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# Characterization of Reference Materials with an Association for Molecular Pathology Pharmacogenetics Working Group Tier 2 Status: *CYP2C9*, *CYP2C19*, *VKORC1*, *CYP2C* Cluster Variant, and *GGCX*

## *A GeT-RM Collaborative Project*

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Pharmacogenetic testing is increasingly available from clinical and research laboratories. However, only a limited number of quality control and other reference materials are currently available for many of the variants that are tested. The Association for Molecular Pathology Pharmacogenetic Work Group has published a series of papers recommending alleles for inclusion in clinical testing. Several of the alleles were not considered for tier 1 because of a lack of reference materials. To address this need, the Division of Laboratory Systems, Centers for Disease Control and Prevention—based Genetic Testing Reference Material (GeT-RM) program, in collaboration with members of the pharmacogenetic testing and research communities and the Coriell Institute for Medical Research, has characterized 18 DNA samples derived from Coriell cell lines. DNA samples were distributed to five volunteer testing laboratories for genotyping using three commercially available and laboratory developed tests. Several tier 2 variants, including *CYP2C9*13*, *CYP2C19*35*, the *CYP2C* cluster variant (rs12777823), two variants in *VKORC1* (rs61742245 and rs72547529) related to warfarin resistance, and two variants in *GGCX* (rs12714145 and rs11676382) related to clotting factor activation, were identified among these samples. These publicly available materials complement the pharmacogenetic reference materials previously characterized by the GeT-RM program and will support the quality assurance and

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quality control programs of clinical laboratories that perform pharmacogenetic testing. *(J Mol Diagn 2021, 23: 952–958; https://doi.org/10.1016/j.jmoldx.2021.04.012)*

Pharmacogenetic tests are used to help predict an individual's reaction to drugs by interrogating the presence or absence of known genetic variants in genes that encode drug-metabolizing enzymes, drug transporters, drug receptors, or targets of drug action. Physicians use the results of these tests to determine appropriate drugs and doses for their patients, which may help to prevent drug toxic effects or ineffective treatments.

Most genetic tests, including pharmacogenetic tests, are developed in individual laboratories, and are often referred to as laboratory developed tests or procedures. Clinical testing laboratories are required by regulations, accreditation standards, and professional guidance to use reference materials for assay development and validation, quality control, and proficiency testing[1–4] (American College of Medical Genetics and Genomics, *https://www.acmg.net/ACMG/Medical-Genetics-Practice-Resources/Technical_Standards_and_Guidelines.aspx*, last accessed February 24, 2020; Washington State Legislature, *http://app.leg.wa.gov/WAC/default.aspx?cite=246-338-090*, last accessed February 24, 2020; College of American Pathologists, *https://www.cap.org/*, last accessed February 24, 2020; New York State Clinical Laboratory Evaluation Program, *https://www.wadsworth.org/regulatory/clep*, last accessed February 24, 2020; Mortality and Morbidity Weekly Reports, *https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5806a1.htm*, last accessed March 24, 2021). The Centers for Disease Control and Prevention's (CDC's) Genetic Testing Reference Material (GeT-RM) program has led multiple efforts[5–7] to characterize publicly available DNA samples for use as reference materials for pharmacogenetic testing. Pharmacogenetic information and clinical pharmacogenetic testing are rapidly progressing, so the need for additional reference materials is also evolving.

The Association for Molecular Pathology (AMP) Pharmacogenetic Working Group developed a series of documents that recommend a minimum set of variant alleles to include in clinical pharmacogenetic test panels. The working group published recommendation documents for cytochrome P450 *CYP2C19*,[8] *CYP2C9*,[9] and variants in genes important for warfarin testing.[10] The AMP Pharmacogenetic Working Group uses a two-tier strategy and selection criteria for recommending pharmacogenetic variants for clinical testing. Tier 1 pharmacogenetic variant alleles are a minimum set of alleles recommended for clinical testing, whereas tier 2 variant alleles are additional alleles that do not meet all criteria for inclusion in tier 1 but that may be considered for clinical testing. Tier 1 recommended alleles are those that are i) well characterized and have a significant effect on the function of the protein and/or gene, leading to an alteration in the drug response phenotype; ii) have an appreciable minor allele frequency in a population/ethnicity group; and iii) have publicly available reference materials. Tier 2 variant alleles meet at least one but not all three of the tier 1 criteria. Tier 2 alleles may be moved to tier 1 if reference materials or additional information becomes available.

