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

AGES Best Practices
UNICOM WP4

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and many other experts from our agency who contributed to this success!
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Welcome
➢ Georg Neuwirther

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• OMS
• RMS
• SMS
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Exporting Medicinal Product Data in FHIR 5.0 format – Outlook
➢ Noel Diamant

Take Home Message
➢ Georg Neuwirther
**AGES MEA** is a division of the Austrian Agency for Health and Food Safety (AGES), which is the leading expert organisation for risk minimisation in the fields of health, food safety and consumer protection.

**AGES** is wholly owned by the Republic of Austria.

The **AGES MEA** business unit is the service provider for the **Federal Office for Safety in Health Care (BASG)**.
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UNICOM deliverables covered in the presentation

- Refactoring, Extending the national core IT-System PHAROS
  - User-Interface
  - Business Logic
  - Database Model

- Updating SOPs, training material

- Extending existing data exports for usage in eHealth use case to support cross-border-prescription according to eHDSI

- Prototyping an FHIR 5.0 compliant data export

- SPOR data management services
  - Delivering quality data management services for substances, products, organisations
  - The four SPOR data management services are:
    - Substance Management Services (SMS)
    - Product Management Services (PMS)
    - Organisation Management Services (OMS)
    - Referential Management Services (RMS)

- eAF import based on FHIR XML
- Mapping eAF-DES to FHIR

- Data on medicines (ISO IDMP standards): Overview
  - Implementation based on EU IDMP Guidelines

- Welcome to PLM Portal
  - A secure online portal for managing electronic Anders forms, electronic Product Information (eAF) and authorised product data (APD) in the European Union, in collaboration with the European Medicines Regulatory Network.
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.

AGES (Noel Diamant) is acting as **Network Product Owner** for the implementation of the new eAF-creation tool and message exchange format → see UNICOM WP3
PHAROS - Implementation of ISO-IDMP concepts

Georg Neuwirther
Status of implementation in PHAROS

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Key Changes in PHAROS

► Implementing *Administrable Product* (Pharmaceutical Product)
  ➢ Based on existing concepts of the former database concept “RDM v3”

► Detailing *Package* structure

► Implementing *Indication Elements*

► Detailing *Manufacturer Details*

► Implementing *Part Names*

► Implementing *Additional Monitoring Attribute*
  ➢ Additional attribute can be stored according to 1.8. Additional monitoring indicator from EU IG chapter 2

► Migration legacy data into IDMP-compliant database model
Implementing Administrable Product (AP)
(Pharmaceutical Product - PhP)

- AP-concept had to be added to the PHAROS-world
  - Before: the Manufactured Item (MI) was the leading class

- Following principles were applied while refactoring:
  - Find synergies with business rules for legacy data migration
  - Ensure compatibility for eAF data import
  - Usage of RMS dictionaries is mandatory
  - Minimise administrative effort for data lifecycle management
  - Find a good balance in enriching the user interface
    ✓ (complexity vs. usability)

Source: EAM EU IG ch.2
Implementation of Administrable Product (AP)

<table>
<thead>
<tr>
<th>National ID for AP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placeholder for PMS identifiers</td>
</tr>
</tbody>
</table>

Consists of following Manufactured Items (MI):

- Strength denominator (presentation, concentration) *only defined once, for all ingredients in the PhP*

List of ingredients of the AP

Route of Administration of AP

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Implementation of Manufactured Item (MI)

This screenshot demonstrates the following scenario:

The Administrable Product is also the Manufactured Item
(applicable for all tablet presentations and any product without reconstitution)

Goal: minimizing administrative effort and error reduction

<table>
<thead>
<tr>
<th>Manufactured Item Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Art</td>
</tr>
<tr>
<td>Wirkstoff</td>
</tr>
<tr>
<td>ESCITALOPRAM OXALAT</td>
</tr>
<tr>
<td>mg</td>
</tr>
<tr>
<td>Hilfsstoff</td>
</tr>
<tr>
<td>LACTOSE</td>
</tr>
<tr>
<td>mg</td>
</tr>
</tbody>
</table>

Flag to mark that MI = AP

Concepts from AP were duplicated – see slide before

Notice: the AP attribute „Route of Administration“ can be entered here – only available for the scenario MI=AP
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### Implementation of Package

| Ebene       | Packungsgröße | Reihenfolge (Packungsreihe) | Beschreibung DE | Container | Container Material | Container Teil | Container Teil Material | Manufactured Item Quantity | Manufactured Item Referenz | Art des Device | Anzahl | Device | Device Referenz | Art der Laufzeit |
|-------------|---------------|----------------------------|-----------------|-----------|-------------------|---------------|------------------------|----------------------------|--------------------------|----------------|---------|--------|----------------|-----------------
| Packung     | 1             | Stück                      | 1 Durchstechflasche mit 250 IE: Pulver + 1 Durchstechflasche mit 30 ml Lösungsmittel + 1 Transferfolie + 1 Sterilitatenscheider |

