*

7 **Closing**
11:50 – 12:00

➤ *Georg Neuwirther*

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Speaker

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*(AGES Head of IT - Austrian Medicines and Medical Devices Agency,
Chair eAF Maintenace Group, UNICOM Workpackage Lead)*

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(AGES, Product Owner, Architect)

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▶ *Gianluca Risi*
*(AEMPS
Senior Developer, Architect)*

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Up-scaling the global univocal identification of medicines

Introduction

Motivation to organise such a training

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- **Data availability in regulator systems (HMA/EMA)** becomes more essential
    - see also HMA/EMA strategy to 2025 and EMA/HMA announcements.

- The **"new" application forms (PLM Portal/DADI)** will provide improved opportunities **to import application and medicinal product data into our IT system**

- A pan-European project **"UNICOM"** and **EMA** are working on the implementation of new data standards called **ISO – IDMP**
    - **This will help us to represent and store medicinal product data in a common approach – like eCTD standards to structure dossiers!**

European medicines agencies network strategy to 2025
Protecting public health at a time of rapid change

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

High-quality data to empower data-driven medicines regulation in the European Union
News 10/10/2022
EMA and the Heads of Medicines Agencies (HMA) in the EU Member States are moving ahead with their ambitious agenda to increase access and improve the quality of the data that underpin decision-making on the benefits and risks of medicines in the European Union (EU).

Source: EMA - High-quality data to empowerdata-drivenmedicines regulation in the European Union | European Medicines Agency (europa.eu)

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unicom-project.eu

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Data on medicines (ISO IDMP standards): Overview ⟨ Share

The European Medicines Agency (EMA) is in the process of implementing the standards developed by the International Organization for Standardization ↗ (ISO) for the identification of medicinal products (IDMP).

Let's use this meeting to understand the new opportunities and get technical info on how we can use them

What is UNICOM?

UNICOM is a project consortium that received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 875299. Further detail can be found here: https://unicom-project.eu/ or on LinkedIn

Focus for the European Medicines Regulatory Network (EMRN) - **is objective ii)** of the project call:

> " …. *This innovation action is expected to support two goals:*
>
> *(i) the cross-border mobility of European patients by offering safer eDispensations across borders,*
>
> *(ii) the implementation of the IDMP standards in Member States drug databases (including a possible linkage to the EU SPOR - Substance, Product, Organisation and Referential master data database) allowing the identification of locally available medicinal products which are equivalent to the one identified in a foreign prescription. …"*

Cooperation of National Medicines Authorities

11 National Competent Authorities

together with e-health organisations, SDOs, industry companies, SW-companies

are working together to implement ISO-IDMP and EU guidance in their medicinal products related IT systems and data repositories

Vision

With compatible IT systems and regulatory processess to ensure data of high quality we will be able to provide IDMP-compatible data and enable various use cases throughout Europe for several stakeholder groups (e.g. eHealth scenarios)
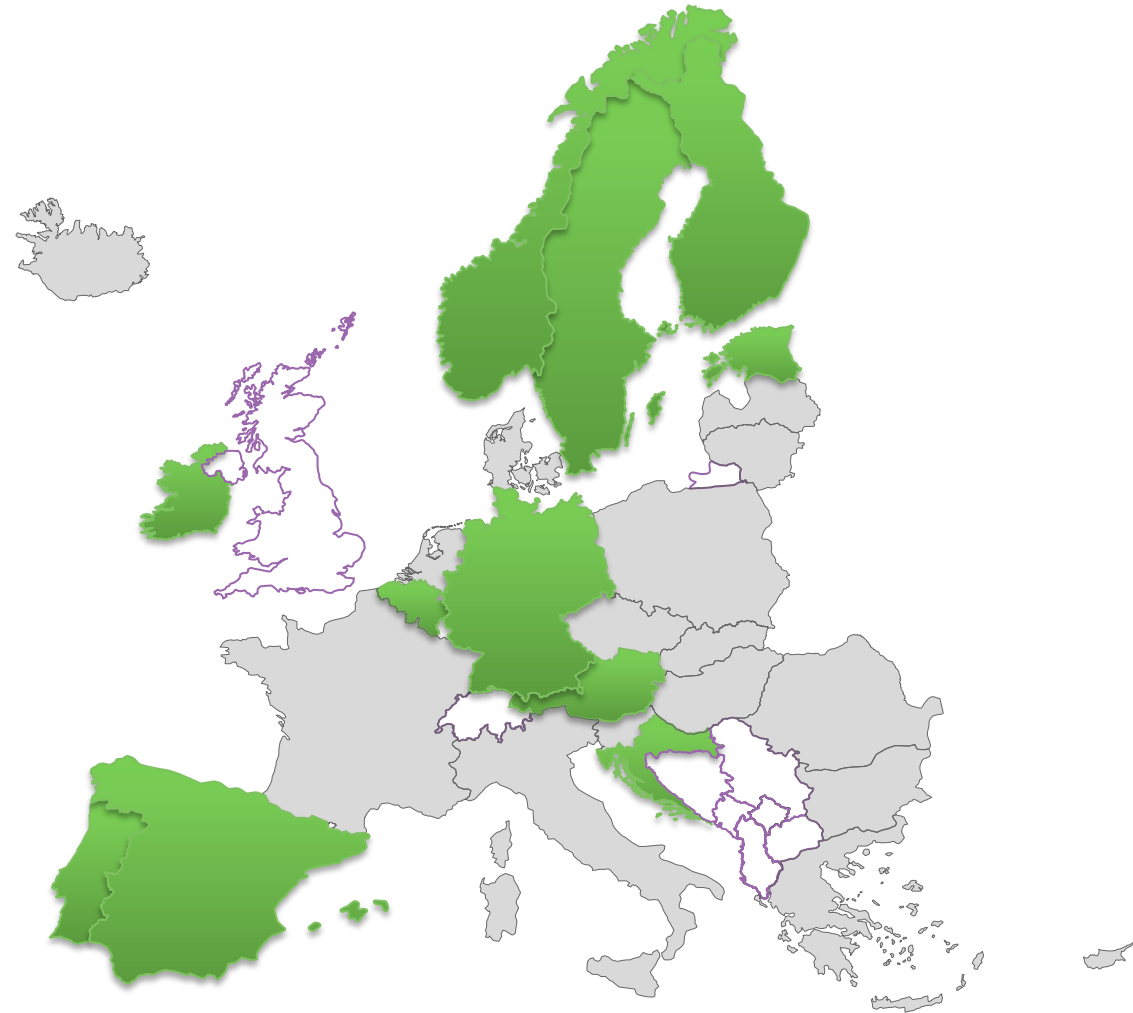
UNICOM objective:
Introducing ISO-IDMP compliant application forms

- At the moment neither application forms nor the tools for initial authorisations, variations and renewals are compliant to the ISO IDMP standards. Thus, it is currently not possible to start, automate and feed regulatory processes with IDMP compliant/structured data and easily re-use the data in EU-wide eHealth services.

The aim of this UNICOM work package is to adapt the application forms and required tools towards the ISO-IDMP / FHIR standards and to increase the usage of EMA's SPOR. It will therefore *deliver web-based application forms compatible with IDMP standards and relevant European Guidance (like EMA IDMP EU IG)*

- **7 National competent authorities** are working together
  - Spain (Development PDF-representation)
  - Austria (Product Owner PLM Product Owner together with a Product Owner from EMA)
  - Netherlands, Germany, Ireland, Sweden, Norway (Contribution of Expertise, Knowledge, Testing, Communication, etc. o)

- **EMA is developing the core IT service Product Lifecycle Management Portal**
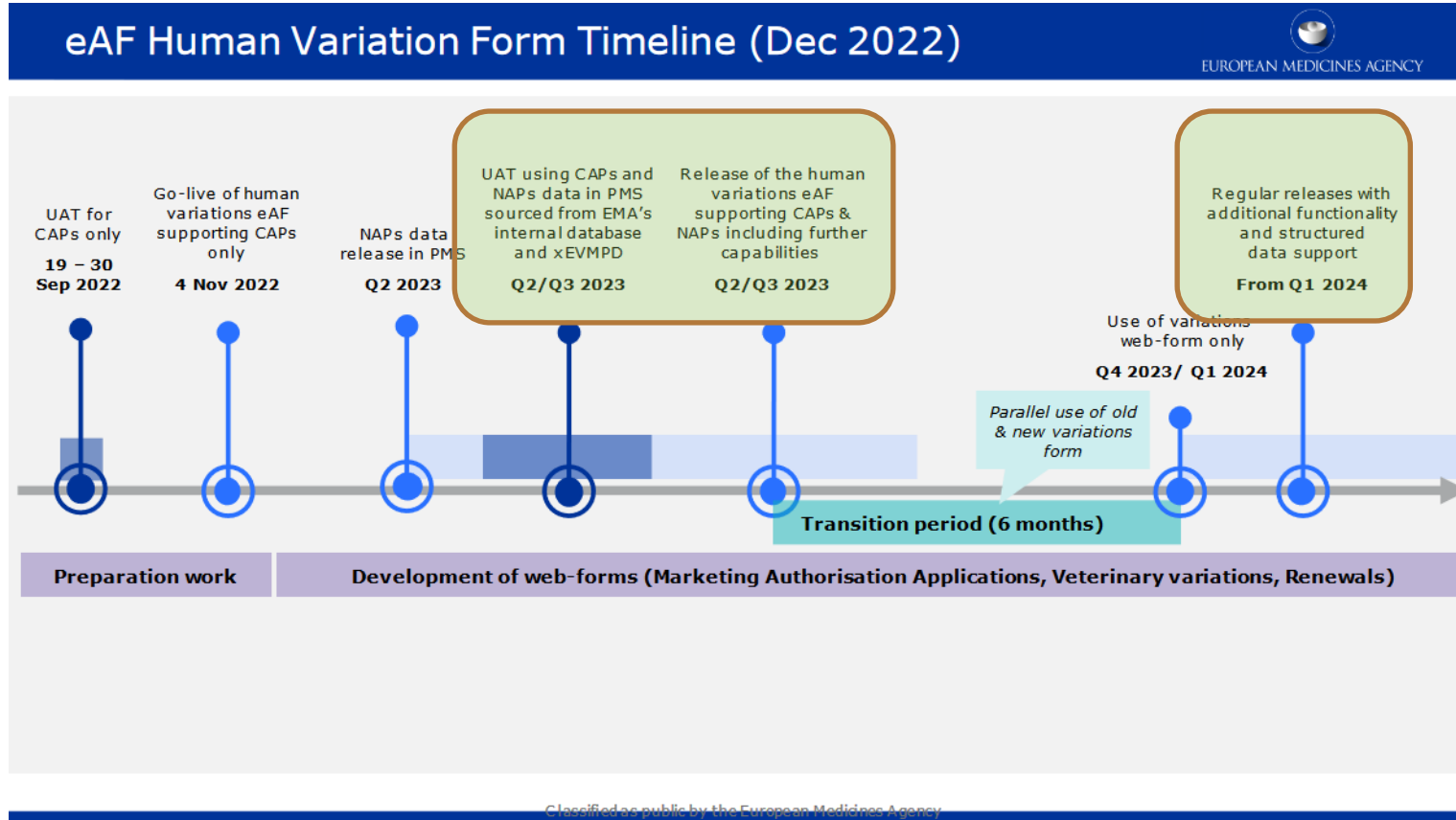 - EMA is not an UNICOM partner!