There were several alleles/variants in the previously published AMP recommendations that did not have available reference materials and thus were categorized as tier 2. In addition, there are alleles of other important pharmacogenes that have not been identified in previous GeT-RM pharmacogenetic studies.[5,6] In this study, the GeT-RM program and the genetic testing community collaborated to characterize genomic DNA samples from 18 publicly available cell lines for some of the previously identified tier 2 alleles: *CYP2C9*13*, *CYP2C19*35, VKORC1* warfarin-resistant variants (rs61742245 and rs72547529), and the *CYP2C* cluster variant rs12777823 that lacked available reference materials. In addition, *GGCX* variants (rs12714145 and rs11676382) were included as well because they have been associated with warfarin sensitivity.[11,12]

## Materials and Methods

### Cell Line DNA and Participating Laboratories

DNA from 18 cell lines were selected from the National Institute of General Medical Sciences and the National Human Genome Research Institute Repositories at the Coriell Institute for Medical Research (Camden, NJ) for this study based on data supplied by the authors or identified by searching the National Center for Biotechnology Information 1000 Genomes Project (*https://www.ncbi.nlm.nih.gov/variation/tools/1000genomes/*, last accessed January 27, 2020) for variants selected for this study. The five laboratories that participated in this follow-up study were as follows: Indiana University (laboratory 1), Mayo Clinic (laboratory 2), Medical College of Wisconsin/RPRD Diagnostics (laboratory 3), Children's Mercy Kansas City (laboratory 4), and University of Cincinnati (laboratory 5). These laboratories used a variety of methods or test platforms as described in this section.

### DNA Preparation

DNA was prepared from each of the selected cell lines by the Coriell Institute for Medical Research using Gentra/Qiagen Autopure (Valencia, CA) per manufacturer's instructions.

### Characterization Protocol

Each of the testing laboratories received one 10-μg aliquot of DNA from each of the cell lines that they volunteered to test. Each laboratory tested the samples using their standard methods and/or additional methods to resolve inconclusive genotype calls. The test platforms and genotyping assays used

**Table 1** Primer Sequences Used for Sanger Sequencing

| Gene/allele | dbSNP[†] | Forward primer | Reverse primer |
|---|---|---|---|
| *CYP2C19*35* | rs12769205 | 5′-TGGAAGAGGCCATTTCCC-3′ | 5′-CAAATTCCCTTGGCTCTCAG-3′ |
| *VKORC1* | rs72547529 | 5′-TGCTGTTGGATTGATTGAGG-3′ | 5′-GACATGGAATCCTGACGTGGC-3′ |
| *VKORC1* | rs61742245 | 5′- GTGCAACGACCCCGCGA-3′ | 5′- GAGATAATGGGCAGCACCTG-3′ |
| *CYP2C9*13* | rs72558187 | 5′-TTTGGCCTGAAACCCATAGT-3′ | 5′-CCATTTCTTTCCATTGCTGAA-3′ |
| *GGCX* | rs12714145 | 5′-TGTAAAACGACGGCCAGTCCGTACC CAGCTAGAAATGC-3′ | 5′-CAGGAAACAGCTATGACCGAACTACTGGGCTAAGGGGACT-3′ |
| *GGCX* | rs11676382 | 5′-TGTAAAACGACGGCCAGTAGAGGAGT TCTAAGGGGAGAGA-3′ | 5′-CAGGAAACAGCTATGACCAAGAAGAATGGCAGGAAAAGA-3′ |

Underlined nucleotides indicate the M13 tail.
[†]Single Nucleotide Polymorphism Database (dbSNP) (*https://www.ncbi.nlm.nih.gov/snp/*, last accessed January 14, 2021).

in the study are described below and in Supplemental Table S1. Two investigators (V.M.P. and L.V.K.) examined the data for quality and discordances and determined the consensus genotype. If discordances were noted, the participating laboratories were asked to reevaluate their data for the sample(s) in question to determine the cause of the inconsistency.