**Packaged Medicinal Product (PMedP) according to EU IG / 2 / ch. 4 (p.127)**

<table>
<thead>
<tr>
<th>Container</th>
<th>Container Teil</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Schachtel</td>
<td>1 Fälschung</td>
</tr>
<tr>
<td>1 Durchstechflasche</td>
<td>1 Glasstopf</td>
</tr>
<tr>
<td>Stopfen</td>
<td>Brombutylk.</td>
</tr>
<tr>
<td>Stopfen</td>
<td>Brombutylk.</td>
</tr>
</tbody>
</table>

**Shelf life of PMedP according to EU IG / 2 / ch. 4 (p.127)**

- **Package Item Layers**
  - e.g. Box with 2 vials (2 MIs)

- **Container Material, Container parts and container part material**

- **Reference to MI including a textual description**

- **Manufactured Item Quantity**
  - (unit is taken from MI; reduces errors)

- **Enrichment of device information**
Implementing Indications

- Indication information is now automatically imported from SMPC (section 4.1)
- Coded indication elements are prepared for future consumption from SPOR PMS
Implementing Name Parts

Part Names are now prepared for future data import from eAF (FHIR)
Detailing *Manufacturer* information

► Prepared for future data import from the new eAF (FHIR)

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Migration into IDMP-compliant database model

► Stepwise migration of legacy data – bottom-up
  ➢ Started with MI enrichment
  ➢ Created APs composed of MIs
  ➢ Finalised with Package layers including links to MIs

► Manual preparing legacy data was needed for:
  ➢ a limited number of “old” products
  ➢ manufactured items to enrich “unit of presentation”
    ✓ existing package information was helpful

► Packages could be brought into the layered structured automatically
  ➢ Manual work was needed to correct “manufactured item quantity” information
SPOR Integration - OMS

Georg Neuwirther
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OMS integration - concept

1. Initial Import of Organisation and address data from eAF MAA, Variation, Renewals

► New organisation records will be taken ONLY from e.g.,
  ➢ eAF, CTs, other applications, ..

► For official letters PHAROS data is used – might deviate from OMS data (see challenges in next slides)

► All relevant organisation records in PHAROS are linked to an OMS-ID/LOC-ID reference

2. Regular OMS syncs to keep PHAROS data aligned with SPOR OMS

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SPOR data management services

- Substance Management Services (SMS)
- Product Management Services (PMS)
- Organisation Management Services (OMS)
- Referentials Management Services (RMS)
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Synchronisation: OMS --> PHAROS

Gap-analysis compares
- **daily** – timestamps OMS/PHAROS
- **weekly** – exists ORG/LOC-combination? (merge, split, active/inactive)

Getting OMS data via
OMS-API calls including error handling
- on a daily basis
- Receiving and processing a CSV-file payload

Process results
- manually via workflow tasks or fully automatically
Findings and challenges

► Processing the CSV payload is not optimal but more stable than separate OMS-calls
  ➢ Open service ticket that CSV data is different from OMS UI data

► High administrative manual effort when handling OMS data quality topics
  ➢ e.g. Active/inactive, lost IDs
  ➢ e.g. rejected OMS requests for new entries or updates

► Umlauts in names and addresses [Ö/Ü/Ä -> OE/UE/AE]
  ➢ ß in addresses [Straße; ß -> Strasse; ss]

► Semantics in address lines do not match PHAROS address structure

► “Districts” are included in address lines which creates manual effort to delete it again
  ➢ Otherwise districts would be included in PHAROS street elements

► Differences between DE and EN names and addresses
Findings and challenges

- Business logic to deal with names and alternative names
  - eAF story exists in PLM backlog

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**Organisation Details**

<table>
<thead>
<tr>
<th>Organisation ID:</th>
<th>OBG-100002269</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organisation Name:</td>
<td>Angelini Pharma Italia AzIende Chirurgico Riuniti</td>
</tr>
<tr>
<td>Status:</td>
<td>ACTIVE</td>
</tr>
<tr>
<td>Organisation Type:</td>
<td>Industry</td>
</tr>
<tr>
<td></td>
<td>Pharmaceutical company</td>
</tr>
</tbody>
</table>
We now have OMS data in PHAROS 😊

- OMS attributes
- LOC address lines
- GPS-coordinates
PHAROS - Importing eAF data based on the new FHIR format (Variation of CPs)

Noel Diamant
Motivation

Data availability in regulator systems (HMA/EMA) is essential for multiples use cases and of strategic importance. The eAF is a vessel to provide that data.
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The FHIR variation message attached to the eAF has been developed in FHIR version 4.6.0 is being released in 5.0.0 in Q2 this year.

