The RxNorm Time Machine

*Issues in using RxNorm for analytics*

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Disclaimer

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Analytics use cases

◆ Example
  ● Evolution of the prescription of opioid drugs over time

◆ Implementation
  ● Claims databases (e.g., Medicare VRDC, Truven)
    ◦ NDC ↔ RxCUI [↔ drug class]
  ● Clinical data warehouses
    ◦ [Compendia ID ↔] RxCUI [↔ drug class]

◆ Requires to make sense of obsolete codes
  ● Obsolete NDCs mapped to current drugs
  ● Identity criteria for obsolete RxCUIs (ingredient + strength + dose form)
NDCs and RxCUIs turnover rate

**NDC**
- High
- Changes in
  - Manufacturer
  - Packaging

**RxCUI**
- Low
- Changes in normal forms (ingredient / strength / dose form [+QnF, QlD])
- Terminology updates (code changes due to editorial policies)
E-prescribing vs. analytics

◆ E-prescribing
  ● Restrict to currently marketed drugs
  ● Restrict to drugs marketed in a given region

◆ Analytics
  ● All drugs ever marketed
  ● All drugs marketed in all regions

RxNorm
RxNorm APIs

◆ Terminology updates
  (code changes due to editorial policies)
RxNorm dataset (Full monthly)

- Limited support for analytics
- Obsolete RxNorm concepts and relations still present in the RxNorm dataset
  - Concepts marked obsolete
    - SUPPRESS=Y and SUPPRESS=O
  - Non-prescribable entities (unquantified forms)
    - SUPPRESS=E
- Obsolete NDCs are removed from the set of NDCs curated by RxNorm (SAB=RXNORM)
- No cumulative history metadata
  - With start and end data for each RxCUI and NDC
- Retired RxCUI data (File = RXNCUI.RRF)
  - Used as the basis for remapping RxCUIs
RxNav

- Biased towards e-prescribing
  - Until very recently
- Only active RxNorm concepts and NDCs can be retrieved
  - Support for remapped concepts
- Only active concepts can be linked to other concepts
Welcome to RxNav

<table>
<thead>
<tr>
<th>IN/MIN</th>
<th>Ingredient</th>
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<tbody>
<tr>
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<thead>
<tr>
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<table>
<thead>
<tr>
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<th>Brand Name</th>
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<tr>
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<table>
<thead>
<tr>
<th>SCDC</th>
<th>Clinical Drug Component</th>
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<tbody>
<tr>
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</table>

<table>
<thead>
<tr>
<th>SBDC</th>
<th>Branded Drug Component</th>
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<tbody>
<tr>
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<table>
<thead>
<tr>
<th>SCD/GPCK</th>
<th>Clinical Drug or Pack</th>
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<tr>
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<table>
<thead>
<tr>
<th>SBD/BPCK</th>
<th>Branded Drug or Pack</th>
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<table>
<thead>
<tr>
<th>SCDG</th>
<th>Clinical Dose Form Group</th>
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<tbody>
<tr>
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<table>
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<th>Dose Form Group</th>
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<tbody>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>SBDG</th>
<th>Branded Dose Form Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
</tbody>
</table>
RxNorm API support for analytics

◆ NDC

- **getNDCStatus**(NDC, startDate, endDate, latest_only)
  - Indicate if an NDC is Active, Obsolete, Alien, or Unknown
    - Optionally restricted to a given time interval
  - RxNorm versions when the NDC was active
  - Original RxCUI(s) the NDC was associated with
    - All RxCUIs vs. latest RxCUI

- **getAllHistoricalNDCs**(RxCUI, active_only)
  - Return all NDCs ever associated with a given RxCUI
    - Optionally restricted to active NDCs
  - RxNorm versions when the NDC was active
**getNDCStatus(00364666854)**

```
{
  "ndcStatus": {
    "status": "Obsolete",
    "comment": "RxCUI (312656) is still active",
    "ndcHistory": {
      "activeRxcui": "312656",
      "originalRxcui": "312656",
      "startDate": "200706",
      "endDate": "201101"
    }
  }
}
```

312656
Promazine 50 MG/ML
Injectable Solution

**getNDCStatus(00143314501)**

```
{
  "ndcStatus": {
    "status": "Active",
    "comment": "",
    "ndcHistory": {
      "activeRxcui": "1116191",
      "originalRxcui": "1116191",
      "startDate": "201108",
      "endDate": "201709"
    },
    {
      "activeRxcui": "1116191",
      "originalRxcui": "198918",
      "startDate": "200706",
      "endDate": "201107"
    }
  }
}
```

