Inheritest® Carrier Screen

Genetic testing services and support, from preconception to prenatal
The way many think about carrier screening is changing.

Carrier screening, once thought to be a test primarily for specific ethnic groups, is now recommended for every patient. The American College of Obstetricians and Gynecologists (ACOG) states that carrier screening for spinal muscular atrophy (SMA), in addition to cystic fibrosis (CF), "should be offered to all women who are considering pregnancy or are currently pregnant."

**Comprehensive, versatile, covering what matters**

Inheritest® provides carrier screening for more than 110 severe, primarily early onset disorders, that can cause cognitive or physical impairment and/or require surgical or medical intervention.

<table>
<thead>
<tr>
<th>Panel</th>
<th>Genes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CF/SMA Panel</strong></td>
<td>2</td>
<td>Includes CF and SMA, which are among the most common genetic disorders</td>
</tr>
</tbody>
</table>
| **CORE Panel**               | 3     | Focuses on mutations for CF, SMA, and fragile X syndrome, with the following carrier risks:  
|                              |       | • CF: as high as 1 in 24\(^{10}\) (varies by ethnicity)                   |
|                              |       | • SMA: as high as 1 in 47\(^{11}\) (varies by ethnicity)                  |
|                              |       | • Fragile X syndrome: approximately 1 in 259 females (all ethnicities)      |
| **Society-guided Panel**     | 14    | This multi-ethnic panel allows for a consistent screening approach as recommended by ACOG |
| **Ashkenazi Jewish Panel**   | 48    | Enhanced panel includes mutations for more than 40 disorders relevant to patients of Ashkenazi Jewish descent |
| **Comprehensive Panel**      | 144   | Includes mutations for more than 110 disorders across 144 different genes—includes all disorders in Core, Society-guided, and Ashkenazi Jewish Panels |
“The primary goal of carrier screening is to facilitate informed reproductive decision making by identifying those couples at risk of having an affected child with an (autosomal or X-linked) recessive disorder.”

According to ACOG, each provider or practice should “establish a standard approach that is consistently offered to and discussed with each patient, ideally before pregnancy.”

The case for ethnic-neutral carrier screening

While some providers may only screen for CF and SMA, or select screening based on ethnicity, the case for more comprehensive screening is becoming clear. According to a bulletin from the World Health Organization, the global prevalence at birth of all single-gene disorders is about 10 per 1000.³

In a recent Practice Resource, ACMG recommends that “carrier screening paradigms should be ethnic and population neutral and more inclusive of diverse populations...”⁴

Ancestry and family history can be a mystery

An absence of disorders in a patient’s family can be an insufficient guide for targeted screening. For example, more than 80% of infants with CF are born to families with no prior family history.⁷ In addition, early studies estimated that each person carries three to five mutations, which, if passed along in a pregnancy, could lead to a genetic disorder.⁸

<table>
<thead>
<tr>
<th>When summarizing the disorders the Comprehensive Panel identifies:*</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>115</td>
<td>can result in severe early onset, increased childhood mortality, or shortened lifespan</td>
</tr>
<tr>
<td>78</td>
<td>may cause intellectual disability</td>
</tr>
<tr>
<td>77</td>
<td>are metabolic disorders that may have treatment benefit with early medical intervention</td>
</tr>
<tr>
<td>62</td>
<td>may cause loss of vision/ eye problems in affected individuals—early identification could be beneficial</td>
</tr>
<tr>
<td>39</td>
<td>may cause deafness/ hearing loss—early identification could be beneficial</td>
</tr>
<tr>
<td>6</td>
<td>are X-linked, meaning only the mother has to be a carrier for the child to be at risk</td>
</tr>
</tbody>
</table>

Some disorders will have characteristics of multiple categories.