This is the best time to start thinking about an automated import to be ready for the MRP / DCP / national variations from the PLM portal.

Latest release notes on the eAF FHIR XML: Bookmark this Link!

In the release notes you will find extensive examples (here)
FHIR Trainings for NCAs provided by AGES & AEMPS

Get an overview of the medicinal product
The basics of the medicinal product and its references
--> (recording) <--

The procedure envelop
Get an overview of the variation message:
--> (recording) <--

What to start importing
Top 10 most wanted IDMP fields
--> (recording) <--

What has changed in a variation?
How to track changes on a medicinal product using FHIR provenances
--> (recording) <--
Demo on Variation (CP)

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RMS - Integration of EMA SPOR services

Noel Diamant
Sporify API
In order to avoid the RMS throttling of 50 requests per minute as well as recent unexpected downtimes SPORIFY was chosen as an API “Proxy”

National Extensions
Even though we want to use RMS lists, we need national values and extensions for many lists that require its own database and UI (developed in Oracle APEX)

Synchronise changes
A method was chosen to only request changes since the last synchronisation: "v1/lists/search-terms?modified-after=$date"
A Detail algorithm can be found in the next slide

Validate every change
New terms, updated names / descriptions in german or changes in status need to be validated. Terms can be blacklisted if they should never be overwritten.
Get new terms since last week

Existing Term Id

- Text update
- Status update (Non-current)

New Term Id

- If name exists: update Term Id; If not: check me!

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SMS - Integration of EMA SPOR services

Noel Diamant
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**Figures on Substances**

**SMS: Substance List**

EMA’s SPOR SMS List contains over 70,000 Substances

**Positive:** A complete List, stable IDs, mappings

**Challenges:** A lot of duplicates exist, that are constantly being merged

**PHAROS: CTL Substance**

Our national database Pharos contains ~ 20,000 Substances. Some are used in Lifecycle management, some in Inspections, some are not used

**PHAROS: Substance Master Folder**

Substances used in the lifecycle of a medicinal product have a “Master Folder”. These are enriched with Information on:

- Synonyms, Doping, Narcotics, Psychotropics, drug interactions, PHV Issues, IDs, type, base substance calculations and documentations

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70,000+

20,000+

10,000+
SMS-Sync: Principles

We handle SMS like any other RMS list (with some additional attributes)

We only synchronise substances on-demand (keep it clean)

We use the “Comment” field from SMS to understand merges of non-current substances

Substance Name source, Type, Weight and Formular will be synced if available.

The sync checks if the updated substance is used to facilitate necessary master folder updates
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Substance Structure - WMUOPVGLPLDJIX-UHFFFAOYSA-N

How to find a substance in Pubchem using the structure from SMS:


How add into an existing web application:

<iframe class="pubchem-widget" src="https://pubchem.ncbi.nlm.nih.gov/compound/aspirin#section=3D-Conformer&embed=true" style="width: 600px; max-width: 100%; height: 900px;">"/>

How to get only the image via REST:

Exporting Medicinal Product Data in FHIR 5.0 format – Outlook

Noel Diamant
How to start your own FHIR export

FHIR version 5.0 has been released and is stable

1. We start with „2024 01 30 AF Data Requirements.xlsx“

2. Chose the fields we want to use:

<table>
<thead>
<tr>
<th>Field</th>
<th>Type</th>
<th>Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of the medicinal product</td>
<td>Header</td>
<td>n</td>
</tr>
<tr>
<td>Country</td>
<td>Select</td>
<td>m</td>
</tr>
<tr>
<td>Language</td>
<td>Select</td>
<td>n, m</td>
</tr>
<tr>
<td>Full Product Name</td>
<td>Header</td>
<td>n, m</td>
</tr>
<tr>
<td>Name Parts</td>
<td>Header</td>
<td>n</td>
</tr>
<tr>
<td>Name Part</td>
<td>Text</td>
<td>n, m</td>
</tr>
<tr>
<td>Name Part Type</td>
<td>Select</td>
<td>1, m</td>
</tr>
</tbody>
</table>

