S87 – Data Integration and Exchange

November 17, 2010

RxNav

Browser and Application Programming Interfaces for RxNorm

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Acknowledgments

- Lee Peters
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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

- http://www.nlm.nih.gov/research/umls/rxnorm/index.html

and RxNorm APIs

- http://rxnav.nlm.nih.gov/

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

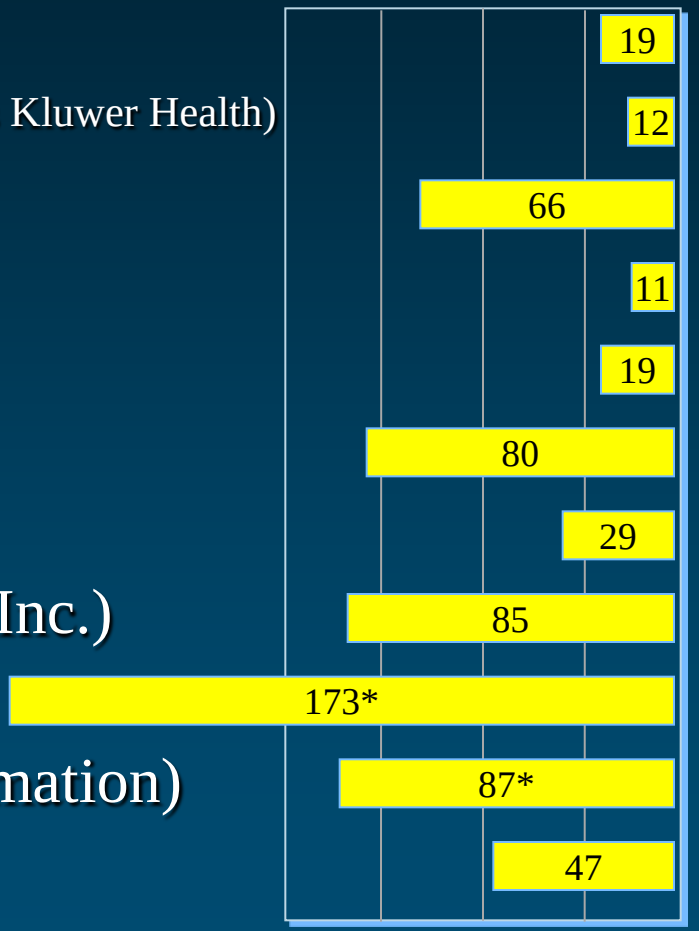
- 11 source vocabularies
- Synonymous names grouped into an RxNorm concept
- Unique identifiers (RxCUI)
- RRF format

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

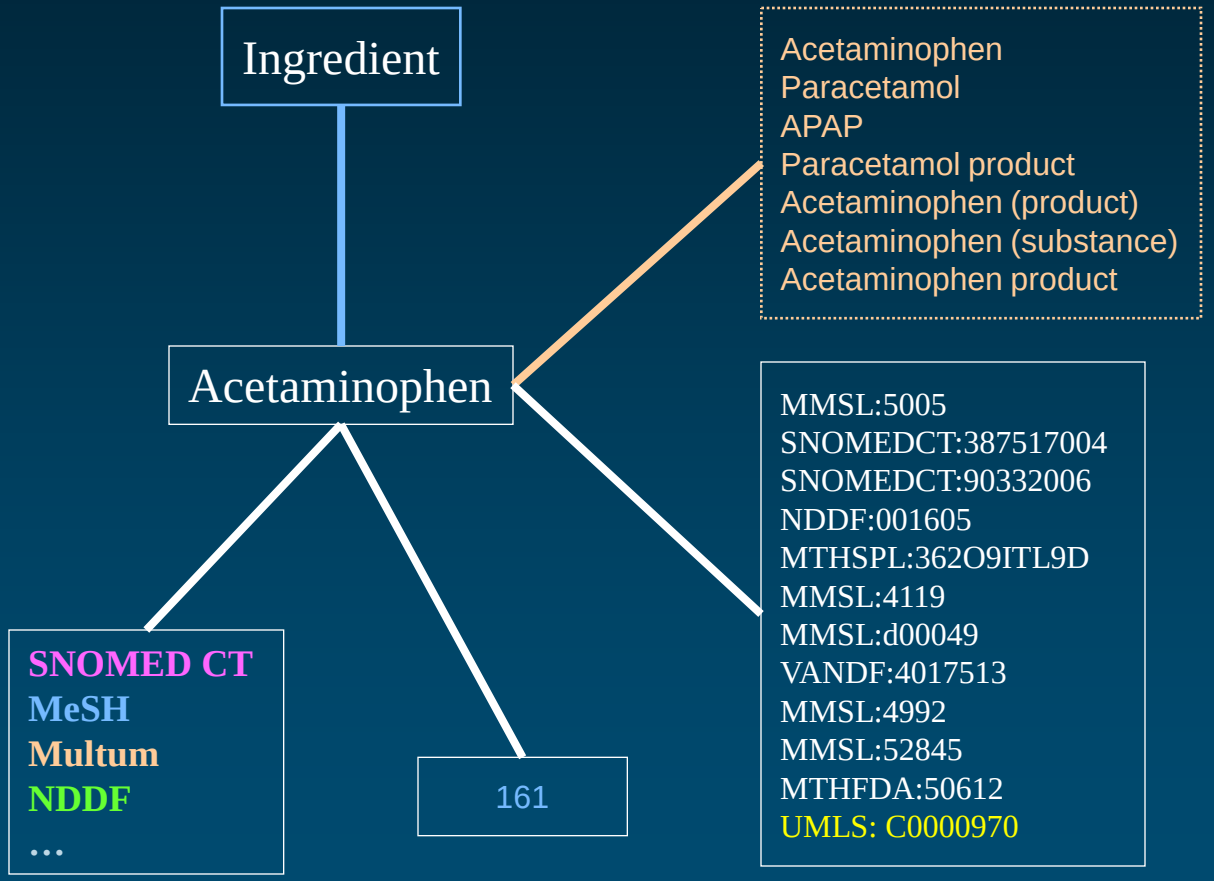
Source vocabularies in RxNorm

(terms in thousands, as of June 2010)

