BfArM‘s Challenges within the Integration in the European Network
Overview

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3. Regulatory World (SPOR context)
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   II. Organisation Database
   III. Catalogue Database
   IV. Medicinal Product Database
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5. Medication Data for Crossborder Data Exchange
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1. About us
As independent higher federal authority the BfArM is part of the portfolio of the Federal Ministry of Health.
The BfArM is the largest European authority in the field of licensing and safety of medicinal products and medical devices.
Roughly 1,300 employees are involved in providing patients with safe and effective drugs and medical devices.
Central tasks of the BfArM:

→ To license and to improve the safety of drugs
→ To register and to evaluate the risks of medical devices
→ To monitor the traffic with narcotics and precursors
→ To establish classifications, terminologies, standards and data based information systems for health care
2. German National Health Care Structure
German National Health Care Structure*

*only relevant aspects for this presentation
German National Health Care Structure in European Context

BfArM

Regulatory world

Health care world

PEI
PI
KP
ISO IDMP
DE-SRS
BVL
AmAnDa

IFA
Gematik
ABDA
pharmacies
hospitals
physicians
eHealth

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3. Regulatory World
Database Landscape

**EMA**

- **S** Veterinary & Human Substances
  - SMS

- **P** Veterinary Medicinal Products
  - UPD
  - PMS

- **O** Human Medicinal Products
  - OMS

- **R** Organizations
  - RMS

**BfArM**

- **DE-SRS** Veterinary & Human Substances
- **AmAnDa** Veterinary & Human Medicinal Products
- **PI** Organizations
- **KP** Referentials
Substance Database - SPOR

Substances are basis for medicines, high quality substance data is crucial!

- Substance names
- Basis for eAF
- Includes national translations
- Transfer of EU-SRS hosting from BfArM to EMA - Jan 2023
- SVG-SRS: all SMS substances (internal)
- EU-SRS: only cleansed SMS substances
- ISO IDMP
- Chemical structure
- Hierarchy of substances
- Relationships between substances
- References (scientific)
- Code & Names
- Create & maintain substances by HMA SVG
- High quality data
**Substance Database - SPOR**

- Substance database since 1980s
- Since 2020 G-SRS software in use (the same software as EU-SRS)
- Approx. 47,000 substances, not all relevant for medicinal product but required by ISO IDMP

**Current process:**

**DE-SRS input**
- EUTCT/SMSID/xEVMPD mapping data since 2019
- Monitoring of SMS changes regarding substance status
- DE-SRS software development for better data exchange between systems

**DE-SRS output**
- Regular submission of German translations to SMS
- New substance request
- Applying for substance corrections in SMS
Substance Database - Challenges

• Mapping by name alone is not sufficient
  • EU-SRS includes high quality data, better source for mapping than SMS

• SMS cleansing in progress
  • Implementation of SMS changes in national substance databases
  • Difficult mapping of not-cleansed substances (e.g. homeopathics - a lot of duplicates, herbal substances/extracts - not clear naming rules)

• Not-cleansed substances can be selected by applicant → cleansing of SMS substances should have high priority for all of us

• SMSID should be basis substance ID for eHealth

Proposal for future process within EU network:
Organisation Database - SPOR

- National pharmaceutical companies database (Partnerinformationen - PI)
- PNR (Pharmaceutical Company Number) as national identifier
- Since early 1980s: 30 000 PNRs in total
- Integration of SPOR data possible since 03/2020
- Start of mapping procedure in 04/2021
Organisation Database - SPOR

- Historical versions are not considered here (mapping rate is higher)
- Checking of each single entry before mapping
- Round about 100 requests/month addressed to EMA

Total amounts of PNRs: 9285
PNRs with ORG-IDs: 5066
PNRs with LOC-IDs: 4728

PNRs used in active medicinal products
Challenges in OMS Mapping Progress

- Different data quality rules between EMA and BfArM (especially with regard to the legally registered address)
- Changes of IDs in OMS (due to mergers or inactivation and creating of new IDs)
- Non-transparent changes of OMS-data
- Data without possibility to verification (e.g. postal code)
- Rejections of creating new entries without documentation (e.g. intermediate manufacturers in China from CEPs)
National Catalogue Database - SPO

- Katalogportal (KP) contains 95 catalogues
- Basis for several consuming systems
- Goes back to first catalogues created in the early 1980s
- Integration of RMS data since 2017
- System requirements need to be updated – new database under construction
National Catalogue Database - SPO\textsubscript{R}

