

Lister Hill National Center for Biomedical Communications  
*Brown Bag Lunch Series*  
August 1, 2008

**RxNav**

*Interfaces to drug information sources*



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# Acknowledgments



- ◆ Stuart Nelson
- ◆ Kelly Zeng
- ◆ Lee Peters
- ◆ Ramez Ghazzaoui

# 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*

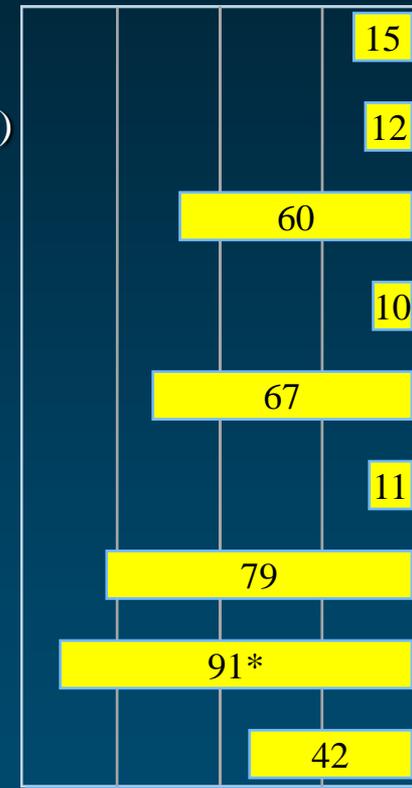


# UMLS-like approach

- ◆ 9 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

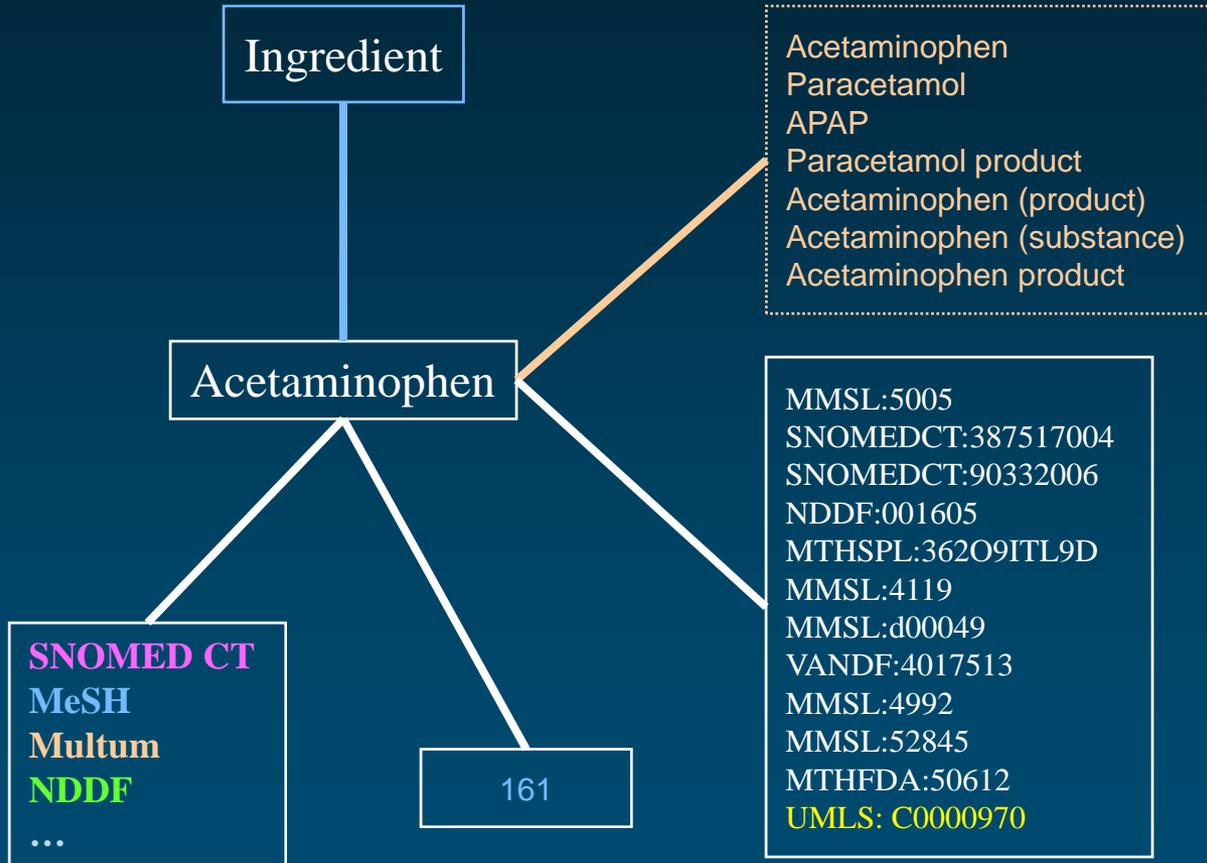
- ◆ Gold Standard Alchemy
- ◆ Master Drug Data Base (Medi-Span, Wolters Kluwer Health)
- ◆ Multum MediSource Lexicon
- ◆ Micromedex DRUGDEX
- ◆ FDA National Drug Code Directory
- ◆ FDA Structured Product Labels
- ◆ Nat'l Drug Data File (First DataBank Inc.)
- ◆ SNOMED Clinical Terms (drug information)
- ◆ Veterans Health Administration Nat'l Drug File



(in thousands,  
as of July 2008)



# RxNorm concept



# Drug vocabulary standardization

*RxNorm*

# Normalization

## ◆ Lexical level

- Conventions for representing strength, units, etc.