- 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



RxNorm concept



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
[…]	[…]

→ 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

Strength **Ingredient** **Dose form**

4mg/ml Fluoxetine Oral Solution

Strength **Ingredient**

Semantic clinical drug component

Ingredient **Dose form**

Semantic clinical drug form

Strength **Ingredient** **Dose form**

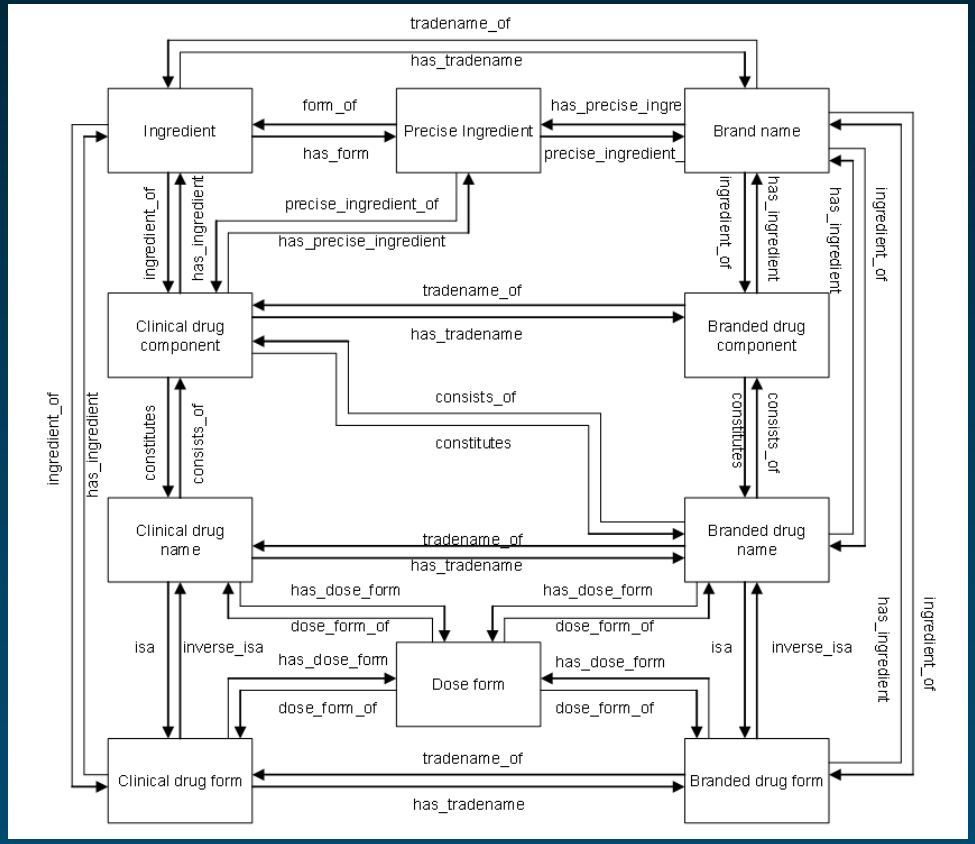
Semantic clinical drug

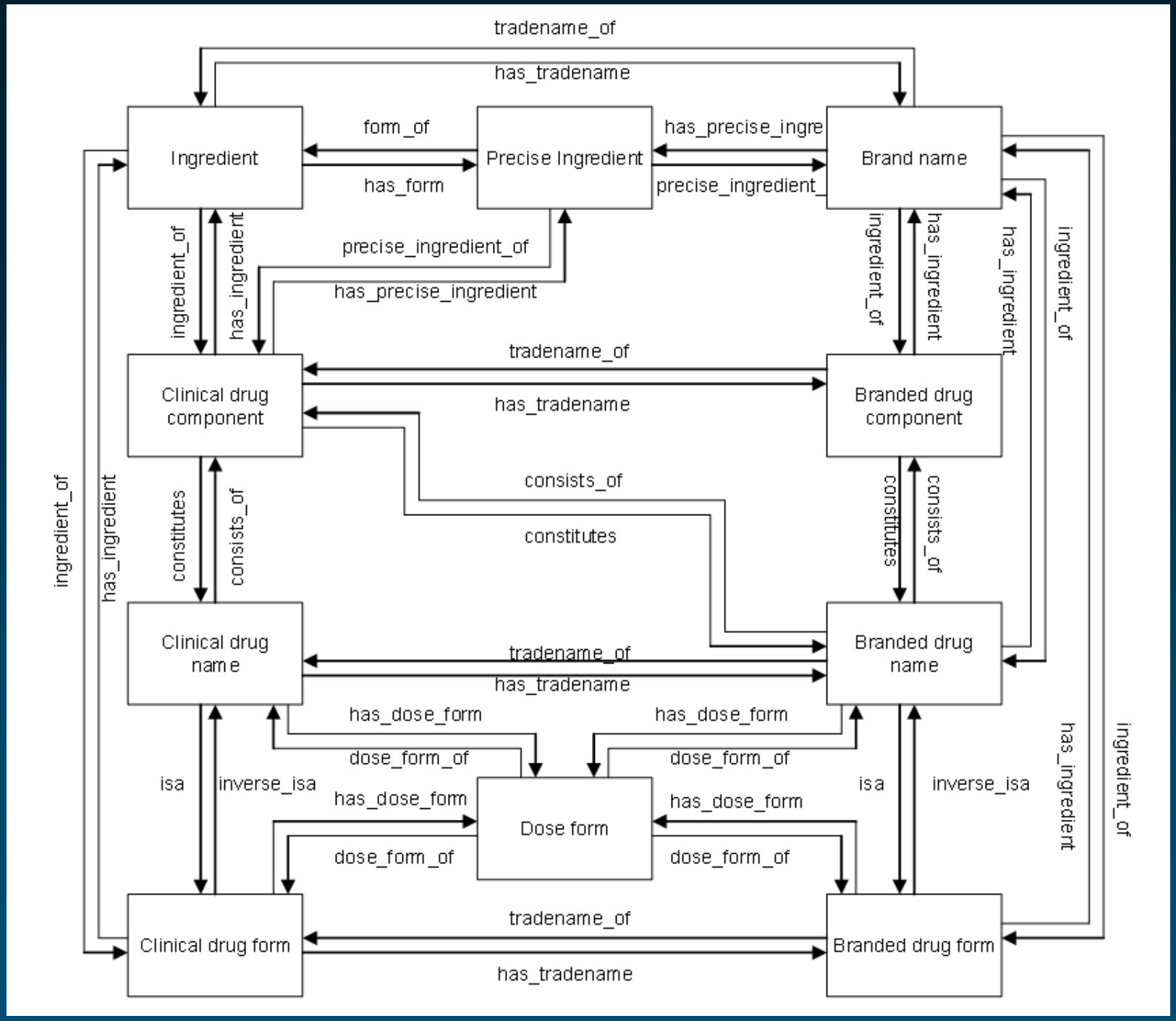
Generic *vs.* Brand

- 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)

