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

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

1. **Introduction, Motivation**
   10:00 – 10:20
   - Georg Neuwirther
     (UNICOM WP3 Lead, Austrian Medicines Agency)

2. **References – Where to start?**
   10:20 – 10:25
   - Noel Diamant
     (Product Co-Owner for DADI, Austrian Medicines Agency)

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. **5 minute break**

6. **Basics - How to read FHIR and use XPath?**
   11:00 – 11:15
   - Gianluca Risi
     (AEMPS, Senior Developer)

7. **A guide to extracting information**
   presented with a UNICOM reference implementation
   11:15 – 11:50
   - Gianluca Risi, Noel Diamant

8. **Closing**
   11:50 – 12:00
   - Georg Neuwirther
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Speaker

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

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

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

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Introduction
Motivation to organise such a training

- 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!

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

unicom-project.eu
Let's use this meeting to understand the new opportunities and get technical info on how we can use them.
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/](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 processes 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).
Introducing ISO IDMP compliant application forms

- 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!

Timelines

- 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

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AS-IS: Electronic Application Forms for Medicinal Products

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

Applicants

Initial Applications

Lifecycle Management

Regulators

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

Regulatory IT-Systems
Web Tool supporting IDMP/FHIR compatible application dataset formats

DADI

Initial Applications
Lifecycle Management

Regulators

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

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

New Retrieving master data
New IDMP/FHIR format

Regulatory IT-Systems

See also collaboration with UNICOM WP4

TO-BE and status of development

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

In progress

pending

10.03.2023

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First Go-Live Release

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

**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.

[Home · PLM (powerappsportals.com)](powerappsportals.com)
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 learn from the product upload to the UPD

Standardisation Focus
• Be part of the Connectathon “Vulcan stream” at HL7
• BR & R group at HL7 also handles the medicinal product
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

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)
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Top 10 Fields in focus of this presentation

This is a collection of essential medicinal product data elements that are currently available in the PLM Portal (Variation form for CAPs) (Except Strength)
Which FHIR Resources do I need?

These top 10 fields are contained in only 4 FHIR resources

- **MedicinalProductDefinition**
  - ✓ Ids, Name, ATC Code

- **PackagedProductDefinition**
  - ✓ Pack Size

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

- **Ingredient**
  - ✓ Substance Name & Strength
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

A worksharing Variation XML can be numerous lines of XML and extracting all information may be challenging at the start.

Example XML:

```xml
<identifier>
  <system value="http://ema.europa.eu/fhir/pmsId" />
  <value value="UAT600010787360" />
</identifier>
```
Concepts to represent master data

2. PRODUCTS CONCERNED BY THIS APPLICATION

Active Substance

<identifier>
  <system value="http://ema.europa.eu/fhir/pmsId" />
  <value value="UAT600010787360" />
</identifier>
Provenance – The list of changes in a variation
Representing changes to master data in so-called FHIR Provenances

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"
XML Data structure to keep the changes

- Every proposed change on master data will know its relation to the Scope, Product and Package.

- 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

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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: 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.

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

5 Minute break
Basics - How to read FHIR and use XPath?

Gianluca
What is FHIR?

- "FHIR is a standard for health care data exchange, published by HL7®" (*)
- Set of rules and specification for exchanging electronic healthcare 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

- **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)

- **References - Use of ‘subject‘**
  - Links between resources are implemented using **reference** elements
  - Reference values are in the form of "**resourceType/resourceId**"
  - Tipically, **subject** element is used to host the reference
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

► 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 XPaths

Open Source Implementations
Most common used libraries to extract FHIR content

- JAVA: [https://github.com/jamesagnew/hapi-fhir](https://github.com/jamesagnew/hapi-fhir) - James Agnew / University Health Network

- .NET Client - Firely .NET SDK: [https://github.com/FirelyTeam/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](https://confluence.hl7.org/pages/viewpage.action?pageId=35718838)

