



**21-HYDROXYLASE GENE (CYP21A2), FULL GENE ANALYSIS,
 PRENATAL
 Test ID: CYCMS**

USEFUL FOR:

- Ambiguous genitalia detected on prenatal ultrasound, particularly when fetus is confirmed XX female by chromosome analysis
- Pregnancies at risk for 21-hydroxylase deficient congenital adrenal hyperplasia based on family history

REFLEX TESTS

Test ID	Reporting Name	Available Separately	Always Performed
MCC	Maternal Cell Contamination, B	Yes	No
FBC	Fibroblast Culture for Genetic Test	Yes	No
AFC	Amniotic Fluid Culture/Genetic Test	Yes	No

TESTING ALGORITHM

- For any prenatal specimen that is received, maternal cell contamination testing (MCC) will be added per lab protocol and charged separately.
- If amniotic fluid (nonconfluent cultured cells) is received, amniotic fluid culture/genetic test (AFC) will be added per lab protocol and charged separately.
- If chorionic villus specimen (nonconfluent cultured cells) is received, fibroblast culture for genetic test (FBC) will be added per lab protocol and charged separately.

METHODOLOGY: Polymerase Chain Reaction (PCR) Amplification/DNA Sequencing and Deletion Detection by Multiplex Ligation-Dependent Probe Amplification (MLPA)

REFERENCE VALUES: An interpretive report will be provided.

SPECIMEN REQUIREMENTS:

Forms:

- 1. CYP21A2 Gene Testing Patient Information Sheet (Supply T663) is required** and available in Special Instructions
- 2. Informed Consent for Genetic Testing (Supply T576) is required** and available in Special Instructions
- 3. New York Clients: Informed consent is required.** Please document on the request form or electronic order that a copy is on file. An Informed Consent for Genetic Testing (Supply T576) is available in Special Instructions.

Due to the complexity of prenatal testing, consultation with the laboratory is required for all prenatal testing. Contact Kate Kotzer, Genetic Counselor; pager: 507-293-5544; phone: 507-293-0215. Prenatal specimens can be sent Monday through Thursday and **must be received by 5 p.m. CST on Friday** in order to be processed appropriately.

Prenatal Specimens

All prenatal specimens **must** be accompanied by parental blood specimens. The maternal sample is required for maternal cell contamination studies (MCC, Maternal Cell Contamination, Molecular Analysis). Both maternal and paternal samples will be tested for CYP21A2 at no charge, if needed for prenatal interpretation.

Maternal whole blood: Order CYPPS - CYP21A2 Full Gene Analysis and MCC, Maternal Cell Contamination

Paternal whole blood: Order CYPPS - CYP21A2 Full Gene Analysis

Submit only 1 of the following acceptable specimens for prenatal testing:

Specimen Type: Amniotic fluid

Container/Tube:

Preferred: Screw-capped, sterile centrifuge tubes

Acceptable: T-25 flasks of confluent cultured cells

Specimen Volume: 20 mL

Collection Instructions:

1. Obtain amniotic fluid.
2. Transfer specimen to 2 sterile centrifuge tubes.

3. Specimen cannot be frozen.

Specimen Stability Information: Refrigerated (preferred)/Ambient

Additional Information:

1. A separate culture charge will be assessed under AFC/80334 Amniotic Fluid Culture for Genetic Testing.
2. Alternatively, we will accept 2 T-25 flasks of confluent cultured cells from another laboratory sent refrigerated.

Specimen Type: Chorionic villi

Container/Tube:

Preferred: 15-mL centrifuge tube

Acceptable: T-25 flasks of confluent cultured cells

Specimen Volume: 20 mg

Collection Instructions:

1. Obtain chorionic villus specimen.
2. Send specimen in transport media in 15-mL centrifuge tube.

3. Specimen cannot be frozen.

Specimen Stability Information: Refrigerated (preferred)

Additional Information:

1. A separate culture charge will be assessed under FBC/80333 Fibroblast Culture for Genetic Testing.
2. Alternatively, we will accept 2 T-25 flasks of confluent cultured cells from another laboratory sent refrigerated.

Specimen Type: Extracted DNA

Container/Tube: Plastic microtube

Specimen Volume: 50 mcL (concentration: > or =80 ng/mcL)

Specimen Stability Information: Refrigerated (preferred)/Ambient

Submit the following specimen for required Maternal Cell Contamination (MCC) Testing:

Specimen must arrive within 96 hours of collection.

Specimen Type: Parental blood

Container/Tube:

Preferred: 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)/Refrigerated

SPECIMEN MINIMUM VOLUME

DNA: 50 mcL/Amniotic Fluid: 10 mL/ Chorionic Villus: 5 mg

SPECIMEN STABILITY INFORMATION:

Specimen Type	Temperature
Varies	Refrigerated (preferred)
	Ambient

CAUTIONS:

- Because of the complexity of the genetic structure of the *CYP21A2* locus, and the possibility that a patient's diagnosis may be due to other gene defects, genetic testing results should be correlated carefully with clinical and biochemical data.
- This testing strategy is superior to approaches previously used, but may still miss some complex and large-scale genetic rearrangements or deletions, as well as genetic changes in intronic regions or in far upstream or downstream gene-regulatory elements that impair *CYP21A2* gene expression. This can lead to false-negative test results.
- Rare polymorphisms in primer binding sites can lead to selective allelic drop-out, which can lead to false-negative or false-positive diagnosis.
- Patients without genetic evidence for disease-causing *CYP21A2* genetic changes may still have congenital adrenal hyperplasia (CAH), but due to a different enzyme defect. Additional and expanded biochemical steroid profiling is, therefore, recommended if the clinical picture is strongly suggestive of CAH.

CPT CODE:

81402-CYP21A2 common variants

81405-CYP21A2 full gene sequence

Amniotic Fluid Culture for Genetic Testing

88235-Tissue culture for amniotic fluid (if appropriate)

88240-Cryopreservation (if appropriate)

Fibroblast Culture for Genetic Testing

88233-Tissue culture, skin or solid tissue biopsy (if appropriate)

88240-Cryopreservation (if appropriate)

Maternal Cell Contamination

81265-Comparative analysis using short tandem repeat (STR) markers; maternal cell contamination of fetal cells)

DAY SET UP: Monday**ANALYTIC TIME:** Varies; DNA: 5 days; Amniotic fluid/chorionic villi (confluent culture): 15 days

QUESTIONS: Contact your Mayo Medical Laboratories' Regional Manager or
David O'Brien, MML Laboratory Technologist Resource Coordinator
Telephone: 800-533-1710