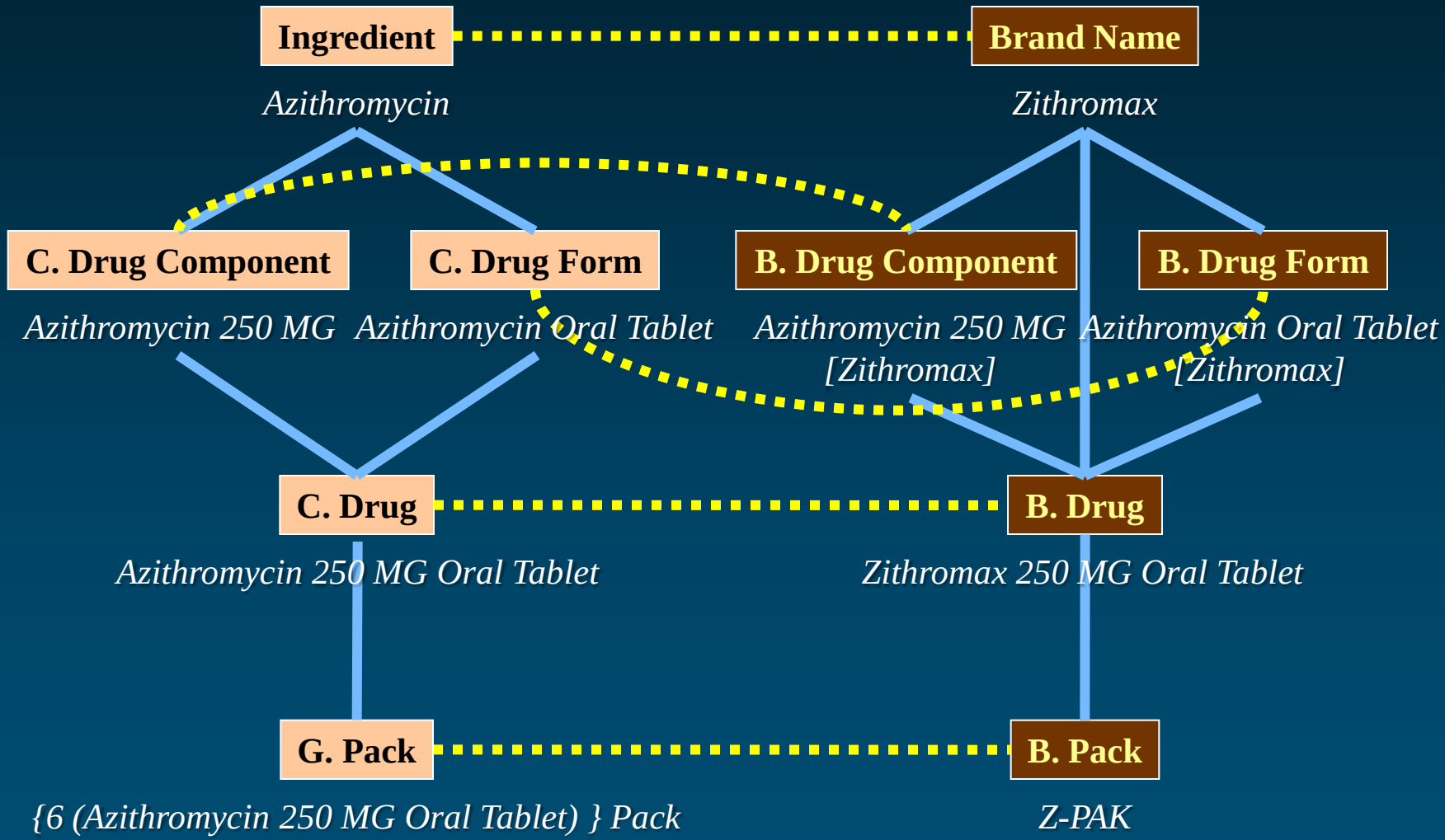
tradename_of

Relations among drug entities




tradename_of
has_tradename
Ingredient
form_of
has_form
Precise Ingredient
has_precise_ingre
precise_ingredient_
Brand name
ingredient_of
has_ingredient
precise_ingredient_of
has_precise_ingredient
ingredient_of
has_ingredient
has_ingredient
ingredient_of
tradename_of
has_tradename
Clinical drug component
Branded drug component
ingredient_of
has_ingredient
constitutes
consists_of
consists_of
constitutes
constitutes
consists_of
Clinical drug name
Branded drug name
tradename_of
has_tradename
has_dose_form
has_dose_form
dose_form_of
dose_form_of
isa
inverse_isa
isa
inverse_isa
has_dose_form
has_dose_form
Dose form
dose_form_of
dose_form_of
has_ingredient
ingredient_of
tradename_of
Clinical drug form
Branded drug form
has_tradename

Relations among drug entities (revisited)



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

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)
  - http://mor.nlm.nih.gov/perl/rxnav_api_demo.pl

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

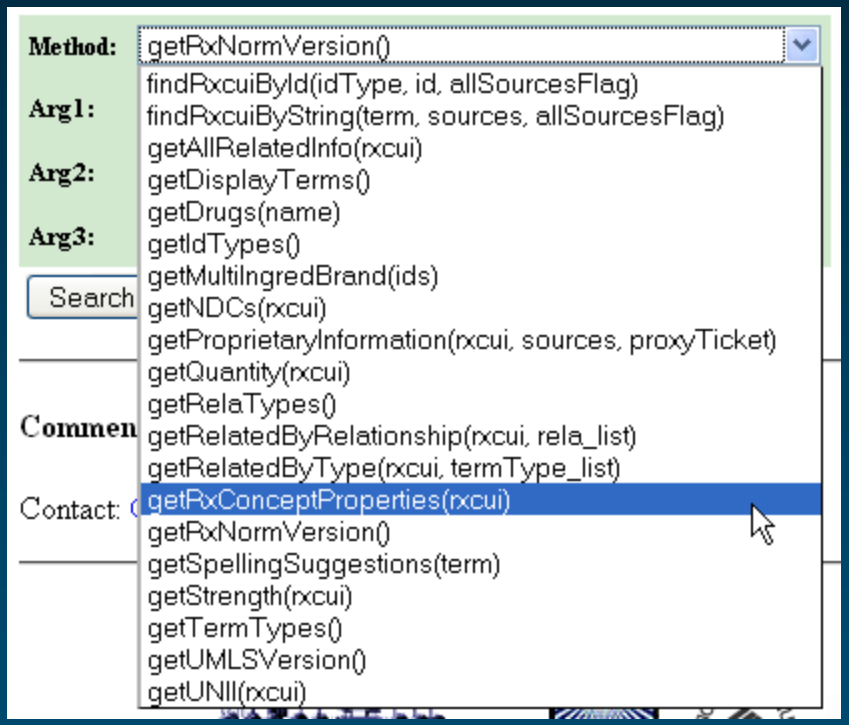
```
import java.net.URL;
import BeanService.*;
import gov.nih.nlm.mor.axis.services.RxNormDBService.*;
```

