Draft Guidance for using IDMP in Medicinal Product Dictionary

Ursula Tschorn
Julie James
Robert Vander Stichele
Jane Millar
Leonora Grandia

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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1. IDMP as driver for MPD Data (Ursula Tschorn)
Introductions to our esteemed colleagues and today’s speakers

Ursula Tschorn (IDMP1)
Julie James (Blue Wave Informatics)
Robert Vander Stichele (clinical pharmacologist)
Jane Millar (Collaboration SNOMED)
Leonora Grandia (Z-Index)

...and our panellist

Frederic Doc (Vidal)
Christian Reich (OHDSI)

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Agenda

1. Identification of Medicinal Product (IDMP) as driver for Medicinal Product Dictionary Data (MPD) (Ursula Tschorn)

2. Mapping, Scenarios and Use Cases
   - 2.1 MPD Structure and Mapping Scenarios (Leonora Grandia)
   - 2.2 MPD and IDMP Data Model (Julie James)
   - 2.3 Mapping Pharmaceutical Dose Forms via Attributes (Robert Vander Stichele)
   - 2.4 Mapping SNOMED – EDQM Activity (Jane Millar)

3. ETL Extraction Process (Ursula Tschorn)

4. Discussion
1 IDMP Controlled Vocabularies + Structure

EMA SPOR Portal
Source: https://spor.ema.europa.eu/sporwi/

SPOR data management services

- Substance Management Services (SMS)
- Product Management Services (PMS)
- Organisation Management Services (OMS)
- Referentials Management Services (RMS)

FHIR - Fast Healthcare Interoperability Resources
1 IDMP Data flow from NCAs to eHealth
Scan with your smartphone
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www.menti.com and type 8294 8006
2.1 MPD Structure and Mapping Scenarios (Leonora Grandia)
## Match on datafields (1)

<table>
<thead>
<tr>
<th>Level</th>
<th>Local MPD</th>
<th>IDMP</th>
</tr>
</thead>
</table>
| Substance | Omeprazol magnesium (76384)  
Omeprazol (as magnesium salt) (76392) | Omeprazole magnesium (100000085918)  
Omeprazole (100000092047) |
| PhP     | Omeprazole magnesium (76384)  
20,6 mg (229)  
Omeprazol (as magnesium salt) (76392)  
20 mg (229)  
Gastro-resistant tablet (250) | Omeprazole magnesium (100000085918)  
20,6 mg (100000110655)  
Omeprazole (100000092047)  
20,6 mg (100000110655)  
Gastro-resistant tablet (100000073667) |
| MPID    | Losec Control 20 mg gastro-resistant tablet (xxx)  
Corden Pharma (xxx)  
etc | Losec Control 20 mg gastro-resistant tablet (xxx)  
Corden Pharma (LOC-100021459)  
Etc |
| PCID    | 1 Blister (37)  
7 ‘each’ [tablets] (245)  
etc | 1 Blister (100000073496)  
7 tablets (200000002152)  
etc |
Match on datafields (2)

- The more structured, the more likely to match to IDMP
  - Risk that the data elements have different interpretation
  - Risk that the content is different

- The more based on international nomenclature, the smaller the gap
  - MPD based on SPC
  - MPD based on SNOMED: you inherit the mapping from SNOMED

- Maintenance: electronic dataflow of all matched datafields is preferred
## Match on ID's of hierarchical levels (1)

<table>
<thead>
<tr>
<th>Level</th>
<th>Local MPD</th>
<th>IDMP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substance</td>
<td>Omeprazol magnesium (76384)</td>
<td>Omeprazole magnesium (100000085918)</td>
</tr>
<tr>
<td></td>
<td>Omeprazol (as magnesium salt) (76392)</td>
<td>Omeprazole (100000092047)</td>
</tr>
<tr>
<td>PhP L1</td>
<td>Omeprazol (as magnesium salt) (76392)</td>
<td>L1 = xxx</td>
</tr>
<tr>
<td>PhP L2</td>
<td>-</td>
<td>L2 = xxx</td>
</tr>
<tr>
<td>PhP L3</td>
<td>-</td>
<td>L3 = xxx</td>
</tr>
<tr>
<td>PhP L4</td>
<td>Omeprazole (as magnesium salt) gastroresistant tablet 20 mg (130648)</td>
<td>L4 = 100000073667</td>
</tr>
<tr>
<td>MPID</td>
<td>1124609</td>
<td>IE-100000833-00000003</td>
</tr>
<tr>
<td>PCID</td>
<td>17082617</td>
<td>IE-100000833-00000003-0001</td>
</tr>
</tbody>
</table>
Match on ID’s of hierarchical levels (2)