3. Use the FHIR paths in the documentation
4. Add national requirements (E.g. PZN Nr for every package)
5. Coordinate with national HL7 FHIR Austria for the extension names
   - E.g. MedicinalProductDefinition.identifier.system=https://www.datacare.at/
   - RegulatedAuthorization.status.extension[url=https://www.ages.at/fhir/extension/positiveAuthStatus]

6. Create the the xml or JSON message using in case of JAVA
Currently medicinal product data will be provided to eHealth-organisations in a proprietary data format („ClaML“):

```xml
<Class code="0012501">
  <Rubric kind="preferred">
    <Label xml:lang="de" xml:space="default">CONTRACTUBEX GEL</Label>
  </Rubric>
  <Meta name="Bedeutung_Zulassung" value="Contractubex -- Gel"/>
  <Meta name="ZulassungsNummer" value="1.2.40.0.34.4.17:13883"/>
  <Meta name="ELGA_Gültigkeit" value="true"/>
  <Meta name="ELGA_MedikationVerpackungsstatusLieferbar" value="true"/>
  <Meta name="Gewicht" value="50"/>
  <Meta name="ELGA_MedikationMengenart_code" value="2.16.840.1.113883.6.8:q"/>
  <Meta name="ELGA_MedikationMengenart_text" value="Gramm"/>
  <Meta name="ELGA_MedikationRezeptpflichtStatus_code" value="1.2.40.0.10.1.4.3.4.3.7:100000072076"/>
  <Meta name="ELGA_MedikationRezeptpflichtStatus_text" value="Arzneimittel zur Abgabe ohne ärztliche Verschreibung"/>
  <Meta name="ELGA_whoATC_D1_code" value="2.16.840.1.113883.6.73:03A"/>
  <Meta name="ELGA_whoATC_D1_text" value="Andere Wundbehandlungsmittel"/>
  <Meta name="ELGA_MedikationArtAnwendung_D1_code" value="1.2.40.0.10.1.4.3.4.3.4:100000073566"/>
  <Meta name="ELGA_MedikationArtAnwendung_D1_text" value="Anwendung auf der Haut"/>
  <Meta name="ELGA_Substanz_1_code" value="1.2.40.0.34.5.156:1712596"/>
  <Meta name="ELGA_Substanz_1_text" value="ALLYL-CEFAR BULBUS (AUSZUG)"/>
  <Meta name="ELGA_Substanz_2_code" value="1.2.40.0.34.5.156:1705858"/>
  <Meta name="ELGA_Substanz_2_text" value="ALLANTOIN"/>
  <Meta name="ELGA_Substanz_3_code" value="1.2.40.0.34.5.156:1708475"/>
  <Meta name="ELGA_Substanz_3_text" value="HEFFARIN-MATRIM"/>
  <Meta name="ELGA_MedikationDarreichungsform_D1_code" value="1.2.40.0.10.1.4.3.4.3.5:100000073726"/>
  <Meta name="ELGA_MedikationDarreichungsform_D1_text" value="Gel"/>
  <Meta name="ELGA_MedikationWachstumsstoffRelevant" value="false"/>
  <Meta name="Domocon" value="human"/>
</Class>
```
New opportunity: FHIR messaging

- With EMA's decision to use FHIR as a messaging format and the ongoing establishment of FHIR in the eHealth domain, FHIR is gaining in importance for the exchange of Medicinal Product Data.

- In a prototyp we will export master data from PHAROS in FHIRv5 format

- The result will be discussed with eHealth-organisations to discuss the benefit und plan next steps:
  - The object oriented structure of FHIR allows for more complex datasets
  - not always needed for eHealth-scenarios!
MVP approach for eHealth exports
Conclusions
Take Home Message

► Implementing ISO-IDMP has not been a sprint, but a marathon and we expect additional effort over the next years, for e.g.

➢ Upcoming EMA’s IDMP Guidelines
➢ Upcoming FHIR versions
➢ UX-improvements
➢ Data enrichment, e.g. importing data from the new eAFs and synchronisation
➢ Sync data with SPOR PMS
➢ OMS improvements
➢ Mapping national terms to SPOR (e.g. for remaining SMS terms)

► PHAROS is now structurally IDMP-ready to store data according to EU IGs

➢ We will use data from the “MAA and Variation eAF” (FHIR) via an automated data import
➢ We are evaluating the use of the PMS-API to download CPs

► IDMP-concepts are complex, perhaps too complex for some data consumers

➢ We are evaluating this together with national eHealth organisations
Thanks for your attention!