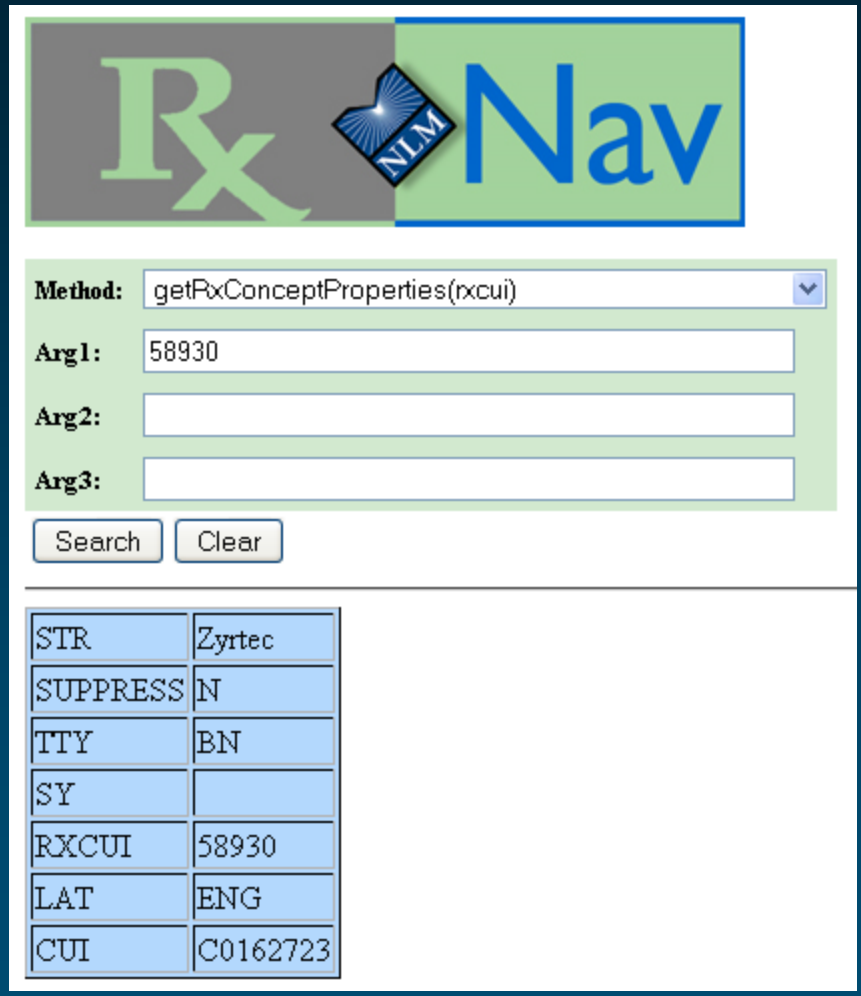
```
String rxhost = "http://mor.nlm.nih.gov";
String rxURI = rxhost + "/axis/services/RxNormDBService";

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

- Perl, .NET

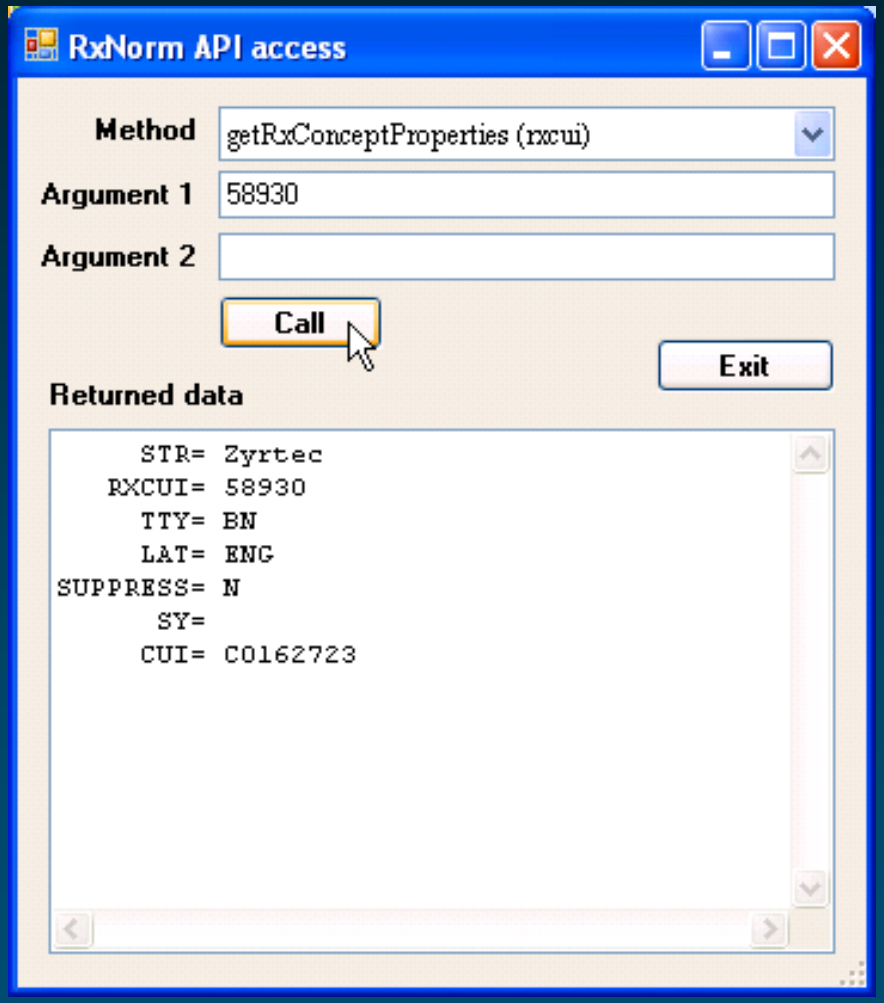
Implementation Perl client

http://mor.nlm.nih.gov/perl/rxnav_api_demo.pl





Implementation .NET client



RESTful API

- Base URI
  - http://rxnav.nlm.nih.gov/REST/
- List of resources
  - http://rxnav.nlm.nih.gov/RxNormRestAPI.html

RESTful resource	SOAP-based function
/	(none)
/version	getRxNormVersion
/displaynames	getDisplayNames
/idtypes	getIdTypes
/relatypes	getRelaTypes
/termtypes	getTermTypes
/rxcui?name=*value*&srclst=*value*&allsrc=*value*&search=*value*	findRxcuiByString
/rxcui?idtype=*value*&id=*value*&allsrc=value	findRxcuiById