1116191
ePHEDrine sulfate 25 MG
Oral Capsule

*RXCIU = 198918 is obsolete and has been remapped to RXCIU = 1116191*
**getAllHistoricalNDCs(1668240)**

```
{
  "historicalNdcConcept": {
    "historicalNdcTime": {
      "status": "indirect",
      "rxcui": "351772",
      "ndcTime": [ {
        "ndc": ["00069040001" ], "startDate": "201401", "endDate": "201510"},
        { "ndc": ["00069040010" ], "startDate": "201401", "endDate": "201510"},
        { "ndc": ["00069315014" ], "startDate": "200706", "endDate": "201510"},
        { "ndc": ["00069315083" ], "startDate": "200706", "endDate": "201510"},
        { "ndc": ["00069315084" ], "startDate": "201304", "endDate": "201510"},
        { "ndc": ["54569468100" ], "startDate": "200706", "endDate": "201101"},
        { "ndc": ["545694652700" ], "startDate": "200810", "endDate": "201510"},
        { "ndc": ["55154271505" ], "startDate": "200706", "endDate": "201206"},
        { "ndc": ["61947315000" ], "startDate": "200708", "endDate": "201206"},
        { "ndc": ["61947315001" ], "startDate": "200706", "endDate": "201206"},
        { "ndc": ["61947315003" ], "startDate": "200706", "endDate": "201206"} ]
    },
    "status": "direct",
    "rxcui": "1668240",
    "ndcTime": [ {
      "ndc": ["00069040001" ], "startDate": "201511", "endDate": "201709"},
      { "ndc": ["00069040010" ], "startDate": "201511", "endDate": "201709"},
      { "ndc": ["00069315014" ], "startDate": "201511", "endDate": "201709"},
      { "ndc": ["00069315083" ], "startDate": "201511", "endDate": "201709"},
      { "ndc": ["00069315084" ], "startDate": "201511", "endDate": "201709"},
      { "ndc": ["545694652700" ], "startDate": "201511", "endDate": "201709"} ]
  }
}
```

RXCUI = 351772 is obsolete and has been remapped to RXCUI = 1668240

1668240
Zithromax 500 MG Injection
RxNorm API support for analytics

◆ RxCUI
  ● `getRx cuiStatus(RxCUI)`
    - Indicate if an RxCUI is Active, Alien, Quantified, Remapped, Retired, or Unknown
    - Last RxNorm versions when active (for Remapped RxCUIs)
    - RxCUI, name and type of the current active RxNorm concept
  ● `RxcuiHistory*(RxCUI)`
    - Indicate if an RxCUI is Active, Retired, Never Active, Non-RxNorm, Unknown
    - Return the canonical representation of any RxNorm concept
      - Identity: ingredient, strength, dose form (+ QnF, QiD)
      - Metadata: source, start and end date
◆ getRxcuiStatus(198918)

RXCUI = 198918 is obsolete and has been remapped to RXCUI = 1116191

◆ getRxcuiStatus(1805014)

RxCUI = 1805014 has been quantified and is remapped to multiple concepts
New RxNav support for obsolete concepts

♦ New Status tab in RxNav
  - Displays the canonical representation and metadata of all active and inactive RxNorm concepts
  - Powered by the *RxcuiHistory* API
**Active Concept**

### Properties

<table>
<thead>
<tr>
<th>Title</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RxCUI</td>
<td>1668240</td>
</tr>
<tr>
<td>Concept Name</td>
<td>Azithromycin 500 MG Injection</td>
</tr>
<tr>
<td>Pack Alias</td>
<td></td>
</tr>
<tr>
<td>Term Type</td>
<td>SBD</td>
</tr>
<tr>
<td>Dose Form</td>
<td>Injection</td>
</tr>
<tr>
<td>Dose Form RxCUI</td>
<td>1649574</td>
</tr>
<tr>
<td>Multiple Ingredient</td>
<td>No</td>
</tr>
<tr>
<td>Branded</td>
<td>Yes</td>
</tr>
<tr>
<td>Quantity Factor</td>
<td></td>
</tr>
<tr>
<td>Quality Distinction</td>
<td></td>
</tr>
<tr>
<td>SCD</td>
<td>Azithromycin 500 MG Injection</td>
</tr>
</tbody>
</table>

### Ingredients

Active Ingredient (AI) & Active Molecule (AM), as well as non-normalized numerator and denominator values, will be available in the future.

