

## Overview

### Useful For

Prediction of response to nicotine replacement therapy for smoking cessation

Investigation of inhibitor dosing for decreasing levodopa metabolism

Research use for assessing estrogen metabolism

### Special Instructions

- [Informed Consent for Genetic Testing](#)
- [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

### Ordering Guidance

This test should not be ordered for pheochromocytoma or paraganglioma assessment. Instead, order 1 of the following:

- METAF / Metanephrines, Fractionated, 24 Hour, Urine
- PMET / Metanephrines, Fractionated, Free, Plasma
- CATU / Catecholamine Fractionation, Free, 24 Hour, Urine
- CATP / Catecholamine Fractionation, Free, Plasma

Testing is available as the single gene assay (this test) and as a part of a psychotropic pharmacogenomics panel.

If genotype testing for psychotropic medications is desired, order PSYQP / Psychotropic Pharmacogenomics Gene Panel, Varies.

### Specimen Required

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

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**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 whole blood specimen in original tube. **Do not aliquot.**

**Specimen Stability Information:** Ambient (preferred) 4 days/Refrigerated 4 days/Frozen 4 days**Additional Information:**

1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.
2. To ensure minimum volume and concentration of DNA are met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.

**Specimen Type:** Saliva**Patient Preparation:** Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.**Supplies:**

DNA Saliva Kit High Yield (T1007)

Saliva Swab Collection Kit (T786)

**Container/Tube:****Preferred:** High-yield DNA saliva kit**Acceptable:** Saliva swab**Specimen Volume:** 1 Tube if using T1007 or 2 swabs if using T786**Collection Instructions:** Collect and send specimen per kit instructions.**Specimen Stability Information:** Ambient (preferred) 30 days/Refrigerated 30 days

**Additional Information:** Saliva specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from saliva, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.

**Specimen Type:** Extracted DNA**Container/Tube:****Preferred:** Screw Cap Micro Tube, 2 mL with skirted conical base**Acceptable:** Matrix tube, 1 mL**Collection Instructions:**

1. The preferred volume is at least 100 µL at a concentration of 75 ng/µL.
2. Include concentration and volume on tube.

**Specimen Stability Information:** Frozen (preferred) 1 year/Ambient/Refrigerated

**Additional Information:** DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). Our laboratory has experience with Chemagic, Puregene, Autopure, MagnaPure, and EZ1 extraction platforms and cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be

reported as failed, and a charge will be applied. If applicable, specific gene regions that were unable to be interrogated due to DNA quality will be noted in the report.

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:  
[-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)  
[-Therapeutics Test Request](#) (T831)

Specimen Minimum Volume

See Specimen Required

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information

Catechol-O-methyltransferase (COMT) is involved in phase II (conjugative) metabolism of catecholamines and catechol drugs, such as dopamine, as well as the catechol-estrogens. COMT transfers a donor methyl-group from S-adenosylmethionine to acceptor hydroxy groups on catechol structures (aromatic ring structures with vicinal hydroxy-groups).(1) Bioactive catecholamine metabolites are metabolized by COMT in conjunction with monoamine oxidase (MAO):

- Norepinephrine is methylated by COMT forming normetanephrine.
- Epinephrine is methylated by COMT forming metanephrine.
- Dopamine is converted to homovanillic acid through the combined action of MAO and COMT.

Parkinsonism patients receiving levodopa (L-Dopa) therapy are frequently also prescribed a COMT inhibitor to minimize metabolism of L-Dopa by COMT, thereby prolonging L-Dopa action.

Catechol-O-methyltransferase is also involved in the inactivation of estrogens. Estradiol can be hydroxylated forming the catechol estrogens 2-hydroxyestradiol and 4-hydroxyestradiol.(2) These hydroxylated estradiols are methylated by COMT, forming the corresponding methoxyestradiols. The gene encoding COMT is transcribed from alternative promoters to produce 2 forms of the enzyme, a soluble short form of the enzyme and a membrane-bound long form. Variants in the *COMT* gene are therefore designated in the literature by the position of the amino acid change in both the short and long form of the enzyme. A single nucleotide variant in exon 4 of the gene produces an amino acid change

from valine to methionine (Val108/158Met). The presence of methionine at this position reduces the maximum activity of the variant enzyme by 25% and also results in significantly less immunoreactive COMT protein, resulting in a 3-fold to 4-fold decrease in activity compared to wild type (valine at this position). This variant has been associated with prediction of response and risk of relapse when using nicotine replacement therapy for smoking cessation.(3)

The following information outlines the relationship between the polymorphism detected in this assay and the effect on the activity of the enzyme produced by that allele:

Amino acid change	cDNA nucleotide change (NM_000754.3)	Effect on enzyme activity/metab olism
None (wild-type)	None (wild type)	Normal activity
p.Val158Met (known as Val108Met)	c.472G>A	Reduced activity

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided.