- Many Implementation tools can be found here: [http://build.fhir.org/downloads.html](http://build.fhir.org/downloads.html)
XPath characteristics

► Important: An XPath interpreter is needed
  ➢ There is at least one library 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 [...] syntax
  ➢ 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

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
<xs:variable name="rs_list_url" select="https://spor.ema.europa.eu/v1/lists/10000000004"/>
<xs:variable name="rs_list_url_e" select="https://spor.ema.europa.eu/v1/lists/100000015442"/>
<xs:variable name="rs_list_url_applicationSubmissionType" select="https://spor.ema.europa.eu/v1/lists/100000159312"/>
<xs:variable name="rs_list_url_applicationIngredientRole" select="https://spor.ema.europa.eu/v1/lists/160000072980"/>
<xs:variable name="rs_list_url_medicalProductNamePartType" select="https://spor.ema.europa.eu/v1/lists/330000000000"/>
<xs:variable name="rs_list_url_productInformationDocumentType" select="https://spor.ema.europa.eu/v1/lists/300000155511"/>
<xs:variable name="rs_list_url_regulatoryEntitlementType" select="https://spor.ema.europa.eu/v1/lists/220000000000000065"/>
<xs:variable name="rs_list_url_parallelApplicationVariationStatus" select="https://spor.ema.europa.eu/v1/lists/290000000000000000"/>
<xs:variable name="rs_list_url_documentation" select="https://spor.ema.europa.eu/v1/lists/290000000000000000"/>
<xs:variable name="rs_list_url_orphanStatus" select="https://spor.ema.europa.eu/v1/lists/orphanStatus"/>
<xs:variable name="rs_list_url_asynchronousOr" select="https://spor.ema.europa.eu/v1/lists/290000000000000000"/>
<xs:variable name="rs_list_url_HarmonisationEntry" select="https://spor.ema.europa.eu/v1/lists/290000000000000000"/>
<xs:variable name="rs_list_url_medicalDeviceClassification" select="https://spor.ema.europa.eu/v1/lists/290000000000000000"/>
<xs:variable name="rs_list_url_medicalDeviceCombinationTypes" select="https://spor.ema.europa.eu/v1/lists/290000000000000000"/>
<xs:variable name="rs_list_url_medicalDeviceDocumentation" select="https://spor.ema.europa.eu/v1/lists/290000000000000000"/>
<xs:variable name="rs_list_url_applicableMedicisicRegulation" select="https://spor.ema.europa.eu/v1/lists/290000000000000000"/>
<xs:variable name="rs_list_url_provenanceType" select="https://spor.ema.europa.eu/v1/lists/900000000000000000"/>
```

---

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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 -->
<variable name="identifierSystem_pid" select="http://ema.europa.eu/fhir/pmid"/>
<variable name="identifierSystemἨο" select="http://ema.europa.eu/fhir/Ήο"/>
<variable name="identifierSystem_applicationIdentifierNumber" select="http://ema.europa.eu/fhir/applicationIdentifierNumber"/>
<variable name="identifierSystem_procedureIdentifierNumber" select="http://ema.europa.eu/fhir/procedureIdentifierNumber"/>
<variable name="identifierSystem_purchaseOrder" select="http://ema.europa.eu/fhir/purchaseOrder"/>
<variable name="identifierSystem_organizationNumber" select="http://ema.europa.eu/fhir/organizationNumber"/>
<variable name="identifierSystem_organizationIdentifierNumber" select="http://ema.europa.eu/fhir/organizationIdentifierNumber"/>
<variable name="identifierSystem_locationId" select="https://spor.ema.europa.eu/v1/organizations"/>
<variable name="identifierSystem_locationIdentifier" select="https://spor.ema.europa.eu/v1/locations"/>
<variable name="identifierSystem_scopedIdentifier" select="http://ema.europa.eu/fhir/scopedIdentifier"/>
<variable name="identifierSystem_marVariationNumber" select="http://ema.europa.eu/fhir/MHPVariationNumber"/>
<variable name="identifierSystem_orphanDesignationNumber" select="http://ema.europa.eu/fhir/orphanDesignationNumber"/>
<variable name="identifierSystem_orphanDesignationProcedureNumber" select="http://ema.europa.eu/fhir/orphanDesignationProcedureNumber"/>
<variable name="identifierSystem_orphanRegisterNumber" select="http://ema.europa.eu/fhir/orphanRegisterNumber"/>
<variable name="identifierSystem_marketingAuthorizationNumber" select="http://ema.europa.eu/fhir/MarketingAuthorizationNumber"/>
<variable name="identifierSystem_deviceIdentifier" select="http://ema.europa.eu/fhir/DeviceIdentifier"/>
<variable name="identifierSystem_plDecisionNumber" select="http://ema.europa.eu/fhir/plDecisionNumber"/>
<variable name="identifierSystem_usLabelDecisionNumber" select="http://ema.europa.eu/fhir/productSpecificLabelDecisionNumber"/>
<variable name="identifierSystem_classWaeiverNumber" select="http://ema.europa.eu/fhir/classWaeiverDecisionNumber"/>
<variable name="identifierSystem_notifiedBodyNumber" select="http://ema.europa.eu/fhir/notifiedBodyNumber"/>
<variable name="identifierSystem_dunNumber" select="http://ema.europa.eu/fhir/dunNumber"/>
<!-- END f:identifier/f:system/value urls -->
```
A guide to extracting information