Redesign of Catalogue Database

<table>
<thead>
<tr>
<th>Katalognummer</th>
<th>Katalogname</th>
<th>Katalogversion</th>
<th>Aktionen</th>
</tr>
</thead>
<tbody>
<tr>
<td>2090000000</td>
<td>ATC-Codes - ATC-Codes (ATC)</td>
<td>166</td>
<td></td>
</tr>
<tr>
<td>2760000000</td>
<td>Allgemeine Hinweise (Pi) - General Notes (GEN)</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>2220000000</td>
<td>Altersbereich bei Menschen - Human Age Range (ARE)</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>2020000000</td>
<td>Altersbereiche bei Tieren - Animal Age Ranges (AAR)</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>2805000000</td>
<td>AstraZenDa-Benutzermasken - AMANDA_MASKS</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>2050000000</td>
<td>Anhaftende Gewebe - Appendent Tissue (ATE)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>2430000000</td>
<td>Anwendungsarten - Route of Administration (RAM)</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>2330000000</td>
<td>Applikationstfitsmittel - Name of Admin Device (NAD)</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>2120000000</td>
<td>Arzneimittellklationen - Classifications (CLS)</td>
<td>136</td>
<td></td>
</tr>
</tbody>
</table>
RMS Mapping Progress

- Mapped catalogues based on delivery for UPD
- Highly prioritised catalogues
  - Routes of Administration
  - Pharmaceutical dose form
  - Authorisation status
  - Record status
  - Product information document type
  - Contact party role
  - Legal basis
Challenges in RMS Mapping Progress

• Missing data in existing lists (shelf life/special precautions for storage)
• Missing lists in RMS (Location of ingredient)
• Merged lists in our national database (Pharmaceutical dose form, combined Pharmaceutical forms, combined terms, Basic dose form)
• National terms in addition to Standard terms
• Missing resources due to development of new system
Medicinal Product Database SPOR I

- Medicinal Product Database with entries dating from the late 1970s
- New database called AmAnDa (Arzneimittel- und Antragsdatenbank) since March 2020

* Due to data protection only test data are shown.
Medicinal Product Database SPOR II

AmAnDa
- Presentation of the complete life cycle of every medicinal product in one database
- Display and editing are joined
- Considering of IDMP during development
- For full IDMP compatibility further modifications in the database are required

Challenges
- Moving target; IDMP IG is constantly in progress
- Gap between national requirements and IDMP IG
4. PZN Mapping
PZN – Meaning & Mapping I

• PZN (Pharmazentralnummer) = German tag which has to be affixed onto the outer pack of medicinal products according to national legislation
• Logistical identifier for distribution purposes and reimbursement
• Can be done via Code 39 and the PZN in clear print underneath
• Provided by IFA (information service provider for the pharmaceutical market)
• Differs per package and pharmaceutical organization
• Link to product logistic and eHealth

→ mapping with regulatory data required
PZN – Meaning & Mapping II

- Implementation procedure in cooperation with IFA
- Additional fields required in AmAnDa → done ✓

<table>
<thead>
<tr>
<th>Vertriebsnummer (PZN)</th>
<th>PNR</th>
<th>Name</th>
<th>PU-Name gemäß IFA</th>
<th>Übermittlungsdatum</th>
</tr>
</thead>
<tbody>
<tr>
<td>01234567</td>
<td>4100017</td>
<td>Musterpharma A</td>
<td>Musterpharma A</td>
<td>28.11.2023</td>
</tr>
</tbody>
</table>

- Focus on medicinal products which are relevant for shortages, eHealth development, Direct Healthcare Professional Communication (DHPC)...
- Step I: Mapping of PZN (so called ‘PZN pool’) to medicinal product → ongoing
- Step II: Mapping of PZN to packages and pharmaceutical organizations → ongoing
- Installation of an interface for regular data update → started
PZN Mapping – Challenges & Benefit

Challenges
- Partially no identical identifier IFA – BfArM (e.g. registration number is missing)
- Different rules for allocation of PZN to MP by IFA e.g.
  - Same pack sizes could have more than one PZN
  - Different PZN for different distributors

Benefit
- Use for shortages, eHealth development, Direct Healthcare Professional Communication (DHPC)...
- Part of IDMP implementation Chapter 4.8.6. Data carrier identifier

5. Medication data for crossborder data exchange
EU Guidelines with reference to EMA SPOR or IDMP – Patient Summary

A.2.1.1 Vaccination/ prophylaxis information

<table>
<thead>
<tr>
<th>A.2.1.1.1 Disease or agent targeted</th>
<th>Disease or agent that the vaccination provides protection against</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.2.1.1.2 Vaccine/prophylaxis</td>
<td>Generic description of the vaccine/prophylaxis or its component(s)</td>
</tr>
<tr>
<td>A.2.1.1.3 Vaccine medicinal product name</td>
<td>Brand name of the vaccine medicinal product</td>
</tr>
<tr>
<td>A.2.1.3.1 Identifier of the vaccine medicinal product</td>
<td>Identifier for the vaccine medicinal product. It could be MPUID according to ISO 11615, EMA PMS ID and/or a national identifier.</td>
</tr>
<tr>
<td>A.2.1.4 Marketing Authorisation holder</td>
<td>Marketing Authorisation Holder</td>
</tr>
</tbody>
</table>

