Noonan syndrome (NS) is characterized by short stature, facial dysmorphisms, and congenital heart defects such as hypertrophic cardiomyopathy, pulmonary valve stenosis, and other structural defects (for example, atrial or ventricular septal defects or tetralogy of Fallot). Additional manifestations of Noonan syndrome include coagulation defects, a short or webbed neck and an unusual chest shape, cryptorchidism in males, hearing loss, ocular abnormalities, lymphatic dysplasias, developmental delay, and mild intellectual disability. Noonan syndrome is estimated to affect between 1 in 1000 and 1 in 2500 individuals.

NS shows clinical overlap with a number of other, rarer syndromes, including LEOPARD (lentigines, ECG abnormalities, ocular hypertelorism, pulmonary stenosis, abnormalities of genitalia, retardation of growth, deafness) syndrome, Costello syndrome (CS), and cardiofaciocutaneous syndrome (CFC). Depending on the actual syndrome present, certain clinical features may be more severe. In addition, each syndrome is associated with specific manifestations or risks, such as bleeding diathesis or increased risk of certain hematological malignancies in the case of NS, increased risk of certain solid tumors in the case of CS, and increased risk of severe skin infections in the case of CFC.

Noonan syndrome and related disorders can be caused by a mutation in one of several different genes. Clinical overlap of the various syndromes is explained by the fact that all of these genes code for components of the same intracellular signaling pathway, namely the RAS/MAPK signaling cascade.

NS and related disorders are autosomal dominant conditions, with many cases of Noonan syndrome and the majority of cases of Costello syndrome and CFS being the result of de novo mutations.

Genetic testing for Noonan syndrome and related disorders may:
- Establish or confirm a clinical diagnosis of Noonan syndrome, LEOPARD syndrome, Costello syndrome, or cardiofaciocutaneous syndrome.
- Identify previously undiagnosed parents, siblings, and other relatives of patients with Noonan syndrome, LEOPARD syndrome, Costello syndrome, or cardiofaciocutaneous syndrome.
- Facilitate appropriate genetic counseling for family members.

**Relevant Assays**

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Test No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>GeneSeq®: Cardio Noonan Syndrome and Related Conditions Profile</td>
<td>451441</td>
</tr>
<tr>
<td>GeneSeq®: Cardio Gene Specific Sequencing, NGS**</td>
<td>452053</td>
</tr>
<tr>
<td>Mutation-specific Sequencing, Whole Blood†</td>
<td>451382</td>
</tr>
</tbody>
</table>

* Visit the online Test Menu at www.LabCorp.com for more information, including a current list of included genes, test methodology, and specimen requirements. To request a sample shipping kit, please call 866-647-0735.

**Full Gene Sequencing for any gene(s) on any of the GeneSeq: Cardio panels

†Known mutation testing for any gene(s) on any of the GeneSeq: Cardio panels

References