RxNav

Browser and application programming interfaces for RxNorm

Olivier Bodenreider
Lister Hill National Center for Biomedical Communications
Bethesda, Maryland - USA
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Outline

◆ **RxNorm**
  - Drug vocabulary integration
  - Drug vocabulary standardization

◆ Visualizing drug information: **RxNav**

◆ Processing drug information: **RxNorm API**

◆ Integrating drug information sources

◆ Applications
RxNorm

Overview
Motivation

- Exchange of information requires standardized names
  - Ordering drugs
  - Checking interactions
  - Inventory management
- No standard naming conventions for drugs
- Integrating drug vocabularies
- Unique identifiers for drugs
- Specify relations among drug entities
Drug vocabulary integration

RxNorm
UMLS-like approach

- 11 source vocabularies
- Synonymous names grouped into an RxNorm concept
- Unique identifiers (RxCUI)
- RRF format

Differences
- RxNorm creates its own names
- Principled use of names relationships
- Limited scope: drug names
Source vocabularies in RxNorm

- Gold Standard Alchemy
- Master Drug Data Base (Medi-Span, Wolters Kluwer Health)
- Multum MediSource Lexicon
- Micromedex DRUGDEX
- Medical Subject Headings
- FDA National Drug Code Directory
- FDA Structured Product Labels
- Nat’l Drug Data File (First DataBank Inc.)
- VHA National Drug File – RT
- SNOMED Clinical Terms (drug information)
- VHA National Drug File

(terms in thousands, as of June 2010)
Drug vocabulary standardization

RxNorm
Normalization

◆ **Lexical level**
  - Conventions for representing names (strength, units, etc.)

◆ **Structural level**
  - Conventions for representing types of drug entities and their interrelations
<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>GS</td>
<td>Digoxin 0.25mg/1mL Solution for injection</td>
</tr>
<tr>
<td>GS</td>
<td>Digoxin 500mcg/2mL Solution for injection</td>
</tr>
<tr>
<td>MDDB</td>
<td>'Digoxin Inj 0.25 MG/ML</td>
</tr>
<tr>
<td>MMSL</td>
<td>digoxin 250 mcg/mL (0.25 mg/mL) injectable solution</td>
</tr>
<tr>
<td>MMSL</td>
<td>Digoxin, 250 mcg/mL (0.25 mg/mL) injectable solution</td>
</tr>
<tr>
<td>MMX</td>
<td>Digoxin 0.25 MG/ML Injection Solution</td>
</tr>
<tr>
<td>MTHFDA</td>
<td>DIGOXIN 0.25 MG INTRAMUSCULAR INJECTION, SOLUTION</td>
</tr>
<tr>
<td>MTHFDA</td>
<td>DIGOXIN 250 MCG INTRAMUSCULAR INJECTION</td>
</tr>
<tr>
<td>MTHFDA</td>
<td>DIGOXIN 250 MCG INTRAVENOUS INJECTION</td>
</tr>
<tr>
<td>MTHSPL</td>
<td>digoxin 0.25 MILLIGRAM In 1.0 MILLILITER INTRAVENOUS INJECTION</td>
</tr>
<tr>
<td>MTHSPL</td>
<td>Digoxin 250 MICROGRAM In 1 MILLILITER INTRAVENOUS INJECTION, SOLUTION</td>
</tr>
<tr>
<td>NDDF</td>
<td>DIGOXIN 250 mcg/mL INJECTION AMPUL (ML)</td>
</tr>
<tr>
<td>NDDF</td>
<td>DIGOXIN 250 mcg/mL INJECTION DISPOSABLE SYRINGE (ML)</td>
</tr>
<tr>
<td>NDDF</td>
<td>DIGOXIN@250 mcg/mL@INJECTION@AMPUL (ML)</td>
</tr>
<tr>
<td>SNOMEDCT</td>
<td>Digoxin 250micrograms/mL injection solution 2mL ampule</td>
</tr>
<tr>
<td>SNOMEDCT</td>
<td>Digoxin 500micrograms/2mL injection</td>
</tr>
<tr>
<td>VANDF</td>
<td>DIGOXIN 0.25MG/ML INJ</td>
</tr>
<tr>
<td>[…]</td>
<td>[…]</td>
</tr>
</tbody>
</table>