presented with a UNICOM reference implementation
Concepts to represent master data

2. PRODUCTS CONCERNED BY THIS APPLICATION

- Active Substance
- Other domains

Business & Domain Experts

Handover to IT Experts

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XPath

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

FHIR Structure

Model

XML Representation

PDF
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Legend

FHIR Resource
- Can be referenced from another resource containing resource
- Use cases can be
  a) To enforce FHIR version
  b) An FHIR resource taxonomy containing multiple resources

Example:
- Package/ProductDefinition
- Product
- Claim

Note: while the FHIR resource is not yet fully implemented in this variation message, it is referenced as a resource for use cases.
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### Medicinal Product - Business context

**Authorised dose form, MRP/DCP/CP Nr, PMS Id**

<table>
<thead>
<tr>
<th>Full Name</th>
<th>Authorised Dose Form</th>
<th>Active Substance</th>
<th>Authorisation Country</th>
<th>MA Holder</th>
<th>MA Nr.</th>
<th>MRP / CP Nr.</th>
<th>PMS ID</th>
<th>MP ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>MINILIVI 200 mg - Powder for concentrate for solut...</td>
<td>Powder for injection</td>
<td>Tafazzanib</td>
<td>European Union</td>
<td>Incyte Biosciences Distribution B.V.</td>
<td>EU/1/21/1570</td>
<td>M/N/0012</td>
<td>60000004682</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MA Number(s)</th>
<th>Full name</th>
<th>MA Holder name</th>
<th>Member state</th>
<th>Pharmaceutical Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>EU/1/14/94/003</td>
<td>Abasaglar 100 Units/ml - Solution for injection</td>
<td>Eli Lilly Nederland B.V.</td>
<td>European Union</td>
<td>Solution for injection</td>
</tr>
</tbody>
</table>

---

**hl7 fhir**

**Product Lifecycle Management Portal**

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Medicinal Product - Business context

Product Full Name

2. PRODUCTS CONCERNED BY THIS APPLICATION

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## Medicinal Product - XML Context