- Less difficulties caused by slightly different datafields
  - How to find out the match between local ID’s and IDMP-ID’s
  - Different algorithm’s per level

- Maintenance: using the algorithm? Filling out the IDMP-PCID by manufacturer? Retrieve ID’s via NCA based on registration number?
Conclusion

► Different approaches
► Keep in mind the use cases for the mapping
2.2 Medicinal Product Dictionaries and IDMP Data Model (Julie James)
MPDs evolved with computing in medicine
1. The “linear” (backbone) model

- Therapeutically active SUBSTANCE
- Therapeutically active SUBSTANCE SET
- SUBSTANCE(S) + STRENGTH(S) + DOSE FORM
- AUTHORISED PRODUCTS
- AUTHORISED PACKAGED PRODUCTS
Example of the “linear” (backbone) model

simvastatin

simvastatin + ezetimibe

simvastatin 20mg + ezetimibe 10mg oral tablet

INEGY® 10mg/20mg Tablets (Organon)

INEGY® 10mg/20mg Tablets x 28 (Organon)

ezetimibe

simvastatin + ezetimibe

simvastatin 20mg + ezetimibe 10mg oral tablet

INEGY® 10mg/20mg Tablets (Organon)

INEGY® 10mg/20mg Tablets x 28 (Organon)
Expansion of the main classes in the “linear” model

As the linear model is populated, it “fans out” from a single substance to many packages.
Z-Index – uses the linear model

- Substance
  - morphine
- Substance + grouped RoA
  - morphine parenteral
- Substance(s) + grouped RoA
  - morphine dexamethasone parenteral
- Active ingredients + strength + units + dose form + RoA
  - Morphine/dexamethasone solution for injection 5/0.04 mg/ml
- As GPK + some more details
  - Morphine/dexamethasone solution for injection 5/0.04 mg/ml cass 100ml
- Medicinal product
- Packaged medicinal product
“Truncated” linear MPD models with an examples
2. The “mirror image” model

- Substance(s) + Strengths
- Dose Form [+ Unit of Presentation]

ABSTRACT PRODUCTS

AUTHORISED PRODUCTS

ABSTRACT PACKAGED PRODUCTS

AUTHORISED PACKAGED PRODUCTS

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Example of the “mirror image” model

- simvastatin 20mg + ezetimibe 10mg
- oral tablet [tablet]

- simvastatin 20mg + ezetimibe 10mg oral tablet
- simvastatin 20mg + ezetimibe 10mg oral tablet x28

- INEGY® 10mg/20mg Tablets (Organon)
- INEGY® 10mg/20mg Tablets x 28 (Organon)

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The “5 box” variation of the “mirror image” model

- Therapeutic Moiety
- Abstract Products
- Authorized Products
- Abstract Packaged Products
- Authorized Packaged Products

Substance(s) + Strengths
Dose Form [+ Unit of Presentation]
Example of the “5 box” variation of the “mirror image” model

simvastatin + ezetimibe

simvastatin 20mg + ezetimibe 10mg oral tablet

simvastatin 20mg + ezetimibe 10mg oral tablet x28

INEGY® 10mg/20mg Tablets (Organon)

INEGY® 10mg/20mg Tablets (Organon) x28

Substance(s) + Strengths

Dose Form [+ Unit of Presentation]
The NHS dm+d – uses the “5 box” model

The dm+d Browser

Prescription Services

Search in progress

VTM
- View Simvastatin + Ezetimibe

VMP
- View Simvastatin 20mg / Ezetimibe 10mg tablets
- View Simvastatin 40mg / Ezetimibe 10mg tablets
- View Simvastatin 80mg / Ezetimibe 10mg tablets

