

**From:** Relling, Mary [mailto:Mary.Relling@STJUDE.ORG]  
**Sent:** Wednesday, September 21, 2011 3:14 PM  
**To:** Genetic Testing Registry (NIH/OD/OSP)  
**Cc:** Roden, Dan; Long, Rochelle (NIH/NIGMS) [E]; 'Teri Klein'  
**Subject:** Request for comments on GTR

Amy P. Patterson, M.D.  
Associate Director for Science Policy  
NIH by mail to the Office of Biotechnology Activities  
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Re: GENETIC TESTING REGISTRY (GTR) REQUEST FOR COMMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
National Institutes of Health  
Request for Comments Under the Paperwork Reduction Act, Section 3506  
*Proposed Collection: Title: The Genetic Testing Registry*  
*Type of Information Collection Request: New collection*

Dear Dr. Patterson,

This letter is in response to the July 21, 2011, Request for Comments on the design and implementation of the forthcoming 'Genetic Testing Registry (GTR)' by the National Institute of Health (NIH) [FR Doc. 2011-18970 Filed 7-26-11; 8:45 am].

A previous letter (August 2010) was submitted to the GTR working group on behalf of The Clinical Pharmacogenetics Implementation Consortium (CPIC) of the NIH's Pharmacogenomics Research Network (PGRN), which introduced the CPIC and detailed our interest in collaboration with the GTR. As mentioned, the CPIC evaluates current levels of evidence for specific pharmacogenetic gene/drug pairs and publishes clinical practice guidelines to facilitate the practical implementation of clinical pharmacogenetic testing. CPIC guidelines are published in their entirety at [www.pharmgkb.org](http://www.pharmgkb.org) and are periodically updated online based on new developments in the field. In addition, all guidelines are peer-reviewed for publication; so far, all published in the journal *Clinical Pharmacology & Therapeutics*.

A published overview of the CPIC and the currently available CPIC practice guidelines are listed below:

1. Relling MV, Klein TE. CPIC: Clinical Pharmacogenetics Implementation Consortium of the Pharmacogenomics Research Network. *Clin Pharmacol Ther.* 2011 Mar;89(3):464-7.
2. Relling MV, Gardner EE, Sandborn WJ, Schmiegelow K, Pui CH, Yee SW, Stein CM, Carrillo M, Evans WE, Klein TE; Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium guidelines for thiopurine methyltransferase genotype and thiopurine dosing. *Clin Pharmacol Ther.* 2011 Mar;89(3):387-91.
3. Scott SA, Sangkuhl K, Gardner EE, Stein CM, Hulot JS, Johnson JA, Roden DM, Klein TE, Shuldiner AR. Clinical Pharmacogenetics Implementation Consortium guidelines for cytochrome

P450-2C19 (CYP2C19) genotype and clopidogrel therapy. *Clin Pharmacol Ther.* 2011 Aug;90(2):328-32.

4. Johnson JA, Gong L, Carrillo M, Gage BF, Scott SA, Stein CM, Anderson JL, Kimmel SE, Lee MT, Pirmohamed M, Wadelius M, Klein TE, Altman RB. Clinical Pharmacogenetics Implementation Consortium guidelines for CYP2C9 and VKORC1 genotypes and warfarin dosing. *Clin Pharmacol Ther*, in press.

Our primary suggestions have to do with clarifying the role that CPIC could play in ensuring GTR's point (3) *enhancing the quality, utility, and clarity of the information to be collected*:

1. In addition to providing clinical practice recommendations based on pharmacogenetic test results, all CPIC guidelines also include a list of possible testing options, including both molecular test manufacturers and CLIA-approved testing providers, when known. These lists are currently available via a link to testing sites on [www.pharmgkb.org](http://www.pharmgkb.org). Given this is also a planned function of the GTR, there is an excellent opportunity for synergy between the CPIC guidelines and the clinical pharmacogenetic testing menus housed within the GTR. As such, we would like to link the "Available Genetic Test Options" sections of the existing and forthcoming CPIC practice guidelines with the GTR.
2. CPIC practice guidelines are authored by experts, follow a standard format, peer reviewed, evidence-based with standard scales for grading evidence and for grading drug dosing recommendations, freely available, and updated, they represent state-of-the-art "gene reviews" guidelines for pharmacogenes. We suggest that the appropriate CPIC guidelines be linked from the relevant pharmacogenetic 'Test' pages of the GTR, that they constitute the "GeneReviews" link for pharmacogenes, and that they be available via the "practice guideline" column planned for the GTR. The link should probably go to the guideline's posting on [www.pharmgkb.org](http://www.pharmgkb.org), which will include the published material in CPT and any updates.
3. In an effort to decrease the burden of data entry time, the GTR proposes to transfer test and laboratory information from the NCBI's GeneTests database to the GTR. As this will facilitate less time required for data entry by providers and manufacturers, we certainly encourage this action. However, given that the expert-authored GeneReviews for known genetic disorders do not currently include drug response phenotypes, pharmacogenes, or any other pharmacogenetic traits, the CPIC would like to work directly with the GTR and GeneTests to review its "phenotype" terms so that we can ensure users may search by drugs for drug-related pharmacogenes. The CPIC has a variety of experts in its membership willing to participate in this initiative.
4. CPIC encourages regular and current updates (and will do so through the Pharmacogenomics Knowledge Base (PharmGKB), and we support GTR having regular (at least every 2 years) reviews and updates by participating laboratories making entries for their tests.
5. CPIC does NOT recommend listing any test pricing, particularly since this can be negotiated. Links to laboratory websites will be sufficient for the marketplace to decide.
6. CPIC recognizes PharmGKB as an authoritative, community-driven, neutral body and convener/aggregator in the pharmacogenetics field, and bridges a gap (as do other resources) as a translator between "research results" and "implementation".
7. CPIC also supports internet URLs in the GTR that provide quality information. CPIC discourages any inappropriate "marketing" of genetic tests. Any links in the GTR must clearly distinguish neutral scholarly parties from company advertising.
8. Given some of the requested information directly overlaps with the peer-reviewed content of the GeneReviews, it seems appropriate to populate the requested 'Indication' information with previously authored GeneReviews text; for pharmacogenes, CPIC offers assistance in populating the "indications" field with appropriate drug terms.

9. The 'Methodology' section requests information on 'Test Targets', specifically defining gene symbols, reference sequences, interrogated exons, and applicable variants. Although this information is very important, it is possible that different laboratories use different reference sequences for the same molecular targets as well as different nomenclature systems for sequence alterations (e.g., HGVS vs. historical/'legacy' nomenclature; nucleotide vs. protein alterations, etc.). As such, it may be challenging to interpret these different test submissions by clinicians looking for specific genetic tests. A mechanism in the GTR that allows for side-by-side comparison of tests between different laboratories may be useful for this and other related issues.
10. The GTR has the potential to fulfill its goals of publicly sharing information about the availability and utility of genetic tests and providing an information resource for the public, health care providers, patients, and researchers. Its success will be predominantly driven by the degree of data submission volunteered by genetic testing providers. Therefore, designing the GTR with these entities in mind will only benefit this public resource and help facilitate continued and accurate data entry. Including functions in the GTR that can benefit the genetic testing community, such as tools for mutation nomenclature and sequence variation interpretation (e.g., intuitive links to the Human Gene Mutation Database (HGMD), the Database of Genomic Variants (DGV), DECIPHER, PharmGKB, and the forthcoming NCBI ClinVar database, etc.), has the potential to incentivize the laboratories and actual individuals who will be carrying the burden of data entry.

In an effort to facilitate continued collaboration and synergy between the CPIC and the GTR, particularly as it relates to the clinical pharmacogenetic testing resources of the GTR, we would be happy to participate in any meetings or workshops to improve the GTR as it is implemented. To discuss this further, please contact me at [mary.relling@stjude.org](mailto:mary.relling@stjude.org).

Sincerely,

Mary Relling, on behalf of the Clinical Pharmacogenetics Implementation Consortium (CPIC)  
[http://www.pharmgkb.org/contributors/consortia/cpic\\_profile.jsp](http://www.pharmgkb.org/contributors/consortia/cpic_profile.jsp)

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