RxNav

Browser and application programming interfaces for RxNorm

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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)
RxNorm concept

Ingredient

Acetaminophen

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

SNOMED CT
MeSH
Multum
NDDF
...

161
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>

Semantic clinical drug component

Semantic clinical drug form

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)

Ingredient
Azithromycin

Brand Name
Zithromax

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]

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
  - 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

$RxNav$
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
- 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( 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( rx cui , rel-list )
  ● By type: getRelatedByType( rx cui , type-list )
  ● All: getAllRelatedInfo( rx cui ) .

◆ Miscellaneous functions
  ● getDrugs( name )
  ● getDisplayTerms()
  ● getMultiIngredBrand( rx cui-list )
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);
Implementation Perl client

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

![RxNorm API access interface](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 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>getRxCxConceptProperties</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>
<tbody>
<tr>
<td>&lt;?xml version=&quot;1.0&quot; encoding=&quot;UTF-8&quot; standalone=&quot;yes&quot; ?&gt;</td>
</tr>
<tr>
<td>&lt;rxnormdata&gt;</td>
</tr>
<tr>
<td>&lt;idGroup&gt;</td>
</tr>
<tr>
<td>&lt;name&gt;bactrim&lt;/name&gt;</td>
</tr>
<tr>
<td>&lt;rxcui&gt;151399&lt;/rxcui&gt;</td>
</tr>
<tr>
<td>&lt;/idGroup&gt;</td>
</tr>
<tr>
<td>&lt;/rxnormdata&gt;</td>
</tr>
</tbody>
</table>
REST output JSON


```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)
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 VA Class
- Blood Products / Modifiers / Volume Expanders
  - Platelet Aggregation Inhibitors

Drug Products by Generic Ingredient Combinations
- Clopidogrel
  - Clopidogrel Bisulfate
    - Clopidogrel Bisulfate 75mg Tab

External Pharmacologic Classes
- Anti-coagulant
  - 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

 isa (stated)
 isa (inferred)

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

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

?≡

getRelatedByRelationship( \( r; \text{inverse isa} \) ) \( \circ \) getRelatedByRelationship( \( *, \text{has ingredient} \) )
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”
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

Medical Ontology Research

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