## ◆ Structural level

- Generic vs. Brand names
- Atomic elements: Ingredient, Strength, Dose form
- Combinations
- Principle set of relationships among the different types



# 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

- Generic vs. Brand names
- Atomic elements: Ingredient, Strength, Dose form
- Combinations
- Principle set of relationships among the different types

# Normalized form

**Strength**

4mg/ml

**Ingredient**

Fluoxetine

**Dose form**

Oral Solution

**Strength**

Semantic clinical drug component

**Ingredient**

**Ingredient**

**Dose form**

Semantic clinical drug form

**Strength**

Semantic clinical drug

**Ingredient**

**Dose form**



# Generic vs. Brand

## ◆ Generic

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

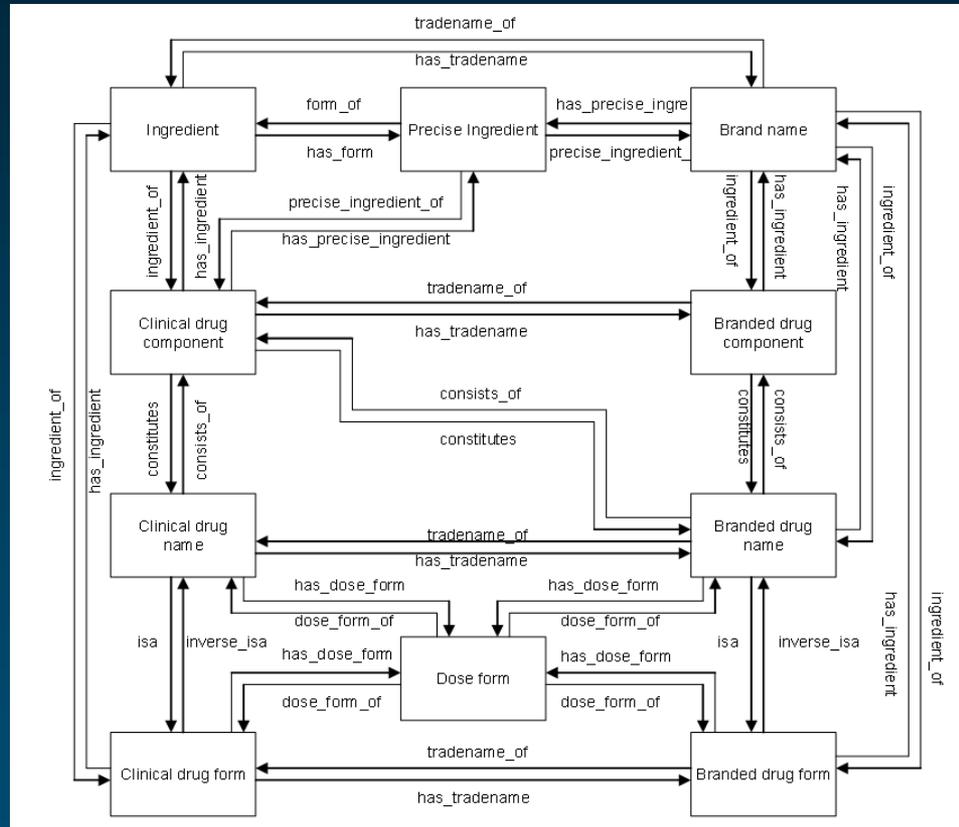
## ◆ Brand

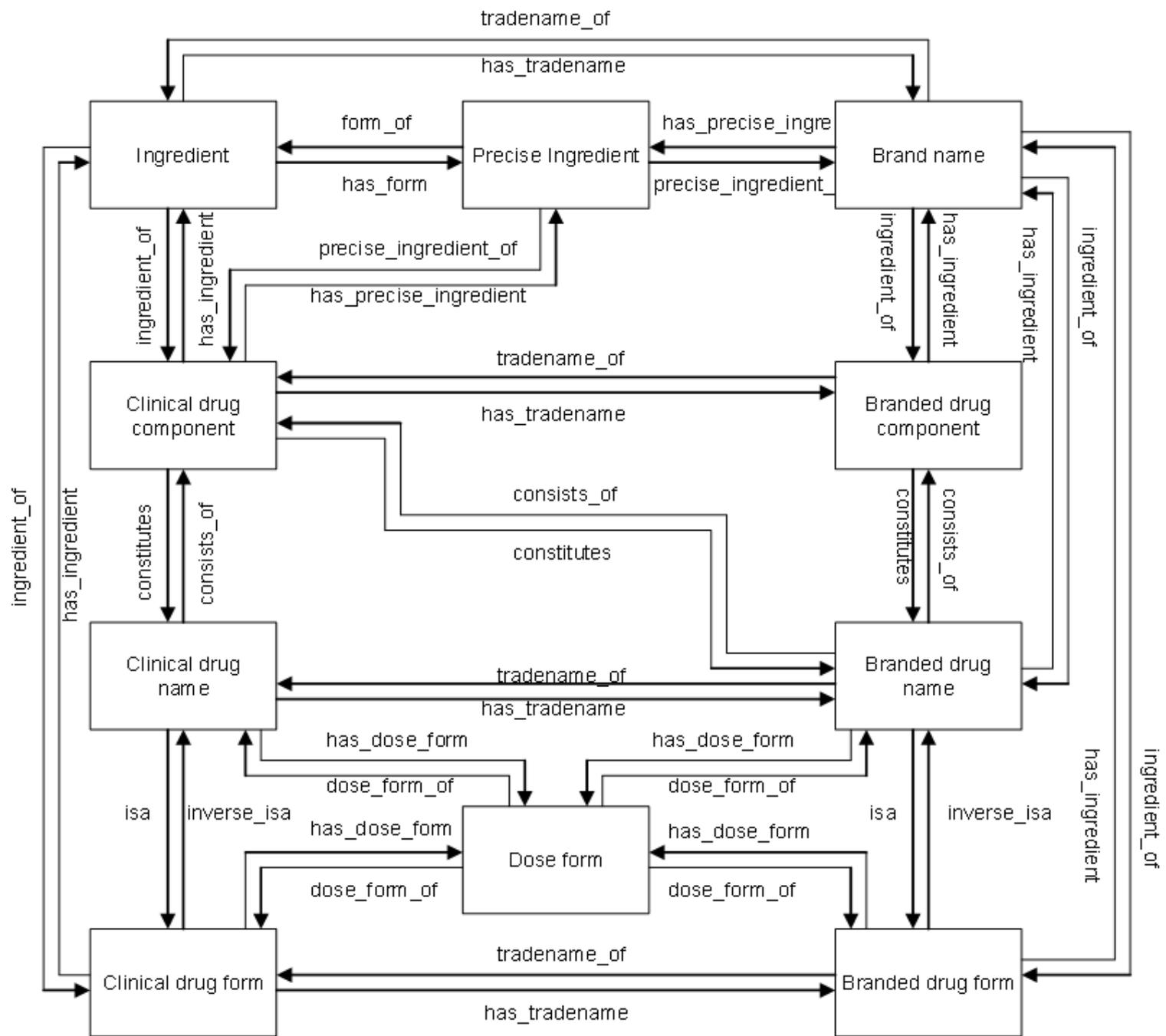
- Brand name (BN)
- Branded drug form (SBDF)
- Branded drug component (SBDC)
- Branded drug (SBD)

