Aligning RxNorm with the SNOMED CT drug model and IDMP

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Disclaimer

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International drug standards

- Identification of medicinal products (IDMP)
  - Set of ISO standards for
    - substances (ISO 11238)
    - pharmaceutical dose forms, units of presentation, routes of administration and packaging (ISO 11239)
    - units of measurement (ISO 11240)
    - regulated pharmaceutical product information (ISO 11616)
    - regulated medicinal product information (ISO 11615)
  - Used by the European Medicines Agency (EMA)

*SNOMED CT aims to be compliant with IDMP*
International drug standards

- **ISO/TS 19256:2016**
  - Health informatics - Requirements for medicinal product dictionary systems for health care
  - “provides information to MPD-system developers, to help them design MPD-systems which are better able to meet the ISO IDMP standards and the needs of multiple use cases”

- **EDQM Standard Terms**
  - European Directorate for the Quality of Medicines
  - Standard terms for
    - Pharmaceutical dose form
    - Route or method of administration
    - Packaging items (Container, Closure, Administration device)
SNOMED CT drug model

**Previous model**
- Substance/product duality
- Most products are primitive concepts
- Limited set of attributes
  - Has_active_ingredient
  - Has_dose_form
  - No explicit BoSS information
  - No explicit strength information

**Current model**
- Substance/product duality
- All products are fully defined concepts
- Extensive set of attributes
  - Has_active_ingredient
  - Has_manufactured_dose_form
  - Has_BoSS
  - Has.presentation_strength_*
    - Numerator (value, unit)
    - Denominator (value, unit)
RxNorm vs. SNOMED CT

**RxNorm**
- Substance/product implicit duality
- Not based on description logics
- Attributes
  - Has_ingredient
  - Has_dose_form
  - No explicit BoSS information
  - Strength (attribute)
    - Normalized (not presentation*)
    - Combines value and unit, numerator and denominator
- Generic + branded drugs

**SNOMED CT**
- Substance/product explicit duality
- All products are fully defined concepts
- Extensive set of attributes
  - Has_active_ingredient
  - Has_manufactured_dose_form
  - Has_BoSS
  - Has_presentation_strength
    - Numerator (value, unit)
    - Denominator (value, unit)
- Generic drugs only
### RxNorm vs. SNOMED CT

<table>
<thead>
<tr>
<th>RxNorm</th>
<th>SNOMED CT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical drug (SCD)</strong></td>
<td><strong>Clinical drug</strong></td>
</tr>
<tr>
<td>Atorvastatin 10 mg oral tablet</td>
<td>Product containing atorvastatin 10 mg/1 each oral tablet</td>
</tr>
<tr>
<td><strong>Ingredient (IN) and Precise ingredient (PIN)</strong></td>
<td><strong>[Single] Medicinal product (or Substance)</strong></td>
</tr>
<tr>
<td>Atorvastatin; Ergotamine tartrate</td>
<td>Product containing atorvastatin</td>
</tr>
<tr>
<td><strong>Multi-ingredient (MIN)</strong></td>
<td><strong>[Multi] Medicinal product</strong></td>
</tr>
<tr>
<td>amlODIPine / atorvastatin</td>
<td>Product containing ergotamine tartrate</td>
</tr>
<tr>
<td><strong>Clinical dose form group (SCDG)</strong></td>
<td><strong>Medicinal product form</strong></td>
</tr>
<tr>
<td>Atorvastatin Oral Product</td>
<td>Product containing amlodipine and atorvastatin</td>
</tr>
<tr>
<td></td>
<td>Product containing atorvastatin in oral dosage form</td>
</tr>
</tbody>
</table>
RxNorm vs. SNOMED CT

### Ingredient
- Azithromycin

### C. Drug Comp.
- Azithromycin 250 MG

### C. Dose Form Group
- Azithromycin Oral Product

### Clinical Drug
- Azithromycin 250 MG Oral Tablet

### Medicinal Product
- Product containing azithromycin

### Med. Product Form
- Product containing azithromycin in oral dosage form

### Clinical Drug
- Product containing azithromycin 250 mg/1 each oral tablet
Atorvastatin 10 mg oral tablet

Strength, split into
- Numerator (unit, value)
- Denominator (unit, value)