*Based on information on the relevant disorders compiled from Genetics Home Reference and GARD.⁵ ⁶
### SMA Gene in Normal and Carrier States

<table>
<thead>
<tr>
<th>State</th>
<th>SMN1 Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-Carrier</strong></td>
<td>2 copies of SMN1, each on a different chromosome</td>
</tr>
<tr>
<td><strong>SMA Carrier</strong></td>
<td>1 copy of SMN1 on one chromosome and 0 copies of SMN1 on other chromosome</td>
</tr>
<tr>
<td><strong>SMA Silent Carrier</strong></td>
<td>2 copies of SMN1 on the same chromosome</td>
</tr>
</tbody>
</table>

**Next-generation sequencing is used for the Comprehensive, Ashkenazi Jewish, and Society-guided Panels. PCR with reflex to Southern blot is used for fragile X syndrome analysis, quantitative PCR analysis is used for SMA analysis and deletion/duplication analysis is used for alpha-thalassemia analysis. While all panels include CF analysis, the Core and CF/α-thalassemia Panels use a bead-based array that identifies 97 common CF mutations.**

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**One fast result for fragile X risk assessment**

Inheritest Carrier Screen offers a fast turnaround time for a complete and final fragile X result with both CGG and AGG repeats reported.

Inheritest Carrier Screen Lab report including a final CGG/AGG fragile X result (when appropriate)

\~ 14 days

**Prenatal diagnosis**

Additionally, once an at-risk pregnancy is identified, we can perform prenatal diagnostic testing—for any of the disorders in the Inheritest panels—to deliver insights regarding the baby’s condition.

Where some testing service providers are unable to offer single gene testing, VUS identification, or prenatal diagnosis—sometimes resulting in time-consuming retesting—Labcorp offers a continuum of care for patients that can both save time and reduce anxiety.

**Enhanced SNP analysis to identify patients at risk to be silent (2+0) SMA carriers**

- Potential identification of more couples at risk for having a child with SMA\(^{13}\)
- Enhanced residual risk estimates to inform genetic counseling and support patient education\(^{13}\)
- Improved prenatal and neonatal management, including early diagnosis and early referral for new therapies

**NGS and appropriate confirmations for greater accuracy**

Inheritest Carrier Screen uses next-generation sequencing (NGS)† and other appropriate technologies to capture a broad spectrum of mutations, including rare variants. Positive results are confirmed with an orthogonal technology as recommended by ACMG, to deliver optimal sensitivity and specificity.

**Focused partner testing**

If your patient’s result is positive, Labcorp can offer her partner full gene sequencing for most autosomal recessive genes in the Inheritest panels.

Full gene sequencing detects disease-causing variants as well as variants of uncertain significance, to identify a greater number of potentially at-risk pregnancies.

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\(^{1}\)Next-generation sequencing is used for the Comprehensive, Ashkenazi Jewish, and Society-guided Panels. PCR with reflex to Southern blot is used for fragile X syndrome analysis, quantitative PCR analysis is used for SMA analysis and deletion/duplication analysis is used for alpha-thalassemia analysis. While all panels include CF analysis, the Core and CF/α-thalassemia Panels use a bead-based array that identifies 97 common CF mutations.
## Inheritest CF/SMA Panel
- Cystic fibrosis (97 mutations)
- Spinal muscular atrophy

## Inheritest Core Panel
- Cystic fibrosis (97 mutations)
- Spinal muscular atrophy
- Fragile X syndrome (females only)

## Inheritest Society-guided Panel
- Alpha-thalassemia
- Beta hemoglobinopathy; includes sickle cell disease, hemoglobins C, D, E, and O, and beta thalassemias
- Bloom syndrome
- Canavan disease
- Cystic fibrosis
- Familial dysautonomia
- Fanconi anemia group C
- Fragile X syndrome (females only)
- Gaucher disease
- Mucolipidosis type IV
- Niemann-Pick disease types A and B
- Spinal muscular atrophy
- Tay-Sachs disease

