Webinar Series
February 2, 2011

RxNav
Browser and Application Programming Interfaces for Drug Information Sources

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Acknowledgments

- Lee Peters
- Thang Nguyen
- Kelly Zeng
- Ramez Ghazzaoui
- Stuart Nelson, John Kilbourne (RxNorm)
- Kin Wah Fung (RxTerms)
- Mark Erlbaum (NDF-RT)
Outline

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

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

◆ Visualizing drug information: **RxNav**

◆ Processing drug information: **RxNorm API**

◆ Applications
References

- **RxNav** and RxNorm APIs

- **RxNorm**

- **RxTerms**

- **NDF-RT**
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 named relationships
- Limited scope: drug names
Source vocabularies in RxNorm

- Gold Standard Alchemy
- Medi-Span Master Drug Data Base
- Multum MediSource Lexicon
- Micromedex RED CODE
- Medical Subject Headings
- FDA National Drug Code Directory
- FDA Structured Product Labels
- First DataBank NDDF Plus
- VHA National Drug File-Ref. Terminology
- SNOMED Clinical Terms (drug information)
- VHA National Drug File

RxNorm

(terms in thousands, as of January 2011)

- Gold Standard Alchemy: 23
- Medi-Span Master Drug Data Base: 13
- Multum MediSource Lexicon: 66
- Micromedex RED CODE: 11
- Medical Subject Headings: 19
- FDA National Drug Code Directory: 86
- FDA Structured Product Labels: 44
- First DataBank NDDF Plus: 87
- VHA National Drug File-Ref. Terminology: 133*
- SNOMED Clinical Terms (drug information): 87*
- VHA National Drug File: 48

Total: 113
RxNorm concept

Ingredient

Acetaminophen

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

SNOMED CT:387517004
SNOMED CT:90332006
NDDF:001605
MTHSPL:362091T9D
MMSL:4119
MMSL:d00049
VANDF:4017513
MMSL:4992
MMSL:52845
MTHFDA:50612
UMLS: C0000970

161

SNOmed CT
MeSH
Multum
NDDF

...
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
Normalization Lexical level

- GS Digoxin 0.25mg/1mL Solution for injection
- GS Digoxin 500mcg/2mL Solution for injection
- MDDB 'Digoxin Inj 0.25 MG/ML
- MMSL digoxin 250 mcg/mL (0.25 mg/mL) injectable solution
- MMSL Digoxin, 250 mcg/mL (0.25 mg/mL) injectable solution
- MMX Digoxin 0.25 MG/ML Injection Solution
- MTHFDA DIGOXIN 0.25 MG INTRAMUSCULAR INJECTION, SOLUTION
- MTHFDA DIGOXIN 250 MCG INTRAMUSCULAR INJECTION
- MTHFDA DIGOXIN 250 MCG INTRAVENOUS INJECTION
- MTHSPL digoxin 0.25 MILLIGRAM In 1.0 MILLILITER INTRAVENOUS INJECTION
- MTHSPL Digoxin 250 MICROGRAM In 1 MILLILITER INTRAVENOUS INJECTION, SOLUTION
- NDDF DIGOXIN 250 mcg/mL INJECTION AMPUL (ML)
- NDDF DIGOXIN 250 mcg/mL INJECTION DISPOSABLE SYRINGE (ML)
- NDDF DIGOXIN@250 mcg/mL@INJECTION@AMPUL (ML)
- SNOMEDCT Digoxin 250micrograms/mL injection solution 2mL ampule
- SNOMEDCT Digoxin 500micrograms/2mL injection
- VANDF DIGOXIN 0.25MG/ML INJ
- [...] [...]
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>

Clinical drug component

Clinical drug form

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)

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

◆ 11 data sources
  ● Gold Standard Alchemy
  ● Medi-Span Master Drug Data Base
  ● Multum MediSource Lexicon
  ● Micromedex RED BOOK
  ● Medical Subject Headings
  ● FDA National Drug Code Directory
  ● FDA Structured Product Labels
  ● First DataBank NDDF Plus
  ● VHA NDF – RT
  ● SNOMED Clinical Terms
  ● VHA National Drug File

◆ Content
  ● 4,942 ingredients
  ● 14,667 brand names
  ● 19,862 clinical drugs
  ● 16,275 branded drugs
  ● 307 generic packs
  ● 388 branded packs
  ● 15,715 clinical drug comp.
  ● 14,680 branded drug comp.
  ● 8,478 clinical drug forms
  ● 12,188 branded drug forms
  ● 100 dose forms

(as of January 26, 2011; excluding obsolete data)
Other drug information sources accessible through RxNav