/rxcui/*{rxcui}*	(none)
/rxcui/*{rxcui}*/properties	getRxConceptProperties
/rxcui/*{rxcui}*/ndcs	getNDCs
/rxcui/*{rxcui}*/allrelated	getAllRelatedInfo
/rxcui/*{rxcui}*/related?tty=*values*	getRelatedByType
/rxcui/*{rxcui}*/related?rela=*values*	getRelatedByRelationship
/rxcui/*{rxcui}*/unii	getUNII
/rxcui/*{rxcui}*/quantity	getQuantity
/rxcui/*{rxcui}*/strength	getStrength
/rxcui/*{rxcui}*/proprietary?srclist=*values*&ticket=*value*	getProprietaryInformation
/spellingsuggestions?name=*value*	getSpellingSuggestions
/brands?ingredientids=*value*	getMultiIngredBrand
/drugs?name=*value*	getDrugs

REST output XML

http://rxnav.nlm.nih.gov/REST/rxcui?name=bactrim

XML output

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

REST output JSON

http://rxnav.nlm.nih.gov/REST/rxcui?name=bactrim

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*)

RxNormNorm Paper

S95 – Foundational Elements of NLP
November 17, 2010 10:30am-12:00pm
Lincoln East

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

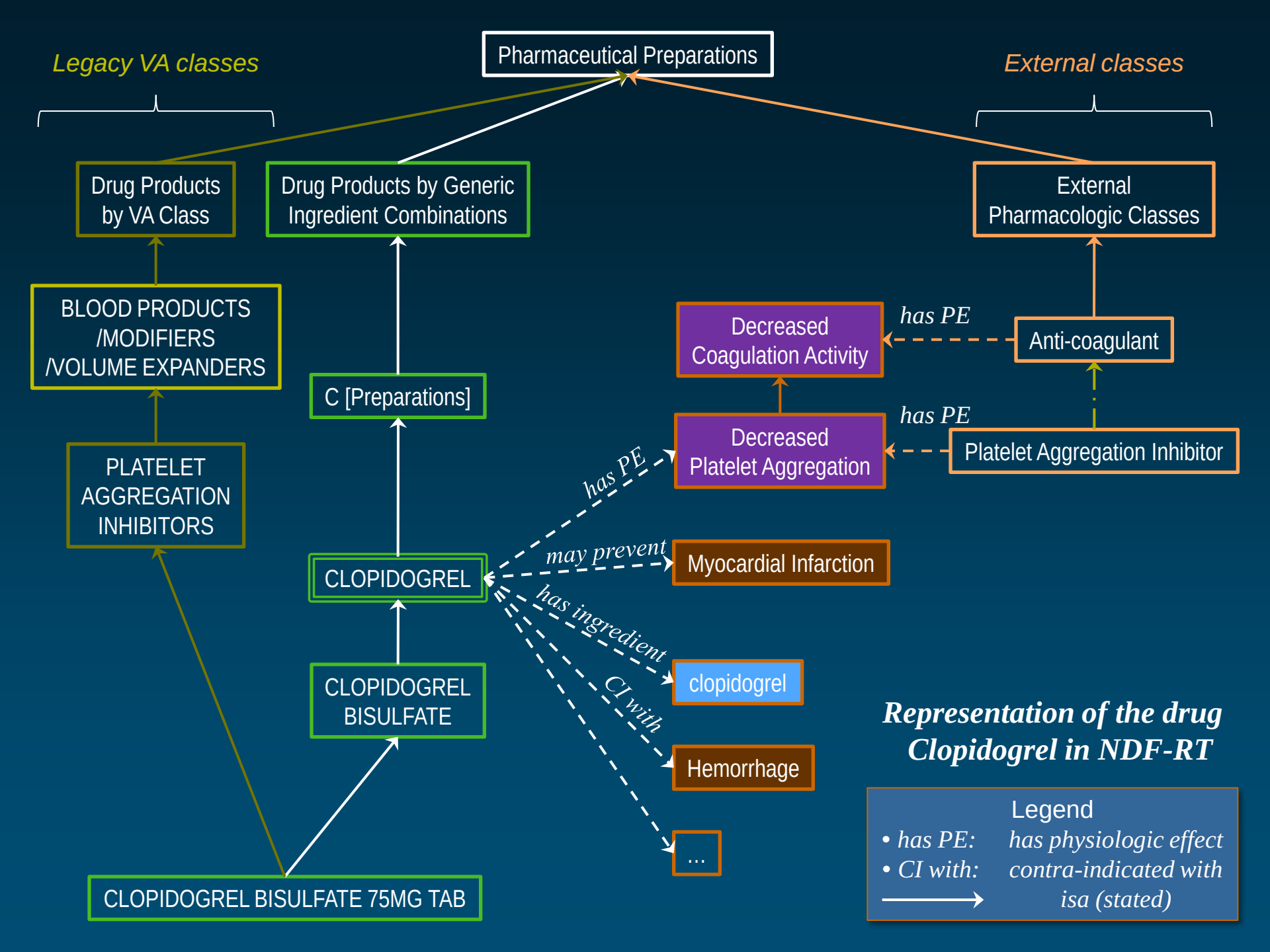
Other drug information sources accessible through RxNav

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*


Legacy VA classes
Pharmaceutical Preparations
External classes
Drug Products by VA Class
Drug Products by Generic Ingredient Combinations
External Pharmacologic Classes
BLOOD PRODUCTS /MODIFIERS /VOLUME EXPANDERS
C [Preparations]
Decreased Coagulation Activity
has PE
Anti-coagulant
Decreased Platelet Aggregation
has PE
Platelet Aggregation Inhibitor
PLATELET AGGREGATION INHIBITORS
has PE
may prevent
