

Pipeline for knowledge curation and decision support in pharmacogenomics

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Motivation

The introduction of whole-genome sequencing in clinical practice has opened a path for preemptive pharmacogenomic (PGx) testing. The Pharmacogenomics Knowledgebase (PharmGKB) distributes clinical dosing guidelines, and provides a link between these guidelines and genomic variants that can be used for automated PGx decision support. Before applying this knowledge in healthcare, it is necessary to adapt and harmonize the guidelines to local clinical practices. We describe a pipeline for translating knowledge from knowledge databases such as PharmGKB into a system that is valid for PGx decision support in our clinic.

Knowledge curation

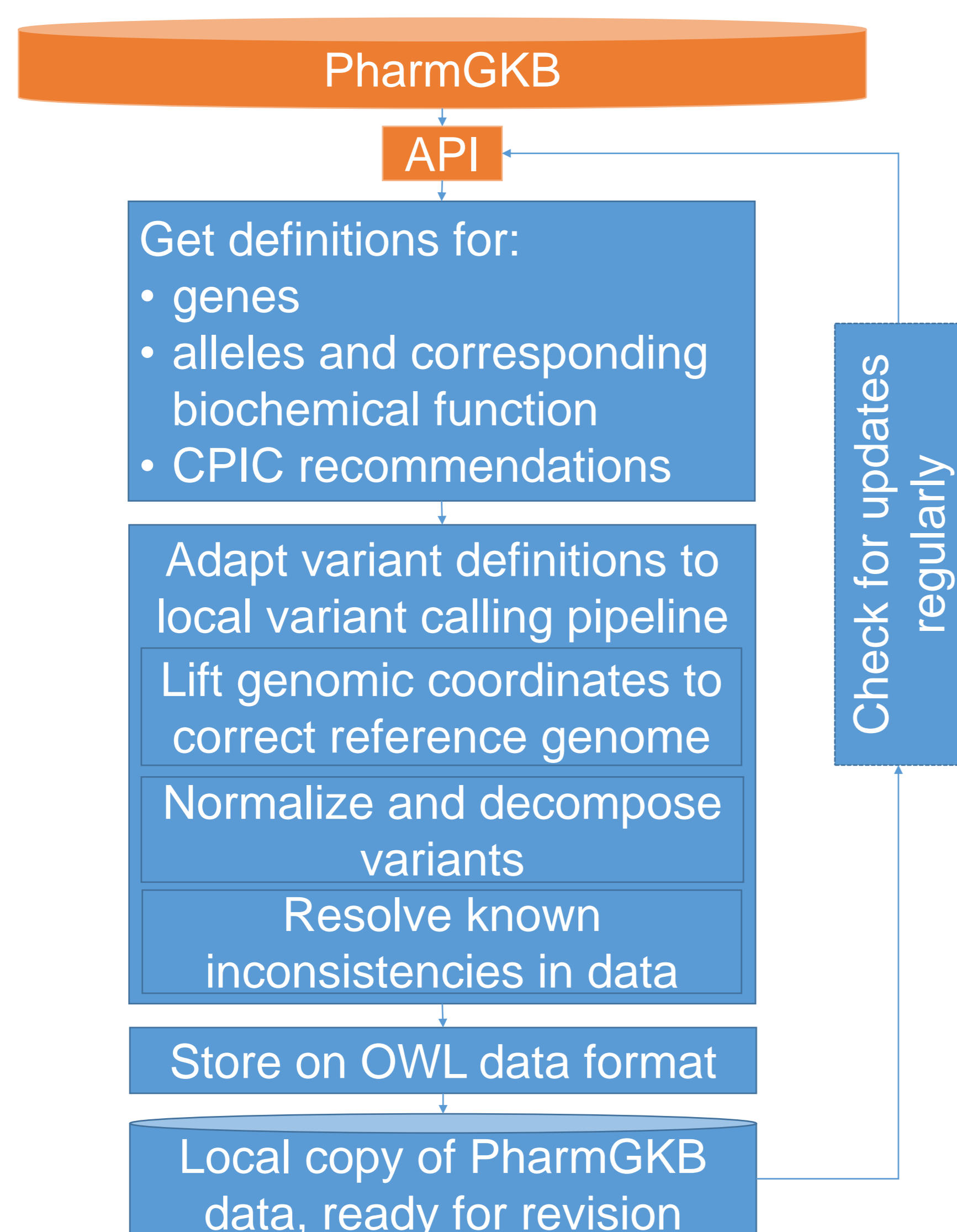


Figure 1: PGx knowledge is downloaded via api.pharmgkb.org, and automatically adapted to the knowledge curation pipeline of our clinic. Internationally recognized PGx guidelines are provided by the Clinical Pharmacogenetics Implementation Consortium (CPIC)

