Other Natera Products

PANORAMA™, a non-invasive prenatal screen, can be used at 9+ weeks gestation to screen the fetus for common aneuploidies and microdeletions. Horizon and Panorama combination collection kits are available.

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Knowing Matters

Five panels plus a la carte options:

<table>
<thead>
<tr>
<th>Panel</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>500+ MUTATIONS</td>
<td>for Cystic Fibrosis</td>
</tr>
<tr>
<td>DUCHENNE MUSCULAR DYSTROPHY</td>
<td>on every panel</td>
</tr>
<tr>
<td>ENHANCED 2+0 SCREENING</td>
<td>for Spinal Muscular Atrophy</td>
</tr>
<tr>
<td>HEMOGLOBINOPATHIES</td>
<td>on many panels</td>
</tr>
<tr>
<td>274 CONDITIONS</td>
<td>on the Pan-ethnic Extended Panel</td>
</tr>
</tbody>
</table>
Horizon™ Carrier Screening

Knowing your patient’s carrier status matters.

This information allows you to provide comprehensive care, and it enables your patient to make more informed reproductive decisions. The Horizon carrier screen supports you by offering different screening options to best fit the needs of your patients.

All of the panels include Cystic Fibrosis (CF), Spinal Muscular Atrophy (SMA), Fragile X Syndrome, and Duchenne Muscular Dystrophy (DMD). Hemoglobinopathies – including Alpha Thalassemia, Beta Thalassemia, and Sickle Cell Disease - are included in many of the Horizon panels. CF, SMA, and Tay-Sachs Enzyme can also be ordered individually.

<table>
<thead>
<tr>
<th>Panels/ # of Conditions</th>
<th>CF</th>
<th>SMA</th>
<th>Fragile X</th>
<th>DMD</th>
<th>Hemoglobinopathies</th>
<th>Suitable for</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horizon 4 (Pan-ethnic Basic)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>Patients of any ethnic background</td>
</tr>
<tr>
<td>Horizon 27 (Pan-ethnic Standard)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>Patients of any ethnic background</td>
</tr>
<tr>
<td>Horizon 106 (Comprehensive Jewish)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>Patients of Ashkenazi or Sephardic Jewish descent</td>
</tr>
<tr>
<td>Horizon 137 (Pan-ethnic Large)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>Patients of any ethnic background</td>
</tr>
<tr>
<td>Horizon 274 (Pan-ethnic Extended)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>Patients of any ethnic background OR Jewish patients who prefer more coverage than the Horizon 106</td>
</tr>
</tbody>
</table>

Note: Please visit Horizonscreen.com to access specific variants screened for by condition and by panel.

Choose Horizon and Receive More than a Carrier Screen

**Horizon’s sample collection process is simple.** Saliva or blood samples are accepted. Complimentary, on-demand shipping is available to and from your clinic.

**Horizon refines your patients’ risks.** Fragile X automatic AGG interruption testing, enhanced SMA (2+0) screening, and combined Tay-Sachs DNA and enzyme testing provide you with more information than standard screening.

**Horizon includes Duchenne Muscular Dystrophy.** DMD is more common than SMA in boys, and almost as common as CF. Horizon is one of the first carrier screens to include this condition.

**Horizon provides options.** The five panels and à la carte ordering options allow you to screen for just what the guidelines recommend or for a broad number of conditions.

**Genetic counselors are here to support your practice.** At no additional cost, Natera’s board-certified genetic counselors are here to answer your or your patients’ questions about Horizon.
Duchenne Muscular Dystrophy Carrier Screening

DMD carrier screening is now available on Horizon. DMD, a severe, X-linked condition, is the most common muscular dystrophy in children¹. The incidence of DMD is approximately 1/3500 in boys². It affects families of all ethnicities. Approximately 2/3 of clinically diagnosed cases of DMD are attributable to a carrier mother.

The DMD (Dystrophin) Gene and DMD Phenotype

DMD is caused by a mutation in the DMD gene. The DMD gene, which encodes the protein dystrophin, is located on the X chromosome and is the largest protein-coding gene. Boys with DMD present in early childhood with delayed milestones, such as sitting and standing. There is progressive symmetrical proximal muscle weakness and atrophy. Cardiomyopathy typically presents by the teenage years. Survival into the 30s and 40s is becoming more common.

DMD has a Similar Incidence to CF, Fragile X and SMA

The American College of Medical Genetics and Genomics (ACMG) and the American Congress of Obstetricians and Gynecologists (ACOG) recommend all women be screened for CF. ACMG recommends all women be screened for SMA. With a ~1/3500 incidence, DMD is similar in incidence and severity to CF, Fragile X, and SMA.

Carrier Screening Can Detect >90% of Inherited Mutations

Mutations causing DMD are a mix of deletions, duplications, and point mutations³.⁴. Carrier screening can detect >90% of inherited mutations⁵. It is important to note that approximately 33% of cases of DMD are de novo, i.e., having occurred for the first time in the affected male child, and not inherited from a carrier mother.

Identifying Carriers Promotes Proactive Patient Care

Up to 20% of carriers may experience symptoms that range in severity. Symptoms can include muscle weakness and/or cardiomyopathy. Finding out if your patient is a carrier early allows you to proactively manage her care path.

TO WATCH a brief video about DMD, text “DMD” to 67076
More Comprehensive SMA Screening Results

Enhanced (2+0) SMA Screening

SMA is a serious childhood disorder that causes progressive muscle weakness, decreased ability to breathe, loss of motor skills, and in many cases, early death. **Horizon’s SMA carrier screening can help detect SMA ‘silent’ (2+0) carriers**, which are not detected through routine SMA carrier screening. Enhanced SMA carrier screening looks for a single nucleotide polymorphism (SNP) that can be seen in SMA ‘silent’ carriers - those with two copies of SMN1 on one chromosome and none on the other chromosome.