Dose form
Active ingredient (?)
BoSS
Atorvastatin 10 mg oral tablet

- Ingredient:
  - BoSS info (implicit)

- Dose form:
  - No explicit BoSS info

- Strength:
  - Numerator (unit, value) together
  - No denominator

- Active ingredient (implicit)
Atorvastatin 10 mg oral tablet

### INGREDIENTS AND APPEARANCE

#### ATORVASTATIN CALCIUM
atovastatin calcium tablet, film coated

<table>
<thead>
<tr>
<th>PRODUCT INFORMATION</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Product Type</td>
<td>HUMAN PRESCRIPTION DRUG</td>
</tr>
<tr>
<td>Item Code (Source)</td>
<td>NDC:42291-143(NDC:62175-890)</td>
</tr>
<tr>
<td>Route of Administration</td>
<td>ORAL</td>
</tr>
</tbody>
</table>

#### ACTIVE INGREDIENT/ACTIVE MOIETY

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin Calcium (UNII: 48A5M73Z4Q) (Atorvastatin - UNII:A0JWA85V8F)</td>
<td>Atorvastatin</td>
<td>10 mg</td>
</tr>
</tbody>
</table>

**Active ingredient**: Atorvastatin Calcium

**Active moiety**: Atorvastatin

**Dose form**: Oral tablet, film coated

**BoSS**: Atorvastatin

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*Image credit: Lister Hill National Center for Biomedical Communications*
Extracting BoSS and presentation strength information

- From SPLs whenever available (XML) [~2/3]
  - `<manufacturedProduct>` tag
    - `<quantity>` → presentation strength
      (numerator + denominator; value + unit)
    - `<ingredientSubstance>` → active ingredient
    - `<activeMoiety>` → active moiety
    - `classCode` attribute (`<ingredient>`) → BoSS
      - ACTIB → BoSS = active ingredient
      - ACTIM → BoSS = active moiety
      - ACTIR → BoSS = other (specified) reference substance

- From similar SPLs or other reference information sources otherwise [~1/3]
BoSS inconsistencies in SPLs

- A given RxCUI (SCD) is linked to multiple NDCs
- These NDCs are associated with multiple SPLs
- BoSS or presentation strength information is sometimes inconsistent across labels
  - Different, but functionally equivalent
    - Units are different, but values reflect equivalent strengths
    - ACTIB vs. ACTIM when AI = AM
    - ACTIR points to a reference that is the AI or AM (as opposed to another reference substance)
  - Different and not equivalent
    - Require manual review
    - Not all SPLs are high-quality
Summary

- Some information had never been recorded explicitly in RxNorm
  - BoSS (+ active ingredient and active moiety)
  - Presentation strength [except through PSNs]
- Extracted from Structured Product Labels whenever possible
- Future work
  - Harmonization of dose forms with EDQM’s
- This information will be made available in RxNorm after completion of the project
Summary

- **Opportunity for alignment with**
  - New SNOMED CT drug model
  - International standards for medicinal products

- **Contribution to SNOMED CT**
  - RxNorm drug content will be converted to and loaded in SNOMED CT

- **Opportunity for quality assurance**
  - Comparison with DM+D (UK) and AMT (Australia) once also converted to and loaded in SNOMED CT

- Will also facilitate the publication of RxNorm as a set of FHIR medication resources
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      "display": "Alprazolam 0.25mg Oral Tablet"
    }
  },
  "isBrand": false,
  "form": {
    "coding": {
      "system": "http://snomed.info/sct",
      "code": "385055001",
      "display": "Tablet dose form (qualifier value)"
    }
  },
  "ingredient": {
    "itemCodeableConcept": {
      "coding": {
        "system": "http://snomed.info/sct",
        "code": "386983007",
        "display": "Alprazolam [substance]"
      }
    },
    "amount": {
      "numerator": {
        "value": 0.25,
        "system": "http://unitsofmeasure.org",
        "code": "mg"
      },
      "denominator": {
        "value": 1,
        "system": "http://snomed.info/sct",
        "code": "Tablet dose form (qualifier value)"
      }
    }
  }
}
```
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