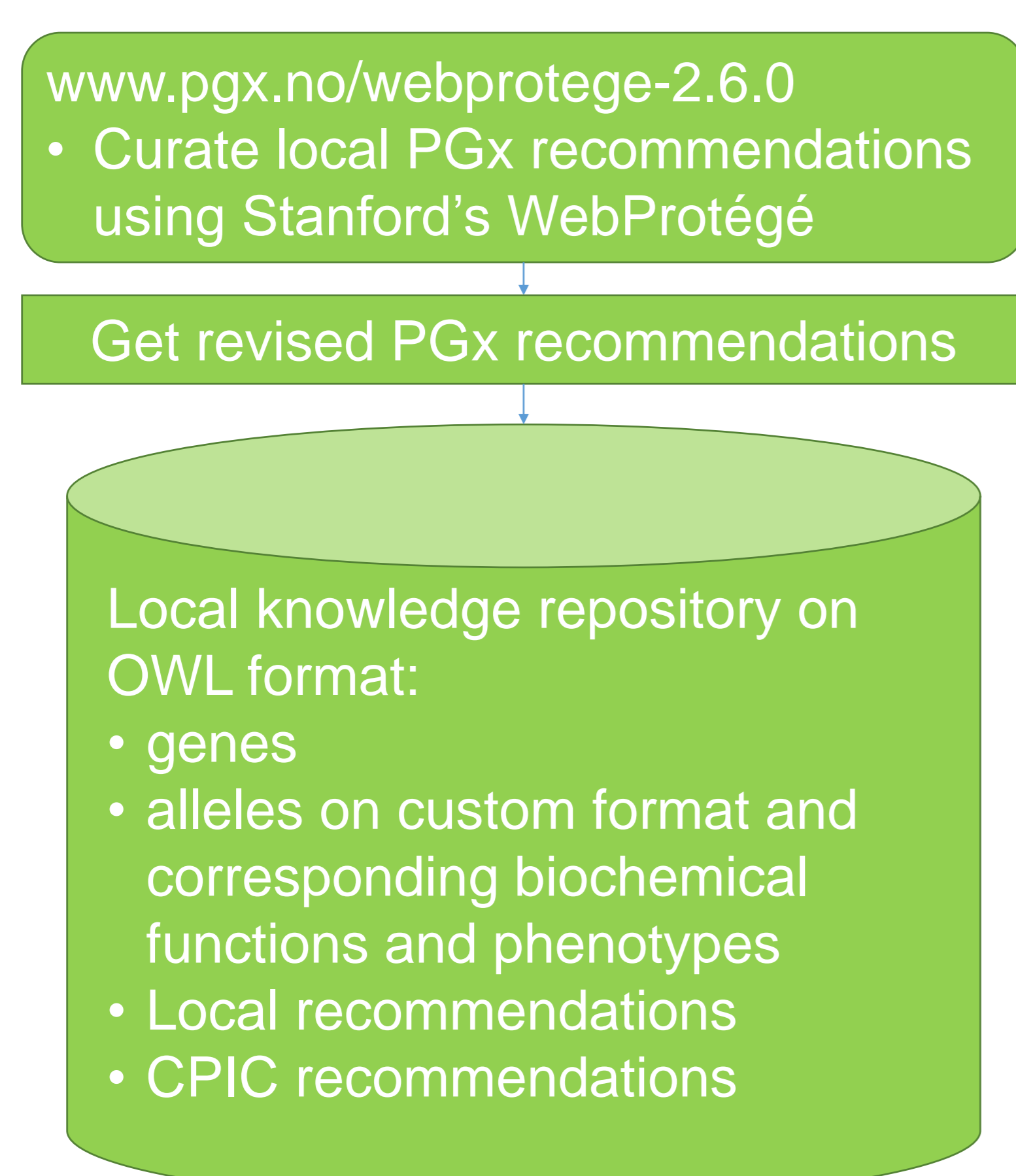


Figure 2: PGx knowledge is manually evaluated, curated and translated to adhere to the standard operating procedures of our clinic. Currently, guidelines for the drugs azathioprine and clopidogrel are ready for use in the clinic. An advantage of the Web Ontology Language (OWL) for knowledge curation, is that the PGx medication recommendation for a patient can be obtained directly by Description Logics (DL) queries via the OWL API.

