National metadata repository for databases of registers and trials

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• **Empirical medical research**
  - is based on the collection of observations stored in DBMS;
  - needs services for the maintenance of item collections and improvement of semantic interoperability:
    • Reuse of item`s definitions
    • Quality improvement through harmonization and standardization,
    • Integration and use of controlled vocabularies as value lists for items
    • Use of terminologies as buildings blocks for data elements

• **MDR-Project in Germany** launched in 2009 by the Federal Ministry of Education and Research to set up a national Metadata repository for the support of empirical research.
  - ISO/IEC 11179 V3 “Information technology - Metadata Registries (MDR)” part 3 “Registry Metamodel and basic attributes”
Use cases

• Single organization
  – Maintain metadata - to specify a CRF or a catalogue of variables
  – Import metadata - to establish a pool of metadata
  – Mapping of metadata - to transform data from one model to another
  – Queries for multiple versions of metadata - to support study series

• Multiple organizations
  – Queries for multiple metadata - to support pooling of data
  – Select projects - to identify projects covering specific variables
  – Review of metadata - to harmonize variables and value lists

• National level
  – Queries for multiple metadata - to support pooling of data
  – Select projects - to identify projects covering specific variables
  – Maintain standards - to harmonize CRFs and databases
  – Improve standards - to identify gaps in data standards or terminologies
Core of the metamodel of ISO/IEC 11179 V3

```
object_class
  person
    0..1
    *
    0..1
    *

characteristic
  sex

data_clement_concept
  gender
    *
    *

conceptual_domain
  karyotype
    <men|women>

representation layer

data_element
  gender <male|female>
    *
    1

value_domain
  <male|female>
```

- `object_class`: person
- `characteristic`: sex
- `data_clement_concept`: gender
- `conceptual_domain`: karyotype
- `representation layer`: data_element
- `value_domain`: gender <male|female>
Project plan

- to check ISO/IEC 11179-3 V3 - done
- to adjust ISO/IEC 11179-3 V3 - not consented
- to implement the MDR - on the way
Tested material in the metadata architecture

Layer 0: information

Layer 1: model

- HIVNET register
- Documentation scheme
- ISO 13606

Layer 2: metamodel

- CDISC ODM
- RIM

Layer 3: meta-metamodel

- ClaML

VOCABULARIES

- MedDRA
- ICD-10-GM
- SNOMED CT
- TNM
- LOINC
• Mapping of model elements (metamodels)
• Import of models into an MDR-database
Disease registers

- no problem in general
- but in particular
  - OIDs
  - layout information of CRFs
  - relationships between data_elements
EHR

- RIM of HL7
- ISO 13606 Health informatics - Electronic health record communication

- no problem in general
- but
  - inheritance
  - complex information objects not explicitly mentioned
Classifications and Terminologies

- **ICD-10-GM**: International Statistical Classification of Diseases and Related Health Problems 10th Revision German Modifications

- **OPS**: German procedure classification


- **MedDRA**: Medical Dictionary for Regulatory Activities, the international medical terminology used to classify adverse events associated with the use of biopharmaceuticals and other medical products.

- **SNOMED-CT**: Systematized Nomenclature of Medicine-Clinical Terms, a multilingual clinical healthcare terminology, essential for electronic health records.
Classification Markup Language (ClaML) is attractive as interface standard for the import of classifications (ICD-10-GM, OPS) into the MDR.


<?xml version="1.0" encoding="utf-8"?>
<!DOCTYPE ClaML SYSTEM "claml.dtd"[]>
<ClaML version="2.0.0">
  <Meta name="TopLevelSort" value="I II III IV V VI VII VIII IX XI XII XIII XIV XV XVI XVII XVIII XIX XX XXI XXII" />
  <Meta name="lang" value="en" />
  <Meta name="titleLong" value="International Statistical Classification of Diseases and Related Health Problems 10th Revision"/>
  <Identifier authority="WHO" uid="SRFSFto be added later" />
  <Title date="2008-05-13" name="ICD-10-2008-EN" version="2008" />
  <Class code="B27" kind="category">
    <SuperClass code="B25-B34" />
    <SubClass code="B27.0" />
    <SubClass code="B27.1" />
    <Rubric id="D0000588" kind="preferred">
      <Label xml:lang="en" xml:space="default">Infectious mononucleosis</Label>
    </Rubric>
  </Class>
</ClaML>
• some problems
  – representation of the code
• **some problems:**
  - representation of the code
  - rules not covered
    • coding standards
    • exclusions, inclusions, special codes
    - reconstruction not possible
  - intermediate levels not supported
  - direct use of classes not possible, doubling required
ISO/IEC 11179 V3

object_class

characteristic

conceptual_domain

karyotype

<men | women>

concept layer

representation layer

data_element

gender <male | female>

value_domain

<male | female>
Terminological systems

- no problem in general
- reconstruction to some extent possible
- but
  - SNOMED CT elements not covered
    - relationship_type
    - refinability for data entry
  - Medical Dictionary for Regulatory Activities (MedDRA)
    - versioning of coding systems and their relationship to the data description package
  - TNM
    - composition of concepts
Conclusion

- ISO/IEC 11179 V3 is powerful and contributes many useful ideas for the definition of a national MDR.
- An extension of ISO/IEC 11179 V3 metamodel to meet the predefined needs of a national MDR might be necessary.
• The presented work is part of the project MDR - Metadata Repository funded by the German Federal Ministry of Education and Research (BMBF).