## Laboratory Developed Test for Taqman Platform (Laboratories 1, 2, and 4)

DNA samples were analyzed using QuantStudio 12K Flex software version 1.2.2 and subjected to Taqman allele discrimination using individual reagents or in a custom-designed OpenArray format (Thermo Fisher Scientific, Waltham, MA). Genomic DNA was amplified and mixed with dual-labeled oligonucleotides that hybridize to a specific target sequence. Hydrolysis by the 5′-3′ exonuclease activity of *Taq* polymerase releases the fluorescent reporter signal, permitting quantitative measurement of the accumulation of the PCR product via the fluorophore signal. Software used includes Genotyper version 1.3 (Thermo Fisher Scientific) and Alleletyper version 1.0 (Thermo Fisher Scientific) or a custom-designed proprietary GINger version 1.0 software (Mayo Clinic, Rochester, MN).

**Table 2** Consensus Genotypes for *CYP2C19*, *CYP2C9*, *VKORC1*, and *CYP2C* Cluster Variant

| Coriell no. | *CYP2C9* | *CYP2C19* | *VKORC1* rs61742245 (warfarin resistant) | *VKORC1* rs72547529 (warfarin resistant) | *CYP2C* cluster variant rs12777823 |
|---|---|---|---|---|---|
| HG01456 | *1/*1 | *1/*1 | G/G | **G/A** | G/G |
| HG01697 | *1/*1 | *17/*17 | **G/T** | G/G | G/G |
| HG01809 | *1/*13 | *2/*2 | G/G | G/G | **A/A** |
| HG02087 | *1/*13 | *1/*2 | G/G | G/G | **A/G** |
| HG02852 | *1/*11 | ***2/*35** | G/G | G/G | **A/A** |
| HG02861 | *1/*11 | ***2/*35** | G/G | G/G | **A/A** |
| HG03370 | *1/*1 | ***2/*35** | G/G | G/G | **A/A** |
| NA18877 | *1/*1 | *1/*17 | G/G | **G/A** | G/G |
| NA19075 | *1/*13 | *1/*2 | G/G | G/G | **A/G** |
| NA19327 | *1/*1 | ***2/*35** | G/G | G/G | **A/A** |
| NA19395 | *1/*1 | *1/*3 | **G/T** | G/G | G/G |
| NA19466 | *1/*9 | *1/*9 | G/G | **G/A** | G/G |

Alleles targeted in this study are highlighted in bold.

## PharmacoScan Array (Laboratory 3)

Following the manufacturer's instructions, genomic DNA was first amplified (DNA amplification and multiplex PCR). The amplified products were pooled, purified, fragmented, labeled, and hybridized to the PharmacoScan Array (Thermo Fisher Scientific) per the manufacturer's recommendations. Arrays were stained with a fluorescent antibody and scanned on the GeneTitan Multi-Channel Instrument (Thermo Fisher Scientific). Data were analyzed using the Axiom Analysis Suite 3.1 (Thermo Fisher Scientific). Analysis was performed using the commercially released allele translation table version r8. A complete list of all variants genotyped on the PharmacoScan Array (Thermo Fisher Scientific) in this analysis are described in the annotation file provided by the manufacturer (PharmacoScan_24F.na36. r8. a3. annot).

## Sanger Sequencing (Laboratories 1 and 5)

DNAs were Sanger sequenced for the specific variant using BigDye Terminator version 3.1 (Thermo Fisher Scientific) and run on 3500xL or 3930xL genetic analyzers (Thermo Fisher Scientific). The sequence of the primers used is provided in Table 1. Mutation Surveyor version 4.0.7 (SoftGenetics, State College, PA) or Sequencher version 5.0 (Gene Codes, Ann Arbor, MI) was used.

**Table 3** Consensus Genotypes for *GGCX*

| Coriell no. | *GGCX* rs12714145 (clotting factor activation) | *GGCX* rs11676382 (clotting factor activation) |
|---|---|---|
| NA10854 | **T/T** | C/C |
| NA12236 | C/C | C/C |
| NA12813 | **T/C** | **C/G** |
| NA12873 | C/C | **C/G** |
| NA15245 | **T/T** | C/C |
| NA23313 | **T/C** | **C/G** |

Alleles targeted in this study are highlighted in bold.

