The *NF1* (Neurofibromin 1) gene encodes neurofibromin, a cytoplasmic protein that is predominantly expressed in neurons, Schwann cells, oligodendrocytes, and leukocytes. It is a multidomain molecule with the capacity to regulate several intracellular processes including cell proliferation. Neurofibromin acts as a negative regulator of the RAS signal transduction pathway and also plays a role in cardiac development. *NF1* gene contains 58 coding exons and spans 282.75 kb genomic distance on chromosome 17q11.2. Mutations in *NF1* gene cause neurofibromatosis type 1 characterized by the absence of neurofibromin protein, juvenile myelomonocytic leukemia and Watson syndrome. *NF1* mutations demonstrate autosomal dominant inheritance with a broad range of clinical severity both within and between families. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for *NF1* mutations. Individuals are tested by DNA sequencing of the coding exons of the *NF1* gene. We strongly recommend initial testing of a clearly affected individual, if available, in order to provide the greatest test sensitivity and clearest interpretation of results for subsequent family members. Genetic counseling is recommended for all individuals.

**REASONS FOR REFERRAL**

Molecular confirmation of the diagnosis of congenital heart diseases (CHD).

**METHODOLOGY**

Genomic DNA is analyzed for *NF1* mutations by DNA sequencing of the coding exons of the *NF1* gene, as well as the exon/intron junctions and a portion of the 5’ and 3’ untranslated region. Patient DNA is sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members are analyzed only for the familial mutation by automatic fluorescent DNA sequencing.

**SERVICE FEES**

<table>
<thead>
<tr>
<th></th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$1,600 per sample</td>
<td>81408</td>
</tr>
<tr>
<td>Additional Family Members</td>
<td>$300 per sample; known familial mutation only</td>
<td>81403</td>
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</table>

**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-58 of *NF1*.

**SPECIMEN REQUIREMENTS**

**Blood (preferred):** EDTA (purple-top) tubes:  
- **Adult:** 5 cc  
- **Child:** 5 cc  
- **Infant:** 2-3 cc  

**Tissue:** Frozen (preferred), RNAlater  
**Other Body Fluids or Formalin-fixed, Paraffin-embedded Tissue:** Call to inquire