RxTerms
NDF-RT
RxTerms

◆ 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
    ◆ ChlorproMAZINE
    ◆ ChlorproPAMIDE
◆ Developed at NLM
National Drug File Reference Terminology

- Developed by the Veterans Health Administration
- Part of the VA clinical information system
- Available from the NCI web site (XML, OWL)
- Integrated in RxNorm since June 2010
Clinical information

- Pharmacologic class, Ingredients (isa)
- Therapeutic intent (may_treat, may_diagnose, may_prevent)
- Chemical ingredient (has_ingredient, has_active_metabolites)
- Mechanism of action (has_MoA)
- Physiologic effect (has_PE)
- Pharmacokinetics/Metabolism (has_PK, site_of_metabolism)
- Dose form (has_dose_form)
- Contraindications (CI_with, CI_MoA, CI_PE, induces)
- Drug-drug interactions
NDF-RT Examples

◆ Clopidogrel
  - *may_prevent* Cerebral Infarction
  - *may_prevent* Coronary Thrombosis
  - *may_prevent* Myocardial Infarction
  - *Cl_with* Blood Coagulation Disorders
  - *Cl_with* Drug Hypersensitivity
  - *Cl_with* Hemorrhage
  - *has_Ingredient* clopidogrel
  - *has_MoA* G-Protein-linked Receptor Interactions
  - *has_PE* Decreased Platelet Aggregation

◆ CLOPIDOGREL BISULFATE 75MG TAB,UD
  - *isa* PLATELET AGGREGATION INHIBITORS
CLOPIDOGREL BISULFATE 75MG TAB

Drug Products by Generic Ingredient Combinations

C [Preparations]

Decreased Coagulation Activity

Decreased Platelet Aggregation

Myocardial Infarction

Hemorrhage

Legend
- has PE: has physiologic effect
- CI with: contra-indicated with
- isa (stated)

Representation of the drug Clopidogrel in NDF-RT
Visualizing drug information

RxNav
RxNav

◆ Visualization and navigation
  ● RxNorm browser
    ■ Integrated with RxTerms and NDF-RT
  ● Auto-completion and spelling correction
  ● Search on names and codes (including proprietary)
  ● Standalone application
  ● Queries databases at NLM (RxNorm, RxTerms, NDF-RT)
  ● Links to external sources (DailyMed)

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

http://rxnav.nlm.nih.gov/
## RxNorm Properties

**RxCIUI= 309362**

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>RxNorm Name</td>
<td>clopidogrel 75 MG Oral Tablet</td>
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<tr>
<td>RxCUI</td>
<td>309362</td>
</tr>
<tr>
<td>TTY</td>
<td>SCD</td>
</tr>
<tr>
<td>UMLSCUI</td>
<td>C0976741</td>
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<td>Source</td>
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RxCUI: 309362
Name: clopidogrel 75 MG Oral Tablet

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CLOPIDOGREL BISULFATE 75MG TAB,UD

Properties Table

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<td>Units</td>
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<td>RxNorm_Name</td>
<td>clopidogrel 75 MG Oral Tablet</td>
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<td>VANDF_Record</td>
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<tr>
<td>VA_National_For...</td>
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### CLOPIDOGREL BISULFATE 75MG TAB,UD

#### Relations Table

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<th>Predicate</th>
<th>Object</th>
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<td>Drug</td>
<td>CLOPIDOGREL</td>
<td>isa</td>
<td>C [Preparations]</td>
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<td>CLOPIDOGREL BISULFATE</td>
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<td>CLOPIDOGREL</td>
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<td>Drug</td>
<td>CLOPIDOGREL BISULFATE 75MG TAB,UD</td>
<td>isa</td>
<td>PLATELET AGGREGATION INHIBITORS</td>
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<tr>
<td>Disease</td>
<td>CLOPIDOGREL</td>
<td>C_l_with</td>
<td>Blood Coagulation Disorders</td>
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<td>Disease</td>
<td>CLOPIDOGREL</td>
<td>C_l_with</td>
<td>Drug Hypersensitivity</td>
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<td>Cerebral Infarction</td>
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<td>Coronary Thrombosis</td>
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<td>Disease</td>
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<td>Myocardial Infarction</td>
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<td>Mechanism of Action</td>
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<td>has_MoA</td>
<td>G-Protein-linked Receptor Interactions</td>
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<td>Physiologic Effect</td>
<td>CLOPIDOGREL</td>
<td>has_PE</td>
<td>Decreased Platelet Aggregation</td>
</tr>
</tbody>
</table>
CLOPIDOGREL BISULFATE 75MG TAB,UD