VMPP
- View 28 tablet
- View 30 tablet

AMP
- View Inegy 10mg/20mg tablets (DE Pharmaceuticals)
- View Inegy 10mg/20mg tablets (Mavdsley-Brooks & Company Ltd)
- View Inegy 10mg/20mg tablets (Organon Pharma (UK) Ltd)

AMPP
- View 28 tablet (2 x 14 tablets)
The “6 box” variation of the “mirror image” model
Example of the “6 box” variation of the “mirror image” model

- Substance(s) + Strengths
- Dose Form [+ Unit of Presentation]
The SAM – uses the “6 box” model
USA RxNorm: a hybrid model
How does the IDMP model fit?

More “linear” than “mirror image”
But the philosophy is different as the central/starting concept is the Medicinal Product
Maybe the “step shape?”
2.3 Mapping Pharmaceutical Dose Forms via Attributes

(Robert Vander Stichele)
Challenges for MPDs to standardise the dose forms to EDQM

► Even if EDQM dose forms will be communicated to NCAs via SPOR, the work of standardization still needs to be done in every country at the national level.

One can get the full set of EDQM Standard Terms directly:

Internal controlled vocabularies for pharmaceutical dose forms (Version 1.2.0 – 28 January 2019)

https://www.edqm.eu/sites/default/files/standard_terms_internal_vocabularies_for_pharmaceutical_dose_forms.pdf
Dilemmas for the providers of Medicinal Product Dictionaries

► MPD providers have 2 options
  ▶ Wait for the NCAs to do the job
  ▶ Start experimenting themselves with this aspect of IDMP implementation

► Motives for MPD providers to anticipate
  ▶ willingness to produce minimal data sets for cross border pilots
  ▶ service to the NCA
  ▶ mapping to SNOMED-CT for clinical care applications

► Standardisation of the dose forms to EDQM is not an easy task
  Especially when performed by inexperienced coders

**Intercoder Reliability of Mapping Between Pharmaceutical Dose Forms in the German Medication Plan and EDQM Standard Terms.**

An example of standardization:
Amlodipine products from Belgium

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amlodipine Krka</td>
<td>tabl. (deelb.)</td>
</tr>
<tr>
<td>Amlodipine Teva</td>
<td>tabl. (deelb.)</td>
</tr>
<tr>
<td>Amlodipin AB</td>
<td>tabl.</td>
</tr>
<tr>
<td>Amlodipine EG</td>
<td>tabl. (deelb.) Besilate</td>
</tr>
<tr>
<td>Amlodipin Sandoz</td>
<td>tabl. (deelb.) Besilaat</td>
</tr>
<tr>
<td>Amlor</td>
<td>harde caps.</td>
</tr>
<tr>
<td>Amlogal</td>
<td>omh. tabl. (deelb.) Divule</td>
</tr>
<tr>
<td>Amlodipine Mylan</td>
<td>tabl. (deelb.) Besilate</td>
</tr>
</tbody>
</table>
## An example of standardization: Amlodipine products from Belgium

<table>
<thead>
<tr>
<th>Company</th>
<th>Formulation</th>
<th>Code</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amlodipine Krka</td>
<td>tabl. (deelb.)</td>
<td>10219000</td>
<td>tablet</td>
</tr>
<tr>
<td>Amlodipine Teva</td>
<td>tabl. (deelb.)</td>
<td>10219000</td>
<td>tablet</td>
</tr>
<tr>
<td>Amlodipin AB</td>
<td>tabl.</td>
<td>10219000</td>
<td>tablet</td>
</tr>
<tr>
<td>Amlodipine EG</td>
<td>tabl. (deelb.) Besilate</td>
<td>10219000</td>
<td>tablet</td>
</tr>
<tr>
<td>Amlodipin Sandoz</td>
<td>tabl. (deelb.) Besilaat</td>
<td>10219000</td>
<td>tablet</td>
</tr>
<tr>
<td>Amlor</td>
<td>harde caps.</td>
<td>10210000</td>
<td>capsule, hard</td>
</tr>
<tr>
<td>Amlogal</td>
<td>omh. tabl. (deelb.) Divule</td>
<td>10220000</td>
<td>coated tablet</td>
</tr>
<tr>
<td>Amlodipine Mylan</td>
<td>tabl. (deelb.) Besilate</td>
<td>10219000</td>
<td>tablet</td>
</tr>
</tbody>
</table>
An example of standardization: Amlodipine products from Belgium

