### Overview

#### Useful For
Identifying individuals who are poor, intermediate, normal (extensive) or rapid metabolizers of drugs metabolized by CYP1A2 to assist drug therapy decision making

#### Special Instructions
- [Informed Consent for Genetic Testing](#)
- [Pharmacogenomic Associations Tables](#)
- [Multiple Genotype Test List](#)
- [Informed Consent for Genetic Testing (Spanish)](#)

### Method Name
Real-Time Polymerase Chain Reaction (PCR) with Allelic Discrimination Analysis

### NY State Available
Yes

### Specimen

#### Specimen Type
Varies

#### Advisory Information
Testing is available as the single gene assay (this test) or as a part of a focused pharmacogenomics panel, which includes testing for the following genes: CYPs 1A2, 2C9, 2C19, 2D6, 3A4, 3A5, 4F2, SLCO1B1, and VKORC1. Order PGXFP / Focused Pharmacogenomics Panel if multiple pharmacogenomic genotype testing is desired.

#### Specimen Required
Multiple genotype tests can be performed on a single specimen after a single extraction. See [Multiple Genotype Test List](#) in Special Instructions for a list of tests that can be ordered together.

**Submit only 1 of the following specimens:**

- **Specimen Type:** Whole blood
- **Container/Tube:** Lavender top (EDTA)
- **Specimen Volume:** 3 mL

#### Collection Instructions:
1. Invert several times to mix blood.
2. Send specimen in original tube.

**Specimen Stability Information:** Ambient (preferred) 9 days/Refrigerated 30 days
Specimen Type: Saliva

Patient Preparation: Patient should not eat, drink smoke, or chew gum 30 minutes prior to collection.

Supplies: Saliva Swab Collection Kit (T786)

Specimen Volume: 1 swab

Collection Instructions: Collect and send specimen per kit instructions.

Specimen Stability Information: Ambient 30 days

Specimen Type: DNA

Container/Tube: 2 mL screw top tube

Specimen Volume: 100 mcL (microliters)

Collection Instructions:
1. The preferred volume is 100 mcL at a concentration of 50 ng/mcL.
2. Include concentration and volume on tube.

Specimen Stability Information: Frozen (preferred)/Ambient/Refrigerated

Forms
1. New York Clients-Informed consent is required. Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:
   - Informed Consent for Genetic Testing (T576)
   - Informed Consent for Genetic Testing-Spanish (T826)
2. If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:
   - Neurology Specialty Testing Client Test Request (T732)
   - Pharmacogenomics Test Request (T797)
   - Therapeutics Test Request (T831)

Specimen Minimum Volume
Blood: 0.4 mL
Saliva: 1 swab

Reject Due To
All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information
Clinical and Interpretive

Clinical Information

The cytochrome P450 (CYP) family is involved in the primary metabolism of many drugs. The CYPs are a group of oxidative/dealkylating enzymes localized in the microsomes of many tissues including the intestines and liver. One of these CYP enzymes, CYP1A2, is wholly or partially responsible for the hydroxylation or dealkylation of many commonly prescribed drugs.

CYP1A2-mediated drug metabolism is highly variable. A number of variants have been identified in the CYP1A2 gene that results in increased, diminished, or abolished catalytic activity and substrate metabolism. The frequency of these variants varies by ethnicity.

Dosing of drugs that are metabolized through CYP1A2 may require adjustment based on the CYP1A2 genotype. Individuals who are poor metabolizers may require lower than usual doses to achieve optimal response, whereas individuals who are ultrarapid metabolizers may benefit from increased doses. CYP1A2 phenotype is predicted based upon the number of functional, partially functional, nonfunctional, and inducible alleles present in a sample. In the absence of clear guidance on dosing for various metabolizer phenotypes, patients with either rapid or poor metabolism also may benefit by switching to another comparable drug that is not primarily metabolized by CYP1A2 or by therapeutic drug monitoring where applicable.

The following table outlines the relationship between the variations (star alleles) detected in this assay and the effect on the activity of the enzyme produced by that allele.

