

The NIH Pharmacogenomics Research Network (PGRN)* is making comments on the Genetic Testing Registry (GTR) after consultation with our membership and other leaders in the genetics community. NIH's vision of Personalized Medicine includes a prominent emphasis on pharmacogenomics, and the GTR plans to include pharmacogenomic tests. The PGRN has the expertise needed to include pharmacogenomic tests in the GTR.

The PGRN is an interdisciplinary network with a core mission to identify and understand genomic variation that contributes to drug responses, and ultimately to make that knowledge and its impact available for translation into clinical practice. The PGRN works closely with PharmGKB** (www.pharmgkb.org), a knowledge base that serves as the premier information source in the field. Part of PGRN's mission is to facilitate the use of genomic data in personalized medicine and routine clinical practice.

The Clinical Pharmacogenetics Implementation Consortium (CPIC) was started in 2009 and consists of PGRN members, PharmGKB staff, and external experts in pharmacogenetics and pharmacogenomics. Some areas of pharmacogenomics have advanced to the point that pharmacogenomic tests are in use in clinical practice. CPIC was created to establish a framework for understanding levels of evidence needed to incorporate pharmacogenetics to clinical practice, and to address the need to provide very specific guidance to clinicians and laboratories so that pharmacogenetic tests can be used wisely in the clinic.

CPIC shares its expertise to create, curate, review, and update written summaries and recommendations for implementing specific pharmacogenomic tests and practices. Summaries are gene-centric, drug-centric, or both. A formalized process for evaluating levels of evidence (linking gene variation to phenotypes) and strength of recommendations (linking genotypes to drug dosing recommendations) is incorporated into CPIC gene/drug reviews. Current CPIC focus is on genotyping tests that are already in use in clinical settings, with comprehensive evaluations and curation of methods for pharmacogenetic testing. CPIC guidelines will be published in their entirety on www.pharmgkb.org and regularly reviewed and updated on-line, and in addition will be peer-reviewed as publications. CPIC will link its guidelines to NCBI's GeneTests Laboratory Directory section for updates on laboratories offering clinical pharmacogenetic tests, and CPIC will provide the "gene reviews" content. As NIH's GTR takes on this Laboratory Directory function of GeneTests, we propose that GTR include links to CPIC gene/drug reviews, and CPIC's gene/drug reviews would of course link to the GTR.

CPIC guidelines include extensive details on gene-specific interpretation of genetic tests, and how to translate gene-specific information into drug-specific information on dosing and/or drug choice. To generate these peer-reviewed clinical guidelines, annotated to individual genes and being generated on a per-gene basis, takes considerable effort. Pharmacogenetic gene-specific knowledge is best curated on a consensus basis and evaluated by experts, and such expertise cannot (and should not) be duplicated among various genetic test registry initiatives. It should be noted that currently only a modest number of pharmacogenes have sufficient evidence that they are offered in a CLIA-approved environment, and of these, only a few (< 10) are presently

deemed to have sufficient evidence that they should be used routinely for drug prescribing. CPIC members feel it is important not to endorse pharmacogenetic tests that do not yet have sufficient evidence for their clinical use. It is important to recognize the substantial time and effort that is required in curating gene test-related information so that it is clinically valuable; it is likewise time-consuming but an important service to the public to filter out those pharmacogenetic tests that falsely claim to have clinical utility.

PGRN's CPIC therefore proposes to take the lead to provide expertise in pharmacogenomic test interpretation, and would like to see its gene/drug specific guidelines linked with GTR, as appropriate. We are eager to participate in workshops and meetings to improve the utility of the GTR as it moves forward. To discuss this further, please contact the CPIC Chair, Mary Relling at mary.relling@stjude.org.

*The NIH PGRN was formed in 2000 to enable a network of multi-disciplinary research groups to conduct studies addressing research questions in pharmacogenetics and pharmacogenomics. The PGRN has support from NIGMS, NHLBI, NCI, NIDA, NIMH, NIAMS, NICHD, NHGRI, and ORWH. One major long-term goal is to translate this knowledge and identify safe and effective drug therapies designed for individual patients.

** PharmGKB has a highly skilled group of curators and contributors that have built and continually update extensive annotations for genes that are particularly important for pharmacogenetics. The annotation on very important variants in pharmacogenes (VIPs) is particularly valuable for interpreting pharmacogenetic test results being offered by clinical laboratories.