Myocardial Infarction
CLOPIDOGREL
has ingredient
clopidogrel
CI with
Hemorrhage
CLOPIDOGREL BISULFATE
...
CLOPIDOGREL BISULFATE 75MG TAB
Representation of the drug Clopidogrel in NDF-RT
Legend
• has PE: has physiologic effect
• CI with: contra-indicated with
isa (stated)

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)
- http://wwwcf.nlm.nih.gov/umlslicense/rxtermApp/rxTerm.cfm
- 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

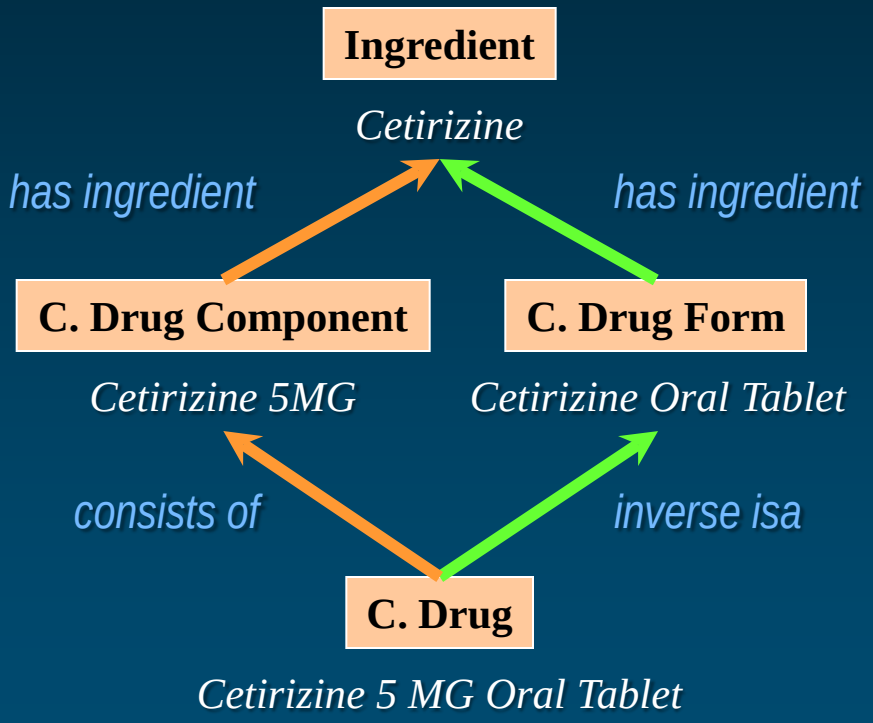
Quality control in RxNorm

- Multiple equivalent paths between RxNorm entities

getRelatedByRelationship(*r*, *consists of*) o
getRelatedByRelationship(*, *has ingredient*)

?≡

getRelatedByRelationship(*r*, *inverse isa*) o
getRelatedByRelationship(*, *has ingredient*)



Examples of application

