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**Overview****Useful For**

Evaluation of individuals with episodic or chronic Coombs-negative nonspherocytic hemolytic anemia

Rapid testing to assess glucose-6-phosphate dehydrogenase (G6PD) enzyme capacity prior to Rasburicase or other therapies that may cause hemolysis or methemoglobinemia in G6PD deficient patients

May aid in the creation of a comprehensive patient profile and can ensure appropriate patient monitoring for developing anemia

**Method Name**

Only orderable as part of a profile. For more information see:

-HAEV1 / Hemolytic Anemia Evaluation, Blood

-EEEV1 / Red Blood Cell (RBC) Enzyme Evaluation, Blood

Kinetic Spectrophotometry

**NY State Available**

Yes

**Specimen****Specimen Type**

Whole Blood ACD-B

**Specimen Required**

Only orderable as part of a profile. For more information see:

-HAEV1 / Hemolytic Anemia Evaluation, Blood

-EEEV1 / Red Blood Cell (RBC) Enzyme Evaluation, Blood

**Specimen Minimum Volume**

1 mL

**Reject Due To**

Gross hemolysis	Reject
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**Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Whole Blood ACD-B	Refrigerated (preferred)	20 days	

## Clinical & Interpretive

### Clinical Information

Hemolytic anemia may be associated with deficiency of erythrocyte enzymes. The most common enzyme defect worldwide is a deficiency of glucose-6-phosphate dehydrogenase (G6PD).

As an enzyme in the hexose monophosphate pathway, G6PD plays a key role in the generation of reduced nicotinamide adenine dinucleotide phosphate (NADPH). Because red blood cells lack the citric acid cycle, this NADPH generation is critical for protection against oxidative stress. Normal conditions require approximately 2% of capacity, leaving 98% reserve for stressor events. More than 400 molecular variants of G6PD are known, and the clinical and laboratory features of G6PD deficiency vary according to the degree to which enzyme reserve is decreased. G6PD deficiency (OMIM 300908, X-linked) therefore results in various forms of anemia and is classified by World Health Organization (WHO) criteria according to enzyme activity and chronic versus acute episodic clinical course.(1,2)

WHO Classes of G6PD deficiency:

Class I: severe, associated with chronic extravascular non-spherocytic hemolytic anemia

Class II: severe, associated with episodic acute hemolytic anemia (enzyme level <10%)

Class III: moderate, associated with episodic acute hemolytic anemia (enzyme level 10%-60%)

Class IV: normal activity (enzyme level 60%-150%). Normal

Class V: increased activity (enzyme level >150%). No known clinical sequelae

The *G6PD* locus is located on the X chromosome and, therefore, G6PD deficiency is a sex-linked disorder. Most people with G6PD deficiency are asymptomatic until a stressor event occurs resulting in acute hemolytic anemia that resolves after stimulus removal. Symptoms can include neonatal jaundice (presents at 1-4 days of age) or acute hemolysis triggered by medications (antimalarials, sulfonamides, dapsone, nitrofurantoin, and naphthalene), infection (hepatitis, cytomegalovirus, typhoid), or fava bean ingestion. Hemolysis and jaundice begin 24 to 72 hours after a triggering stimulus, with accompanying dark urine/hemoglobinuria. Anemia worsens for approximately one week and begins to recover ten days after cessation. Splenomegaly, gallstones, and recurrent jaundice are additional clinical symptoms. Because it is X-linked, males are usually more severely affected but homozygous females are seen due to the prevalence of genetic variants. Heterozygous females (carriers) range from asymptomatic to severe anemia due to mosaicism/lyonization. Acquired G6PD may occur due to increasing X inactivation in aging females.(3) Acute episodic G6PD deficiency (WHO class II and III) is not expected to affect length or quality of life. Less commonly seen are genetic variants that result in chronic nonspherocytic hemolytic anemia which manifest similarly to other enzyme deficiencies (WHO class I).

The major *G6PD* variants occur in specific ethnic groups. Thus, knowledge of the ethnic background of the patient is helpful. G6PD deficiency has very high frequency in persons of southeast Asian, African, southern European, and Middle Eastern descent.