Welcome to PLM Portal

A secure online portal for managing electronic Application Forms, electronic Product Information (ePI) and authorised product data (PMS) in the European Union, in collaboration with the European Medicines Regulatory Network.
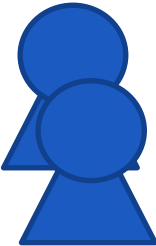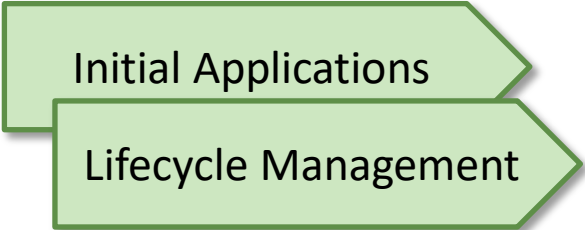
Sign In >

https://plm-portal.ema.europa.eu/

Timelines

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eAF Human Variation Form Timeline (Dec 2022)

EUROPEAN MEDICINES AGENCY

UAT for CAPs only
19 – 30 Sep 2022

Go-live of human variations eAF supporting CAPs only
4 Nov 2022

NAPs data release in PMS
Q2 2023

UAT using CAPs and NAPs data in PMS sourced from EMA's internal database and xEVMPD
Q2/Q3 2023

Release of the human variations eAF supporting CAPs & NAPs including further capabilities
Q2/Q3 2023

Regular releases with additional functionality and structured data support
From Q1 2024

Use of variations web-form only
Q4 2023/ Q1 2024

Parallel use of old & new variations form

Transition period (6 months)

Preparation work

Development of web-forms (Marketing Authorisation Applications, Veterinary variations, Renewals)

Classified as public by the European Medicines Agency

- **1st: Variations for CAPs**
  - Online!

- **2nd Variation CAPs+NAPs and start of transition phase**

- **3rd: Variations CAP/NAP in structured format!**
  - Minimizing free text changes

- 4th: MAA
- 5th: Renewal

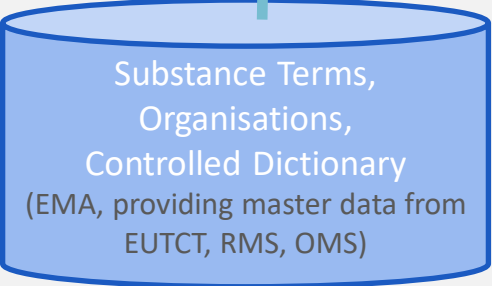Source: EMA, https://plm-portal.ema.europa.eu/

10.03.2023

AS-IS: Electronic Application Forms for Medicinal Products

PDF-based forms including a **PDF-proprietary Data Exchange Format**

Applicants

EUROPEAN COMMISSION
HEALTH AND FOOD SAFETY DIRECTORATE-GENERAL

EUROPEAN COMMISSION
HEALTH AND FOOD SAFETY DIRECTORATE-GENERAL

EUROPEAN COMMISSION
HEALTH AND FOOD SAFETY DIRECTORATE-GENERAL

Health systems, medical products and innovation
eAF Version Number: 1.24.0.0

Revision 13

NOTICE TO APPLICANTS

Medicinal Products for Human Use

Initial Applications

Lifecycle Management

Regulators

Substance Terms, Organisations, Controlled Dictionary
(EMA, providing master data from EUTCT, RMS, OMS)

Regulatory IT-Systems

TO-BE and status of development

UAT partly achieved, **first Variation Application From release in production since 04/11/2022**
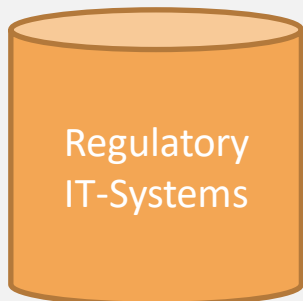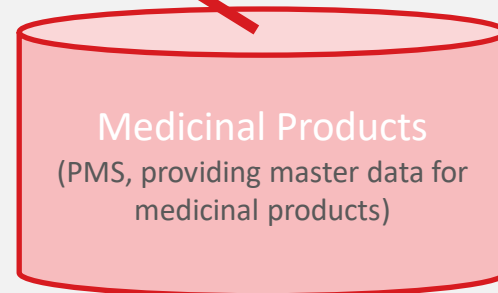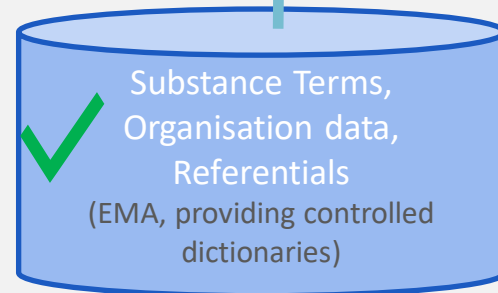
In progress

pending

Web Tool supporting IDMP/FHIR compatible application dataset formats

DADI

Variation Application
Initial Application
Renewal Application

Initial Applications

Lifecycle Management

Regulators

New Retrieving master data

New IDMP/FHIR format

Substance Terms, Organisation data, Referentials
(EMA, providing controlled dictionaries)

Medicinal Products
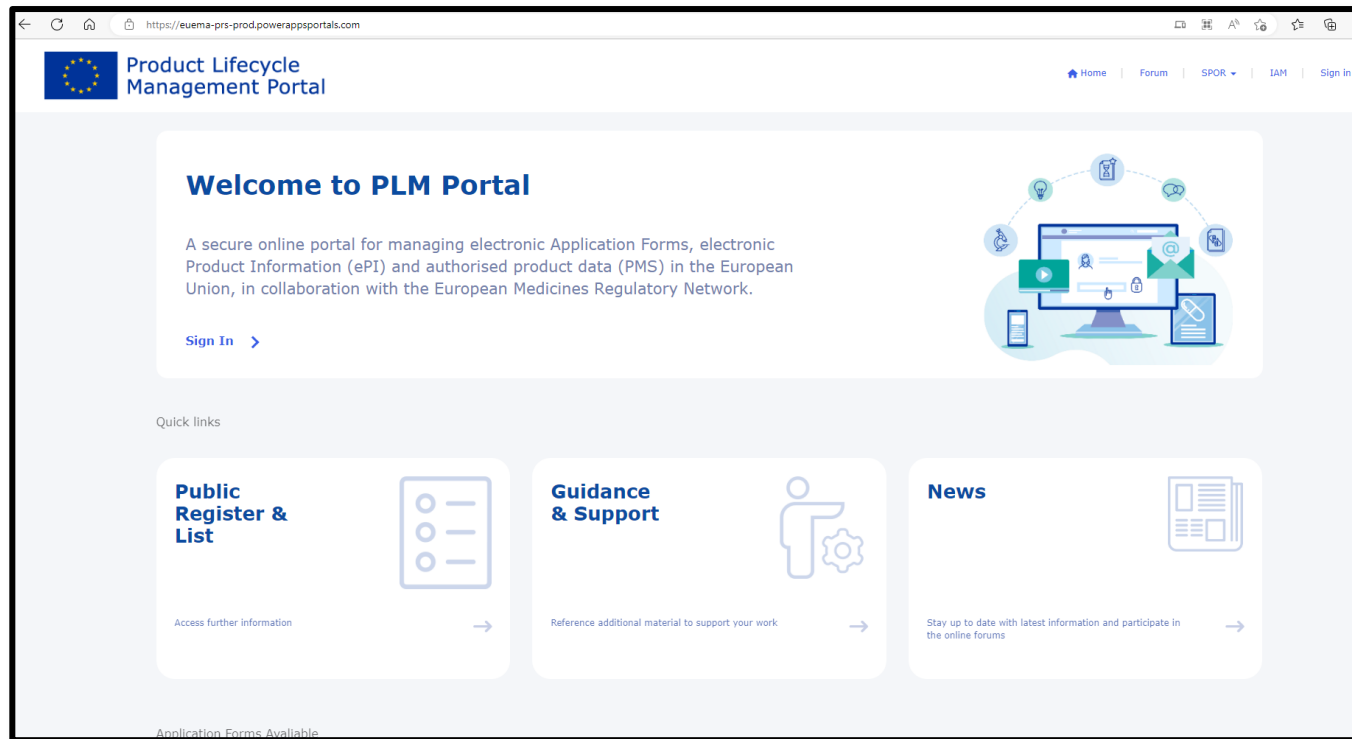(PMS, providing master data for medicinal products)

Regulatory IT-Systems
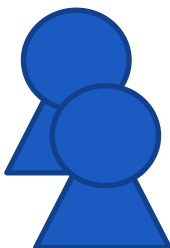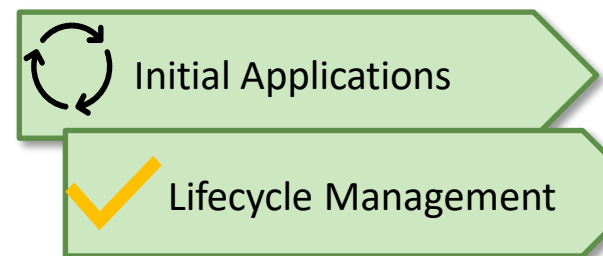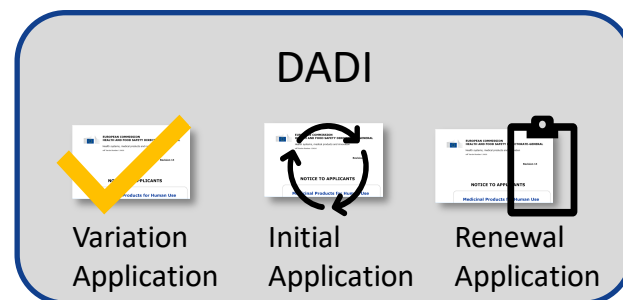
See also collaboration with UNICOM WP4

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- The first release of **Variation Application Forms** is successfully online since 04.11.2022
  - This version covers variations of **centrally authorised medicinal products**

Link: Home · PLM (powerappsportals.com)

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References – Where to start?

How to get involved?

Previous Trainings

The following training will focus on specific elements of the medicinal product part of the variation message.

Previous trainings were given to

Get an overview of the full product:

- FHIR Training: The **Medicinal Product part of FHIR** --> (recording) <--

Get an overview of the variation message:

- FHIR Training: **FHIR on Variations** --> (recording) <--

How to contribute

Business Focus

- Give your input to
  - PMS SMEs and Network PO
  - eAF SMEs and Network PO
- Get in contact with veterinary colleagues and fearn from the product upload to the UPD

Standardisation Focus

- Be part of the Connecthatons "Vulcan stream" at HL7
- BR & R group at HL7 also handles the medicinal product

Cost-free References – Where to start?