Cautions

Samples may contain donor DNA if obtained from patients who received non-leukoreduced blood transfusions or allogeneic hematopoietic stem cell 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 hematopoietic stem cell transplantation, a pretransplant DNA specimen is recommended for testing.

COMT genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's catechol-O-methyltransferase (COMT) status.

This test does not detect variants other than those listed. Variants in primer binding may affect test results and ultimately the genotyping calls made.

Absence of a detectable variant does not rule out the possibility that a patient has an intermediate or poor metabolizer phenotype. Patients with a normal (extensive) or intermediate metabolizer genotype may have COMT enzyme activity inhibited by a variety of medications, or their metabolites. The following is a partial listing of drugs known to affect COMT activity.

Drugs that undergo metabolism by COMT:

- Alpha-methyl DOPA
- Apomorphine

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-Benserazide  
-Bitolterol  
-Dihydroxyphenylserine  
-Dobutamine  
-Dopamine  
-Epinephrine  
-2-Hydroxyestrogens  
-4-Hydroxyestrogens  
-Isoetherine  
-Isoprenaline  
-Isoproterenol  
-Norepinephrine  
-Rimiterol

Coadministration may decrease the rate of elimination of other drugs metabolized by COMT.

Drugs that undergo structural modification but are not metabolized by COMT:

-Albuterol  
-Metaproterenol  
-Methoxamine  
-Phenylephrine  
-Perbuterol  
-Terbutaline

Coadministration will not decrease the rate of elimination metabolism of other drugs metabolized by COMT.

Drugs known to inhibit COMT activity:

-Entacapone  
-Tolcapone  
-Nitecapone

Dietary components that inhibit COMT activity:

-Quercetin  
-Tea catechins

Coadministration will decrease the rate of metabolism of COMT metabolized drugs, increasing the possibility of toxicity, including in heterozygous individuals.

### Clinical Reference

1. Weinshilboum RM, Otterness DM, Szumlanski CL. Methylation pharmacogenetics: catechol O-methyltransferase, thiopurine methyltransferase, and histamine N-methyltransferase. *Annu Rev Pharmacol Toxicol.* 1999;39:19-52. doi:10.1146/annurev.pharmtox.39.1.19
2. Sun H, Guo S, Chen D, et al. Association of functional COMT Val108/Met polymorphism with smoking cessation in a nicotine replacement therapy. *J Neural Transm (Vienna).* 2012;119(12):1491-1498. doi:10.1007/s00702-012-0841-8
3. Herman AI, Jatlow PI, Gelernter J, Listman JB, Sofuoglu M. COMT Val158Met modulates subjective responses to intravenous nicotine and cognitive performance in abstinent smokers. *Pharmacogenomics J.* 2013;13(6):490-497. doi:10.1038/tpj.2013.1

4. Worda C, Sator MO, Schneeberger C, Jantschev T, Ferlitsch K, Huber JC. Influence of the catechol-O-methyltransferase (COMT) codon 158 polymorphism on estrogen levels in women. Hum Reprod. 2003;18(2):262-266.  
doi:10.1093/humrep/deg059
5. Shield AJ, Thomae BA, Eckloff BW, Wieben ED, Weinshilboum RM. Human catechol O-methyltransferase genetic variation: gene resequencing and functional characterization of variant allozymes. Mol Psychiatry. 2004;9(2):151-160.  
doi:10.1038/sj.mp.4001386
6. Crews KR, Monte AA, Huddart R, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6, OPRM1, and COMT Genotypes and Select Opioid Therapy. Clin Pharmacol Ther. 2021;110(4):888-896.  
doi:10.1002/cpt.2149

## Performance

### Method Description

Genomic DNA is extracted from whole blood or saliva. Genotyping for *COMT* alleles is performed using a polymerase chain reaction (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. (Unpublished Mayo method)

### PDF Report

No

### Day(s) Performed

Monday through Friday

### Report Available

3 to 8 days

### Specimen Retention Time

Whole blood/Saliva swab: 30 days (if available), Extracted DNA: 3 months

### Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

## Fees & 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 account representative. For assistance, contact [Customer Service](#).

# Test Definition: COMTQ

Catechol-O-Methyltransferase (COMT)  
Genotype, Varies

### Test Classification

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

### CPT Code Information

0032U

### LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
COMTQ	COMT Genotype, V	74511-7

Result ID	Test Result Name	Result LOINC® Value
610124	COMT Genotype	74511-7
610125	COMT Phenotype	93411-7
610126	Interpretation	69047-9
610127	Additional Information	48767-8
610128	Method	85069-3
610129	Disclaimer	62364-5
610130	Reviewed by	18771-6