Decision support

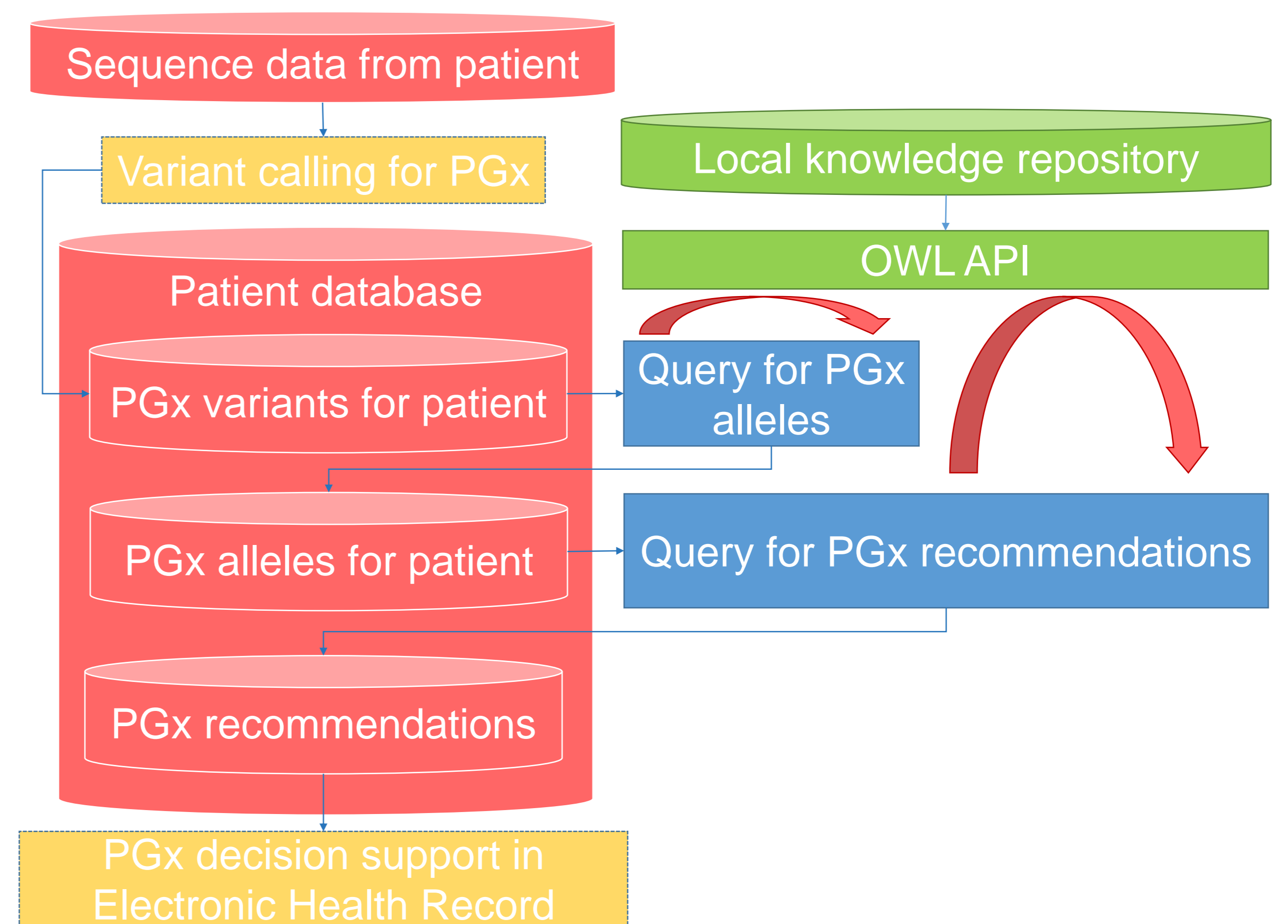


Figure 3: We are planning to adapt our variant calling to PGx. Appropriate PGx alleles and PGx recommendations are acquired by DL queries to the curated knowledge repository. A PGx decision support module for communicating PGx recommendations to the patient at the time of drug prescription is also being developed.