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ISO IDMP EU IG v2.1.1
Start by looking at the ISO diagram in the EU IG Chapter 2 Page 30
Link to EU IG

FHIR Documentation
Get familiar with the basics in FHIR or attend a training
Getting started: http://build.fhir.org/documentation.html
Product in Version 4.6: https://hl7.org/fhir/2021May/medicinalproductdefinition.html

Data models and Mappings (eAF & DES to FHIR)
List of all fields and mappings
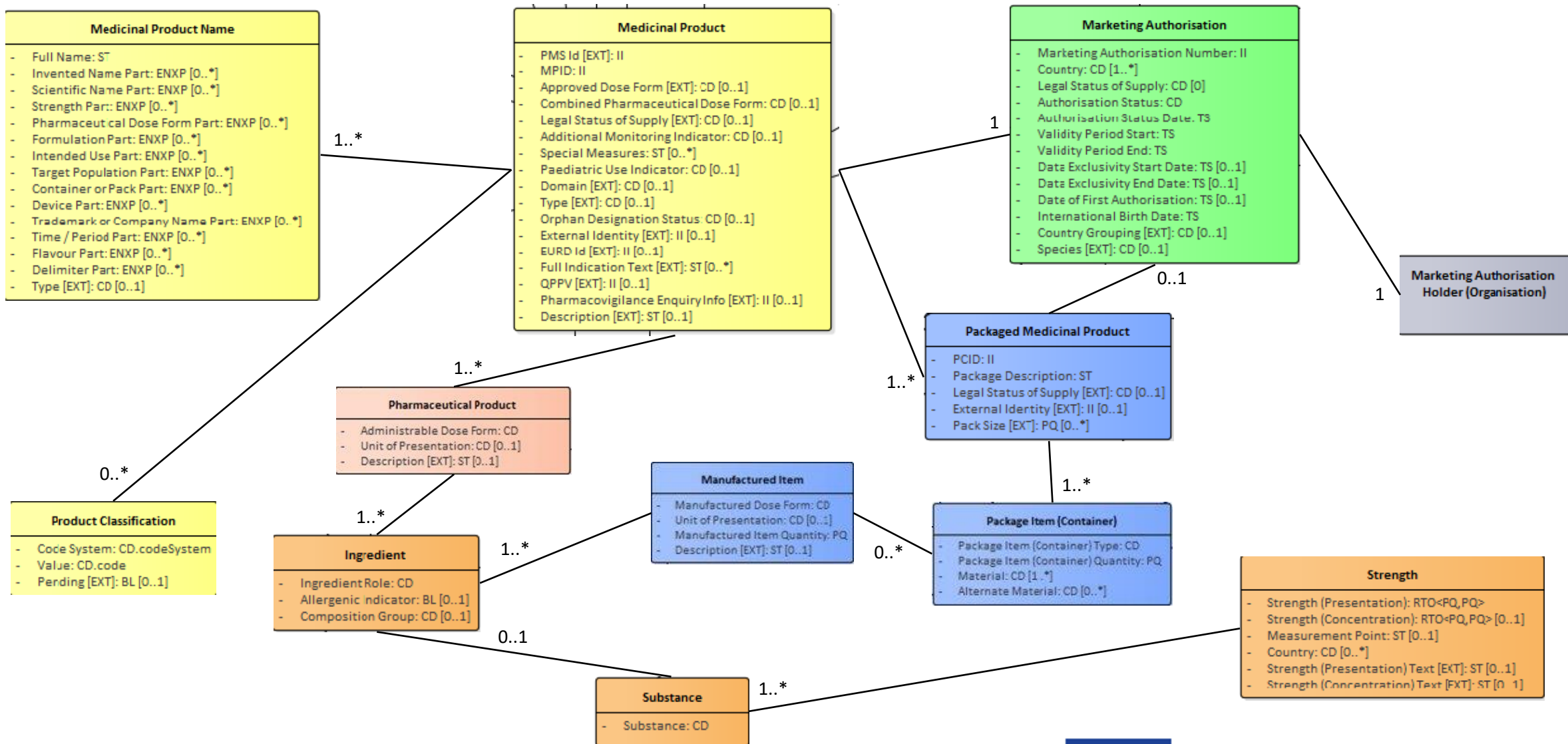A Conceptual data model of the human Variation FHIR message
A Conceptual data model of the medicinal product in a Variation

Top 10 most wanted product data elements

(and where to find them)

Medicinal Product Name
- Full Name: ST
- Invented Name Part: ENXP [0..*]
- Scientific Name Part: ENXP [0..*]
- Strength Part: ENXP [0..*]
- Pharmaceutical Dose Form Part: ENXP [0..*]
- Formulation Part: ENXP [0..*]
- Intended Use Part: ENXP [0..*]
- Target Population Part: ENXP [0..*]
- Container or Pack Part: ENXP [0..*]
- Device Part: ENXP [0..*]
- Trademark or Company Name Part: ENXP [0..*]
- Time / Period Part: ENXP [0..*]
- Flavour Part: ENXP [0..*]
- Delimiter Part: ENXP [0..*]
- Type [EXT]: CD [0..1]

Medicinal Product
- PMS Id [EXT]: II
- MPID: II
- Approved Dose Form [EXT]: CD [0..1]
- Combined Pharmaceutical Dose Form: CD [0..1]
- Legal Status of Supply [EXT]: CD [0..1]
- Additional Monitoring Indicator: CD [0..1]
- Special Measures: ST [0..*]
- Paediatric Use Indicator: CD [0..1]
- Domain [EXT]: CD [0..1]
- Type [EXT]: CD [0..1]
- Orphan Designation Status: CD [0..1]
- External Identity [EXT]: II [0..1]
- EURD Id [EXT]: II [0..1]
- Full Indication Text [EXT]: ST [0..*]
- QPPV [EXT]: II [0..1]
- Pharmacovigilance Enquiry Info [EXT]: II [0..1]
- Description [EXT]: ST [0..1]

Marketing Authorisation
- Marketing Authorisation Number: II
- Country: CD [1..*]
- Legal Status of Supply: CD [0]
- Authorisation Status: CD
- Authorisation Status Date: TS
- Validity Period Start: TS
- Validity Period End: TS
- Data Exclusivity Start Date: TS [0..1]
- Data Exclusivity End Date: TS [0..1]
- Date of First Authorisation: TS [0..1]
- International Birth Date: TS
- Country Grouping [EXT]: CD [0..1]
- Species [EXT]: CD [0..1]

Marketing Authorisation Holder (Organisation)

Packaged Medicinal Product
- PCID: II
- Package Description: ST
- Legal Status of Supply [EXT]: CD [0..1]
- External Identity [EXT]: II [0..1]
- Pack Size [EXT]: PQ [0..*]

Pharmaceutical Product
- Administrable Dose Form: CD
- Unit of Presentation: CD [0..1]
- Description [EXT]: ST [0..1]

Manufactured Item
- Manufactured Dose Form: CD
- Unit of Presentation: CD [0..1]
- Manufactured Item Quantity: PQ
- Description [EXT]: ST [0..1]

Package Item (Container)
- Package Item (Container) Type: CD
- Package Item (Container) Quantity: PQ
- Material: CD [1..*]
- Alternate Material: CD [0..*]

Product Classification
- Code System: CD.codeSystem
- Value: CD.code
- Pending [EXT]: BL [0..1]

Ingredient
- Ingredient Role: CD
- Allergenic Indicator: BL [0..1]
- Composition Group: CD [0..1]

Substance
- Substance: CD

Strength
- Strength (Presentation): RTO<PQ,PQ>
- Strength (Concentration): RTO<PQ,PQ> [0..1]
- Measurement Point: ST [0..1]
- Country: CD [0..*]
- Strength (Presentation) Text [EXT]: ST [0..1]
- Strength (Concentration) Text [EXT]: ST [0..1]

This is a collection of essential medicinal product data elements that are currently available in the PLM Portal (Variation form for CAPs)
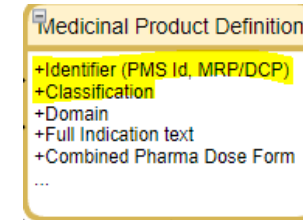
(Except Strength)

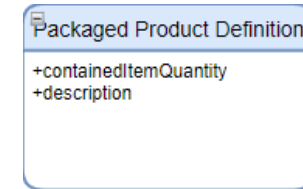**These top 10 fields are contained in only 4 *FHIR resources***

MedicinalProductDefinition
- ✓ Ids, Name, ATC Code

Medicinal Product Definition
+Identifier (PMS Id, MRP/DCP)
+Classification
+Domain
+Full Indication text
+Combined Pharma Dose Form
...

PackagedProductDefinition
- ✓ Pack Size

Packaged Product Definition
+containedItemQuantity
+description

RegulatedAuthorisation
- ✓ MA Holder, Number, Country for both Product and Package

Regulated Authorisation (Marketing Authorisation)
+ MA Nr
+ MA Country
+ MA Date
+ International Birth date
+ Date of first Authorisation

Organization (MAH / Applicant)
+ LOC ID
+ Name
+ Address ...
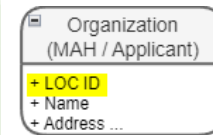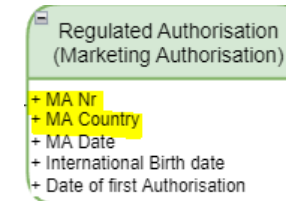
Ingredient
- ✓ Substance Name & Strength

Ingredient Definition (e.g. Active Substance)
+role
+grouping

Substance
+Substance (RMS)

Strength
+presentation
+concentration
+ high limits...
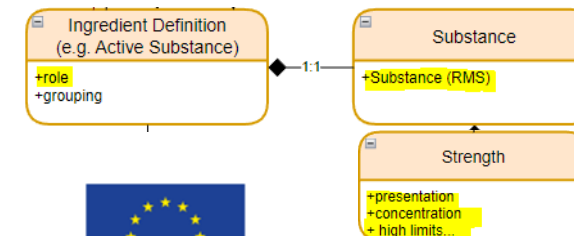
What is a FHIR Resource?

Example: Medicinal Product → PMS Id
(A stable unique Identifier used by systems)

Resources are represented in XML Language in a special template format

Medicinal Product Definition
+Identifier (PMS Id, MRP/DCP)
+Classification
+Domain
+Full Indication text
+Combined Pharma Dose Form
...

```
<identifier>
  <system value="http://ema.europa.eu/fhir/pmsId" />
  <value value="UAT600010787360" />
</identifier>
```
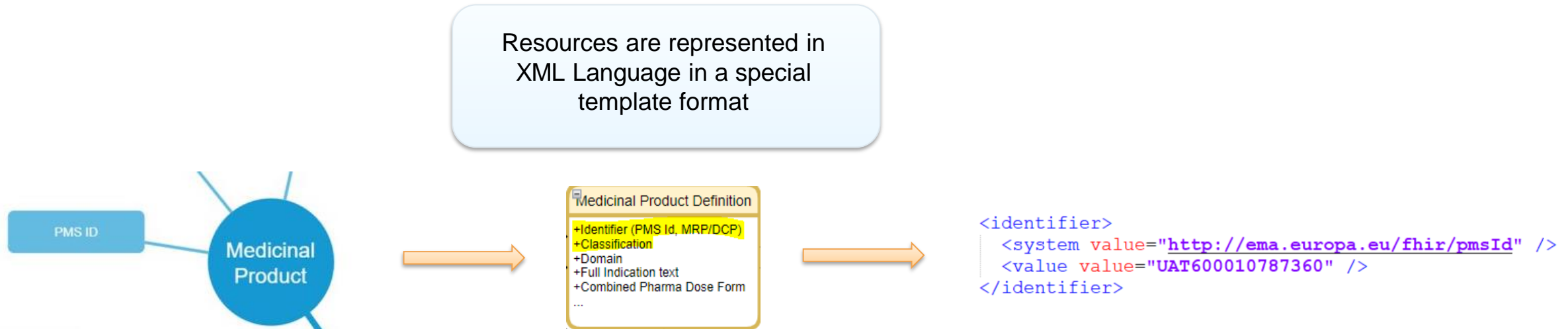
A worksharing Variation XML can be numerous lines of XML and extracting all information may be challenging at the start

Concepts to represent master data

Business & Domain Experts

PDF

2. PRODUCTS CONCERNED BY THIS APPLICATION'

Active Substance
Ceftazidime

MA Number(s) [8] Full name [21]	MA Holder name	Member state	Pharmaceutical Form [22]
BE168122UAT	Glazidim 1 g Pulver zur Herstellung einer Injektions-oder Infusionslösung	UAT ORG (ORG-200036101) LOC	Belgium	Powder for solution for injection/infusion

Model

Medicinal Product Definition
+Identifier (PMS Id, MRP/DCP)
+Classification
+Domain
+Full Indication text
+Combined Pharma Dose Form
...

Contact
(QPPV)

Op
(Manufact
+Manufacturi
+Confidentiali

FHIR Structure

Name	Flags	Card.	Type	Description & Constraints
Identifier	Σ N		Element	An identifier intended for computation Elements defined in Ancestors: id, extension
use	?! Σ	0..1	code	usual | official | temp | secondary | old (If known) IdentifierUse (Required)
type	Σ	0..1	CodeableConcept	Description of identifier IdentifierType (Extensible)
system	Σ	0..1	uri	The namespace for the identifier value
value	Σ	0..1	string	The value that is unique
period	Σ	0..1	Period	Time period when id is/was valid for use
assigner	Σ	0..1	Reference(Organization)	Organization that issued id (may be just text)

XML Representation

```
<identifier>
  <system value="http://ema.europa.eu/fhir/pmsId" />
  <value value="UAT600010787360" />
</identifier>
```

Search Criterias - XPath

Handover to IT Experts

Element/Collection	Xpath	Description
$product	1. $allProducts[1] 2. $allProducts[f:identifier[f:system/@value = $identifierSystem_pmsId and f:value/@value = 'xyz']]	Get a concrete producto by some criteria: 1. The first producto of the list of affected products 2. Product whose PmsId is "xyz"

Provenance – The list of changes in a variation

Representing changes to master data in so called FHIR Provenances

Present & Proposed

The future variation application form minimises free text changes and enables applicants to directly propose changes in structured data elements.

