RxNav
Browser and Application Programming Interfaces for RxNorm

Olivier Bodenreider, MD, PhD
Lee Peters, MS
Lister Hill National Center for Biomedical Communications
Bethesda, Maryland - USA
Acknowledgments

- Lee Peters
- Thang Nguyen
- Kelly Zeng
- Ramez Ghazzaoui
- Stuart Nelson
- John Kilbourne
- Tammy Powell
Outline

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

◆ **Visualizing drug information: RxNav**

◆ **Processing drug information: RxNorm API**

◆ **Other drug information sources accessible through RxNav**
  - RxTerms
  - NDF-RT

◆ **Applications**
References

RxNorm


and RxNorm APIs

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)
RxNorm concept

Ingredient

Acetaminophen

SNOMED CT
MeSH
Multum
NDDF
...

161

Acetaminophen
Paracetamol
APAP
Paracetamol product
Acetaminophen (product)
Acetaminophen (substance)
Acetaminophen product

MMSL:5005
SNOMEDCT:387517004
SNOMEDCT:90332006
NDDF:001605
MTHSPL:362O9ITL9D
MMSL:4119
MMSL:d00049
VANDF:4017513
MMSL:4992
MMSL:52845
MTHFDA:50612
UMLS: C0000970
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>Brand</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>

**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
Normalized form

<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

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Dose form</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oral Solution</td>
</tr>
</tbody>
</table>

Semantic clinical drug form

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Dose form</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oral Solution</td>
</tr>
</tbody>
</table>

Semantic clinical drug
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)

**C. Drug Component**
- Azithromycin 250 MG

**C. Drug Form**
- Azithromycin Oral Tablet

**B. Drug Component**
- Azithromycin 250 MG

**B. Drug Form**
- Azithromycin Oral Tablet [Zithromax]

**B. Pack**
- Zithromax 250 MG Oral Tablet

**G. Pack**
- 6 (Azithromycin 250 MG Oral Tablet) Pack

**Brand Name**
- Zithromax

**Ingredient**
- Azithromycin
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
  - 4,932 ingredients
  - 14,339 brand names
  - 15,403 clinical drug comp.
  - 14,422 branded drug comp.
  - 19,413 clinical drugs
  - 15,978 branded drugs
  - 8,383 clinical drug forms
  - 11,958 branded drug forms
  - 294 generic packs
  - 381 branded packs
  - 100 dose forms

(as of November 1, 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, searchType )
  ● By code: findRxcuiById( idType, id, allSourcesFlag )
  ● Help: getSpellingSuggestions( searchString )
List of functions (SOAP) 2/3

◆ Get RxNorm concept properties

- getRxConceptProperties( rxcui )
- getStrength( rxcui )
- getQuantity( rxcui )
- getNDCs( rxcui )
- getUNII( rxcui )
- getProprietaryInformation( rxcui, source-list, 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: BN
- LAT: ENG
- SUPPRESS: N
- SY:
- CUI: C0162723
RESTful API

◆ Base URI

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


XML output

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


<table>
<thead>
<tr>
<th>JSON output</th>
</tr>
</thead>
<tbody>
<tr>
<td>{</td>
</tr>
<tr>
<td>&quot;idGroup&quot; : {</td>
</tr>
<tr>
<td>&quot;rxcui&quot; : &quot;151399&quot;,</td>
</tr>
<tr>
<td>&quot;name&quot; : &quot;bactrim&quot;</td>
</tr>
<tr>
<td>}</td>
</tr>
<tr>
<td>}</td>
</tr>
</tbody>
</table>

Lister Hill National Center for Biomedical Communications
RxNormNorm Recently released

- 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*)
Methods for Managing variation in Clinical Drug Names

Lee Peters and Olivier Bodenreider
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
Other drug information sources accessible through RxNav
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)
NDF-RT Examples

◆ 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 Generic Ingredient Combinations

CLOPIDOGREL

BLOOD PRODUCTS /MODIFIERS /VOLUME EXPANDERS

PLATELET AGGREGATION INHIBITORS

CLOPIDOGREL BISULFATE

CLOPIDOGREL BISULFATE 75MG TAB

Decreased Coagulation Activity

Decreased Platelet Aggregation

Myocardial Infarction

Hemorrhage

Legend

• has PE: has physiologic effect
• CI with: contra-indicated with

Representation of the drug Clopidogrel in NDF-RT

External Pharmacologic Classes

Anti-coagulant

Platelet Aggregation Inhibitor

Legacy VA classes

Drug Products by VA Class

Drug Products by Generic Ingredient Combinations

C [Preparations]
NDF-RT  New in RxNav

◆ Integrated in RxNorm since June 2010

◆ Integration in RxNav
  ● Beta version
  ● http://rxnav.nlm.nih.gov/rxnavdemo_virtuoso.jnlp
  ● Feedback welcome
RxTerms New 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
- Beta version 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

getRelatedByRelationship( r; consists of ) \( \circ \) getRelatedByRelationship( *, has ingredient )

\[ ?\equiv \]

getRelatedByRelationship( r; inverse isa ) \( \circ \) getRelatedByRelationship( *, has ingredient )

Ingredient

\( \text{Cetirizine} \)

has ingredient

C. Drug Component

Cetirizine 5MG

consists of

C. Drug Form

Cetirizine Oral Tablet

inverse isa

C. Drug

Cetirizine 5 MG Oral Tablet
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”
Contact: RXNAVINFO@LIST.NIH.GOV
Web: http://rxnav.nlm.nih.gov/

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