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Carrier Frequency(^a,^b)</th>
<th>Detection Rate w/out Enhanced(^c,^d)</th>
<th>Residual Risk w/ Negative Result(^e,^f)</th>
<th>Detection Rate w/ Enhanced(^c,^d)</th>
<th>Residual Risk w/ Negative(^e,^f)</th>
<th>Residual Risk w/ Positive(^e,^f)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashkenazi Jewish</td>
<td>1 in 41</td>
<td>90%</td>
<td>1 in 345</td>
<td>94%</td>
<td>1 in 580</td>
<td>Likely carrier</td>
</tr>
<tr>
<td>Asian</td>
<td>1 in 53</td>
<td>92%</td>
<td>1 in 628</td>
<td>93%</td>
<td>1 in 702</td>
<td>Likely carrier</td>
</tr>
<tr>
<td>African American</td>
<td>1 in 66</td>
<td>71%</td>
<td>1 in 121</td>
<td>&gt;71%</td>
<td>1 in 396</td>
<td>1 in 34</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1 in 117</td>
<td>91%</td>
<td>1 in 1061</td>
<td>&gt;91%</td>
<td>1 in 1762</td>
<td>1 in 140</td>
</tr>
<tr>
<td>Caucasian</td>
<td>1 in 35</td>
<td>95%</td>
<td>1 in 632</td>
<td>&gt;95%</td>
<td>1 in 769</td>
<td>1 in 29</td>
</tr>
</tbody>
</table>

**SCHEMATIC OF SMN1 GENE CONFIGURATION**

Modified from chart provided by Mt. Sinai Genetic Testing Laboratory

**RESIDUAL RISK ESTIMATES WITH ENHANCED SMA SCREENING**

A More Accurate Fragile X Risk Assessment

Fragile X with Automatic AGG Interruption Testing

Fragile X syndrome is the most common form of inherited intellectual disability in males and occurs when the CGG repeat tract in the FMR1 gene located on the X chromosome contains over 200 CGG repeats. **Horizon’s Fragile X screening provides the number of AGG interruptions, providing refined risk information to help counsel your patients.**

Women typically have <45 CGG repeats. When a woman has between 55-200 CGG repeats, she is considered a ‘premutation carrier’ and is at risk to have a child with Fragile X syndrome. Women who have between 45-54 CGG repeats, while not at risk to have a child with Fragile X syndrome, are at risk for the repeat size to expand in future generations.

When a woman is found to have between 45-90 CGG repeats, AGG interruption testing is performed. If a woman has Fragile X carrier testing without AGG interruption testing and is found to have 68 CGG repeats, she would be counseled that her chance to pass Fragile X on to her child is around 6% \(^g\,^h\). When the number of AGGs are known, her risk can either go up (0 AGGs increases the chance for expansion to full mutation to about 20%) or go down (1 or 2 AGGs reduces the chance for expansion to full mutation to about 5% and less than 1%, respectively).

**FRAGILE X FMR1 GENE: IMPACT OF AGG INTERRUPTIONS ON CGG REPEAT EXPANSION**

Chart and Data provided by Asuragen\(^a\)
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Cystic Fibrosis Screening

The American Congress of Obstetricians and Gynecologists (ACOG) and the America College of Genetics and Genomics (ACMG) recommend Cystic Fibrosis (CF) carrier screening for all patients regardless of ethnicity. **Horizon's CF carrier screening includes 500+ mutations.** These mutations include the 23 mutations recommended by ACOG and ACMG in addition to many others to increase detection rates in all ethnic groups.

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Detection Rate (ACOG/ACMG mutations)</th>
<th>Detection Rate (Horizon 500+ mutations)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td>&gt;88%</td>
<td>&gt;94%</td>
</tr>
<tr>
<td>African American</td>
<td>&gt;64%</td>
<td>&gt;87%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>&gt;71%</td>
<td>&gt;87%</td>
</tr>
<tr>
<td>Asian</td>
<td>&gt;48%</td>
<td>&gt;65%</td>
</tr>
<tr>
<td>Ashkenazi Jewish</td>
<td>&gt;94%</td>
<td>&gt;97%</td>
</tr>
<tr>
<td>General Population</td>
<td>&gt;84%</td>
<td>&gt;86%</td>
</tr>
</tbody>
</table>

Comprehensive Jewish Panel

Some of your patients may not know their Jewish heritage. Horizon’s Comprehensive Jewish Panel is appropriate for patients of Ashkenazi Jewish and Sephardic descent. The Comprehensive Jewish Panel screens for **more than 100 Jewish conditions** to provide your patients with more comprehensive screening. The diseases screened for on this panel have a combined carrier risk of 1 in 2 in the Ashkenazi Jewish population.

This panel includes:
- 37 conditions recommended by the Victor Center and many other conditions that have higher incidence in Jewish populations
- Tay-Sachs DNA and enzyme testing to increase detection rates
- Hemoglobinopathies since they are more common in people from the Mediterranean and Sephardic Jews are from this region

**TO WATCH a brief video about the Comprehensive Jewish Panel, text “PANEL” to 67076**

9. Internal data courtesy of Asuragen, Inc, Austin, TX.
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TO WATCH a brief video about the Horizon and Panorama combination collection kits, text “COMBO” to 67076