*tradename\_of*

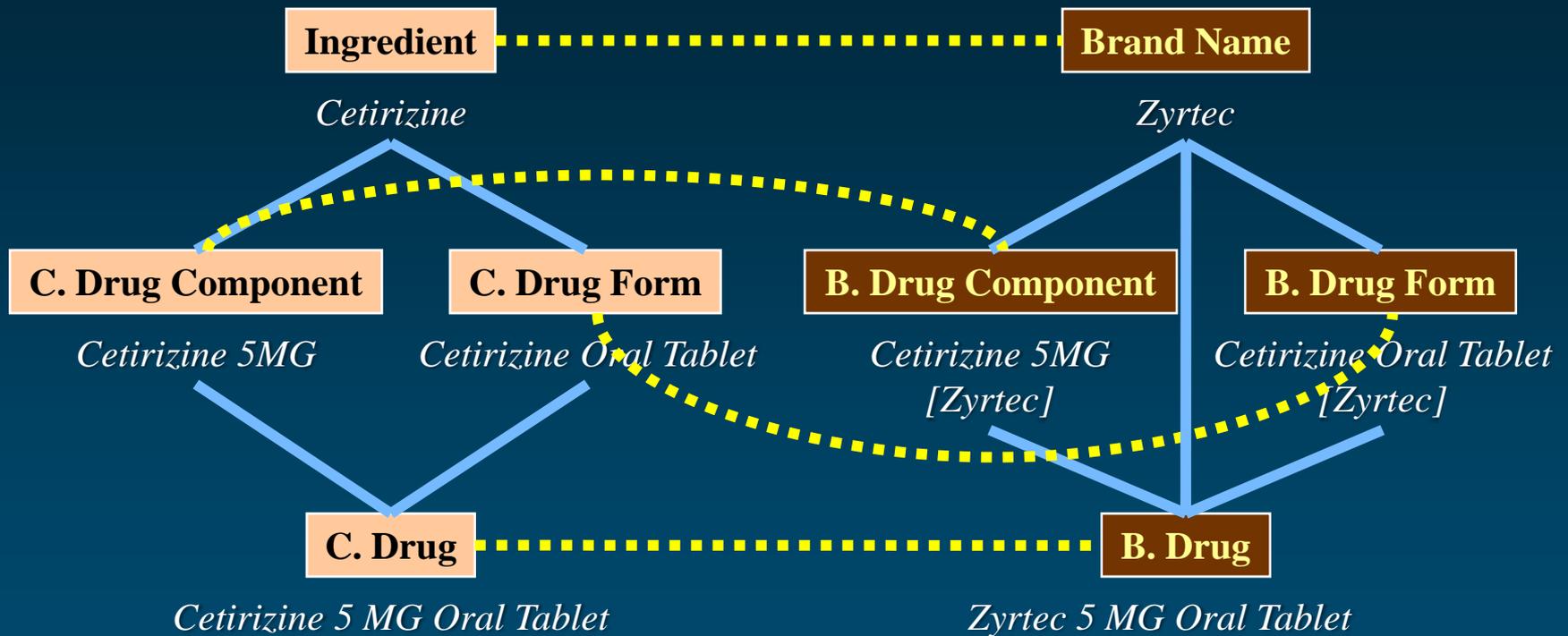


# Relations among drug entities





# Relations among drug entities (revisited)



# RxNorm database

## ◆ 9 data sources

- Gold Standard Alchemy
- Master Drug Data Base
- Multum MediSource Lex.
- Micromedex DRUGDEX
- FDA National Drug Code Directory
- FDA Structured Product Labels
- National Drug Data File Plus Source Vocabulary
- SNOMED Clinical Terms
- VA National Drug File

## ◆ Content

- 4,109 ingredients
- 9,845 brand names
- 13,380 clinical drug comp.
- 14,036 branded drug comp.
- 18,245 clinical drugs
- 14,769 branded drugs
- 8,193 clinical drug forms
- 11,520 branded drug forms
- 104 dose forms