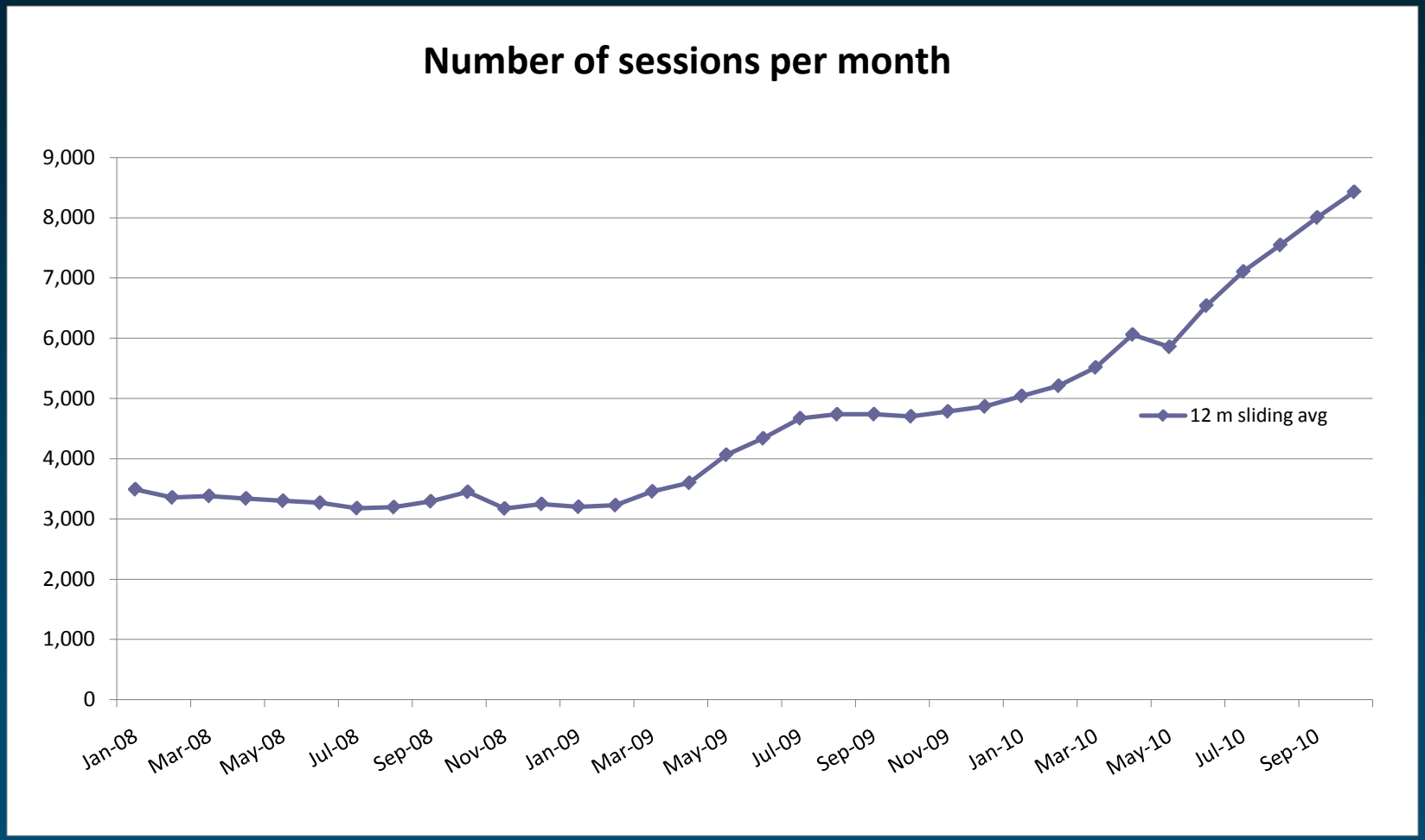
- Quality control in RxNorm: Results
  - 35,000 pairs of paths investigated
  - Few discrepancies detected
  - Types of errors
    - Obsolete brand names
    - Obsolete branded drug forms
    - Erroneous relations
  - Discrepancies reported to the RxNorm team

[Peters, JAMIA 2009]

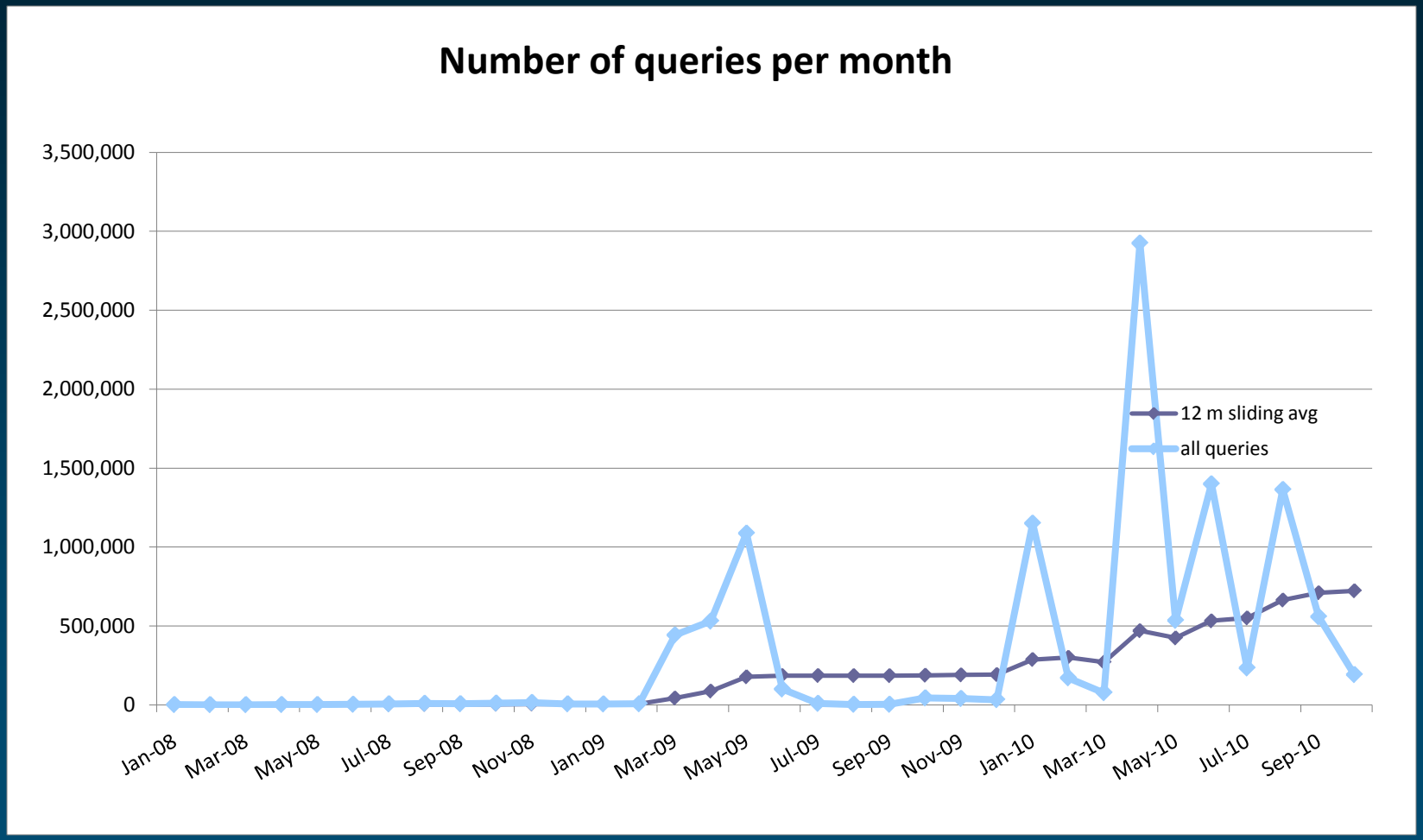
Applications outside NLM

- RxSafe (OHSU)
  - “improve medication safety for patients”
  - http://www.ohsu.edu/RxSafe/
- My-Medi-Health (Vanderbilt)
  - “Child-Centered Medication Management”
  - http://www.projecthealthdesign.org/projects/overview-2006_2008/405594/406293

Usage statistics Sessions



Usage statistics Queries



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

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