### Allele Designations and Diplotype Reporting

Allele designations are according to those described by the Pharmacogene Variation (PharmVar) Consortium (*www.PharmVar.org*, last accessed March 24, 2021).[13–15]

## Results

DNA from 12 cell lines were tested for *CYP2C19*35*, *CYP2C9*13*, and *VKORC1* warfarin-resistance variants (rs61742245 and rs72547529) using clinical genotyping assays and Sanger sequencing. The same 12 DNA samples were tested for the *CYP2C* cluster variant (rs12777823) using only genotyping methods. Genomic DNA samples from six additional cell lines were tested for *GGCX* variants (rs12714145 and rs11676382) using genotyping and Sanger sequencing. All variant alleles in this study were assigned a consensus genotype based on assay results (Tables 2 and 3). The results of all assays used to determine the consensus genotypes are given in Supplemental Table S2. Except for differences attributable to assay design, all results were concordant.

Most targeted genotyping was performed as part of a panel. Therefore, additional data were generated for genes and variants outside the scope of this report and are available on the GeT-RM website (Get-RM, *https://www.cdc.gov/labquality/get-rm/index.html*, last accessed March 24, 2021).

## Discussion

As pharmacogenetic information evolves, so does pharmacogenetic testing and the need for reference materials with important variants. Although two previous GeT-RM pharmacogenetic studies[5,6] included *CYP2C19*, *CYP2C9* and *VKORC1*, the tests used to characterize the samples were not designed to detect all known variants of these genes. In addition, variants such as the *CYP2C* cluster variant and *GGCX* were not included in the previous studies. Thus, the goal of this project was to supplement the set of available reference materials for *VKORC1*, *CYP2C9,* and *CYP2C19* previously characterized by GeT-RM, identify samples with variants included in the AMP Pharmacogenetic Working Group recommendations,[8–10] and identify variants in *GGCX* related to clotting factor activation. The commonly tested alleles for warfarin metabolism, clotting factor activation and *CYP2C19*, availability of reference materials from this or a previous GeT-RM study, and their AMP Pharmacogenetic Working Group tier 1 or tier 2 status are given in Table 4.

The tier 2 alleles have an identified functional variant with a well-characterized alteration of activity but are not recommended because of an unknown or low allele frequency and/or the lack of available reference material. This study targeted several of the tier 2 pharmacogenetic alleles without characterized reference materials, namely *CYP2C9*13, CYP2C19*35*, *VKORC1* rs72547529 or rs61742245, and the *CYP2C* cluster variant rs12777823.

*CYP2C9*13* has been classified by Clinical Pharmacogenetics Implementation Consortium guideline authors as a no function allele (PharmGKB, *https://www.pharmgkb.org/page/cyp2c9RefMaterials*, last accessed January 15, 2021). This allele is relatively rare and appears to be present only in Asians (0.33%) (PharmGKB, *https://www.pharmgkb.org/page/cyp2c9RefMaterials*, last accessed January 15, 2021). *CYP2C19*35* is a nonfunctional allele that occurs in African populations at frequencies ranging from 1.59% to 3.21% and appears to be absent in European and Asian populations (PharmGKB Gene-specific Information Tables for CYP2C19, *https://www.pharmgkb.org/*, last accessed March 24, 2021)). *VKORC1* variants rs72547529 and rs61742245 are associated with warfarin resistance.[16] Variant rs72547529 is found at a frequency of 0.25% in African/African Americans and lower frequencies in Latino/admixed Americans (0.014%) and South Asians (0.0033%) (gnomAD, *https://gnomad.broadinstitute.org*, last accessed January 15, 2021), and *VKORC1* rs61742245 has an approximate frequency of 0.0045% in African/African American, 0.09% in South Asian, 0.17% in Latino, and 3.8% in Ashkenazi Jewish populations (gnomAD). The *CYP2C* cluster variant rs12777823 is present in many populations at frequencies up to 30.6% in East Asians and 25.8% in African/African Americans (gnomAD). It is associated with reduced warfarin dose requirements in individuals with West African ancestry but not in other populations.[10,17] The inclusion of this allele can be considered for testing of African American populations to improve dosing algorithms, such as those developed by the International Warfarin Pharmacogenetics Consortium (*http://www.warfarindosing.org/Source/InitialIWPC.aspx*, last accessed January 30, 2021).[18,19]

Two *GGCX* variants were also included in the study. Although rare *GGCX* variants lead to coagulation factor deficiency,[20] the more common *GGCX* variants, including rs699664, rs12714145, and rs11676382, affect warfarin dose requirements in several populations, but the data are inconsistent.[11,12] *GGCX* variants were not part of the AMP recommendations, but they were included in this study because some laboratories are testing for these alleles in clinical testing and research studies.