The proposed changes are automatically logged and are made human readable in the PDF form.

"Behind the scenes" they are not text only but also **references to data elements in order to consume them in IT systems.**

The changes are represented in "**FHIR Provenances**"

Lookup records   ×

| | L03AB1 | 🔍 |

Choose one record and click Select to continue

✔	Name	Source ID ↑
☐	peginterferon alfa-2b	L03AB10
☑	peginterferon alfa-2a	L03AB11
☐	albinterferon alfa-2b	L03AB12
☐	peginterferon beta-1a	L03AB13
☐	cepeginterferon alfa-2b	L03AB14
☐	ropeginterferon alfa-2b	L03AB15
☐	peginterferon alfacon-2	L03AB16

Select   Cancel   Remove value

	Cosentyx 150 mg - Powder for solution for injection	
	Created new	Classification: ATC code: L03AB11

```
<extension url="http://ema.europa.eu/fhir/extension/targetElement">
  <extension url="http://ema.europa.eu/fhir/extension/targetActivity">
    <valueCoding>
      <system value="http://terminology.hl7.org/CodeSystem/v3-DataOperation" />
      <code value="CREATE" />
    </valueCoding>
  </extension>
  <extension url="url">
    <valueUrl value="#13889352-c13a-4f0f-8649-00dab76976e5" />
  </extension>
</extension>
<reference value="MedicinalProductDefinition/UAT600000000986" />
```

10.03.2023

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 875299

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XML Data structure to keep the changes

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► Every proposed change on master data will know its relation to the **Scope**, **Product** and P**ackage**

► There are 3 types of changes:

➢ Text changes
  ✓ Rich text & Pictures

➢ Organisation changes
  ✓ Rich text & Pictures
  ✓ OMS link

➢ Product changes
  ✓ What kind of change? --> Create, Update, Delete
  ✓ What was is before? --> present data
  ✓ What is it now? --> Link to the new data element in the proposed product entity

Provenance Conceptual Model

Variation - A FHIR CDM (Conceptual Data Model)

created by - noel.diamant@ages.at - part of UNICOM WP3
last update: 23.02.2023

IT Experts
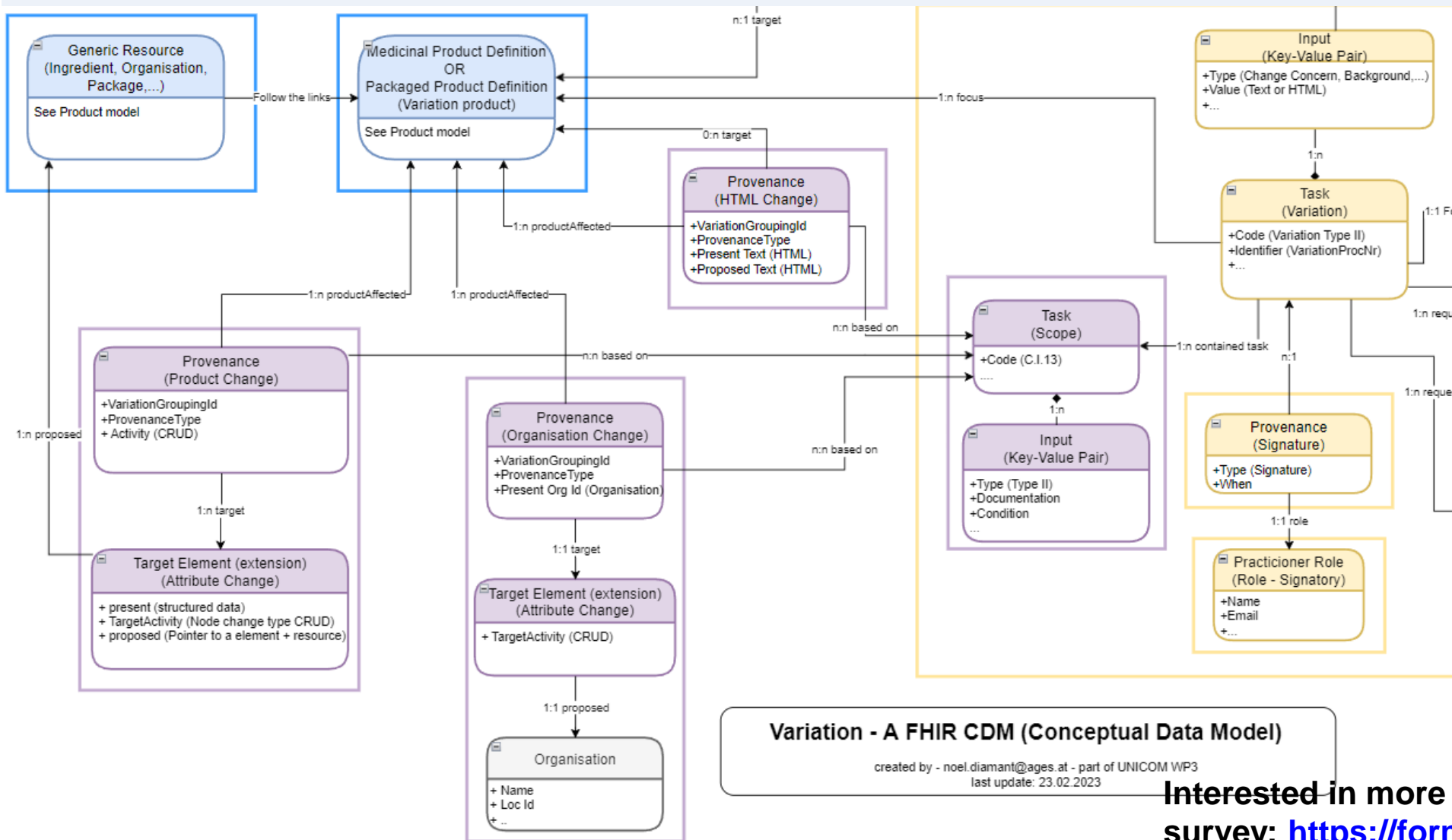
Interested in more information? Please find this survey: https://forms.office.com/r/pT37im2FSr

What you will learn today

With the following training you will be able to Import
data from eAFs into your local IT systems.

Understand IDMP
Implementations

Read FHIR Structure

Find XML Elements

Extract data
with XSL and XPath

Target audience

Target audience:

IT experts

We recommend that business experts involved in national implementations stay,
although the following slides are quite technical.

Business experts

Business experts will benefit from the implementation by reducing administrative effort of typing product data and enable automatic case allocation

During the national implementation a common view and a good collaboration between business experts and technical experts will be essential

5 Minute break

Basics - How to read FHIR and use XPath?

Gianluca

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FHIR standard

▶ **What is FHIR?**

➢ *"FHIR is a standard for health care data exchange, published by HL7®"* **(*)**

➢ Set of rules and specification for exchanging electronic heathcare data

➢ Data is organized in *resources*. Each resource group information related to a same business entity (medicine, package, substance,…)

➢ Each resource comprises:

  ✓ Simple properties (e.g.: identifier)

  ✓ Complex properties (aka: backbone elements – e.g.: *package*)

  ✓ References to other resources

➢ Resources can be seen as object types in an OO paradigm
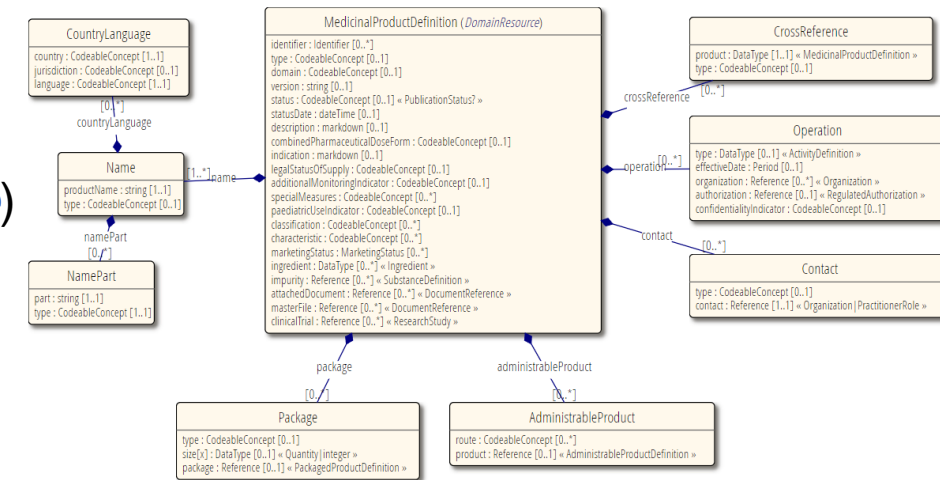
▶ Using **FHIR** as a standard, communication parties agree on a shared contract that rules the information exchange

(*) Taken from https://hl7.org/fhir/2021May/index.html

FHIR types

▶ **Codeable concept**

- ➤ Used to describe a property of a resource
- ➤ Can be **text** or **coding**
- ➤ Element **coding** is a reference to a code in a terminology

```xml
<domain>
  <coding>
    <extension url="http://ema.europa.eu/fhir/extension/codeSystemName">
    <system value="https://spor.ema.europa.eu/v1/lists/100000000004" />
    <code value="100000000012" />
    <display value="Human use" />
  </coding>
</domain>
```

▶ **Identifiers and systems**

- ➤ **identifier** elements provide Id values for resources (e.g.: Pms Id)
- ➤ The Id value always refers to a (classification) **system** (e.g.: PMS)

```xml
<identifier>
  <system value="http://ema.europa.eu/fhir/pmsId" />
  <value value="900000999999" />
</identifier>
```

▶ **References - Use of 'subject'**

- ➤ Links between resources are implemented using **reference** elements
- ➤ Refecence values are in the form of `"resourceType/resourceId"`
- ➤ Tipically, **subject** element is used to host the reference

```xml
<PackagedProductDefinition>
  <id value="56132" />
  <subject>
    <reference value="MedicinalProductDefinition/600000001169" />
  </subject>
  <marketingAuthorization>
```

Consuming FHIR messages - Alternatives

▶ **Alternative #1: *FHIR-agnostic* approach**

 ➢ Consume a message like any XML document

 ➢ Document oriented strategy (XML technologies: XPath, XSLT, XSD,…)

 ➢ Query using XPath

*We went this way
And propose to
share the expertise
and best-practices in
the network*

▶ **Alternative #2: *FHIR-aware* approach**

 ➢ Use of third party libraries to handle (read) FHIR resources and relationships among them

 ➢ Object oriented strategy (OO languages/technologies must be used)

 ➢ Query using objects/object properties

Alternative to XPath

▶ Open Source Implementations
Most common used libraries to extract FHIR content

  ➢ **JAVA**: **https://github.com/jamesagnew/hapi-fhir** - James Agnew / University Health Network

  ➢ **.NET Client - Firely .NET SDK**: **https://github.com/FirelyTeam/firely-net-sdk**

▶ Many other libraries can be found here:
https://confluence.hl7.org/pages/viewpage.action?pageId=35718838

▶ Many Implementation tools can be found here:
http://build.fhir.org/downloads.html

XPath characteristics

► **Important:** An XPath interpreter is needed

  ➢ There is at least one libvrary for each technology

► XPath rules (some of them):

  ➢ All elements belong to a namespace

  ➢ Nodes are targeted by their node name

  ➢ Location paths are defined using the **/** symbol between node names in the path