Amlodipine Krka tabl. (deelb.) 10219000 tablet
Amlodipine Teva tabl. (deelb.) 10219000 tablet
Amlodipin AB tabl. 10219000 tablet
Amlodipine EG tabl. (deelb.) Besilate 10219000 tablet
Amlodipin Sandoz tabl. (deelb.) Besilaat 10219000 tablet
Amlor harde caps. 10210000 capsule, hard
Amlogal omh. tabl. (deelb.) Divule 10220000 coated tablet
Amlodipine Mylan tabl. (deelb.) Besilate 10219000 tablet

Additional information for EDQM dose form “tablet”

Descriptors: Administrable / solid / Tablet  Characteristics: No transformation / Conventional / Oral / Swallowing

Definition: Solid single-dose uncoated preparation obtained by compressing uniform volumes of particulate solids or by other means such as extrusion or moulding. Tablets include single-layer tablets resulting from a single compression of particles and multi-layer tablets consisting of concentric or parallel layers obtained by successive compressions of particles of different composition. Tablets are intended for oral use to release active substance(s) in the gastrointestinal fluids by a rate depending essentially on the intrinsic properties of active substance(s) (conventional release).
The process of standardization of national value sets for dose form in national medicinal products to EDQM dose forms can be facilitated

► by making use of the definitions and characteristics of the EDQM dose forms
► by training experts
► by developing supporting tools for coders
► by using maps with
  • Snomed-CT
  • RxNorm (US)
  • OMOP (Common Data Model for drugs in big data)
► by comparing results of standardisation efforts between countries
► by using an ontology of EDQM dose forms
Proposal for an ontology of dose forms

3 levels of granularity

- 22 high level entries
- 69 intermediate level entries
- Accommodating for 248 granular EDQM Dose Forms

(Submitted for publication)
Developing an EDQM to SNOMED CT map for Dose Forms

(A collaboration between SNOMED International and EDQM)

Jane Millar
Collaboration & Clinical Engagement, SNOMED International

snomedexpo.org  @snomedct  linkedin.com/company/ihtsdo/
Requirements for the map

Requirements identified by SNOMED International member countries in Drug Extension User Support Group (DEUSG):
- EDQM (Pharmaceutical Dose Form or PDF) Standard Terms (Source) to SNOMED CT (Target)map
- Scope - Dose Forms relevant to clinical care

Use cases identified by SNOMED International DEUSG:
- To represent real / branded medication products in a SNOMED CT drug extension, based on the registered product information (where EDQM dose forms are used for regulatory purposes)
- To map medicinal products from a national or local medicinal product dictionary to international SNOMED CT Clinical Drugs, for interoperability purposes, such as the sharing of medication lists for cross-border patient-care, pharmacovigilance and clinical research
- To map from an IDMP-compliant regulatory database of medicinal products to SNOMED CT drug concepts (which include the dose form)
Summary of approach

- SNOMED International members in DEUSG, with input from EDQM
- Development of mapping guidance to ensure consistency, focused on ‘Exact’ semantic matches between EDQM and SNOMED CT
- Existing maps from a number of Member Countries provide a ‘candidate’ map for review
  - Scope - EDQM pharmaceutical dose forms relevant for clinical care
- 431 EDQM Pharmaceutical Dose Forms (13-07-2021) analyzed:
  - 379 in scope
  - 52 out of scope at this time e.g.
    - Live animals (leeches etc.) and herbal materials
    - Dose forms associated with radiopharmaceuticals
    - ‘Solvent’ and ‘Concentrate’ dose forms
- Spreadsheet basis but will be transferred to new tool, Snap-2-SNOMED, for maintenance and updating, and to facilitate release and distribution.
Examples of challenges