**Normalization Lexical level**

Digoxin 0.25 MG/ML Injectable Solution
Normalization Structural level

◆ Structural level
  ● Atomic elements
    ■ Ingredient
    ■ Strength
    ■ Dose form
  ● Generic vs. Brand names
  ● Principle set of relationships among the different types
<table>
<thead>
<tr>
<th>Strength</th>
<th>Ingredient</th>
<th>Dose form</th>
</tr>
</thead>
<tbody>
<tr>
<td>4mg/ml</td>
<td>Fluoxetine</td>
<td>Oral Solution</td>
</tr>
</tbody>
</table>

Semantic clinical drug component

Semantic clinical drug form

Semantic clinical drug

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Generic vs. Brand

- **Generic**
  - Ingredient (IN)
  - Clinical drug form (SCDF)
  - Clinical drug component (SCDC)
  - Clinical drug (SCD)

- **Brand**
  - Brand name (BN)
  - Branded drug form (SBDF)
  - Branded drug component (SBDC)
  - Branded drug (SBD)

*tradename_of*
Relations among drug entities
Relations among drug entities (revisited)

- **Ingredient**: Azithromycin
- **Brand Name**: Zithromax
- **C. Drug Component**: Azithromycin 250 MG
- **C. Drug Form**: Azithromycin Oral Tablet
- **C. Drug**
- **B. Drug Component**: Azithromycin 250 MG [Zithromax]
- **B. Drug Form**: Azithromycin Oral Tablet [Zithromax]
- **B. Drug**
- **G. Pack**: {6 (Azithromycin 250 MG Oral Tablet) } Pack
- **B. Pack**: Z-PAK

Diagram:
- Azithromycin 250 MG (C. Drug Component) connected to Azithromycin Oral Tablet (C. Drug Form)
- Azithromycin 250 MG (B. Drug Component) connected to Azithromycin Oral Tablet [Zithromax] (B. Drug Form)
- B. Drug Component connects to B. Drug Form directly.
- The relationship between Ingredient (Azithromycin) and Brand Name (Zithromax) is depicted through the Drug entities.

Note: The diagram shows the relations among drug entities with specific components and forms, illustrating the connection between ingredients, drug names, and packaging.
RxNorm database

- 11 data sources
  - Gold Standard Alchemy
  - Master Drug Data Base
  - Multum MediSource Lexicon
  - Micromedex DRUGDEX
  - Medical Subject Headings
  - FDA National Drug Code Directory
  - FDA Structured Product Labels
  - Nat’l Drug Data File Plus
  - VHA NDF – RT
  - SNOMED Clinical Terms
  - VHA National Drug File

- Content
  - 4,857 ingredients
  - 13,770 brand names
  - 14,842 clinical drug comp.
  - 14,133 branded drug comp.
  - 18,841 clinical drugs
  - 15,627 branded drugs
  - 8,242 clinical drug forms
  - 11,659 branded drug forms
  - 278 generic packs
  - 357 branded packs
  - 100 dose forms

(as of June 7, 2010; excluding obsolete data)
Visualizing drug information

RxNav
- Visualization and navigation
  - RxNorm browser
  - Auto-completion and spelling correction
  - Search on names and codes (including proprietary)
  - Standalone application
    - RxNorm database at NLM
    - Local RxNorm database

- Drug information processing
  - API to the RxNorm database
  - Web services (SOAP, REST)
RxNav demo

http://rxnav.nlm.nih.gov/
Processing drug information

RxNorm Application Programming Interface
RxNorm APIs

- Made available in March 2008
- Based on Web Services
  - SOAP, REST
  - Independent of any programming language
- Used by *RxNav* and other applications
- Enable access to all information displayed in RxNav
- Documentation
  - SOAP  http://rxnav.nlm.nih.gov/RxNormAPI.html
  - REST  http://rxnav.nlm.nih.gov/RxNormRestAPI.html
- Testing environment (SOAP client demo)
List of functions (SOAP) 1/3

◆ Housekeeping functions

  - getRxNormVersion()
  - getIdTypes()
  - getRelaTypes()
  - getTermTypes()

◆ Find RxNorm concepts

  - By name: findRxcuiByString( searchString, source-list, allSourcesFlag )
  - By code: findRxcuiById( idType, id, allSourcesFlag )
  - Help: getSpellingSuggestions( searchString )
List of functions (SOAP) 2/3

◆ Get RxNorm concept properties
  ● getRxConceptProperties( \textit{rxcui} )
  ● getStrength( \textit{rxcui} )
  ● getQuantity( \textit{rxcui} )
  ● getNDCs( \textit{rxcui} )
  ● getUNII( \textit{rxcui} )
  ● getProprietaryInformation( \textit{rxcui}, \textit{source-list}, \textit{proxyTicket} )
List of functions (SOAP) 3/3