  ➢ Attributes are targeted by their attribute name prefixed by the **@** symbol

  ➢ Predicates (filters) can be defined using the **[…]** sintaxis

  ➢ Support for functions (e.g.: **trim()**, **local-name()**…)

  ➢ Several versions of the specification

► More info:

  ➢ See **https://en.wikipedia.org/wiki/XPath**

XPath example - Demo

► Try it at https://scrapinghub.github.io/xpath-playground/

```xml
<root>
    <artist name="Peter Gabriel">
        <album title="Us" year="1992" />
        <album title="New Blood" year="2011" />
    </artist>
    <artist name="Pink Floyd">
        <album title="The Dark Side of the Moon" year="1973" />
        <album title="The Wall" year="1979" />
        <album title="A Momentary Lapse of Reason" year="1987" />
    </artist>
</root>
```

► /root/artist/@name

  ➢ Peter Gabriel

  ➢ Pink Floyd

► /root/artist[@name = 'Pink Floyd']/album[3]/@title

  ➢ A Momentary Lapse of Reason

Friendly Names for RMS Lists and Term IDs

UNICOM

Best practice advice to work with Lists and Terms in XSLT

Note: FHIR message has a namespace `xmlns="http://hl7.org/fhir"` prefixed with `f` in the examples

▶ Use of variables to "friendly name" the RMS codes and RMS list URLs

```xml
<!--******************* (START) RMS list urls: -->
<xsl:variable name="rmsList_domain" select="'https://spor.ema.europa.eu/v1/lists/100000000004'"/>
<xsl:variable name="rmsList_euRegulatoryAuthorization" select="'https://spor.ema.europa.eu/v1/lists/100000154442'"/>
<xsl:variable name="rmsList_submissionMode" select="'https://spor.ema.europa.eu/v1/lists/100000155553'"/>
<xsl:variable name="rmsList_applicationSubmissionType" select="'https://spor.ema.europa.eu/v1/lists/100000155688'"/>
<xsl:variable name="rmsList_ingredientRole" select="'https://spor.ema.europa.eu/v1/lists/100000072050'"/>
<xsl:variable name="rmsList_medicinalProductNamePartType" select="'https://spor.ema.europa.eu/v1/lists/220000000000'"/>
<xsl:variable name="rmsList_productInformationDocumentType" select="'https://spor.ema.europa.eu/v1/lists/100000155531'"/>
<xsl:variable name="rmsList_regulatoryEntitlementType" select="'https://spor.ema.europa.eu/v1/lists/220000000060'"/>
<xsl:variable name="rmsList_parallellApplicationVariationStatus" select="'https://spor.ema.europa.eu/v1/lists/200000020000'"/>
<xsl:variable name="rmsList_documentation" select="'https://spor.ema.europa.eu/v1/lists/200000003964'"/>

<xsl:variable name="rmsList_orphanStatus" select="'https://spor.ema.europa.eu/v1/lists/orphanStatus'"/>

<!-- "Local" lists (not present in RMS and having ListId like "9*" (as opposed to "1*") -->
<!-- List below corresponds to "ProcedureDetailType" in Web App/FHIR generation module -->
<xsl:variable name="rmsList_variationTypesMetadata" select="'https://spor.ema.europa.eu/v1/lists/200000027891'"/>

<xsl:variable name="rmsList_declarationEntries" select="'https://spor.ema.europa.eu/v1/lists/200000027815'"/>

<xsl:variable name="rmsList_medicalDeviceClassification" select="'https://spor.ema.europa.eu/v1/lists/200000025960'"/>
<xsl:variable name="rmsList_medicalDeviceCombinationTypes" select="'https://spor.ema.europa.eu/v1/lists/200000025965'"/>
<xsl:variable name="rmsList_medicalDeviceDocumentation" select="'https://spor.ema.europa.eu/v1/lists/200000027957'"/>

<xsl:variable name="rmsList_applicablePaediatricRegulation" select="'https://spor.ema.europa.eu/v1/lists/applicablePaediatricRegulation'"/>
<xsl:variable name="rmsList_provenanceType" select="'https://spor.ema.europa.eu/v1/lists/90000000995'"/>

<!--******************* (END) RMS list urls -->
```

```xml
<!--******************* (START) RMS Constants: -->
<xsl:variable name="rmsId_ingredientRole_active" select="'100000072072'"/>
<xsl:variable name="rmsId_ingredientRole_excipient" select="'100000072082'"/>

<xsl:variable name="rmsId_namePart_pharmaDoseForm" select="'220000000005'"/>
<xsl:variable name="rmsId_namePart_strength" select="'220000000004'"/>
<xsl:variable name="rmsId_namePart_fullName" select="'220000000001'"/>
<xsl:variable name="rmsId_namePart_inventedName" select="'220000000002'"/>

<xsl:variable name="rmsId_productInfoDocumentType_summaryOfProductChanges" select="'100000155532'"/>
<xsl:variable name="rmsId_productInfoDocumentType_packageLeaflet" select="'100000155538'"/>
<xsl:variable name="rmsId_productInfoDocumentType_mockUps" select="'100000155540'"/>
<xsl:variable name="rmsId_productInfoDocumentType_specimens" select="'200000027914'"/>
<xsl:variable name="rmsId_productInfoDocumentType_labelling" select="'100000155535'"/>
<xsl:variable name="rmsId_productInfoDocumentType_mahBatchReleaser" select="'100000155533'"/>
<xsl:variable name="rmsId_productInfoDocumentType_listOfAllPresentations" select="'200000027915'"/>
<xsl:variable name="rmsId_productInfoDocumentType_restrictionsByMemberStates" select="'200000027916'"/>

<xsl:variable name="rmsId_regulatoryEntitlementType_marketingAuthorization" select="'220000000061'"/>
<xsl:variable name="rmsId_regulatoryEntitlementType_marketProtection" select="'220000000077'"/>

<xsl:variable name="rmsId_preciseScopeForChange" select="'200000027908'"/>
<xsl:variable name="rmsId_backgroundForChange" select="'200000027909'"/>

<xsl:variable name="rmsId_extendedDataExclusivity_art10_1" select="'200000027929'"/>
<xsl:variable name="rmsId_extendedDataExclusivity_art10_5" select="'200000027930'"/>
<xsl:variable name="rmsId_extendedDataExclusivity_art74_a" select="'200000027931'"/>
<xsl:variable name="rmsId_extendedDataExclusivity_notApplicable" select="'90000000066'"/>

<!--
    Possible value of the "Procedure Type" checkboxes in a scope:
    IA IAIN IB IBun II IIart29 art5
-->
<!--
    // List = 100000155688: Application Submission Type.
-->
<xsl:variable name="rmsId_typeIA" select="'100000155690'"/>
<xsl:variable name="rmsId_typeIAIN" select="'100000155691'"/>
<xsl:variable name="rmsId_typeIB" select="'100000155692'"/>
<xsl:variable name="rmsId_typeII" select="'100000155693'"/>
<xsl:variable name="rmsId_art5" select="'100000155694'"/>
<xsl:variable name="rmsId_typeIBun" select="'100000155695'"/>
<xsl:variable name="rmsId_typeIIart29" select="'200000026016'"/>

<xsl:variable name="rmsId_thereAreNoOtherChanges" select="'200000027822'"/>
<xsl:variable name="rmsId_allConditionsFullfilled" select="'200000027823'"/>
<xsl:variable name="rmsId_allDocumentsSubmitted" select="'200000027824'"/>
<xsl:variable name="rmsId_feesHaveBeenPaid" select="'200000027825'"/>
<xsl:variable name="rmsId_notificationSubmittedSimultaneously" select="'200000027826'"/>
<xsl:variable name="rmsId_concernedMAsBelongToSameMAH" select="'200000027827'"/>
<xsl:variable name="rmsId_allPIsAnonymised" select="'200000027967'"/>
```

The Key to the Key-Value principle in the FHIR message

► Each Key is named after a URL that identifies a business attribute

```xml
<!--******************* (START) f:identifier/f:system/@value urls: -->
<xsl:variable name="identifierSystem_pmsId" select="'http://ema.europa.eu/fhir/pmsId'"/>
<xsl:variable name="identifierSystem_mpId" select="'http://ema.europa.eu/fhir/mpId'"/>

<xsl:variable name="identifierSystem_applicationIdentifierNumber" select="'http://ema.europa.eu/fhir/applicationIdentifierNumber'"/>
<xsl:variable name="identifierSystem_procedureIdentifierNumber" select="'http://ema.europa.eu/fhir/procedureIdentifierNumber'"/>

<xsl:variable name="identifierSystem_poNumber" select="'http://ema.europa.eu/fhir/purchaseOrder'"/>

<xsl:variable name="identifierSystem_organizationVatNumber" select="'http://ema.europa.eu/fhir/organizationVatNumber'"/>
<xsl:variable name="identifierSystem_organizationAccountNumber" select="'http://ema.europa.eu/fhir/organizationAccountNumber'"/>

<xsl:variable name="identifierSystem_organizationOrgId" select="'https://spor.ema.europa.eu/v1/organizations'"/>
<xsl:variable name="identifierSystem_organizationLocId" select="'https://spor.ema.europa.eu/v1/locations'"/>
<xsl:variable name="identifierSystem_scopeIdentifier" select="'http://ema.europa.eu/fhir/scopeIdentifier'"/>

<!--<xsl:variable name="identifierSystem_mrpVariationNumber" select="'http://ema.europa.eu/fhir/MRPVariationNumber'"/>-->

<xsl:variable name="identifierSystem_orphanDesignationNumber" select="'http://ema.europa.eu/fhir/orphanDesignationNumber'"/>
<xsl:variable name="identifierSystem_orphanDesignationProcedureNumber" select="'http://ema.europa.eu/fhir/orphanDesignationProcedureNumber'"/>
<xsl:variable name="identifierSystem_orphanRegisterNumber" select="'http://ema.europa.eu/fhir/orphanRegisterNumber'"/>
<xsl:variable name="identifierSystem_marketingAuthorizationNumber" select="'http://ema.europa.eu/fhir/marketingAuthorizationNumber'"/>
<xsl:variable name="identifierSystem_manufacturingAuthorizationNumber" select="'http://ema.europa.eu/fhir/manufacturingAuthorizationNumber'"/>

<xsl:variable name="identifierSystem_deviceIdentifier" select="'http://ema.europa.eu/fhir/deviceIdentifier'"/>

<xsl:variable name="identifierSystem_pipDecisionNumber" select="'http://ema.europa.eu/fhir/pipDecisionNumber'"/>
<xsl:variable name="identifierSystem_waiverDecisionNumber" select="'http://ema.europa.eu/fhir/productSpecificWaiverDecisionNumber'"/>
<xsl:variable name="identifierSystem_classWaiverNumber" select="'http://ema.europa.eu/fhir/classWaiverDecisionNumber'"/>

<xsl:variable name="identifierSystem_notifiedBodyNumber" select="'http://ema.europa.eu/fhir/notifiedBodyNumber'"/>

<xsl:variable name="identifierSystem_dunsNumber" select="'http://ema.europa.eu/fhir/dunsNumber'"/>

<!--******************* (END) f:identifier/f:system/@value urls -->
```

A guide to extracting information

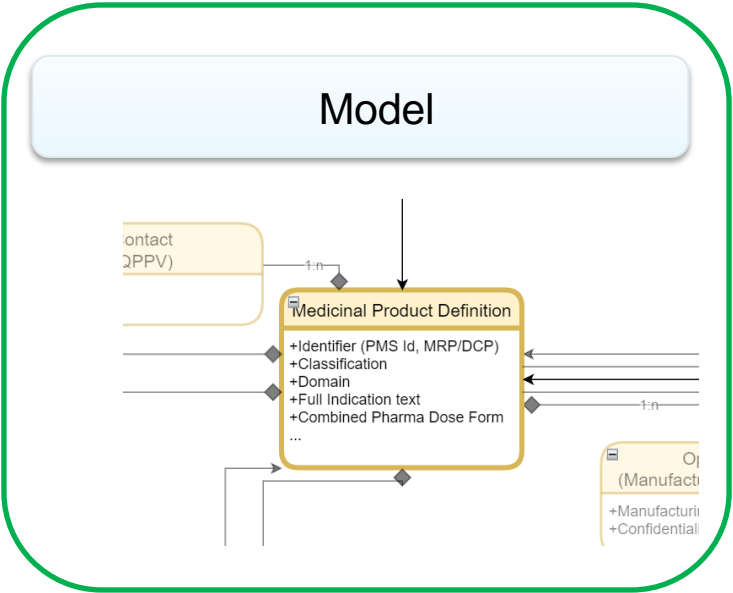presented with a UNICOM reference implementation

Concepts to represent master data

Business & Domain Experts

Handover to IT Experts

PDF

2. **PRODUCTS CONCERNED BY THIS APPLICATION**

Active Substance
Ceftazidime

MA Number(s) [8] Full name [21]		MA Holder name	Member state	Pharmaceutical Form [22]
BE168122UAT	Glazidim 1 g Pulver zur Herstellung einer Injektions-oder Infusionslösung	UAT ORG (ORG-200036101) LOC	Belgium	Powder for solution for injection/infusion

Model

Medicinal Product Definition
+Identifier (PMS Id, MRP/DCP)
+Classification
+Domain
+Full Indication text
+Combined Pharma Dose Form
...