Rasburicase therapy is contraindicated in patients with G6PD deficiency. Food and Drug Administration (FDA) guidelines

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state to screen patients at higher risk for G6PD deficiency (eg, patients of African or Mediterranean ancestry) prior to starting therapy.(4)

Deficiency can be assessed by enzymatic and/or genetic assays. Due to limitations of genetic testing, in most cases it is preferential to perform G6PD enzyme testing to assign G6PD status. However, enzyme activity can be affected by recent red blood cell transfusion, marked reticulocytosis and very high white blood cell count. In these settings, genotyping may be useful for correlation with the red blood cell enzyme level.(5,6)

Due to historic issues with other similar antimalarial medications, questions arise if hydroxychloroquine (HCQ) or chloroquine (CQ) therapy may trigger acute hemolytic episodes in some G6PD subtypes. Data is limited in this regard. Available published data did not find hemolytic episodes associated with HCQ therapy in G6PD deficient African American(7) or CQ therapy in G6PD deficient African(8) patients. Both studied populations were assumed to have mild forms of the disorder. Data regarding these medications in populations with more severe G6PD phenotypes is lacking. While patients receiving HCQ do not routinely need G6PD levels checked before initiating therapy, testing may be considered in patients who are from ethnic backgrounds with high G6PD variant rates such as those from Mediterranean, African, or Asian descent. Although specific details are not described, hemolysis has been reported in at least one individual with G6PD deficiency during the post-approval use of hydroxychloroquine sulfate tablets, United States Pharmacopeia (USP) per FDA label information.(9)

### Reference Values

Only orderable as part of a profile. For more information see:

- HAEV1 / Hemolytic Anemia Evaluation, Blood
- EEEV1 / Red Blood Cell (RBC) Enzyme Evaluation, Blood

> or =12 months of age: 8.0-11.9 U/g Hb

Reference values have not been established for patients who are less than 12 months of age.

### Interpretation

The World Health Organization (WHO) classification of glucose-6-phosphate dehydrogenase (G6PD) deficiency is historically based on enzyme activity level and in most cases enzyme activity level is sufficient. Accurate classification requires correlation with clinical, and in certain cases, genetic data.

Baseline enzyme levels less than 10% of mean normal are either WHO class I (chronic hemolysis) or WHO class II (episodic hemolysis) variants.(1,2,10)

Enzyme levels between 10% and 60% of mean normal can be seen in WHO class III (episodic) variants or female carrier states.

Enzyme levels greater than 60% are considered sufficient and can be seen in normal persons, female carrier states or G6PD variants with subclinical effect (WHO class IV).

Although G6PD deficiency is an X-linked recessive disorder and most often seen in hemizygous males, some females are affected. In addition, older women who are heterozygous can develop deficiency due to differential X-skewing with age.(3) It is important to note that clinically significant G6PD deficiency can be masked in the setting of significant

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reticulocytosis, markedly elevated WBC count or recent red blood cell transfusion. If any of these are present in the setting of a history of neonatal, chronic or episodic jaundice or anemia, genotyping for G6PD genetic alterations is recommended. If desired, order G6PDB / Glucose-6-Phosphate Dehydrogenase (*G6PD*) Full Gene Sequencing, Varies.

**Cautions**

During hemolytic events normal glucose-6-phosphate dehydrogenase (G6PD) activity values may be measured for several weeks following hemolysis.

Reticulocytosis from any cause can mask some G6PD deficiency cases by raising the activity level. Comparison to other RBC enzyme activity levels may be useful.

Recent transfusion may mask the patient's intrinsic enzyme activity and cause unreliable results.

A very high white blood cell count can cause interference and falsely raise the G6PD activity, thereby masking a deficiency.

**Clinical Reference**

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12. Mehta A, Mason PJ, Vulliamy TJ: Glucose-6-phosphate dehydrogenase deficiency. *Baillieres Best Pract Res Clin Haematol*. 2000 Mar;13(1):21-38
13. Koralkova P, van Solinge WW, van Wijk R: Rare hereditary red blood cell enzymopathies associated with hemolytic anemia-pathophysiology, clinical aspects and laboratory diagnosis. *Int J Lab Hematol*. 2014;36:388-397

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## Performance

### Method Description

Glucose-6-phosphate dehydrogenase (G6PD) in a hemolysate catalyzes the oxidation of glucose-6-phosphate to 6-phosphogluconate. Concomitantly, nicotinamide adenine dinucleotide phosphate (NADP[+]) is changed to its reduced form, NADPH, and the reaction is measured spectrophotometrically on an automated chemistry analyzer. (Beutler E: Red cell metabolism: A Manual of Biochemical Methods. 3rd ed. Grune and Stratton; 1984:68-71; van Solinge WW, van Wijk: Enzymes of the red blood cell. In: Rifai N, Horvath AR, Wittwer CT: eds. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 6th ed. Elsevier; 2018:chap 30)

### PDF Report

No

### Day(s) Performed

Monday through Friday

### Report Available

5 days

### Specimen Retention Time

28 days

### Performing Laboratory Location

Rochester

## 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 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 US Food and Drug Administration.

### CPT Code Information

82955

### LOINC® Information

## Test Definition: G6PDC

Glucose 6 Phosphate Dehydrogenase Enzyme  
Activity, Blood

Test ID	Test Order Name	Order LOINC® Value
G6PDC	G6PD Enzyme Activity, B	32546-4

Result ID	Test Result Name	Result LOINC® Value
G6PCL	G6PD Enzyme Activity, B	32546-4