*(as of July 1, 2008;  
excluding obsolete data)*



# Recent changes

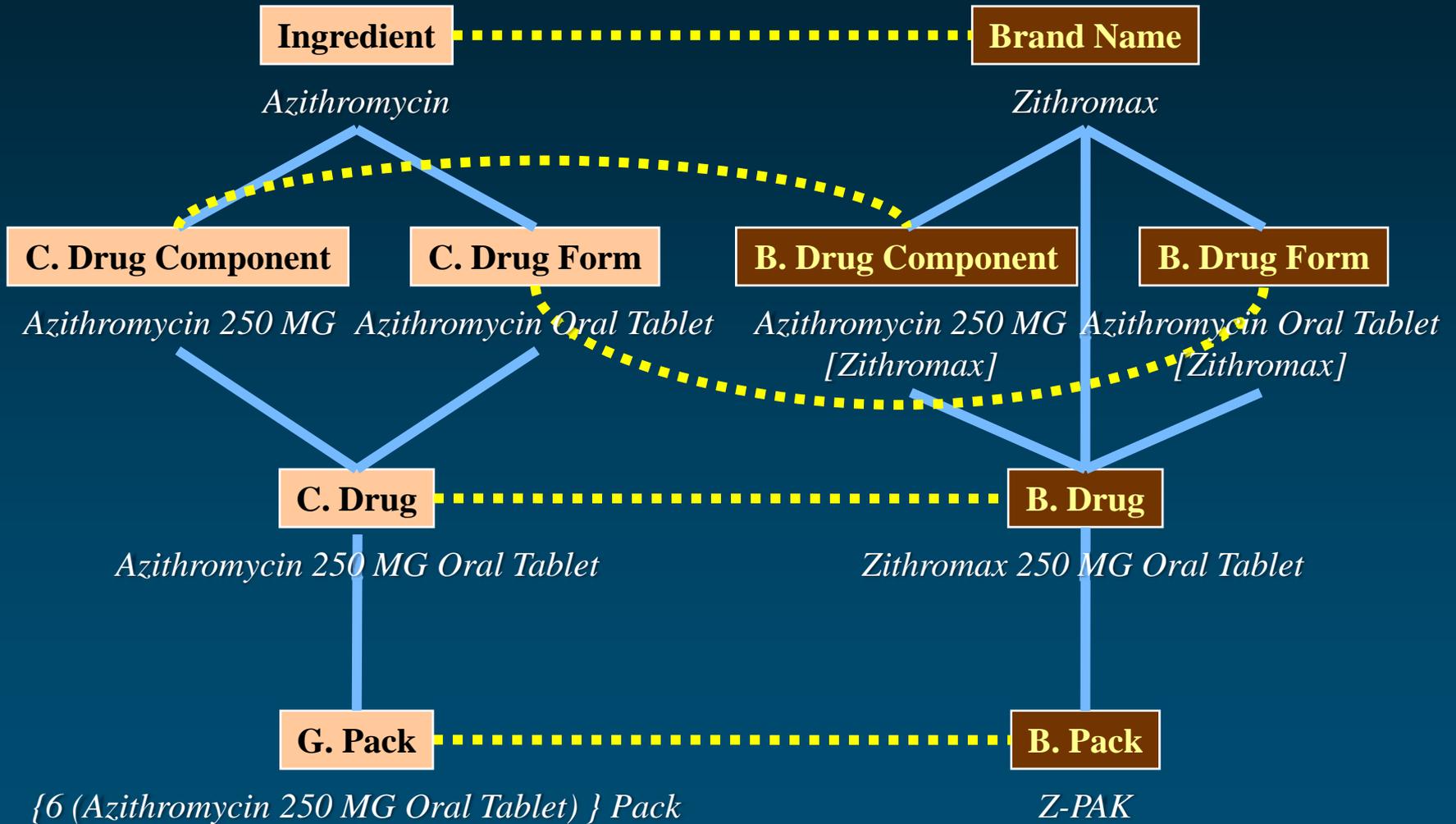
## ◆ Generic/Branded Pack

- Collection of drugs prescribed as one unit
  - Z-PAK =  
{6 (Azithromycin 250 MG Oral Tablet [Zithromax]) } Pack [Z-PAKS]
  - Nordette-28 =  
{21 (Ethinyl Estradiol 0.03 MG / Levonorgestrel 0.15 MG Oral Tablet) / 7 (Inert Ingredients 1 MG Oral Tablet) } Pack [Nordette 28 Day]
  - Triphasil-21 =  
{6 (Ethinyl Estradiol 0.03 MG / Levonorgestrel 0.05 MG Oral Tablet) / 10 (Ethinyl Estradiol 0.03 MG / Levonorgestrel 0.125 MG Oral Tablet) / 5 (Ethinyl Estradiol 0.04 MG / Levonorgestrel 0.075 MG Oral Tablet) } Pack [Triphasil 21 Day]

Active GPCCK forms	217
Active BPCCK forms	279



# Generic/Branded packs



# Visualizing drug information

*RxNav*





# RxNav

- ◆ Visualization and navigation
  - RxNorm browser
  - 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





# RxNav demo

<http://mor.nlm.nih.gov/download/rxnav/>



Terminology

Search



Search By: **String**

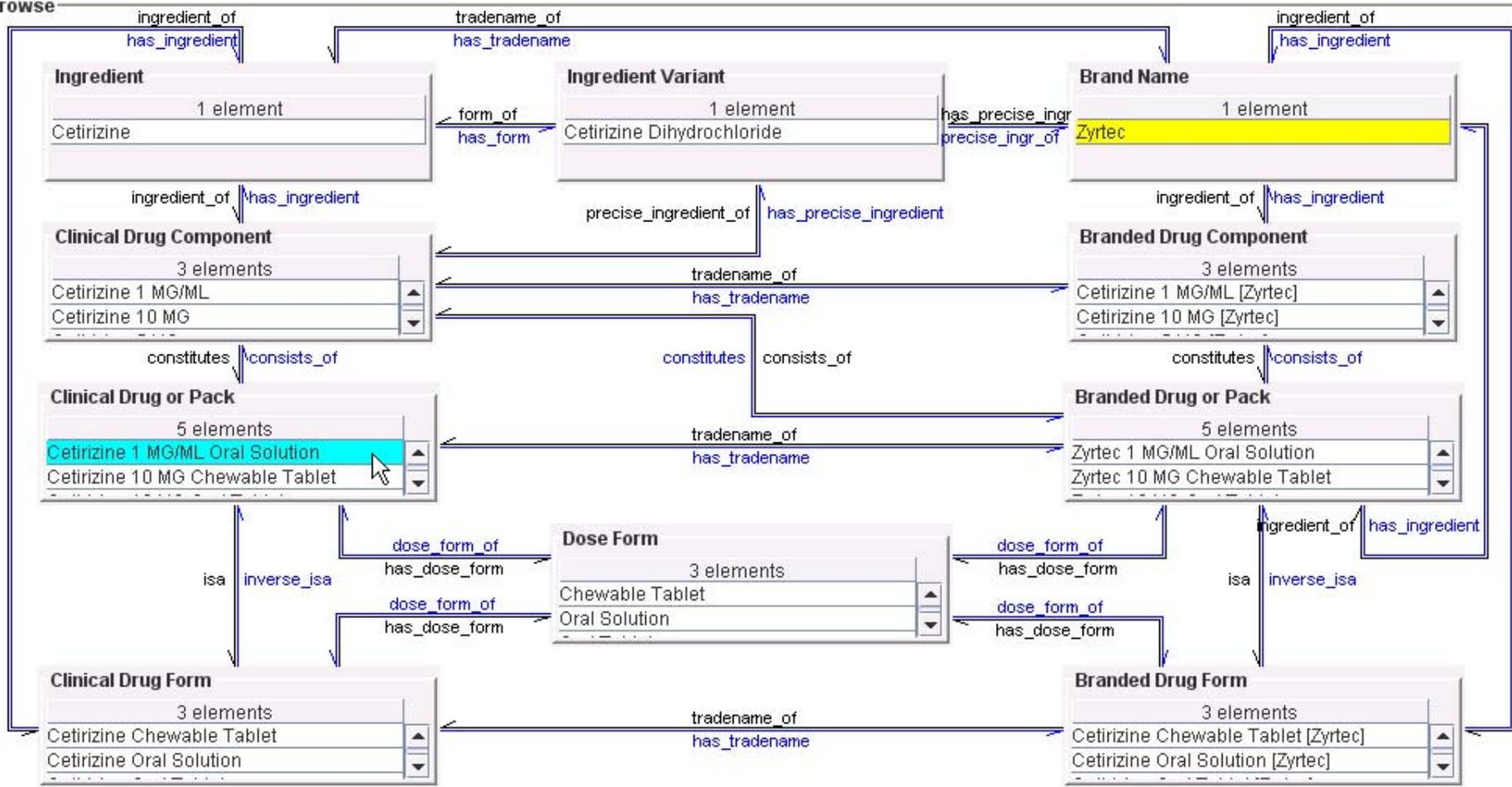
Help

Enter Search String:

Search



Browse



Retrieval Status or Detailed View of an RxNorm Entry ( RxNorm Concept Unique Identifier (RXCUI) | UMLS Concept Unique Identifier (UMLSCUI): 2008AA | RxNorm S 250637|C0792562||Cetirizine 1 MG/ML Oral Solution

Terminology

Search



Search By: **String**

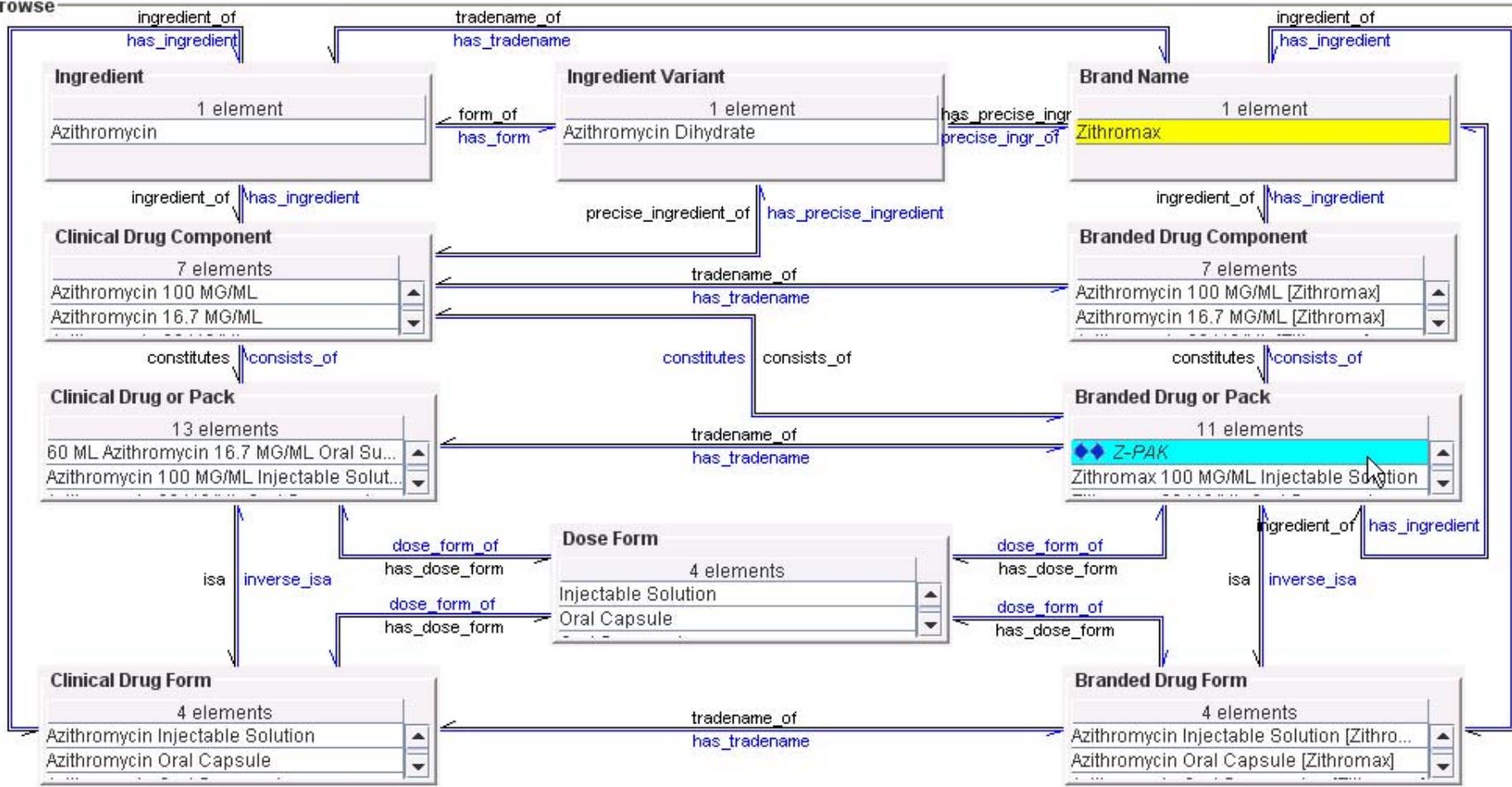
Help

Enter Search String: zithromax

Search



Browse



Retrieval Status or Detailed View of an RxNorm Entry ( RxNorm Concept Unique Identifier (RXCUI) | UMLS Concept Unique Identifier (UMLSCUI): 2008AA | RxNorm S 750149|C1878682|Z-PAK|6 (Azithromycin 250 MG Oral Tablet [Zithromax]) ) Pack [Z-PAKS]

# Processing drug information

*RxNorm Application Programming Interface*

# RxNorm API

- ◆ Made available in March 2008
- ◆ Based on Web Services
  - SOAP
  - Independent of any programming language
- ◆ Used by *RxNav* and *MyMedicationList*
- ◆ Enable access to all information displayed in RxNav
- ◆ Documentation  
<http://mor.nlm.nih.gov/download/rxnav/>



# List of functions 1/2

## ◆ Housekeeping functions

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

## ◆ Find RxNorm concepts

- By name: `findRxcuiByString( searchString )`
- By code: `findRxcuiById( idType, id )`
- Help: `getSpellingSuggestions( searchString )`



# List of functions 2/2

- ◆ Get RxNorm concept properties
  - `getRxConceptProperties( rx cui )`
  - `getNDCs( rx cui )`
- ◆ Get RxNorm concept relations
  - By rel.: `getRelatedByRelationship( rx cui, rel-list )`
  - By type: `getRelatedByType( rx cui, type-list )`
  - All: `getAllRelatedInfo( rx cui )`
- ◆ Convenience function
  - `getDrugs( name )`