FHIR Structure

Name	Flags	Card.	Type	Description & Constraints	?
Identifier	Σ N		Element	An identifier intended for computation Elements defined in Ancestors: id, extension	
use	?! Σ	0..1	code	usual	official	temp	secondary	old (If known) IdentifierUse (Required)	
type	Σ	0..1	CodeableConcept	Description of identifier IdentifierType (Extensible)	
system	Σ	0..1	uri	The namespace for the identifier value	
value	Σ	0..1	string	The value that is unique	
period	Σ	0..1	Period	Time period when id is/was valid for use	
assigner	Σ	0..1	Reference(Organization)	Organization that issued id (may be just text)	

XML Representation

```
<identifier>
    <system value="http://ema.europa.eu/fhir/pmsId" />
    <value value="UAT600010787360" />
</identifier>
```
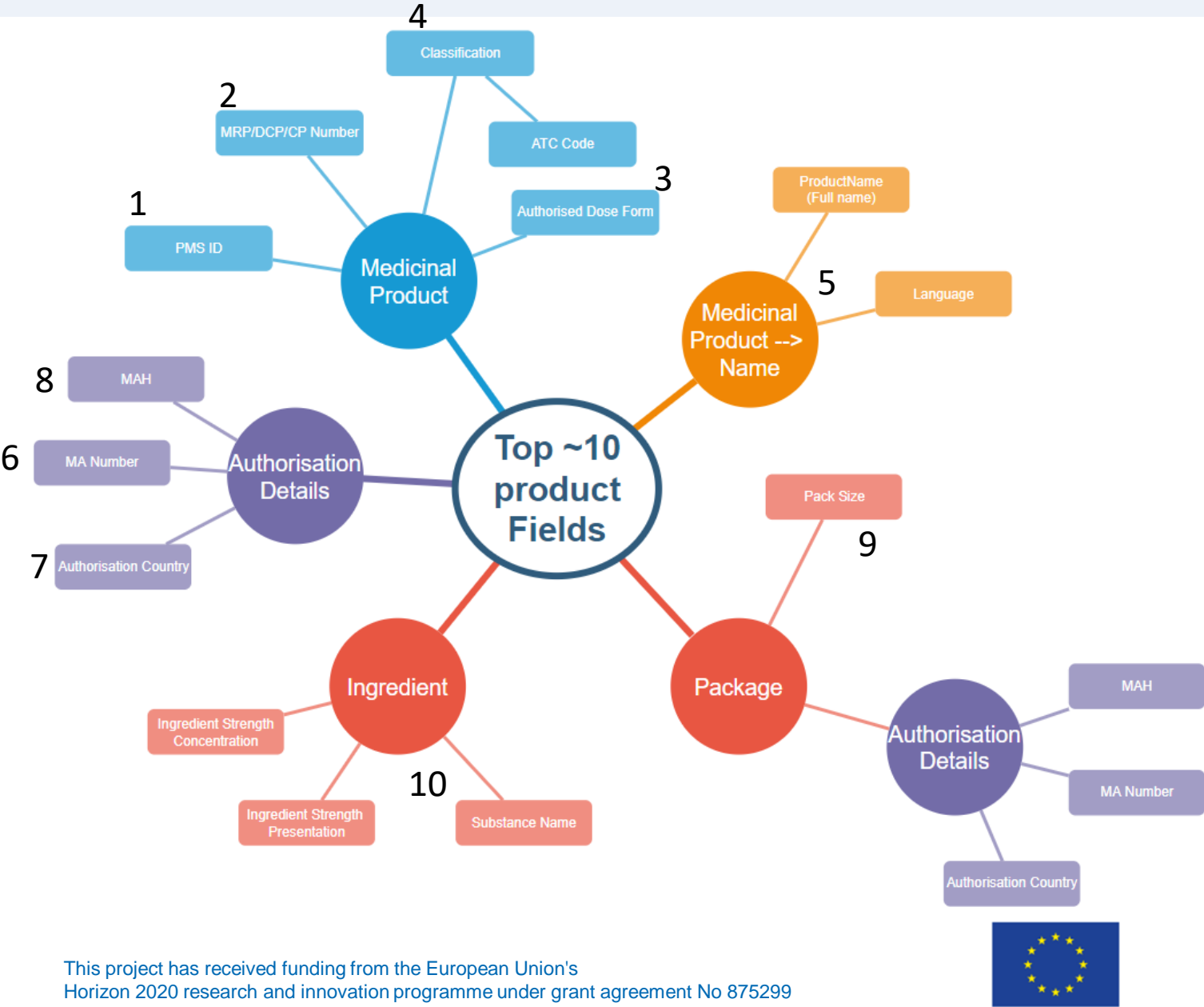
XPath

Element/Collection	Xpath	Description
$product	1. $allProducts[1] 2. $allProducts[f:identifier[f:system/@value = $identifierSystem_pmsId and f:value/@value = 'xyz']]	Get a concrete producto by some criteria: 1. The first producto of the list of affected products 2. Product whose PmsId is "xyz"

PMS Product - A FHIR CDM (Conceptual Data Model)

created by - noel.diamant@ages.at - part of UNICOM WP3
last update: 08.03.2023

PMS Product - A FHIR CDM (Conceptual Data Model)

created by - noel.diamant@ages.at - part of UNICOM WP3
last update: 08.03.2023

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Product Lifecycle Management Portal

Full Name ↑	Authorised Dose Form	Active Substance	Authorisation Country	MA Holder	MA Nr. ⓘ	MRP / CP Nr.	PMS ID	MP ID
MINJUVI 200 mg - Powder for concentrate for solut...	Powder for concentrate for solution for infusion	Tafasitamab	European Union	Incyte Biosciences Distribution B.V.	EU/1/21/1570	EMEA/H/C/005436	600000004682	600000004682

eAF Variation PDF

MA Number(s) [8]	Full name [21]	MA Holder name	Member state	Pharmaceutical Form [22]
EU/1/14/944/003 EU/1/14/944/007 EU/1/14/944/008 EU/1/14/944/009 EU/1/14/944/012 EU/1/14/944/013 EU/1/14/944/014 EU/1/14/944/015	Abasaglar 100 Units/ml - Solution for injection	Eli Lilly Nederland B.V.	European Union	Solution for injection

HL7 FHIR

combinedPharmaceuticalDoseForm Σ 0..1 CodeableConcept

Name	Flags	Card.	Type	Description & Constraints
Identifier	Σ N		Element	An identifier intended for computation Elements defined in Ancestors: id, extension
use	?! Σ	0..1	code	usual | official | temp | secondary | old (If known) IdentifierUse (Required)
type	Σ	0..1	CodeableConcept	Description of identifier IdentifierType (Extensible)
system	Σ	0..1	uri	The namespace for the identifier value
value	Σ	0..1	string	The value that is unique
period	Σ	0..1	Period	Time period when id is/was valid for use
assigner	Σ	0..1	Reference(Organization)	Organization that issued id (may be just text)

Medicinal Product - Business context
ATC Code

UNICOM

PLM eAF portal

Lookup records   ✕

┌───┐
│   │ L03AB1   │ 🔍 │
└───┘

Choose one record and click Select to continue

✓	**Name**	**Source ID ↑**
☐	peginterferon alfa-2b	L03AB10
☑	peginterferon alfa-2a	L03AB11
☐	albinterferon alfa-2b	L03AB12
☐	peginterferon beta-1a	L03AB13
☐	cepeginterferon alfa-2b	L03AB14
☐	ropeginterferon alfa-2b	L03AB15
☐	peginterferon alfacon-2	L03AB16

[Select]   [Cancel]   [Remove value]

eAF Variation PDF

	Cosentyx 150 mg - Powder for solution for injection	
	Created new	Classification: ATC code: L03AB11

FHIR specification

ATC Code

... ⬡ **classification**   Σ   0..*   CodeableConcept

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Product Lifecycle Management Portal

Full Name	Authorised Dose Form	Active Substance	Authorisation Country	MA Holder	MA Nr.	MRP / CP Nr.	PMS ID
Qwerty 30 mg - Gastro-resistant capsule, hard	Gastro-resistant capsule, hard	MERQWERTYAMINE BITARTRATE	European Union	UAT ORG (ORG-200036099)	EU/9/13/777UAT	EMEA/H/C/902777UAT	UAT900000000777
Zwerty 30 mg - Gastro-resistant capsule, hard	Gastro-resistant capsule, hard	MERZWERTYAMINE BITARTRATE	Germany	UAT ORG (ORG-200036099)	PA1077/027/888UAT		UAT00007888

2. PRODUCTS CONCERNED BY THIS APPLICATION[']

Active Substance
Mercaptamine

MA Number(s) [8]	Full name [21]	MA Holder name	Member state	Pharmaceutical Form [22]
EU/9/13/777UAT	Qwerty 30 mg - Gastro-resistant capsule, hard	UAT ORG (ORG-200036099)	European Union	Gastro-resistant capsule, hard
PA1077/027/888UAT	Zwerty 30 mg - Gastro-resistant capsule, hard	UAT ORG (ORG-200036099)	Germany	Gastro-resistant capsule, hard

eAF Variation PDF

HL7® FHIR®

name	Σ	1..*	BackboneElement
productName	Σ	1..1	string
type	Σ	0..1	CodeableConcept
namePart	Σ	0..*	BackboneElement
part	Σ	1..1	string
type	Σ	1..1	CodeableConcept
countryLanguage	Σ	0..*	BackboneElement
country	Σ	1..1	CodeableConcept
jurisdiction	Σ	0..1	CodeableConcept
language	Σ	1..1	CodeableConcept

Medicinal Product - XML Context

Steps to find a specific product

Element/Collection	XPath	Description
$variationTask	`/f:Bundle/f:entry/f:resource/f:Task[1]`	Variation procedure (**Task**) Note: selector [1] is optional, since only one task is expected
$allProducts	`/f:Bundle/f:entry/f:resource/f:MedicinalProductDefinition`	All the **MedicinalProductDefinition** resources contained in the bundle
$affectedProductReferences	`$variationTask/f:contained/f:List/f:entry/f:item/f:reference`	All the rereferences to (concerned) products contained in the procedure task
$affectedProducts	`$allProducts[$affectedProductReferences/@value = concat('MedicinalProductDefinition/', f:id/@value)]`	All the MedicinalProductDefinition resources representing each of the products concerned by the application
$product	1. `$allProducts[1]` 2. `$allProducts[f:identifier[f:system/@value = $identifierSystem_pmsId and f:value/@value = 'xyz']]`	Get a concrete product by some criteria: 1. The first product of the list of affected products 2. The product whose PmsId is "xyz"

