The DIKB is an evidential system

- All assertions are linked to their evidence for or against:
  
  \((\text{FLUCONAZOLE inhibits CYP2C9})\)

- helps assess credibility, draw attention to errors, and establish confidence
All assumptions are linked to evidence

Evidence item 'E'

supports

(Drug-X primary-clearance-enzyme CYP3A4)

assumes

(Drug-Y in-Vivo-selective-inhibitor CYP3A4)

- Enables the system to identify when assumptions are no longer valid
- Helps identify poor uses of evidence
All evidence is classified using a study taxonomy

- Oriented toward user confidence assignment
- 36 types over several sub-hierarchies

A DDI clinical trial
  ...randomized
  ...non-randomized
  ...

A non-traceable statement
  ...in drug product labelling
  ...

A metabolic enzyme inhibition experiment
  ...focusing on CYP450 enzymes
  ...done in human liver microsomes
  ...
Basic quality standards are defined for every evidence type

- Example: Pharmacokinetic clinical trials
  - adequate duration and magnitude of dosing
  - patient genotype/phenotype is noted if the target enzyme is polymorphic

- Example: in vitro enzyme metabolism identification
  - human hepatocyte or recombinant CYP450
  - 'selective' inhibitors and 'probe' substrates
This DIKB's architecture helps identify evidence use strategies

- What evidence is sufficient to justify that a drug possesses certain mechanistic properties in vivo?

- What evidence-use strategy enables the system to make the best predictions?

- How do these predictions compare with the most rigorous treatment of evidence possible?