### Steps to find a specific product

<table>
<thead>
<tr>
<th>Element/Collection</th>
<th>XPath</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Note: selector [1] is optional, since only one task is expected</td>
</tr>
<tr>
<td>$allProducts</td>
<td>/f:Bundle/f:entry/f:resource/f:MedicinalProductDefinition</td>
<td>All the MedicinalProductDefinition resources contained in the bundle</td>
</tr>
<tr>
<td>$affectedProductReferences</td>
<td>$variationTask/f:contained/f:List/f:entry/f:item/f:reference</td>
<td>All the rereferences to (concerned) products contained in the procedure task</td>
</tr>
<tr>
<td>$affectedProducts</td>
<td>$allProducts[$affectedProductReferences/@value = concat('MedicinalProductDefinition/', f:id/@value)]</td>
<td>All the MedicinalProductDefinition resources representing each of the products concerned by the application</td>
</tr>
<tr>
<td>$product</td>
<td>1. $allProducts[1]</td>
<td>Get a concrete product by some criteria:</td>
</tr>
<tr>
<td></td>
<td>2. $allProducts[f:identifier[f:system/@value = $identifierSystem_pmsId and f:value/@value = 'xyz']]</td>
<td>1. The first product of the list of affected products</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. The product whose PmsId is “xyz”</td>
</tr>
</tbody>
</table>
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
   Note: this field is not used in PdfGen

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
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Medicinal Product - IT context
ATC Code, Product Full Name

4. ATC code


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

5. Product full name

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


Returned values is

MINJUVI 200 mg - Powder for concentrate for solution for infusion

When queried for [lang = "EN"]
<table>
<thead>
<tr>
<th>Full Name</th>
<th>Authorised Dose Form</th>
<th>Active Substance</th>
<th>Authorisation Country</th>
<th>MA Holder</th>
<th>MA Number(s)</th>
<th>HRP / CP Nr.</th>
<th>PMS ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qwerty 30 mg - Gastro-resistant capsule, hard</td>
<td>Gastro-resistant capsule, hard</td>
<td>MERQWERTYAMINE BITARTRATE</td>
<td>European Union</td>
<td>UAT ORG (ORG-200036099)</td>
<td>EU/123456789/AT</td>
<td>EMEA/H/012345/AT</td>
<td>UAT900000000777</td>
</tr>
</tbody>
</table>

**MA Number(s):** EU/9/13/777/AT

**Full name:** Qwerty 30 mg - Gastro-resistant capsule, hard

**MA Holder name:** UAT ORG (ORG-200036099)

**Member state:** European Union

**Pharmaceutical Form:** Gastro-resistant capsule, hard
Regulated authorisation - XML context
MA Number, MA Country, MA Holder
Steps to find a marketing authorisation

<table>
<thead>
<tr>
<th>Element/Collection</th>
<th>Xpath</th>
<th>Description</th>
</tr>
</thead>
</table>

Note: steps to get to a package are shown later
Marketing authorisation – IT context
MA Number, MA Country, MA Holder

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

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
<table>
<thead>
<tr>
<th>Full Name</th>
<th>Pack Size</th>
<th>MA Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>QWERTY 30 mg - Gastro-resistant capsule, hard</td>
<td>1 gastro resistant capsule, hard</td>
<td>EU/9/13/777/111UAT</td>
</tr>
</tbody>
</table>

**Scope:** A.2.b) - Variation Type B - 1

<table>
<thead>
<tr>
<th>Product(s) Package(s)</th>
<th>Present</th>
<th>Proposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>QWERTY 30 mg - Gastro-resistant capsule, hard</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All packages listed in section 2 for the product.

---

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 875299.
### Package information - XML context

**Package Size**

**Steps to find a package**

<table>
<thead>
<tr>
<th>Element/Collection</th>
<th>Xpath</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$allPackagedProductDefinitions</td>
<td>/f:Bundle/f:entry/f:resource/f:PackagedProductDefinition</td>
<td>All the PackagedProductDefinition resources contained in the bundle</td>
</tr>
<tr>
<td>$productPackages</td>
<td>$allPackagedProductDefinitions[substring-after(f:subject/f:reference/@value, '/')] = f:id/@value</td>
<td>All the pacages associated with the product $product</td>
</tr>
<tr>
<td>$package</td>
<td>$productPackages[1]</td>
<td>Selection of a package based on some criteria (in the example, the first of them)</td>
</tr>
</tbody>
</table>
9. Pack sizes