Medicinal Product - IT context
Authorised dose form, MRP/DCP/CP Nr, PMS Id

1. PMS Id

`$product/f:identifier[f:system/@value = $identifierSystem_pmsId]/f:value/@value`

Returned value is **AT-16569**

2. MRP/DCP/CP number

`$product/f:identifier[f:system/@value ='http://ema.europa.eu/fhir/mrpCpId']/f:value/@value`

Note: this field is not used in PdfGen

```xml
<entry>
    <!-- <fullUrl value="urn:uuid:c6a838d9-27ca-49a4-a6ba-216448f82000"/> -->
    <resource>
        <MedicinalProductDefinition>
            <!-- Information not available in PHAROS

            <!-- Not in PHAROS
            <id value="Curocef1500mgPulver-A-HL-MedicinalProductDefinition"/>
            <extension url="http://ema.europa.eu/fhir/extension/authorisedDoseForm">

            <identifier>
                <!-- Will be provided by PMS. This is just a placeholder -->
                <system value="http://ema.europa.eu/fhir/mpId"/>
                <value value="AT-16569"/>
            </identifier>
            <!-- Not available in PHAROS
            <identifier>
                <system value="http://ema.europa.eu/fhir/eurdId"/>
                <value value="2215"/>
            </identifier> -->
```

3. Authorised dose form

RMS code: `$product/f:combinedPharmaceuticalDoseForm/f:coding[1]/f:code/@value`

Display value: `$product/f:combinedPharmaceuticalDoseForm/f:coding[1]/f:display/@value`

Returned values are:
- RMS code: **100000073863**
- Display value: **Solution for injection**

```xml
<entry>
    <fullUrl value="urn:uuid:69d04f9a-793f-4b9b-b408-dcff83a957e8" />
    <resource>
        <MedicinalProductDefinition>
            <id value="600000001169" />
            <identifier>
            <identifier>
            <identifier>
            <domain>
            <combinedPharmaceuticalDoseForm>
                <coding>
                    <extension url="http://ema.europa.eu/fhir/extension/codeSystemName">
                        <valueString value="Pharmaceutical Dose Form" />
                    </extension>
                    <system value="https://spor.ema.europa.eu/v1/lists/200000000004" />
                    <code value="100000073863" />
                    <display value="Solution for injection" />
                </coding>
            </combinedPharmaceuticalDoseForm>
```

4. ATC code

ATC code (RMS): `$product/f:classification/f:coding[f:system/@value = $rmsList_classification]/f:code/@value`

ATC code (WHO): `$product/f:classification/f:coding[f:system/@value = $extension_whoAtcClassification]/f:code/@value`

Returned values are:
- RMS: **100000096825**
- WHO: **L03AB11**

For **peginterferon alfa-2a**

```
<entry>
  <resource>
    <MedicinalProductDefinition>
      <id value="600000001169" />
      <identifier>
      <identifier>
      <identifier>
      <domain>
      <combinedPharmaceuticalDoseForm>
      <indication value="Indication example" />
      <legalStatusOfSupply>
      <additionalMonitoringIndicator>
      <paediatricUseIndicator>
      <!-- Example -->
      <classification>
        <extension url="http://ema.europa.eu/fhir/extension/atcPending">
          <valueString value="false" />
        </extension>
        <coding>
          <extension url="http://ema.europa.eu/fhir/extension/codeSystemName">
            <valueString value="Anatomical Therapeutic Chemical classification system - Human" />
          </extension>
          <system value="https://spor.ema.europa.eu/v1/lists/100000093533" />
          <code value="100000096825" />
          <display value="peginterferon alfa-2a" />
        </coding>
        <coding>
          <system value="http://www.whocc.no/atc" />
          <code value="L03AB11" />
          <display value="peginterferon alfa-2a" />
        </coding>
      </classification>
```

5. Product full name

Multiple "name" elements in one product, one for each country/language pair considered

EN: `$product/f:name[f:countryLanguage[f:language/f:coding/f:code/@value = '100000072147']]/f:productName/@value`

DE: `$product/f:name[f:countryLanguage[f:language/f:coding/f:code/@value = '100000072178']]/f:productName/@value`

Returned values is
MINJUVI 200 mg - Powder for concentrate for solution for infusion

When queried for [lang = "EN"]

```
<entry>
  <resource>
    <MedicinalProductDefinition>
      <id value="19ec038b3abcfbe8f8d69a30ce653a8a"/>
      <identifier>
      <identifier>
      <domain>
      <combinedPharmaceuticalDoseForm>
      <legalStatusOfSupply>
      <additionalMonitoringIndicator>
      <paediatricUseIndicator>
      <classification>
      <characteristic>
      <masterFile>
      <contact>
      <name>
        <productName value="MINJUVI 200 mg - Powder for concentrate for solution for infusion"/>
        <namePart>
        <namePart>
        <namePart>
        <namePart>
        <countryLanguage>
          <country>
            <coding>
              <system value="https://spor.ema.europa.eu/v1/lists/100000000002"/>
              <code value="100000000390"/>
              <display value="European Union"/>
            </coding>
          </country>
          <language>
            <coding>
              <system value="https://spor.ema.europa.eu/v1/lists/100000072057"/>
              <code value="100000072147"/>
              <display value="English"/>
            </coding>
          </language>
        </countryLanguage>
      </name>
```

Medicinal Product - Business context
MA Number, MA Country, MA Holder

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Product Lifecycle Management Portal

Full Name	Authorised Dose Form	Active Substance	Authorisation Country	MA Holder	MA Nr. ⓘ	MRP / CP Nr.	PMS ID
Qwerty 30 mg - Gastro-resistant capsule, hard	Gastro-resistant capsule, hard	MERQWERTYAMINE BITARTRATE	European Union	UAT ORG (ORG-200036099)	EU/9/13/777UAT	EMEA/H/C/902777UAT	UAT900000000777

eAF Variation PDF

MA Number(s) [8]	Full name [21]	MA Holder name	Member state	Pharmaceutical Form [22]
EU/9/13/777UAT	Qwerty 30 mg - Gastro-resistant capsule, hard	UAT ORG (ORG-200036099)	European Union	Gastro-resistant capsule, hard

HL7 FHIR

RegulatedAuthorization	TU		DomainResource
identifier	Σ	0..*	Identifier
subject	Σ	0..1	Reference(MedicinalProductDefinition
holder	Σ	0..1	Reference(Organization)
region	Σ	0..*	CodeableConcept

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Regulated authorisation - XML context
MA Number, MA Country, MA Holder

Steps to find a marketing authorisation

Element/Collection	Xpath	Description
$allRegulatedAuthorizations	`/f:Bundle/f:entry/f:resource/f:RegulatedAuthorization`	All the **RegulatedAuthorization** resources contained in the bundle

$allMarketingAuthorizations	`$allRegulatedAuthorizations[`
	`  f:type/f:coding/f:system/@value = $rmsList_regulatoryEntitlementType`
	`and`
	`  f:type/f:coding/f:code/@value =`
	`    $rmsId_regulatoryEntitlementType_marketingAuthorization`
	`]`
		All RegulatedAuthorization resources whose type is "Marketing Authorization"

$productMAuth	`$allMarketingAuthorizations[substring-after(f:subject/f:reference/@value, '/')` `= $product/f:id/@value][1]`	First marketing authorization for the product $product
$packageMAuth	`$allMarketingAuthorizations[substring-after(f:subject/f:reference/@value, '/')` `= $package/f:id/@value][1]`	First marketing authorization for the package $package **Note:** steps to get to a package are shown later

6. Authorisation number

$productMA/f:identifier[f:system/@value =
$identifierSystem_marketingAuthorizationNumber]/f:value/@value

Returned value is **PA999/099/009UAT**

7. Authorisation country

RMS code: $productMA/f:region/f:coding/f:code/@value

Country name: $productMA/f:region/f:coding/f:display/@value

Returned values are
100000000529 for the RMS code
Kingdom of Spain for the country name

```
<entry>
    <resource>
        <RegulatedAuthorization>
            <id value="19ec038b3abcfbe8f8d69a30ce653a8aMKTRA"/>
            <identifier>
                <system value="http://ema.europa.eu/fhir/marketingAuthorizationNumber"/>
                <value value="PA999/099/009UAT"/>
            </identifier>
            <subject>
            <type>
            <region>
                <coding>
                    <system value="https://spor.ema.europa.eu/v1/lists/100000000002"/>
                    <code value="100000000529"/>
                    <display value="Kingdom of Spain"/>
                </coding>
            </region>
            <relatedDate>
            <relatedDate>
```

8. Marketing authorisation holder

Organisation name:

$productMA/f:holder/f:display/@value

OMS Loc-ID:

$productMA/f:holder/f:identifier[f:system/@value =

$identifierSystem_organizationLocId]/ f:value/@value

Returned values are
Acme Inc. for the organisation name
LOC-999999999 for the OMS Loc-ID

Note: both marketing authorisations, for product and package, contain holder information

```
<entry>
    <resource>
        <RegulatedAuthorization>
            <id value="e888c5e53aaa0711f8d69a30ce653a8aMKTRA" />
            <identifier>
            <subject>
            <type>
            <region>
            <relatedDate>
            <holder>
                <reference value="Organization/603bd74a3a2a3ab7f8d69a30addf073a" />
                <identifier>
                    <system value="https://spor.ema.europa.eu/v1/locations" />
                    <value value="LOC-999999999" />
                </identifier>
                <display value="Acme Inc." />
            </holder>
            <regulator>
            <case>
```

UN COM

Product Lifecycle Management Portal

Full Name	Pack Size	MA Number
QWERTY 30 mg - Gastro-resistant capsule, hard	<mark>1 gastro-resistant capsule, hard</mark>	EU/9/13/777/111UAT

eAF Variation PDF

| Scope	A.2.b) - Variation Type IB - 1	
Product(s) Package(s)	Zwerty 30 mg - Gastro-resistant capsule, hard *all packages listed in section 2 for the product*	
	Present [9,10]	Proposed [9,10]

HL7® FHIR®

Name	Flags	Card.	Type
PackagedProductDefinition	TU		DomainResource
identifier	Σ	0..*	Identifier
name	Σ	0..1	string
type	Σ	0..1	CodeableConcept
subject	Σ	0..*	Reference(MedicinalProductDefinition)
status	Σ	0..1	CodeableConcept
statusDate	Σ	0..1	dateTime
<mark>containedItemQuantity</mark>	Σ	0..*	Quantity

Steps to find a package
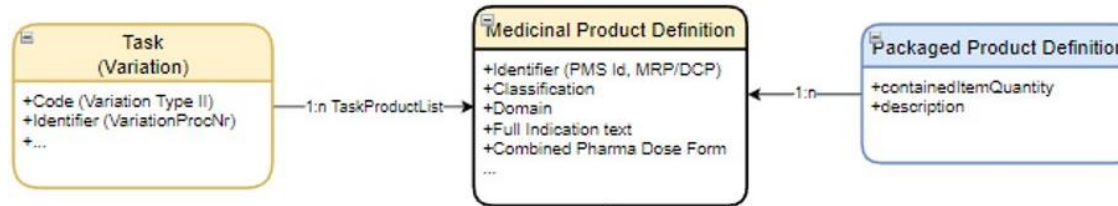
Element/Collection	Xpath	Description
$allPackagedProductDefinitions	`/f:Bundle/f:entry/f:resource/f:PackagedProductDefinition`	All the **PackagedProductDefinition** resources contained in the bundle
$productPackages	`$allPackagedProductDefinitions[substring-after(f:subject/f:reference/@value, '/') = $product/f:id/@value]`	All the pacagest associated with the product $product
$package	`$productPackages[1]`	Selection of a package based on some criteria (in the example, the first of them)