A.2.4 Medication summary

A.2.4.1 Current and relevant past medicines

<table>
<thead>
<tr>
<th>A.2.4.1.3 Brand name</th>
<th>Brand name if biological medicinal product or when justified by the health professional (ref. Commission Directive 2012/52/EU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.2.4.1.4 Active ingredient lists</td>
<td>Substance that alone or in combination with one or more other ingredients produces the intended activity of a medicinal product. Example: <em>paracetamol</em></td>
</tr>
<tr>
<td>A.2.4.1.5 Strength</td>
<td>The content of the active ingredient expressed quantitatively per dosage unit, per unit of volume or per unit of weight, according to the pharmaceutical dose form. Example: 500 mg per tablet</td>
</tr>
<tr>
<td>A.2.4.1.6 Pharmaceutical dose form</td>
<td>The form in which a pharmaceutical product is presented in the medicinal product package (e.g. tablet, syrup)</td>
</tr>
</tbody>
</table>

EU Guideline ePrescription / eDispensation

Crossborder activities in Germany
eHealth Digital Service Infrastructure

Electronic Patient Summary [NFDM / MIO PKA]
eprescription/eDispensiation in pipeline

National Contact Point for eHealth (NCPeH)

Country A – Sender: Mapping of national codesystems/valuesets + „Workaround“ providing English translation

Country B – Receiver: Translation of codesystems/valuesets into German
Crossborder activities in Germany challenges for ePatientSummary

Technical aspects:
- National implementation in HL7 FHIR – EU implementation in HL7 CDA

Most relevant semantic aspects:
- Regulatory brand name is different from brand name in other sources
- Substance valueset will be mapped to SMS
- SNOMED CT is basis terminology for electronic health record and may be used also for substances (necessary granularity of information has still to be verified, eventually mapping required in the future)
- ATC-German Extension contains additional terms (for ex. Herbals or blood products)
- Pharmaceutical form (KBV Darreichungsformen) valueset is different from EDQM-standard Terms
Crossborder activities in Germany challenges for ePrescription

Electronic Prescription data

- **Product Identifier Pharmazentralnummer**: 10203632
- **Product name**: ASPIRIN 500 mg Tabletten
- **Pack size**: 80 Stück
- **Pharmaceutical form**: UIA ... Überzogene Tabletten

ISO IDMP Regulatory Data

- **[Product Identifier] Zulassungsnummer**: 86750.00.00
- **Identifier pharmaceutical product**
- **Identifier packaged pharmaceutical product**
- **[Name of the Product] Arzneimittelname**: ASPIRIN 500 mg überzogene Tabletten
- **[Marketing Authorisation Holder] Zulassungsinhaber**: Bayer Vital GmbH
- **[Active Substance] Wirkstoffcode (EU) + Wirkstoffname**: 00002 + Acetylsalicylsäure (Ph.Eur.)
- **[Strength] + [Reference Strength] Wirkstoff Stärke**: 500 Milligramm
- **[Product Classification] ATC**: N02BA01
- **[pharmaceutical dose form] Pharmazeutische Form (EDQM)**: Überzogene Tablette
- **[Package Size] Packunggröße**: 80
- **[Unit of Presentation] Einheit der Abgabeform (EDQM) überzogene Tablette**
- **[Package Type] Packungstyp (EDQM)**: Blister
Crossborder activities in Germany
Interoperability challenges

- **ePrescription Identifier different to Market Authorisation Identifier**
  
  [ PZN, NTIN --- ZNR?, ENR?, MPID? ]

- **Source and business needs for „Pharmaceutical form“ varies according to intended users needs**
  
  [ recoding for substitution purposes, „imprecision“ in healthcare professional data ]

- **Substances repositories vary according to use cases and intended users needs**
  
  [ different granularity (Active moiety vs. Pharmaceutical substance), limits of ATC + handling „German modification entries“, grouping to pharmaceutical groups for healthcare professionals, patient friendly terms ]

- **Identifiers in use for exchange of structured data**
  
  In EU SPOR (RMS ID) and EU eHDSI CTS (Source system code)
6. Prospect and Conclusion
Tasks For 2024

- Mapping Exercise
- FHIR Server
- Integration of eAF
- Interface to RMS
- Interface to EU-SRS
- Interface to PMS
Prospect

- Necessity to improve co-operation between the two worlds (regulatory and eHealth)
- Transparent communication process for amendments and updates to central EMA systems are necessary
- Mapping activities need to be continued in order to achieve IDMP compatibility
- Constant adjustments to the data model will be necessary

→ UNICOM has lead to an improved interoperability within the EEA and should be continued.
Glossary

**AmAnDa** = Arzneimittelantragsdatenbank (national medicinal products database)

**BfArM** = Federal Institute for Drugs and Medical Devices

**DE-SRS** = German Substance Registration System (national substances database)

**eHDSI** = EU Electronic Health Digital Service Infrastructure

**EMA** = European Medicines Agency

**IFA** = Informationsstelle für Arzneispezialitäten

**KP** = Katalogportal (national referentials database)

**MP** = Medicinal Product

**NCPeH** = National Contact Point for eHealth

**PI** = Partnerinformationen (national pharmaceutical companies database)

**PNR** = pharmaceutical companies number (national identifier used in PI)

**PZN** = Pharmazentralnummer (nationals identifier for distribution purposes and reimbursement)

**SPOR** = Substances, Product, Organisations, Referentials (portal provided by EMA)
Thank you very much for your attention!

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