• Working with the different models of SNOMED CT and EDQM – use cases, structure, definitions etc., for example:
  ➢ Understanding EDQM’s use of some “compound concepts” (like “Intravesical/Urethral” and “Cutaneous/Transdermal”) and EDQM “grouper concepts” (like “Oromucosal” compared to “sublingual” or “buccal”), then being able to confidentially map exactly to more explicitly defined concepts in SNOMED CT based on description and text definition
  ➢ EDQM’s use of particular pharmaceutical concepts (for example, “Dispersions”) and how they relate to other ways to describe other heterogeneous systems (suspensions and emulsions)
• Conforming with the editorial guidance in both SNOMED CT and EDQM
• Identifying and requesting changes to either SNOMED CT or EDQM – thus impacting on timelines and release schedule for the Alpha release
Benefits of a map produced by SNOMED International and EDQM

- Collaboration between two recognized standards bodies who own the products and are committed to the distribution, maintenance and update of the map on a regular basis.
- Provides one standard map that is available globally
- Supports semantic interoperability between regulatory and healthcare systems
- Supporting the information flow between regulation and healthcare facilitates better quality data:
  - Clinical safety reporting
  - Tracing and reporting drug errors
  - Understanding trends and population-based analytics
- Providing a format that is consumable by vendors in a consistent way to use within systems
THANK YOU
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Or go to
www.menti.com and type 8294 8006
3. Extraction Transformation Loading Process (ETL) (Ursula Tschorn)
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 875299
The Observational Health Data Sciences and Informatics (or OHDSI, pronounced "Odyssey") program is a multi-stakeholder, interdisciplinary collaborative to bring out the value of health data through large-scale analytics.

Data experts and CDM experts together design the ETL

People with medical knowledge create the code mappings

All are involved in quality control

A technical person implements the ETL

ETL Step 1: Design the ETL

- Make a gap analysis of the data elements you will get from IDMP product data to your internal product data elements.
- Matching those data elements to your tables, fields, content and data model will be the first part of the ETL design.
ETL Step 2: Create the Code Mappings

- The coding systems in your MPD data need to be aligned with or mapped to IDMP coding systems.
- MPDs may use coding systems that are not in the IDMP vocabularies or in another granularity.
- Check on existing mappings from third parties.
3 Step 3: Implement the ETL

- ETL implementation in a piece of software.
- Experience needed for working with data (particularly large data)
- Note that this is not a one-time expense.
- ETL depends on many factors, no formal recommendation on how best to do it.
ETL Step 4: Quality Control

- Quality control is iterative.
- Typically write logic -> implement logic -> test logic -> fix/write logic.
- 4 eyes control
- Take small sample of medicinal products in the source and target data to control them manually
- Compare overall counts in the source and target data.
3 ETL Maintenance

- IDMP data source content may change (new controlled vocabularies).
- Monitor technical changes e.g. new FHIR resource versions.
- New business processes and with it new data requirements may evolve.
3 Final thoughts on the ETL

► No “one-size-fits-all” solution.
► Use the 80/20 rule (Pareto).
► Plan to allocate resources for changes and maintenance.
► Plan the versioning of the ETL data (change history).
► Calculate much more time than estimated first.
► Think about hiring external expertise for making a first gap analysis.
► Use tools for implementing IDMP which are being developed.
► Let us know what your pain points are!
1 IDMP Tools in Development (Piloting Phase)

IDMP Term Browser (© IDMP1)
www.idmp1.com

IDMP Drug Dictionary (© pharmazie.com)
www.pharmazie.com

IDMP Matching Tool (© IDMP1)
www.idmp1.com
Scan with your smartphone
Or go to
www.menti.com and type 8294 8006
Questions in the Q & A facility, please
For feedback, please go to: https://forms.gle/pruBAY1fvkLk4V3H7

Thanks for your time