<table>
<thead>
<tr>
<th>CYP1A2 Allele</th>
<th>Nucleotide Change (Legacy nomenclature)</th>
<th>cDNA Nucleotide Change</th>
<th>Effect on Enzyme Metabolism(a)</th>
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<tbody>
<tr>
<td>*1</td>
<td>None (wild type)</td>
<td>None (wild type)</td>
<td>Normal (extensive) metabolizer</td>
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<tr>
<td>*1F</td>
<td>-163C-&gt;A</td>
<td>c.-9-154C-&gt;A</td>
<td>Increased inducibility</td>
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<tr>
<td>*1K</td>
<td>-729C-&gt;T</td>
<td>c.-10+113C-&gt;T</td>
<td>Decreased activity and decreased inducibility</td>
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<tr>
<td>*6</td>
<td>5090C-&gt;T</td>
<td>c.1291C-&gt;T</td>
<td>No activity</td>
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<tr>
<td>*7</td>
<td>3533G-&gt;A</td>
<td>c.1253+1G-&gt;A</td>
<td>No activity</td>
</tr>
</tbody>
</table>

a. Effect of a specific allele on the activity of the CYP1A2 enzyme can only be estimated since the literature does not provide precise data. Å

A complicating factor in correlating CYP1A2 genotype to CYP1A2 phenotype is that some drugs or their metabolites are inhibitors of CYP1A2 catalytic activity. These drugs may reduce CYP1A2 catalytic activity. Consequently, an individual may require a dose decrease greater than predicted based upon genotype alone. Another complicating factor is that CYP1A2 is inducible by several drugs and environmental agents (eg, cigarette smoke) and the degree
of inducibility is under genetic control. It is important to interpret the results of testing in the context of other coadministered drugs and environmental factors.

**Reference Values**

An interpretive report will be provided.

**Interpretation**

An interpretive report will be provided.

The genotype, with associated star alleles, is assigned using standard allelic nomenclature as published by the Pharmacogene Variation (PharmVar) Consortium.(1)

CYP1A2 activity is also dependent upon hepatic function status, as well as age. Renal function may be important for drugs that are excreted in urine. Patients may develop drug toxicity if hepatic or renal function is decreased. Drug metabolism is known to decrease with age. It is important to interpret the results of testing and dose adjustments in the context of hepatic and renal function and age.

For additional information regarding pharmacogenomic genes and their associated drugs, see [Pharmacogenomic Associations Tables](#) in Special Instructions. This resource also includes information regarding enzyme inhibitors and inducers, as well as potential alternate drug choices.

**Cautions**

Rare variants may be present that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings (phenotype), additional testing should be considered.

Samples may contain donor DNA if obtained from patients who received heterologous blood transfusions or allogeneic blood or marrow transplantation. Results from samples obtained under these circumstances may not accurately reflect the recipient’s genotype. For individuals who have received blood transfusions, the genotype usually reverts to that of the recipient within 6 weeks. For individuals who have received allogeneic blood or marrow transplantation, a pretransplant DNA specimen is recommended for testing.

CYP1A2 genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient’s CYP1A2 status.

This method may not detect all variants that result in altered CYP1A2 activity. Therefore, absence of a detectable variant does not rule out the possibility that a patient has altered CYP1A2 metabolism due to other CYP1A2 variants that cannot be detected with this method. Furthermore, when 2 or more variants are identified, the cis-/trans- status (whether the variants are on the same or opposite chromosomes) is not always known.

The frequency of variants which cause altered CYP1A2 metabolism has not been fully characterized in all ethnic groups. Patients with a rapid, normal (extensive) or intermediate genotype may have CYP1A2 enzyme activity inhibited or induced by a variety of substances, medications, or their metabolites.

**Clinical Reference**


Performance

Method Description
Genomic DNA is extracted from whole blood or saliva. Genotyping for the CYP1A2 alleles is performed using a PCR-based 5'-nuclease assay. Fluorescently labeled detection probes anneal to the target DNA. PCR is used to amplify the section of DNA that contains the variant. If the detection probe is an exact match to the target DNA, the 5'-nuclease polymerase degrades the probe, the reporter dye is released from the effects of the quencher dye, and a fluorescent signal is detected. Genotypes are assigned based on the allele-specific fluorescent signals that are detected. (User Guide: TaqMan SNP Genotyping Assay, Applied Biosystems, Revision A.0 January 2014)

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Friday; 8 a.m.

Analytic Time
3 days (Not reported Saturday or Sunday)

Maximum Laboratory Time
8 days

Specimen Retention Time
Whole Blood/Saliva swab: 2 weeks; Extracted DNA: 2 months

Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
0031U
### LOINC® Information

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