# 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);
```

## ◆ Coming up soon: Perl, .NET



# Implementation Perl client



Method:

Arg1:

Arg2:

Comment:

Contact:

- findRxcuiById(idType, id)
- findRxcuiByString(term)
- getAllRelatedInfo(rxcui)
- getDrugs(name)
- getIdTypes()
- getNDCs(rxcui)
- getRelaTypes()
- getRelatedByRelationship(rxcui, relationship)
- getRelatedByType(rxcui, termType)
- getRxConceptProperties(rxcui)**
- getRxNormVersion()
- getSpellingSuggestions(term)
- getTermTypes()

Method:

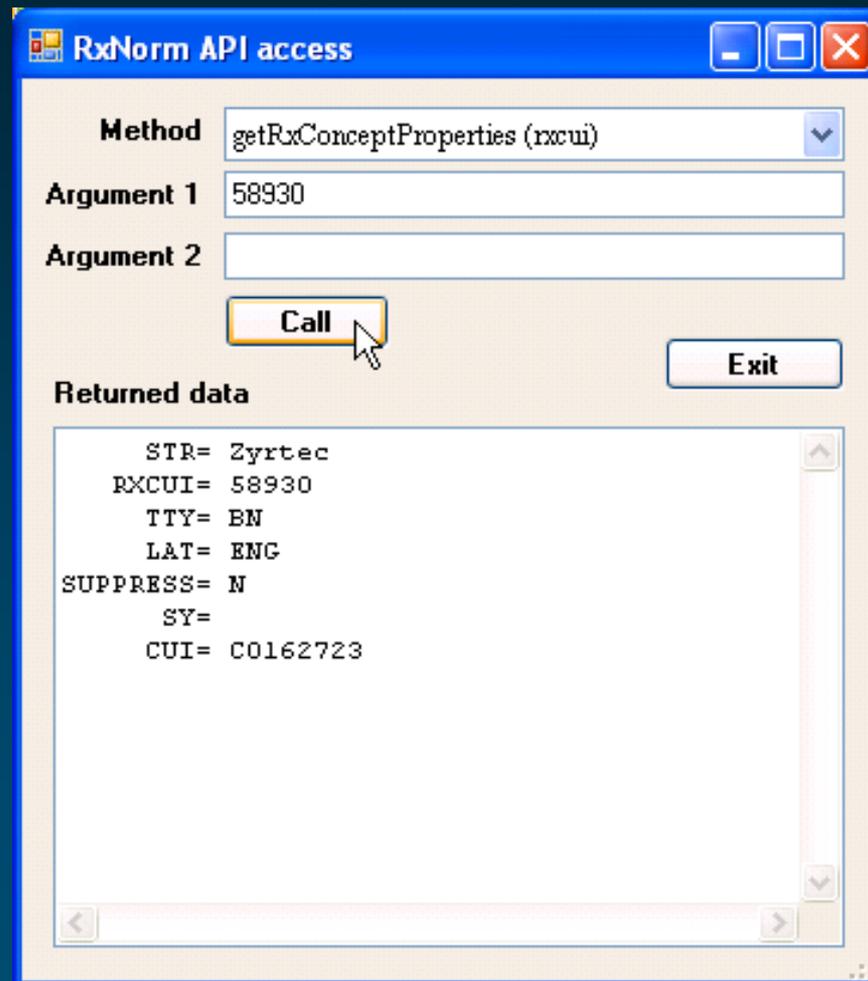
Arg1:

Arg2:

STR	Zyrtec
SUPPRESS	N
TTY	BN
SY	
RXCUI	58930
LAT	ENG
CUI	C0162723



# Implementation .NET client



# Coming up soon

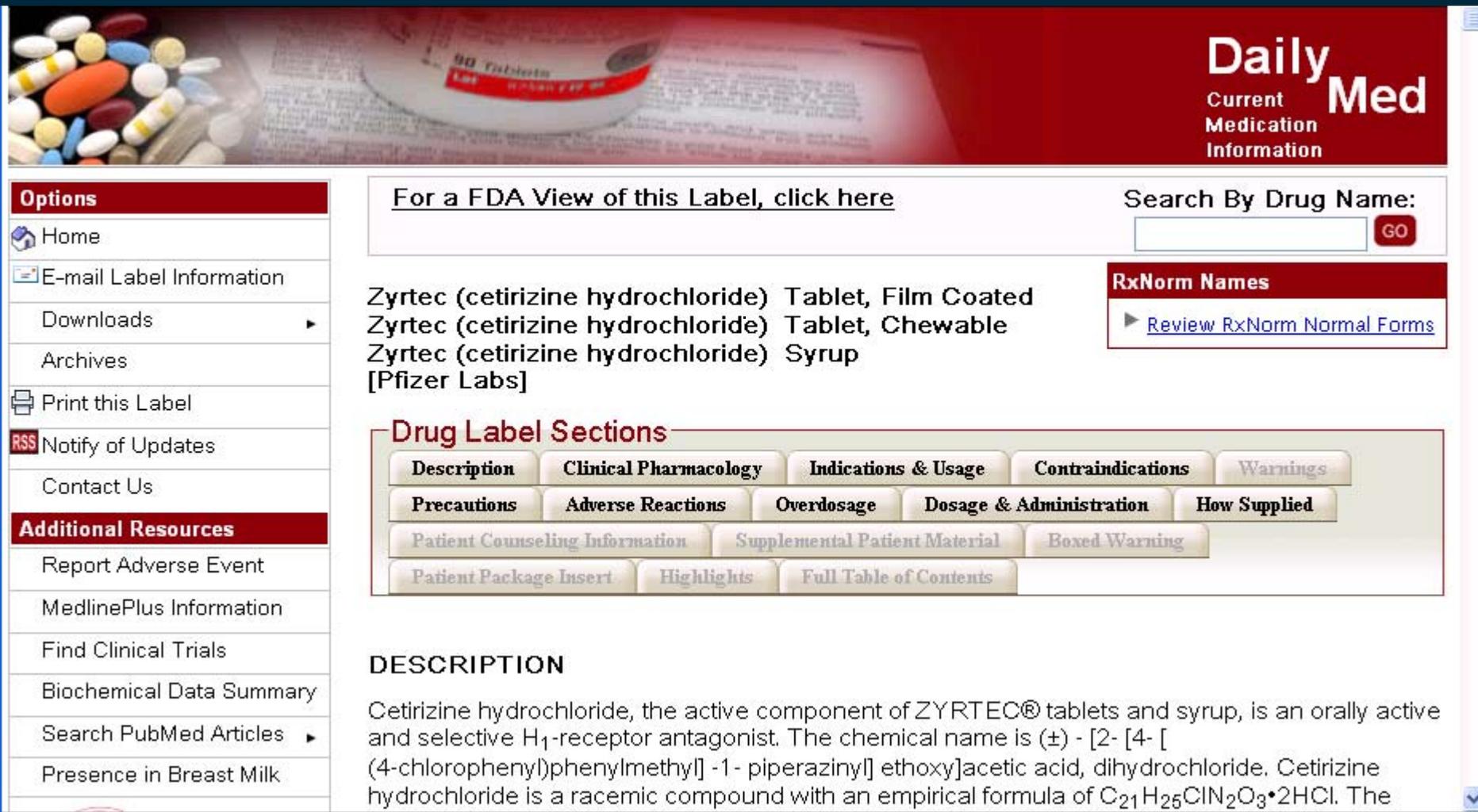
- ◆ Get proprietary information in a given source
  - Subject to UMLS intellectual property restrictions
  - Requires a “ticket” (similar to UMLSKS API)
  - Use cases
    - Access to exact names and codes in a given source
    - Support for mapping across drug vocabularies through RxNorm
      - Code in Multum → code in First Data Bank
- ◆ Multi-ingredient search



# Integrating drug information sources

*Link out*

# FDA Standard product labels



**Daily Med**  
Current Medication Information

Options

- Home
- E-mail Label Information
- Downloads
- Archives
- Print this Label
- Notify of Updates
- Contact Us

Additional Resources

- Report Adverse Event
- MedlinePlus Information
- Find Clinical Trials
- Biochemical Data Summary
- Search PubMed Articles
- Presence in Breast Milk

For a FDA View of this Label, click here

Search By Drug Name:  GO

RxNorm Names

- Review RxNorm Normal Forms

Zyrtec (cetirizine hydrochloride) Tablet, Film Coated  
Zyrtec (cetirizine hydrochloride) Tablet, Chewable  
Zyrtec (cetirizine hydrochloride) Syrup  
[Pfizer Labs]

**Drug Label Sections**

Description	Clinical Pharmacology	Indications & Usage	Contraindications	Warnings
Precautions	Adverse Reactions	Overdosage	Dosage & Administration	How Supplied
Patient Counseling Information	Supplemental Patient Material	Boxed Warning		
Patient Package Insert	Highlights	Full Table of Contents		