◆ Get RxNorm concept relations
  ● By rel.: `getRelatedByRelationship(rxcui, rel-list)`
  ● By type: `getRelatedByType(rxcui, type-list)`
  ● All: `getAllRelatedInfo(rxcui)`

◆ Miscellaneous functions
  ● `getDrugs(name)`
  ● `getDisplayTerms()`
  ● `getMultiIngredBrand(rxcui-list)`
Documentation

◆ Java

```java
import java.net.URL;
import BeanService.*;
import gov.nih.nlm.mor.axis.services.RxNormDBService.*;

String rxhost = "http://mor.nlm.nih.gov";
String rxURI = rxhost + "//axis/services/RxNormDBService";

// Locate the RxNorm API web service
URL rxURL = new URL(rxURI);
DBManagerService rxnormService = new DBManagerServiceLocator();
DBManager dbmanager = rxnormService.getRxNormDBService(rxURL);
```

◆ Perl, .NET
Implementation  Perl client

http://mor.nlm.nih.gov/perl/rxnav_api_demo.pl
Implementation .NET client

![RxNorm API access](image)

Method: `getRxConceptProperties (rxcui)`

Argument 1: 58930

Argument 2: 

Returned data:

```
STR= Zyrtec
RXCUI= 58930
TTY= EN
LAT= ENG
SUPPRESS= N
SY= 
CUI= C0162723
```
RESTful API

- **Base URI**

- **List of resources**
<table>
<thead>
<tr>
<th>RESTful web service resource</th>
<th>SOAP-based web service function</th>
</tr>
</thead>
<tbody>
<tr>
<td>/</td>
<td>(none)</td>
</tr>
<tr>
<td>/brands?ingredientids=value</td>
<td>getMultiIngredBrand</td>
</tr>
<tr>
<td>/displaynames</td>
<td>getDisplayNames</td>
</tr>
<tr>
<td>/drugs?name=value</td>
<td>getDrugs</td>
</tr>
<tr>
<td>/idtypes</td>
<td>getIdTypes</td>
</tr>
<tr>
<td>/relatypes</td>
<td>getRelaTypes</td>
</tr>
<tr>
<td>/rxcui?idtype=value&amp;id=value&amp;allsrc=value</td>
<td>findRxcuiById</td>
</tr>
<tr>
<td>/rxcui?name=value&amp;srclist=value&amp;allsrc=value</td>
<td>findRxcuiByString</td>
</tr>
<tr>
<td>/rxcui/{rxcui}</td>
<td>(none)</td>
</tr>
<tr>
<td>/rxcui/{rxcui}/allrelated</td>
<td>getAllRelatedInfo</td>
</tr>
<tr>
<td>/rxcui/{rxcui}/ndcs</td>
<td>getNDCs</td>
</tr>
<tr>
<td>/rxcui/{rxcui}/properties</td>
<td>getRxConceptProperties</td>
</tr>
<tr>
<td>/rxcui/{rxcui}/proprietary?srclist=values&amp;ticket=value</td>
<td>getProprietaryInformation</td>
</tr>
<tr>
<td>/rxcui/{rxcui}/related?rela=values</td>
<td>getRelatedByRelationship</td>
</tr>
<tr>
<td>/rxcui/{rxcui}/related?tty=values</td>
<td>getRelatedByType</td>
</tr>
<tr>
<td>/rxcui/{rxcui}/quantity</td>
<td>getQuantity</td>
</tr>
<tr>
<td>/rxcui/{rxcui}/strength</td>
<td>getStrength</td>
</tr>
<tr>
<td>/rxcui/{rxcui}/unii</td>
<td>getUNII</td>
</tr>
<tr>
<td>/spellingsuggestions?name=value</td>
<td>getSpellingSuggestions</td>
</tr>
<tr>
<td>/termtypes</td>
<td>getTermTypes</td>
</tr>
<tr>
<td>/version</td>
<td>getRxNormVersion</td>
</tr>
</tbody>
</table>
REST output  XML


<table>
<thead>
<tr>
<th>XML output</th>
</tr>
</thead>
</table>
| ```xml
<?xml version="1.0" encoding="UTF-8" standalone="yes"?>
<rxnormdata>
  <idGroup>
    <name>bactrim</name>
    <rxcui>151399</rxcui>
  </idGroup>
</rxnormdata>
``` |
REST output  JSON