9. Pack sizes

Numeric value: $package/**f:containedItemQuantity/f:value/@value**

Unit: $package/**f:containedItemQuantity/f:unit/@value**

Returned values are
<mark>1</mark> for the numeric value
<mark>Bottle</mark> for the unit

Note:
package size information must be retrieved from the
containedItemQuantity element and not the package element

```
<entry>
  <resource>
    <PackagedProductDefinition>
      <id value="8d5eaac03abeb235f8d69a305a6e1ccbPACK" />
      <identifier>
      <subject>
      <containedItemQuantity>
        <value value="1" />
        <unit value="Bottle" />
        <code value="100000073497" />
      </containedItemQuantity>
      <description value="Omeprazole/Omeprazole/description" />
      <marketingAuthorization>
      <package>
        <identifier>
        <type>          NO
          <coding>
            <system value="https://spor.ema.europa.eu/v1/lists/100000073346" />
            <code value="100000073493" />
            <display value="Bag" />
          </coding>
        </type>
        <quantity value="1" />
        <containedItem>
      </package>
    </PackagedProductDefinition>
  </resource>
</entry>
```

Product Lifecycle Management Portal

| Full Name	Authorised Dose Form	Active Substance	Authorisation Country	MA Holder	MA Nr. ⓘ	MRP / CP Nr.	PMS ID
RoActemra 20 mg/mL concentrate for solution for i...	Concentrate for solution for infusion	Tocilizumab, Tocilizumab	European Union	UAT ORG (ORG-200036101) LOC	EU/1/08/492UAT	EMEA/H/C/000955UAT	UAT600010864424

eAF Variation PDF

Active Substance
Tocilizumab

MA Number(s) [8]	Full name [21]	MA Holder name	Member state	Pharmaceutical Form [22]
EU/1/08/492UAT	RoActemra 20 mg/mL concentrate for solution for infusion	UAT ORG (ORG-200036101) LOC	European Union	Concentrate for solution for infusion

HL7 FHIR

Name	Flags	Card.	Type
Ingredient	TU		DomainResource
identifier	Σ	0..1	Identifier
role	Σ	1..1	CodeableConcept
function	Σ	0..*	CodeableConcept
group	Σ	0..1	CodeableConcept
description	Σ	0..1	markdown
allergenicIndicator	Σ	0..1	boolean
manufacturer	Σ	0..*	Reference(Organization)
substance	Σ	0..1	BackboneElement
code	Σ	1..1	CodeableReference(SubstanceDefinition | Substance)
strength	Σ	0..*	BackboneElement

Substances - XML context
Active Substance Name, Strength
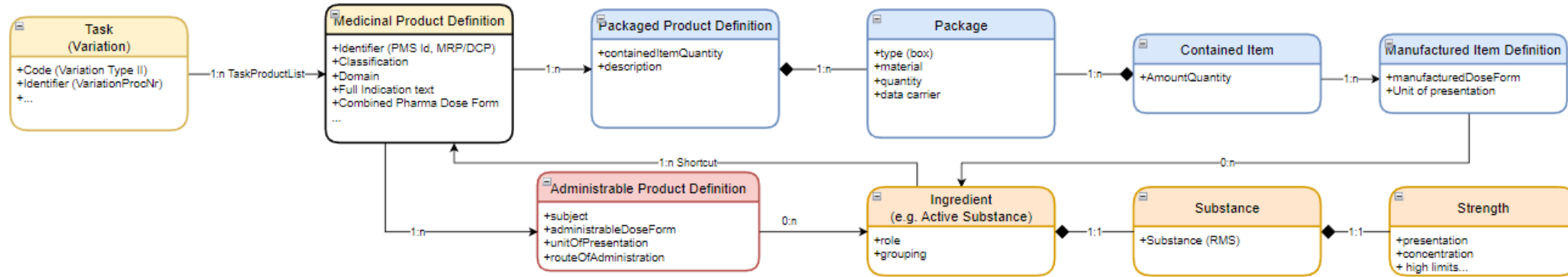
Element/Collection	Xpath	Description
$allIngredients	`/f:Bundle/f:entry/f:resource/f:Ingredient`	All the **Ingredient** resources contained in the bundle

$activeIngredients	`$allIngredients[`
	`    f:role/f:coding/f:system/@value = $rmsList_ingredientRole`
	`    and f:role/f:coding/f:code/@value = $rmsId_ingredientRole_active`
	`]`
		All the ingredients with "active" role

$productIngredients	`$activeIngredients[substring-after(f:extension[@url =` `extension_subject]/f:valueReference/f:reference/@value, '/') = $product/f:id/@value]`	All the active ingredients of the product $product
$ingredient	`$productIngredients[1]`	Any selection mechanism of an ingredient among the ones of **$product** In this example, the first one in the list is selected
$ingredientSubstance	`$ingredient/f:substance`	The "substance" child element of the Ingredient resource

10.1. Active substance name

SMS code:

$ingredientSubstance**/f:code/f:concept/f:coding[f:system/@url =**
'https://spor.ema.europa.eu/v1/lists/SubstanceDefinition']/ <mark>**f:code**</mark>**/@value**

Substance name:

$ingredientSubstance**/f:code/f:concept/f:coding[f:system/@url =**
'https://spor.ema.europa.eu/v1/lists/SubstanceDefinition']/ <mark>**f:display**</mark>**/@value**

Returned values are
<mark>**100000091436**</mark> for the SMS code
<mark>**CEFUROXIME SODIUM**</mark> for the substance name

```xml
<entry>
    <!-- <fullUrl value="urn:uuid:c6a838d9-27ca-49a4-a6ba-216448f82010"/> -->
    <resource>
        <Ingredient>
            <id value="Curocef1500mgPulver-A-HL-Ingredient"/>
            <extension url="http://ema.europa.eu/fhir/extension/masterFile">
            <extension url="http://ema.europa.eu/fhir/extension/subject">
            <status value="active"/>
            <role>
            <substance>
                <code>
                    <concept>
                        <coding>
                            <extension
                                url="http://ema.europa.eu/fhir/extension/substanceVersion">
                            <system value="https://spor.ema.europa.eu/v2/SubstanceDefinition"/>
                            <code value="100000091436"/>
                            <!-- EUTCT or. APEX -->
                            <display value="CEFUROXIME SODIUM"/>
                        </coding>
                    </concept>
                </code>
                <strength>
            </substance>
        </Ingredient>
    </resource>
</entry>
```

Substances – IT context

10.2. Active substance strength

Presentation ratios:

$ingredientSubstance**/f:strength/f:concentrationRatio**

$ingredientSubstance**/f:strength/f:concentrationHighValueRatio**

Concentration ratios:

$ingredientSubstance**/f:strength/f:presentationRatio**

$ingredientSubstance**/f:strength/f:presentationHighValueRatio**

```xml
<entry>
    <resource>
        <Ingredient>
            <id value="0bf46d49d30129e7f8d69a301b942c43"/>
            <role>
            <substance>
                <code>
                <strength>
                    <concentrationRatio>
                    <concentrationHighValueRatio>
                    <presentationRatio>
                    <presentationHighValueRatio>
                </strength>
            </substance>
        </Ingredient>
    </resource>
</entry>
```

Considerations:

☐ There are two distinct groups of information, one for **concentration** strength and another for **presentation** strength

☐ An ingredient can have one, the other or both

☐ Each of those two groups encloses the following:

- A comparator ("greater than", "less than", "equals to", "approximately equals to"…) - an extension for RMS is used instead of the standard attribute that uses a FHIR quantity-comparator list
- A FHIR Ratio[*] element representing a specific value or the lower limit of the range, in case the upper limit is also present
- An optional FHIR Ratio [*] element representing the upper limit of a range

(*) https://hl7.org/fhir/2021May/datatypes.html#Ratio

10.2. Active substance strength – cont.

Let `$ratio` be one of the four above ratios.
Then:

Numerator value: `$ratio/f:numerator/f:value/@value`
Numerator unit code: `$ratio/f:numerator/f:code/@value`
Numerator unit label: `$ratio/f:numerator/f:unit/@value`

Denominator value: `$ratio/f:denominator/f:value/@value`
Denominator unit code: `$ratio/f:denominator/f:code/@value`
Denominator unit label: `$ratio/f:denominator/f:unit/@value`

Comparator code:
`$ratio/f:numerator/f:comparator/f:extension/f:valueCoding/f:code/@value`
Comparator display name:
`$ratio/f:numerator/f:comparator/f:extension/f:valueCoding/f:display/@value`


```xml
<presentationRatio>
    <numerator>
        <value value="0.5000000000"/>
        <comparator>
            <extension url="http://ema.europa.eu/fhir/extension/comparator">
                <valueCoding>
                    <system value="https://spor.ema.europa.eu/v1/lists/100000000008"/>
                    <code value="100000000055"/>
                    <display value="approximately equal to"/>
                </valueCoding>
            </extension>
        </comparator>
        <unit value="millilitre(s)"/>
        <system value="https://spor.ema.europa.eu/v1/lists/100000110662"/>
        <code value="100000110633"/>
    </numerator>
    <denominator>
        <value value="1.0000000000"/>
        <unit value="Ampoule"/>
        <system value="https://spor.ema.europa.eu/v1/lists/200000002164"/>
        <code value="200000000014"/>
    </denominator>
</presentationRatio>
```

Do you want more information on FHIR?

► This was the last planned training 😢

► If you are interested in continuing this kind of information exchange please fill in this survey that was already sent out to all IT Directors 😊

Link to the survey
https://forms.office.com/r/pT37im2FSr

This was the last planned training 😢

If you are interested in continuing this kind of information exchange please tell us in this survey that was sent out to all IT Directors 😊

Link to the survey https://forms.office.com/r/pT37im2FSr

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What's Next?

1. Publication of Xpaths in a Github in the next months
2. Create and publish validation profiles for variation and product
3. Publish a service to check authenticity of the variation PDF using checksums
4. Stricter change process once more member states have the import in production (3 or 6 months lead time?)
5. Update from 4.6.0 to 5.0.0 for eAF
6. Update from 4.2.0 to 5.0.0 for PMS

The full recording of this webinar will be available on the UNICOM youtube channel accessible from the UNICOM website

On the UNICOM website, under resources, you will also find a number of important documents published as « working papers »

Further Information on UNICOM
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Congratulations!
You have made it until the end!
Thank you for your patience!

UNICOM

https://hl7.org/fhir/2021May/resourcelist.html

- **MedicinalProductDefinition**
  - The entry point for the PMS product
- **PackagedProductDefinition**
  - Packages in a product
- **AdministrableProductDefinition**
  - Pharmaceutical Product with links to ingredients
- **ManufacturedItemDefinition**
  - Manufactured Items with links to ingredients
- **Ingredient**
  - Each Ingredient has a substance link and represents a part of the composition
- **RegulatedAuthorization**
  - Any kind of authorisation (e.g. Marketing Authorisation, Manufacturing Authorisation,…)

- **SubstanceDefinition**
  - Contains the substance name and link to SMS
- **ActivityDefinition**
  - The „operation" of a manufacturer
- **DeviceDefinition**
  - Medical Device that is part of the product
- **DocumentReference**
  - Numbers of documents – no actual document or link
- **ClinicalUseIssue**
  - Indications of the product
- **Organization**
  - Contains the link to OMS and a copy of the organisation details
- **PracticionerRole**
  - A person (not part of any master data)

https://hl7.org/fhir/2021May/resourcelist.html

Procedure Management

► Task

➢ Task is the main entry point of the procedure. It contains most details as a key value pair on input type & value

➢ A task can be the subject of regulated authorisations (e.g. orphan, paediatric applications) and payment details

➢ A task has a subtask for every scope in a variation

► Provenance

➢ Each of the 3 types of changes are depicted in a provenance of type HTML change, Organisation change or Product Change

➢ Provenances are bundled in scopes

➢ Each change creates a new provenance

➢ A provenance can link any resource depending on what was changed

➢ A provenance can also be a signature

► PaymentNotice

➢ Payment details within the procedure