**DESCRIPTION**

Cetirizine hydrochloride, the active component of ZYRTEC® tablets and syrup, is an orally active and selective H<sub>1</sub>-receptor antagonist. The chemical name is (±) - [2- [4- [ (4-chlorophenyl)phenylmethyl] -1- piperaziny]] ethoxy]acetic acid, dihydrochloride. Cetirizine hydrochloride is a racemic compound with an empirical formula of C<sub>21</sub>H<sub>25</sub>ClN<sub>2</sub>O<sub>3</sub>•2HCl. The

# Coming up soon

- ◆ Currently no clinical information
  - In RxNorm
  - Processable through RxNav
    - Textual information available through the links to DailyMed and MedlinePlus Drugs
- ◆ Clinical information available in other sources
  - E.g., MedlinePlus drugs, NDF-RT
  - Soon to be integrated in RxNav



# MedlinePlus Drugs

Skip navigation



## MedlinePlus

Trusted Health Information for You

A service of the U.S. NATIONAL LIBRARY OF MEDICINE  
and the NATIONAL INSTITUTES OF HEALTH

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Other drug names: [A](#) [B](#) [C](#) [D](#) [E](#) [F](#) [G](#) [H](#) [I](#) [J](#) [K](#) [L](#) [M](#) [N](#) [O](#) [P](#) [Q](#) [R](#) [S](#) [T](#) [U](#) [V](#) [W](#) [X](#) [Y](#) [Z](#) [0-9](#)

### Cetirizine

(se ti' ra zeen)

 Printer-friendly version  E-mail to a friend

**Contents of this page:**

- [Why is this medication prescribed?](#)
- [How should this medicine be used?](#)
- [Other uses for this medicine](#)
- [What special precautions should I follow?](#)
- [What special dietary instructions should I follow?](#)
- [What should I do if I forget a dose?](#)
- [What side effects can this medication cause?](#)
- [What storage conditions are needed for this medicine?](#)
- [In case of emergency/overdose](#)
- [What other information should I know?](#)
- [Brand names](#)
- [Brand names of combination products](#)

**Why is this medication prescribed?** [Return to top](#)

Cetirizine is used to temporarily relieve the symptoms of hay fever (allergy to pollen, dust, or other substances in the air) and allergy to other substances (such as dust mites, animal dander, cockroaches, and molds). These symptoms include sneezing, runny nose, itchy, red, watery eyes, and itchy nose or throat. Cetirizine is also used



# National Drug File Reference Terminology

- ◆ Developed by the Veterans Health Administration
- ◆ Part of the VA clinical information system