## Inheritest Ashkenazi Jewish Panel
- Abetalipoproteinemia
- Alpha-thalassemia
- Alport syndrome, COL4A3-related
- Arthrogryposis, mental retardation, and seizures (AMRS)
- Ataxia-telangiectasia
- Bardet-Biedl syndrome, BBS2-related
- Beta hemoglobinopathy; includes sickle cell disease, hemoglobins C, D, E, and O, and beta thalassemias
- Bloom syndrome
- Canavan disease
- Carnitine palmitoyltransferase II deficiency
- Congenital amegakaryocytic thrombocytopenia
- Congenital disorder of glycosylation type 1a
- Cystic fibrosis
- Cystinosis
- Dihydrolipoamide dehydrogenase deficiency
- Ehlers-Danlos syndrome type VIIC
- Familial dysautonomia
- Familial hyperinsulinism, ABCC8-related
- Familial Mediterranean fever
- Familial dysautonomia
- Familial hyperinsulinism, ABCC8-related
- Familial Mediterranean fever
- Fanconi anemia group C
- Fragile X syndrome (females only)
- Galactosemia, GAL-T-related
- Gaucher disease
- Glycogen storage disease type Ia
- Glycogen storage disease type III
- Joubert syndrome 2
- Maple syrup urine disease type 1A
- Maple syrup urine disease type 1B
- Metachromatic leukodystrophy
- Mucolipidosis type IV
- Multiple sulphatase deficiency
- Nemaline myopathy, NEB-related
- Niemann-Pick disease types A and B
- Phenylalanine hydroxylase deficiency, includes phenylketonuria (PKU)
- Phosphoglycerate dehydrogenase deficiency, PHGDH-related
- Polycystic kidney disease, autosomal recessive
- Retinitis pigmentosa 59
- Smith-Lemli-Opitz syndrome
- Spinal muscular atrophy
- Tay-Sachs disease
- Tyrosinemia type 1
- Usher syndrome type IF
- Usher syndrome type IIIA
- Walker-Warburg syndrome, FKTN-related
- Wilson disease
- Zellweger spectrum disorder, PEX2-related
- Zellweger spectrum disorder, PEX6-related
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<td><strong>Andersen syndrome</strong></td>
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<td><strong>Arginosuccinic aciduria</strong></td>
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<td><strong>Aspartylglucosaminuria</strong></td>
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<td><strong>Ataxia with vitamin E deficiency</strong></td>
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<td><strong>Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS)</strong></td>
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<td><strong>Bardet-Biedl syndrome, BBS1-related</strong></td>
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<tr>
<td><strong>Bardet-Biedl syndrome, BBS10-related</strong></td>
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<td><strong>Bardet-Biedl syndrome, BBS2-related</strong></td>
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<td><strong>Carnitine acylcarnitine translocase deficiency</strong></td>
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<tr>
<td><strong>Cartilage-hair hypoplasia</strong></td>
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<tr>
<td><strong>Citrininemia type I</strong></td>
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<tr>
<td><strong>Cobalamin C disease</strong></td>
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Test/Panel Name | Test No.
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Inheritest® CF/SMA Panel | 452172
Inheritest Core Panel | 451964
Inheritest Society-guided Panel | 451960
Inheritest Ashkenazi Jewish Panel | 451920
Inheritest Comprehensive Panel | 451950
Gene-specific Sequencing | 451910
Mutation-specific Sequencing | 451382/640

Specimen requirements: 8.5 mL whole blood in a yellow-top (ACD-A) tube or lavender-top (EDTA) tube.

Continuity of care, pioneering science, professional service

Inheritest is available through Labcorp, which delivers continuity of care for your patients, from carrier screening to noninvasive prenatal testing (NIPT, also known as cfDNA testing) to diagnostic testing.

We provide the scientific expertise you need, and the customer experience patients want.

Results reporting

Samples have a turnaround time of ~2 weeks from the date of pickup of a specimen for testing to when the result is released.

Extensive managed care contracts

Help patients maximize their benefits.

Convenient blood draws

We have a nationwide network of patient service centers, allowing for convenient access to sample collection. Visit Labcorp.com to find your nearest location.

Genetic counseling

Patients with a positive test result may be offered counseling, and Labcorp offers the largest national commercial network of genetic counselors to help inform and support patients. Visit our online scheduler at womenshealth.labcorp.com or call 855.422.2557. To learn more about genetic inheritance and carrier screening for genetic disorders visit womenshealth.labcorp.com/videos.

References


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Toll-free (within the US) at 800.848.4436

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Labcorp

3400 Computer Drive
Westborough, Massachusetts 01581