**Numeric value:** $\text{package/f:containedItemQuantity/f:value/@value}$

**Unit:** $\text{package/f:containedItemQuantity/f:unit/@value}$

Returned values are

- 1 for the numeric value
- Bottle for the unit

**Note:**

package size information must be retrieved from the $\text{containedItemQuantity}$ element and not the $\text{package}$ element.
Medicinal Product - Business context

Active Substance Name

Full Name: Tocilizumab

Authorized Dose Form: Concentrate for infusion

Active Substance: Tocilizumab

Authorisation Country: European Union

MA Holder: UAT ORG (ORG-200036101) LOC

MA Nr.: EU/1/08/492UAT

MRP / CP Nr.: EMEA/H/IV/000955UAT

PMS ID: UI1006010864424

MA Number[s]: EU/1/08/492UAT

Full name: RoActemra 20 mg/mL concentrate for solution for infusion

MA Holder name: UAT ORG (ORG-200036101) LOC

Member state: European Union

Pharmaceutical Form: Concentrate for solution for infusion

This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 875299
Substances - XML context
Active Substance Name, Strength

<table>
<thead>
<tr>
<th>Element/Collection</th>
<th>Xpath</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$allIngredients</td>
<td>/f:Bundle/f:entry/f:resource/f:Ingredient</td>
<td>All the Ingredient resources contained in the bundle</td>
</tr>
<tr>
<td>$activeIngredients</td>
<td>$allIngredients[[f:role/f:coding/f:system/@value = $rmsList_ingredientRole and f:role/f:coding/f:code/@value = $rmsId_ingredientRole_active ]</td>
<td>All the ingredients with “active” role</td>
</tr>
<tr>
<td>$productIngredients</td>
<td>$activeIngredients[[substring-after(f:extension[@url = extension_subject]/f:valueReference/f:reference/@value, '/') = $product/f:id/@value]</td>
<td>All the active ingredients of the product $product</td>
</tr>
<tr>
<td>$ingredient</td>
<td>$productIngredients[1]</td>
<td>Any selection mechanism of an ingredient among the ones of $product In this example, the first one in the list is selected</td>
</tr>
<tr>
<td>$ingredientSubstance</td>
<td>$ingredient/f:substance</td>
<td>The “substance” child element of the Ingredient resource</td>
</tr>
</tbody>
</table>
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']/f:code/@value
```

**Substance name:**

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

Returned values are

- **100000091436** for the SMS code
- **CEFUROXIME SODIUM** for the substance name
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

**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 $\text{ratio}$ be one of the four above ratios.

Then:

- **Numerator value:** $\text{ratio}/f: \text{numerator}/f: \text{value}@value$
- **Numerator unit code:** $\text{ratio}/f: \text{numerator}/f: \text{code}@value$
- **Numerator unit label:** $\text{ratio}/f: \text{numerator}/f: \text{unit}@value$

- **Denominator value:** $\text{ratio}/f: \text{denominator}/f: \text{value}@value$
- **Denominator unit code:** $\text{ratio}/f: \text{denominator}/f: \text{code}@value$
- **Denominator unit label:** $\text{ratio}/f: \text{denominator}/f: \text{unit}@value$

**Comparator code:**

- $\text{ratio}/f: \text{numerator}/f: \text{comparator}/f: \text{extension}/f: \text{valueCoding}/f: \text{code}@value$

**Comparator display name:**

- $\text{ratio}/f: \text{numerator}/f: \text{comparator}/f: \text{extension}/f: \text{valueCoding}/f: \text{display}@value$
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
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
http://www.unicom-project.eu
Twitter: @unicom_idmp
linkedin.com/company/unicom-idmp

Congratulations!
You have made it until the end!
Thank you for your patience!
References: All Resources used in PMS

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
- PractitionerRole
  - A person (not part of any master data)
References: Additional Resources used in Variation

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