- ◆ Non-terminological information
  - Pharmacologic class (*isa*)
  - Indications (*may\_treat, may\_diagnose, may\_prevent*)
  - Contraindications (*drug\_contraindicated\_for*)
  - Mechanism of action (*mechanism\_of\_action\_of*)
  - Drug-drug interactions (*contraindicated\_with*)
  - Physiology (*has\_physiologic\_effect*)
  - Metabolism (*metabolic\_site\_of, metabolizes, pharmacokinetics\_of*)



# NDF-RT Examples

## ◆ Cetirizine

- *drug\_contraindicated\_for Drug Allergy*
- *may\_treat Rhinitis, Allergic, Perennial*
- *may\_treat Urticaria*
- *has\_physiologic\_effect Decreased Histamine Activity*

# Applications

# Applications

- ◆ Terminology integration and standardization (RxNorm) enables interoperability and mapping across vocabularies
- ◆ Specific applications
  - Data integration
  - Medication reconciliation
  - Personal Health Record
  - E-prescribing / CPOE
  - CDA R2



# My Medication List


 Home

 Add a Medication

 Save

 Save As

 Print View

Medication Record for:

Bodenreider Olivier



## Current Medications

	Name of Medici...	Start Date	Stop Date	Amount Each Ti...	Frequency	Instruction
<input type="checkbox"/>	Sulfamethoxazo le 400 MG / Trimethoprim 80 MG Oral	06/27/2008	07/05/2008	1	Twice a Day	
<input checked="" type="checkbox"/>	Lipitor 10 MG Oral Tablet	06/27/2008	07/26/2008	1	Once a Day	

## Previous Medications

	Name of Medici...	Start Date	Stop Date	Amount Each Ti...	Frequency	Instruction



Correct/Complete Info



Change Freq or Quantity



Discontinue



View Label



Delete

<http://mml.nlm.nih.gov/>

[Zeng, AMIA 2008]

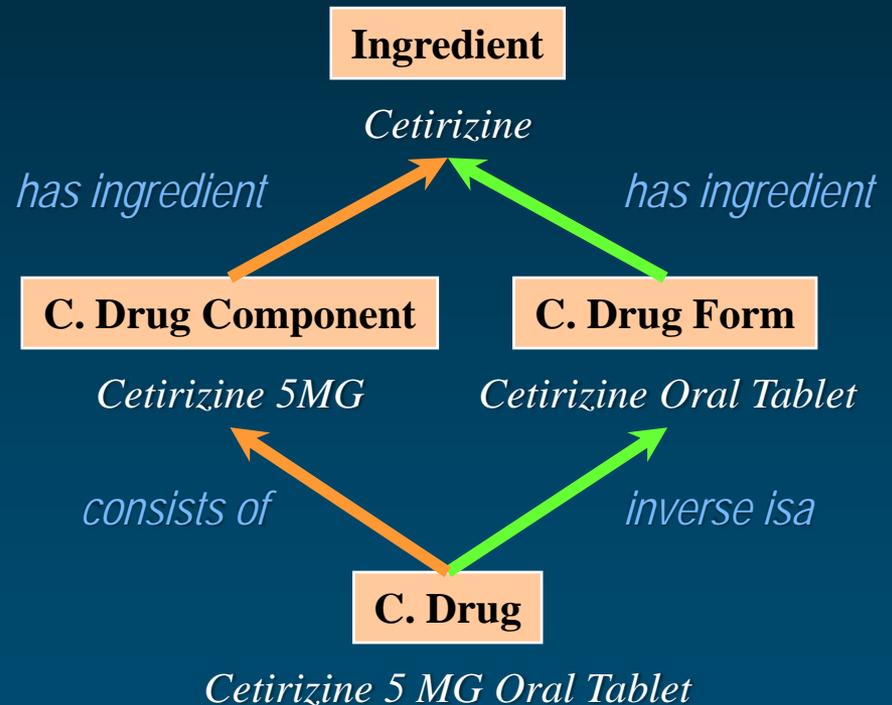
# Quality control in RxNorm

- ◆ Multiple equivalent paths between RxNorm entities

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

?≡

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



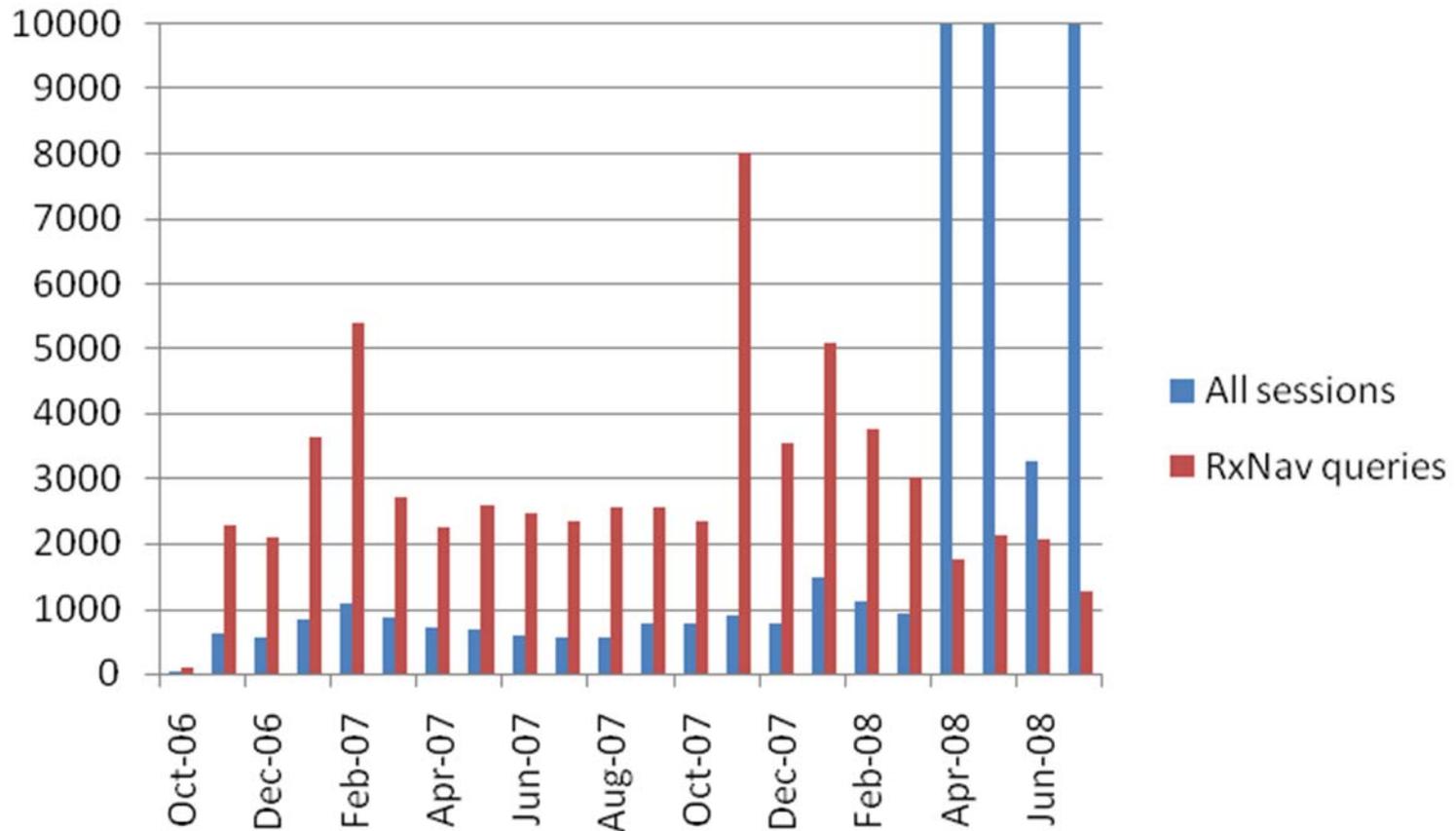
# Examples of application

- ◆ 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, AMIA 2008]



# Usage statistics



# References

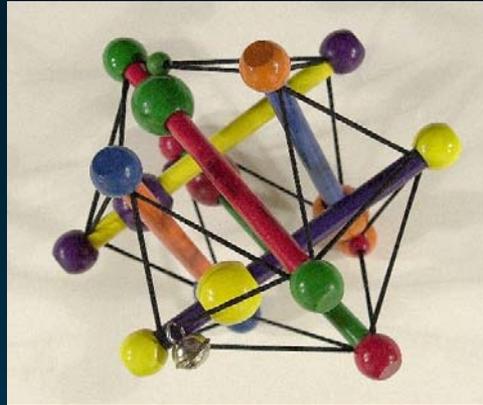
## RxNorm

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



## and RxNorm API

- <http://mor.nlm.nih.gov/download/rxnav/>



# Medical Ontology Research

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