```
{  
  "idGroup" : {  
    "rxcui" : "151399",  
    "name" : "bactrim"  
  }  
}
```
Managing variation in clinical drug names

Use case: mapping of local formularies to RxNorm

Extends the UMLS program norm

Specific normalization rules

- Expansion of abbreviations (e.g., tab to tablet)
- Reformatting of specific elements (e.g., space between number and unit)
- Removal of salt variants (e.g., succinate from metoprolol succinate)
New functions  Coming up soon

- **RxMap**
  - Mapping lists of drug names / identifiers to RxNorm
  - Batch mode version of
    - `findRxcuiByString()`
    - `findRxcuiById()`

- **RxXMap**
  - Mapping across vocabularies through RxNorm
  - Combines
    - `findRxcuiById()`
    - `getProprietaryInformation()`
  - Requires UMLS license
Integrating drug information sources
National Drug File Reference Terminology

- Developed by the Veterans Health Administration
- Part of the VA clinical information system
- Non-terminological information
  - Pharmacologic class (isa)
  - Therapeutic intent (may_treat, may_diagnose, may_prevent)
  - Contraindications (drug_contraindicated_for)
  - Mechanism of action (mechanism_of_action_of)
  - Physiology (has_physiologic_effect)
  - Metabolism (metabolic_site_of, metabolizes, pharmacokinetics_of)
  - Drug-drug interactions (contraindicated_with)
Cetirizine

- `drug_contraindicated_for` Drug Allergy
- `may_treat` Rhinitis, Allergic, Perennial
- `may_treat` Urticaria
- `has_mechanism_of_action` Histamine H1 Antagonists
- `has_physiologic_effect` Decreased Histamine Activity
CLOPIDOGREL BISULFATE 75MG TAB

Pharmaceutical Preparations

Drug Products by VA Class

BLOOD PRODUCTS /MODIFIERS /VOLUME EXPANDERS

Platelet Aggregation Inhibitors

Drug Products by Generic Ingredient Combinations

C [Preparations]

CLOPIDOGREL

CLOPIDOGREL BISULFATE

CLOPIDOGREL BISULFATE 75MG TAB

External Pharmacologic Classes

Anti-coagulant

Platelet Aggregation Inhibitor

Decreased Coagulation Activity

Decreased Platelet Aggregation

Myocardial Infarction

Hemorrhage

Legend

• has PE: has physiologic effect
• CI with: contra-indicated with
• isa (stated)
• isa (inferred)
NDF-RT  Coming up soon in RxNav

◆ Integrated in RxNorm since June 2010
◆ Pilot integration in RxNav
  ● Nov. 2009
◆ Full integration underway
RxTerms Coming up soon in RxNav

- Drug interface terminology derived from RxNorm for prescription writing or medication history recording
  - Commonly used synonyms and abbreviations (e.g. HCTZ for hydrochlorothiazide)
  - "tall man" lettering recommended by FDA to avoid medication errors (e.g. ChlorproMAZINE and ChlorproPAMIDE)
- Developed at NLM
- Soon to be integrated in RxNav
Applications
Examples of application

◆ Terminology integration and standardization (RxNorm) enables interoperability and mapping across vocabularies

◆ Specific applications
  • Information exchange ("meaningful use")
  • Medication lists
  • Medication reconciliation
  • E-prescribing / CPOE
  • CDA R2
  • Personal Health Record
Quality control in RxNorm

- Multiple equivalent paths between RxNorm entities

\[
\text{getRelatedByRelationship}(r; \text{consists of}) \ o \ \text{getRelatedByRelationship}(\ast; \text{has ingredient})
\]

\[
\equiv
\]

\[
\text{getRelatedByRelationship}(r; \text{inverse isa}) \ o \ \text{getRelatedByRelationship}(\ast; \text{has ingredient})
\]
Examples of application

◆ Quality control in RxNorm: Results
  ● 35,000 pairs of paths investigated
  ● Few discrepancies detected
  ● Types of errors
    ▪ Obsolete brand names
    ▪ Obsolete branded drug forms
    ▪ Erroneous relations
  ● Discrepancies reported to the RxNorm team

[Peters, JAMIA 2009]
Applications outside NLM

◆ RxSafe (OHSU)
  • “improve medication safety for patients”
  • http://www.ohsu.edu/RxSafe/

◆ My-Medi-Health (Vanderbilt)
  • “Child-Centered Medication Management”
  • http://www.projecthealthdesign.org/projects/overview-2006_2008/405594/406293
Usage statistics

Sessions

Number of sessions per month

12 m sliding avg
Usage statistics  Queries

Number of queries per month

- 12 m sliding avg
- all queries
References

RxNorm


and RxNorm APIs