There are still several tier 2 alleles that lack reference materials. For example, there are no publicly available reference materials for *CYP2C19*5* and *CYP2C19*7*. Both these alleles are extremely rare. *CYP2C19*5* and **7* have an estimated multiethnic allele frequency of 0.032% and 0.0005%, respectively (gnomAD).[8,21] A publicly available cell line for *CYP2C9*15* (rs72558190), which is estimated to have an allele frequency of 0.0054% in East Asians and 0.000398% overall (gnomAD), could not be identified. As the AMP Pharmacogenetics Working Group continues to recommend alleles for clinical testing, additional publicly available, characterized reference materials will need to be developed.

**Table 4** Commonly Tested Alleles and Available Reference Materials for *CYP2C9, CYP2C19, VKORC1, CYP4F2, CYP2C* Cluster Variant, and *GGCX*

| Gene | Allele | Allele function[†] | Coriell no. | Genotype | GeT-RM study | AMP tier |
|---|---|---|---|---|---|---|
| *CYP2C9* | **2* | Decreased | HG00276 | **1/*2* | 2016[6] | 1 |
| | | | NA10854 | **2/*2* | 2016 | |
| *CYP2C9* | **3* | None | NA18524[‡] | **1/*3* | 2016 | 1 |
| *CYP2C9* | **5* | Decreased | NA18519 | **1/*5* | 2016 | 1 |
| | | | NA23275 | **5/*5* | 2016 | |
| *CYP2C9* | **6* | None | NA19213 | **1/*6* | 2016 | 1 |
| | | | NA19143 | **1/*6* | 2016 | |
| *CYP2C9* | **8*[§] | Decreased | NA12815 | **1/*8* | 2016 | 1 |
| | | | NA17454 | **1/*8* | 2016 | |
| *CYP2C9* | **9* | Normal | NA19700 | **1/*9* | 2016 | None |
| | | | NA19178 | **5/*9* | 2016 | |
| *CYP2C9* | **10* | Uncertain | NA15245 | **10/*12* | 2016 | None |
| *CYP2C9* | **11* | Decreased | HG02861 | **1/*11* | This study | 1 |
| | | | HG02852 | **1/*11* | This study | |
| | | | NA19122 | **1/*11* | 2016 | |
| *CYP2C9* | **12* | Decreased | NA15245 | **10/*12* | 2016 | 2 |
| *CYP2C9* | **13* | None | HG01809 | **1/*13* | This study | 2 |
| | | | HG02087 | **1/*13* | This study | |
| | | | NA19075 | **1/*13* | This study | |
| *CYP2C9* | **15* | None | none | | ND | 2 |
| *CYP2C19* | **2* | None | HG01190 | **1/*2* | 2016 | 1 |
| | | | NA12717 | **2/*2* | 2016 | |
| *CYP2C19* | **3* | None | NA18564 | **2/*3* | 2016 | 1 |
| | | | NA23246 | **3/*17* | 2016 | |
| *CYP2C19* | **4.001* | None | NA23881 | **1/*4.001* | 2016 | 2 |
| | | | NA18552 | **1/*4.001* | 2016 | |
| *CYP2C19* | **4.002* | None | NA23878 | **1/*4.002 (*4/*17)*[¶] | 2016 | 2 |
| *CYP2C19* | **5* | None | none | | ND | 2 |
| *CYP2C19* | **6* | None | NA19178 | **1 (*27)/*6* | 2016 | 2 |
| | | | NA23874 | **2/*6* | 2016 | |
| *CYP2C19* | **7* | None | none | | ND | 2 |
| *CYP2C19* | **8* | None | NA23873 | **1/*8* | 2016 | 2 |
| | | | NA10865 | **8/*17* | 2016 | |
| *CYP2C19* | **9* | Decreased | NA24008 | **9/*17* | 2016 | 2 |
| | | | NA24009 | **2/*9* | 2016 | |
| | | | NA19466 | **1/*9* | This study | |
| *CYP2C19* | **10* | Decreased | NA07439 | **2/*10* | 2016 | 2 |
| *CYP2C19* | **12* | Uncertain | NA17074 | **1(*12)/*17* | 2016 | None |
| | | | NA19700 | *(*12/*27)* | 2016 | |
| *CYP2C19* | **13* | Normal | NA17448 | **1/*13* | 2016 | None |
| | | | NA19239 | **13/*17* | 2016 | |
| *CYP2C19* | **15* | Normal | NA19213 | **1/*15* | 2016 | None |
| | | | NA19143 | **1/*15* | 2016 | |
| *CYP2C19* | **17* | Increased | NA19035 | **17/*17* | 2016 | 1 |
| | | | NA17658 | **1/*17* | 2016 | |
| *CYP2C19* | **35* | None | HG02852 | **2/*35* | This study | 2 |
| | | | NA19327 | **2/*35* | This study | |
| | | | HG03370 | **2/*35* | This study | |
| | | | HG02861 | **2/*35* | This study | |
| *VKORC1* | c.-1639 G>A (rs9923231) | Decreased gene expression | HG00276 | G/A | 2016 | 1 |
| | | | HG00589 | A/A | 2016 | |
| *VKORC1* | rs61742245 | Warfarin resistance | HG01697 | G/T | This study | 2 |
| | | | NA19395 | G/T | This study | |
| *VKORC1* | rs72547529 | Warfarin resistance | HG01456 | G/A | This study | 2 |
| | | | NA18877 | G/A | This study | |
| | | | NA19466 | G/A | This study | |

