Tay-Sachs disease is an autosomal recessive lysosomal storage disorder caused by accumulation of a fatty substance, called glycosphingolipid GM2 ganglioside, in the lysosomes. The fatty GM2 ganglioside substance is normally broken down in the lysosomes, by the enzyme hexosaminidase-A (HEX A). Loss of HEX A enzyme activity results in buildup of the GM2 ganglioside in lysosomes, particularly in tissues of the central nervous system. Tay Sachs disease is characterized by progressive neurodegeneration with symptoms including seizures, spasticity, and blindness as well as loss of motor skills, progressive muscle weakness, decreased attentiveness, and increased startle reflex. A significant physical finding in persons with Tay-Sachs disease is a cherry red spot on the macula of the retina. Treatment of Tay-Sachs disease is supportive only and death usually occurs by 4 years of age. Variant forms of Tay-Sachs disease include chronic, juvenile, and adult-onset. These forms of HEX A deficiency are characterized by later onset and slower progression of variable neurodegenerative symptoms.

There are three protein components to the hexosaminidase complexes: the alpha subunit, the beta subunit and the GM2 ganglioside activator protein. Deficiency of the alpha subunit, due to mutations in the \textit{HEXA} gene, results in deficiency of the hexosaminidase A complex and causes Tay-Sachs disease. Deficiency of the beta subunit, due to mutations in the \textit{HEXB} gene, results in deficiency of both the beta-hexosaminidase A and B complexes and causes Sandhoff disease. Deficiency of the GM2 ganglioside activator protein, due to mutation in the \textit{GM2A} gene, is associated with the rare AB variant form of GM2 gangliosidosis. Enzymatic analysis can distinguish between the GM2 gangliosidoses. Clinically, these diseases are indistinguishable.

For questions about testing for Tay-Sachs disease, call EGL Genetics at 470-378-2200 or 855-831-7447.

For further clinical information about lysosomal storage diseases, including management and treatment, call the Emory Lysosomal Storage Disease Center at (404) 778-8565 or (800) 200-1524.

### Indications

This test is indicated for:

- Children or adults with symptoms of Tay-Sachs Disease.

### Methodology

Specific total Hexosaminidase activities are determined by fluorometric enzyme assay using artificial 4-MU substrate; and \% Hex A activity is determined by the ratio of Hex A/total Hexosaminidase activity to confirm a diagnosis of Tay-Sachs.

### Specimen Requirements

**Type: Whole Blood**

Specimen Requirements:

- In sodium heparin (green top) tube: 3-5 ml

Specimen Collection and Shipping: Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.