

Recommendations to facilitate design and implementation of clinical pharmacogenomic DPYD genotyping assays

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The Association for Molecular Pathology (AMP) has published consensus recommendations to aid in the design and validation of clinical DPYD genotyping assays, promote standardization of testing across different laboratories, and improve patient care.

The manuscript, "[DPYD Genotyping Recommendations](#): A Joint

Consensus Recommendation of the AMP, American College of Medical Genetics and Genomics (ACMG), Clinical Pharmacogenetics Implementation Consortium (CPIC), College of American Pathologists (CAP), Dutch Pharmacogenetics Working Group (DPWG) of the Royal Dutch Pharmacists Association, European Society for Pharmacogenomics and Personalized Therapy (ESPT), Pharmacogenomics Knowledgebase (PharmGKB), and Pharmacogene Variation Consortium (PharmVar)," was released online ahead of publication in *The Journal of Molecular Diagnostics*.

The AMP Clinical Practice Committee's Pharmacogenomics (PGx) Working Group was established to define the key attributes of pharmacogenetic alleles recommended for clinical testing, along with a minimum set of variants that should be included in clinical PGx genotyping assays. The new DPYD report is the latest in a series of recommendations developed by the AMP PGx Working Group to help standardize clinical testing for frequently used genotyping assays.

It builds on the earlier clinical genotyping recommendations for CYP3A4/CYP3A5, TPMT/NUDT15, CYP2D6, genes important for warfarin testing, CYP2C9, and CYP2C19. It is important for health care providers to implement the recommendations along with other relevant clinical guidelines, such as those issued by CPIC and DPWG, both of which have a primary focus on interpreting PGx test results and providing therapeutic recommendations for specific drug-gene pairs.

"Testing for variants in the DPYD gene can help identify individuals who may be at increased risk for severe fluoropyrimidine-related toxicity," said Victoria M. Pratt, Ph.D., Co-Chair of the AMP PGx Working Group, Director of the Scientific Affairs for Pharmacogenetics at Agena Bioscience, and Adjunct Professor of Clinical Pharmacology at Indiana University School of Medicine. "This new report is intended to improve clinical practice and facilitate standardization across clinical

laboratories and ensure that the appropriate variants are included in clinical PGx DPYD assays."

The AMP PGx Working Group used a two-tier categorization of variants recommended for inclusion, as with previous clinical PGx genotyping assay recommendations. The Tier 1 recommended variants were selected because they have a well-characterized effect on functional activity of the protein and/or gene expression, have an appreciable minor allele frequency in a population/ancestral group, have available reference materials for [assay](#) validation, and are technically feasible for clinical laboratories to interrogate using standard molecular testing methods.

The Tier 2 list of optional variants meet at least one, but not all, of the Tier 1 criteria. These recommendations for clinical genotyping assays do not include variants with an unknown effect on protein function or [gene expression](#). They are meant to be a reference guide and not a restrictive list.

"Over the past six years, the AMP PGx Working Group has developed an extensive series of joint consensus guidelines to promote genotype concordance and test standardization between laboratories for the PGx assays most commonly used in clinical practice," said Karen E. Weck, MD, Chair of the AMP PGx Working Group and Director of Molecular Genetics and Pharmacogenomics and Professor of Pathology & Laboratory Medicine and Genetics at the University of North Carolina at Chapel Hill. "We will continue to update the full series of recommendations as new data and reference materials become available."

More information: Victoria M. Pratt et al, DPYD Genotyping Recommendations: A Joint Consensus Recommendation of the Association for Molecular Pathology, American College of Medical Genetics and Genomics, Clinical Pharmacogenetics Implementation

Consortium, College of American Pathologists, Dutch Pharmacogenetics Working Group of the Royal Dutch Pharmacists Association, European Society for Pharmacogenomics and Personalized Therapy, Pharmacogenomics Knowledgebase, and Pharmacogene Variation Consortium, *The Journal of Molecular Diagnostics* (2024). [DOI: 10.1016/j.jmoldx.2024.05.015](https://doi.org/10.1016/j.jmoldx.2024.05.015)

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