<table>
<thead>
<tr>
<th>Base</th>
<th>AI</th>
<th>AM</th>
<th>BoSS</th>
<th>Numerator Value</th>
<th>Numerator Units</th>
<th>Denominator Value</th>
<th>Denominator Units</th>
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<tbody>
<tr>
<td>Azithromycin</td>
<td>Azithromycin</td>
<td>500</td>
<td>MG</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</table>

### Metadata

<table>
<thead>
<tr>
<th>Title</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Status</td>
<td>Active</td>
</tr>
<tr>
<td>Source</td>
<td>RXNORM</td>
</tr>
<tr>
<td>Start Date</td>
<td>11-2015</td>
</tr>
<tr>
<td>End Date</td>
<td></td>
</tr>
<tr>
<td>Is Current</td>
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</table>
### Retired Concept

#### Properties

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<th>Value</th>
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<tbody>
<tr>
<td>RxCUI</td>
<td>857094</td>
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<tr>
<td>Concept Name</td>
<td>Acetaminophen 325 MG / Hydrocodone Bitartrate 5 MG Oral Tablet</td>
</tr>
<tr>
<td>Pack Alias</td>
<td></td>
</tr>
<tr>
<td>Term Type</td>
<td>SBD</td>
</tr>
<tr>
<td>Dose Form</td>
<td>Oral Tablet</td>
</tr>
<tr>
<td>Dose Form RxCUI</td>
<td>317541</td>
</tr>
<tr>
<td>Multiple Ingredient</td>
<td>Yes</td>
</tr>
<tr>
<td>Branded</td>
<td>Yes</td>
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<tr>
<td>Quantity Factor</td>
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<tr>
<td>Quality Distinction</td>
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</tr>
<tr>
<td>SCD</td>
<td>Acetaminophen 325 MG / Hydrocodone Bitartrate 5 MG Oral Tablet</td>
</tr>
</tbody>
</table>

#### Ingredients

Active Ingredient (AI) & Active Moiety (AM), as well as non-normalized numerator and denominator values, will be available in the future.

<table>
<thead>
<tr>
<th>Base</th>
<th>AI</th>
<th>AM</th>
<th>Base Scale System Source</th>
<th>Numerator Value</th>
<th>Numerator Units</th>
<th>Denominator Value</th>
<th>Denominator Units</th>
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</thead>
<tbody>
<tr>
<td>Hydrocodone</td>
<td>Hydrocodone</td>
<td>Bitartrate</td>
<td></td>
<td>5</td>
<td>MG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Acetaminophen</td>
<td></td>
<td></td>
<td>325</td>
<td>MG</td>
<td></td>
<td></td>
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#### Metadata

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<th>Value</th>
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</thead>
<tbody>
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<td>Status</td>
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<tr>
<td>Source</td>
<td>RXNORM</td>
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<tr>
<td>Start Date</td>
<td>08-2009</td>
</tr>
<tr>
<td>End Date</td>
<td>02-2013</td>
</tr>
<tr>
<td>In Current</td>
<td>False</td>
</tr>
</tbody>
</table>
## Hyperlipemia [RxCUI = 1023000]

### Non-RxNorm Concept

#### Properties

<table>
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<tr>
<th>Title</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RxCUI</td>
<td>1023000</td>
</tr>
<tr>
<td>Concept Name</td>
<td>Hyperlipemia</td>
</tr>
<tr>
<td>SCD</td>
<td></td>
</tr>
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</table>

#### Metadata

<table>
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<th>Value</th>
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<tbody>
<tr>
<td>Status</td>
<td>Non-RxNorm</td>
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<tr>
<td>Source</td>
<td>NDFRT</td>
</tr>
<tr>
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<td>End Date</td>
<td>09-2017</td>
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<tr>
<td>Is Current</td>
<td>False</td>
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</table>
Summary

◆ The update model of the RxNorm dataset is biased towards e-prescribing, and does not fully support analytics.

  ● Obsolete NDCs are removed from the set of NDCs curated by RxNorm.
  ● Obsolete RxCUIs and relations persist.
    - No metadata for obsolete RxCUIs.
Summary

- Support for analytics ("Time Machine") built through the RxNorm API
  - NDC
    - NDC → RxCUI(s) + metadata
      - For each NDC ever curated by RxNorm
    - RxCUI → all NDCs ever associated with this RxCUI
      - Including through remapping of RxCUIs
  - RxCUI
    - RxCUI → status (including remapping)
    - RxCUI → definitional properties and metadata (for all active and obsolete RxNorm concepts)

- Displayed in RxNav (new Status tab)
- Canonical representation of RxNorm drugs
  - Can also support a similarity function for drugs
Acknowledgments

◆ RxNav team (development)
  - Lee Peters
  - Richard Rice

◆ External collaborators (use cases)
  - \textit{getRxcuiStatus}
    - Indian Health Service
    - Value Set Authority Center
  - \textit{getNDCStatus}
    - Boston Children’s Hospital/Harvard Medical School (Dr. Ken Mandl)
  - \textit{getAllHistoricalNDCs, RxcuiHistory}
    - Greater Plains Collaborative PCORnet (Dr. Jim Campbell)
Medical Ontology Research

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