(*table continues*)

**Table 4** (*continued*)

| Gene | Allele | Allele function[†] | Coriell no. | Genotype | GeT-RM study | AMP tier |
|---|---|---|---|---|---|---|
| *CYP4F2* | **3* | Possibly decreased | HG01190 | **1/*3* | 2016 | 2 |
| | | | NA07029 | **3/*3* | 2016 | |
| *CYP2C* cluster variant | rs12777823 | Unknown | HG02087 | A/G | This study | 2 |
| | | | HG01809 | A/A | This study | |
| *GGCX* | rs12714145 | Clotting factor activation | NA10854 | T/T | This study | None |
| | | | NA12813 | T/C | This study | |
| *GGCX* | rs11676382 | Clotting factor activation | NA12873 | C/G | This study | None |
| | | | NA23313 | C/G | This study | |

Information about additional reference materials for these genes is available on the GeT-RM website (*https://www.cdc.gov/labquality/get-rm/index.html*, last accessed March 24, 2021).

AMP, Association for Molecular Pathology; GeT-RM, Genetic Testing Reference Material; ND, not detected.

[†]Function shown for CYP2C9 and CYP2C19 corresponds to Clinical Pharmacogenetics Implementation Consortium clinical function as assigned by guideline authors. For all other alleles except GGCX, function information is according to PharmGKB (*https://www.pharmgkb.org/page/pgxGeneRef*, last accessed March 24, 2021) and Clinical Pharmacogenetics Implementation Consortium (*https://cpicpgx.org/content/guideline/publication/warfarin/2017/28198005.pdf*, last accessed March 24, 2021).

[‡]The *CYP2C9*3* tag variant (rs1057910) is present in both the **3* and **18* alleles and is present on multiple Coriell cell lines.

[§]Samples were not genotyped for c.-1766T>C, a second core variant defining *CYP2C9*8*.

[¶]Alleles in parentheses indicate that they were identified by only one laboratory.

The AMP Pharmacogenetics Working Group plans to periodically review the status of the tier 2 variants, and some included in this study may be recategorized to tier 1 based on the availability of reference materials. Availability of the materials developed as part of this study will allow development and validation of more accurate pharmacogenetic tests and facilitate assay standardization across laboratories. It will also help laboratories develop and validate tests that incorporate the tier 1 and 2 alleles recommended for clinical testing by the AMP Pharmacogenetics Working Group.

In conclusion, these 18 genomic DNA reference materials can be used for quality assurance, proficiency testing, test development and research and should help to ensure the accuracy of clinical pharmacogenetic testing. The alleles identified in these samples complement the alleles identified by previous GeT-RM studies, and together these characterized genomic DNA samples form a comprehensive set of reference materials for pharmacogenetic testing. These, as well as other reference materials developed by GeT-RM, are publicly available from the National Institute of General Medical Sciences and National Human Genome Research Institute repositories at the Coriell Institute for Medical Research (Camden, NJ). More information on this and other reference material characterization projects is available at the GeT-RM website (*https://www.cdc.gov/labquality/get-rm/index.html*, last accessed August 31, 2020).

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## Supplemental Data

Supplemental material for this article can be found at *http://doi.org/10.1016/j.jmoldx.2021.04.012*.

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