Example

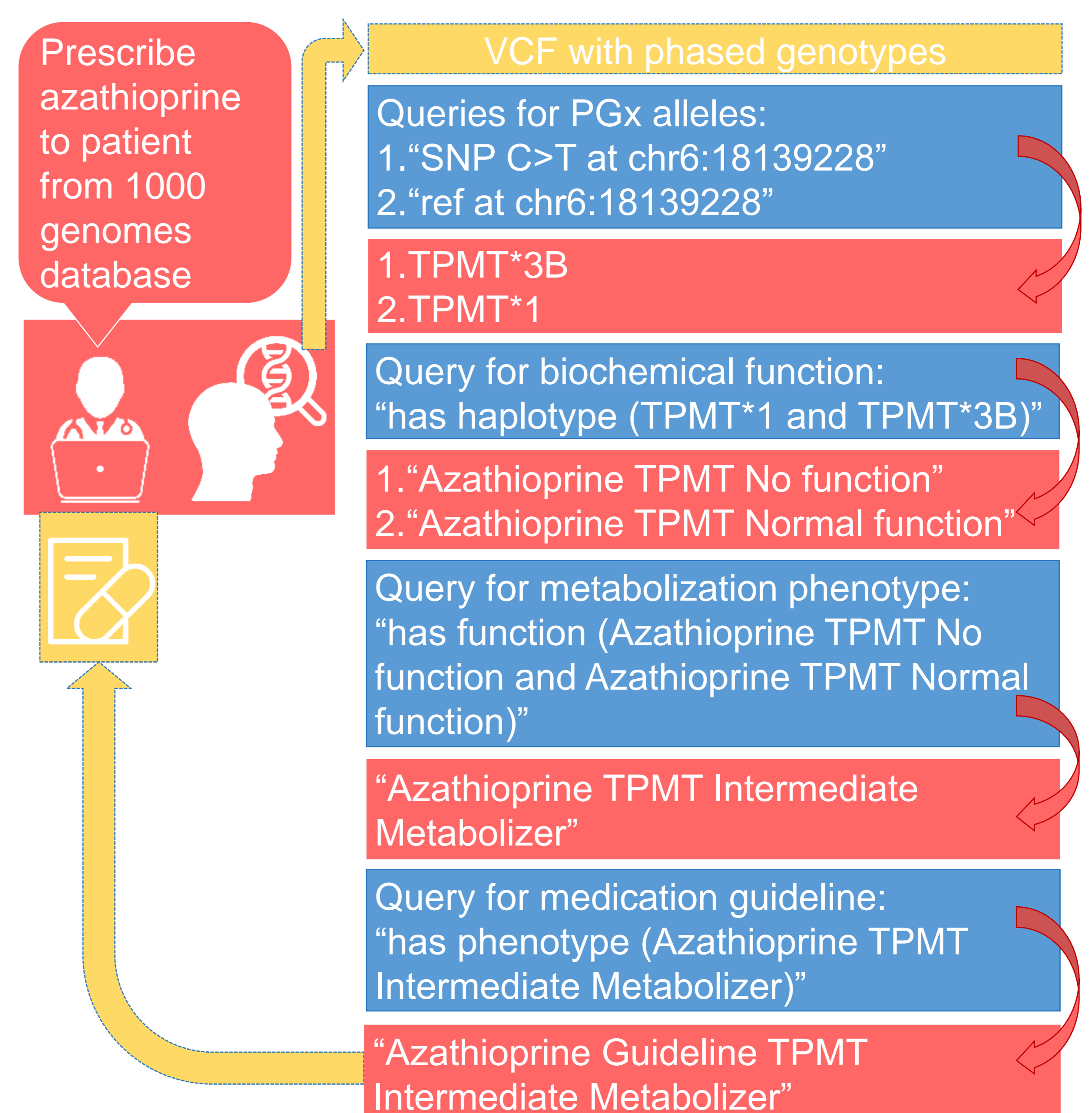


Figure 4: Prescription of azathioprine. The genotype and allele definitions are simplified for the sake of presentation. Human readable queries are translated into DL queries to the locally curated OWL ontology

Next steps

- Modify our standard variant calling pipeline to meet requirements of PGx analysis
- Develop a decision support module in the patient health record, using the openEHR platform
- Develop a process for quality assurance and accreditation.
- Expand database to include locally adapted guidelines for all drugs with CPIC guidelines