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# Association for Molecular Pathology Position Statement: Best Practices for Clinical Pharmacogenomic Testing – September 4, 2019

***Background:***

Pharmacogenomic testing provides information to predict the likelihood of medication response and/or risk for adverse medication reactions based on a person's genetic makeup. Healthcare providers may use information from pharmacogenomic testing to assist in medication and/or dosing decisions. Some examples include choosing a drug that may have better efficacy, avoiding drugs with a high risk of toxicity or adverse drug reaction such as hypersensitivity, adjusting the dose of a drug, or determining when closer monitoring is needed[1].

The field of pharmacogenomics is steadily growing, and the FDA has already approved the inclusion of pharmacogenomic information in the labels of hundreds of medications[2]. As the prevalence of pharmocogenetic testing continues to increase, so will the need for laboratory professionals to translate genetic laboratory results to healthcare providers who make prescribing decisions for patient care. Pharmacogenomic tests that are offered clinically should demonstrate evidence of clinical validity before being offered to patients, the same standard as for other practices of medicine. Such evidence may be established and/or demonstrated through peer-reviewed literature, clinical practice guidelines, and/or FDA drug labels.

One organization that has established levels of evidence for pharmacogenomic tests based on literature review is the Clinical Pharmacogenetics Implementation Consortium (CPIC)[3]. CPIC is an international consortium of individuals with the goal of facilitating the use of pharmacogenomic tests for patient care. CPIC creates and curates peer-reviewed, evidence-based, updatable, and detailed gene/drug clinical practice guidelines. AMP has endorsed CPIC's Term Standardization for Clinical Pharmacogenetics Test Results Project[4] and encourages the use of CPIC's gene-drug practice guidelines.

To build upon these guideline-development and evidence-curation efforts, a working group of AMP leaders examined the current environment of pharmacogenomic testing and determined that clinically meaningful pharmacogenomic tests can improve patient care and professional practice, provided certain conditions are met.

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[1] https://www.fda.gov/drugs/science-research-drugs/pharmacogenomics-overview-genomics-and-targeted-therapy-group
[2] https://www.fda.gov/drugs/science-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling
[3] https://cpicpgx.org/
[4] https://cpicpgx.org/endorsements/

**Recommendations**

**AMP recommends that laboratories providing pharmacogenomic tests adhere to the following conditions to ensure clinical pharmacogenomic testing best practices to promote patient access and improved care.**

- **All health-related pharmacogenomic claims must have well-established clinical validity.** The drug-gene association must be robust and supported by strong scientific evidence in the peer-reviewed literature, in the FDA-approved drug label, and/or in clinical practice guidelines, such as those created by CPIC.

- **The pharmacogenomic testing provider must comply with the CLIA statute and regulations, as is required for all other clinical laboratory tests, including having documented analytical validity, a robust quality management system, and appropriately licensed or credentialed laboratory personnel.** Tests must be verified under the supervision of, and interpreted and reported by, board-certified molecular laboratory professionals. Additionally, as required by CLIA, details regarding analytical methodology, validity, and quality should be readily available to the healthcare providers upon request.

- **The pharmacogenomic test report should be comprehendible by healthcare providers without medical genetics or pharmacogenomics training and include the interpretation of the findings, the significance of the results, as well as the limitations of the test.** Pharmacogenomic testing provides the greatest clinical benefit to patients when the healthcare provider is able to easily determine when an actionable prescribing change and/or treatment decision is indicated by a patient's genotype. Including information regarding the test's interpretation in the laboratory report is required or recommended by federal and accrediting agencies[5,6,7]. AMP strongly supports the practice of including the following information in the test report within the interpretation of the findings and the significance of the pharmacogenomic test results:
    - A statement of the metabolizer status determined by the genotype for the genes that affect drug metabolism;
    - A list of the drugs for which responsiveness may be affected by the genotype;
    - A generalized statement to alert healthcare providers when alternate dosage or drug treatment may be considered based on the results;
    - A list of resources and references that the healthcare provider can utilize to learn more about the genotyping result, the drug-gene association, and how to incorporate the result into actionable decisions. These resources can include pointing healthcare providers to CPIC guidelines and/or peer-reviewed literature.

- **AMP strongly recommends that patients should not change their treatment plan without first talking to their healthcare provider**. Patients currently may have direct access to their laboratory test results. Any result of a pharmacogenomic test should be discussed with the patient's healthcare provider to determine whether changes to the patient's medication plan are recommended.

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[5] CLIA - 42 CFR §493.1291 (e)

[6] The CDC MMWR "Good Practices for Molecular Genetic Testing for Heritable Diseases and Conditions" https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5806a1.htm

[7] CAP Accreditation Program Molecular Pathology Checklist http://elss.cap.org/elss/ShowProperty?nodePath=/UCMCON/Contribution%20Folders/DctmContent/education/OnlineCourseContent/2017/LAP-TLTM/checklists/cl-mol.pdf

***About AMP***

*The Association for Molecular Pathology (AMP) is an international medical and professional association representing approximately 2,500 physicians, doctoral scientists, and medical technologists who perform or are involved with laboratory testing based on knowledge derived from molecular biology, genetics, and genomics. Membership includes professionals from the government, academic medicine, private and hospital-based clinical laboratories, and the in vitro diagnostic industry.*

*The AMP Pharmacogenomics (PGx) Working Group is currently developing a series of evidence-based expert consensus opinion recommendations for alleles that should be included during genotyping for clinical pharmacogenomic tests. To date the PGx Working Group, in collaboration with organizational representatives from the College of American Pathologists (CAP) and the Clinical Pharmacogenetics Implementation Consortium (CPIC), has published recommendations for selection and genotyping of CYP2C19[8] and CYP2C9[9] alleles used in clinical assays. Additionally, there are currently 2 other expert opinion recommendations in development.*

[8] Pratt, V.M., Del Tredici, A.L., Hachad, H., et al. Recommendations for Clinical CYP2C19 Genotyping Allele Selection. *J. of Molecular Diagnostics*. 2018; 20(3): 269-276.

[9] Pratt, V.M., Cavallari, L.H., Del Tredici, A.L., et al. Recommendations for Clinical CYP2C9 Genotyping Allele Selection. *J of Molecular Diagnostics*. 2019; 21: 746-755. DOI: https://doi.org/10.1016/j.jmoldx.2019.04.003.