Drug

Pharmaceutical Preparations

Drug Products by Generic Ingredient Combinations

Drug Products by VA Class

C [Preparations]

BLOOD PRODUCTS/MODIFIERS/VOLUME EXPANDERS

PLATELET AGGREGATION INHIBITORS

CLOPIDOGREL

CLOPIDOGREL BISULFATE

CLOPIDOGREL BISULFATE 75MG TAB,UD

Legend

VA Class

VA Product

DRUG

association

Association
CLOPIDOGREL BISULFATE 75MG TAB,UD
Pharmacokinetics

CLOPIDOGREL

CLOPIDOGREL BISULFATE

CLOPIDOGREL BISULFATE 75MG TAB,UD

Legend
CLOPIDOGREL BISULFATE 75MG TAB,UD

Drug Interactions

CLOPIDOGREL BISULFATE

CIMETIDINE [Significant]
OMEPRAZOLE [Significant]
WARFARIN [Significant]
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**

**Testing environment (SOAP client demo)**
List of functions (SOAP) 1/3

- **Housekeeping functions**
  - `getRxNormVersion()`
  - `getIdTypes()`
  - `getRelaTypes()`
  - `getTermTypes()`
  - `getSourceTypes()`

- **Find RxNorm concepts**
  - **By name:** `findRxcuiByString(searchString, source-list, allSourcesFlag, searchType)`
  - **By code:** `findRxcuiById(idType, id, allSourcesFlag)`
  - **Help:** `getSpellingSuggestions(searchString)`
  - **Versioning:** `findRemapped(rxcui)`
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( rxr cui, rel-list )
  ● By type:  getRelatedByType( rxr cui, type-list )
  ● All:  getAllRelatedInfo( rxr cui )

◆ Miscellaneous functions
  ● getDrugs( name )
  ● getDisplayTerms()  
  ● getMultiIngredBrand( rxr cui-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 (rxnui)`

**Argument 1**
- 58930

**Argument 2**
- 

**Returned data**
- STR = Zyrtec
- RXCUI = 58930
- TTY = BN
- LAT = ENG
- SUPPRESS = N
- SY =
- CUI = C0162723
RESTful API

◆ Base URI
  ● http://rxnav.nlm.nih.gov/REST/

◆ List of resources
  ● http://rxnav.nlm.nih.gov/RxNormRestAPI.html
<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>
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<tr>
<td>/displaynames</td>
<td>getDisplayNames</td>
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<td>/idtypes</td>
<td>getIdTypes</td>
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<td>/relatatypes</td>
<td>getRelaTypes</td>
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<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>
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<td>getNDCs</td>
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<td>/rxcui/{rxcui}/allrelated</td>
<td>getAllRelatedInfo</td>
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<td>getRelatedByType</td>
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<td>/drugs?name=value</td>
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REST output XML


<table>
<thead>
<tr>
<th>XML output</th>
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|     <rxcui>151399</rxcui>
|   </idGroup>
| </rxnormdata> |
REST output  JSON


```
JSON output
{
    "idGroup" : {
        "rxcui" : "151399",
        "name" : "bactrim"
    }
}
```
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)
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
New APIs  Coming up soon

◆ **RxTerms**
  - SOAP + REST
  - List of RxTerms properties for a given RxCUI

◆ **NDF-RT**
  - SOAP + REST
  - Find NDF-RT entity by name, NUI, RxCUI
  - Get properties for a given NDF-RT drug entity
  - Get relations for a given NDF-RT drug entity
  - Find drug interactions
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 ) o getRelatedByRelationship( *, has ingredient )

?= getRelatedByRelationship( r; inverse isa ) o getRelatedByRelationship( *, 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”
Usage statistics  All queries

Number of queries per month

- all queries
- REST queries
- 12 m sliding avg

Lister Hill National Center for Biomedical Communications
Usage statistics  Interactive queries

Number of interactive queries per month

- 0
- 1,000
- 2,000
- 3,000
- 4,000
- 5,000
- 6,000
- 7,000
- 8,000
- 9,000
- 10,000

Jan-08 Feb-08 Mar-08 Apr-08 May-08 Jun-08 Jul-08 Aug-08 Sep-08 Oct-08 Nov-08 Dec-08 Jan-09 Feb-09 Mar-09 Apr-09 May-09 Jun-09 Jul-09 Aug-09 Sep-09 Oct-09 Nov-09 Dec-09 Jan-10 Feb-10 Mar-10 Apr-10 May-10 Jun-10 Jul-10 Aug-10 Sep-10 Oct-10 Nov-10 Dec-10

12 m sliding...
Contact: RXNAVINFO@LIST.NIH.GOV
Web: http://rxnav.nlm.nih.gov/

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