The problem – Incomplete or missing information in drug package inserts

“Both clopidogrel and ticlopidine significantly inhibited the CYP2B6-catalyzed bupropion hydroxylation. Patients receiving either clopidogrel or ticlopidine are likely to require dose adjustments when treated with drugs primarily metabolized by CYP2B6.” [1]

Search bupropion drug package inserts for “clopidogrel”
- No mention at all in Aplenzin ER insert [2]
- Mention in the generic tablet insert [3], but refers only to hypothetical interaction

 Aren’t package inserts for regulatory purposes only?
- No – they are primarily intended to be a reference for prescribing clinicians [11]

Who reads the package insert anyway?
- 14% of prescribers that were surveyed reported using the package insert for information on drug-drug interactions (DDIs) [12]
- Also, we have found that the agreement among drug information databases on DDIs is strongly correlated with mention in the package insert

So what?

The PI for citalopram [7] notes age-related pharmacokinetic changes
“…subjects ≥ 60 years of age were compared to younger subjects in two normal volunteer studies. In a single-dose study, citalopram AUC and half-life were increased in the elderly subjects by 30% and 50%, respectively”

However, clearance (Cl) would be the preferred measure of age-related change – is there literature on this?
- Yes! [8-10]

How can Semantic Web technology help address this problem?

Using the Structured Product Label (SPL) standard and Linked Data to provide a “mash-up” view of package inserts that alerts the reader to evidence that is more up-to-date or completes claims in the drug package insert:

1. Identify the types of scientific claims that belong in each section of a Structured Product Label (http://pur.org/net/nlp/repository/linkedSPL)

   1. SPL Header
      - FDA/USP Unique Identifier (identifier of the active ingredients)
      - LOINC Section headings
      - content (unstructured)
   2. Extract claims from linked data versions of drug information sources
      - ClinicalTrials.gov
      - PubMed
      - DrugBank
      - Drug Interaction Knowledge Base
   3. Combine claims with provenance data into a new linked data set and create views

W3C HCLSIG Scientific Discourse Use Case proof of concept: http://dbmi-icde-01.dbmi.pitt.edu/dikb-evidence/outfits/