GENETICS & WOMEN'S HEALTH

Inheritest® Carrier Screen

Genetic testing services and support, from preconception to prenatal

labcorp

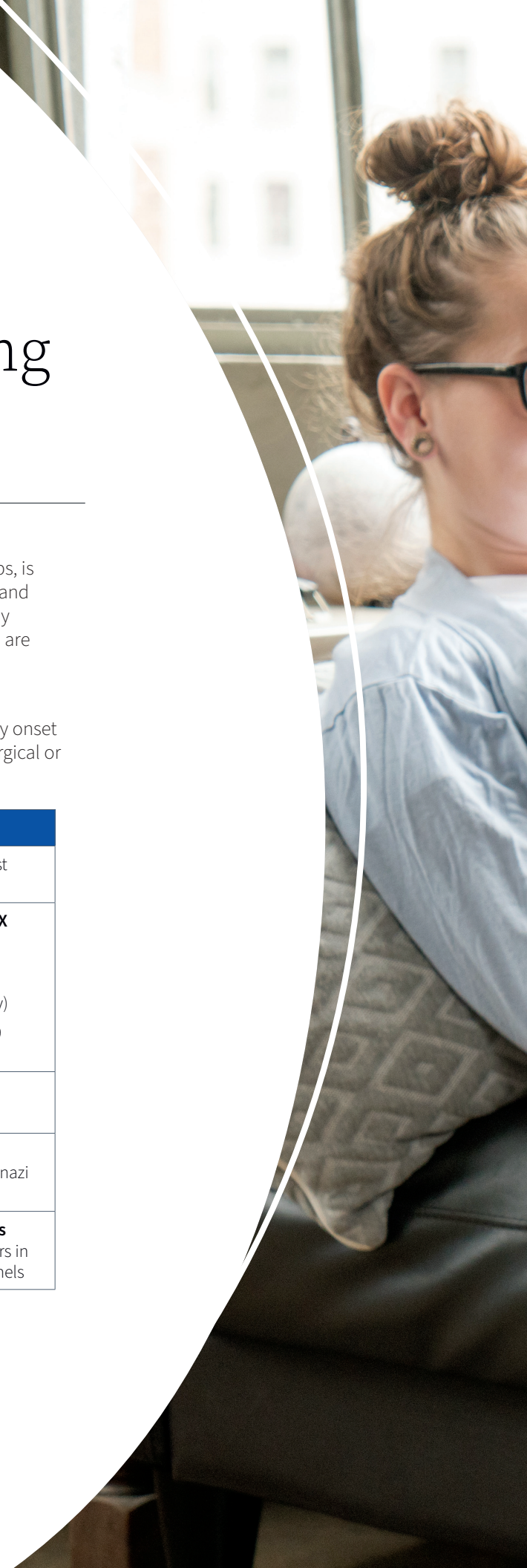
The way many think about carrier screening is changing.

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."[9]

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.

Inheritest offers multiple panels to suit the diverse needs of your patients:		
CF/SMA Panel	**2 genes**	Includes CF and SMA, which are among the most common genetic disorders
CORE Panel	**3 genes**	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)[12]
Society-guided Panel	**14 genes**	This multi-ethnic panel allows for a consistent screening approach as recommended by ACOG
Ashkenazi Jewish Panel	**48 genes**	Enhanced panel includes mutations for **more than 40 disorders** relevant to patients of Ashkenazi Jewish descent
Comprehensive Panel	**144 genes**	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."[1]

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."[2]

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]

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

Some disorders will have characteristics of multiple categories.

*Based on information on the relevant disorders compiled from Genetics Home Reference and GARD.[5,6]

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]

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.

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.

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

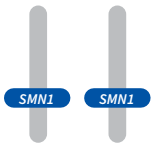
- Potential identification of more couples at risk for having a child with SMA[13]
- Enhanced residual risk estimates to inform genetic counseling and support patient education[13]
- Improved prenatal and neonatal management, including early diagnosis and early referral for new therapies

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.

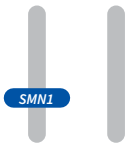
Full gene sequencing detects disease-causing variants as well as variants of uncertain significance, to identify a greater number of potentially at-risk pregnancies.

SMN1 Gene in Normal and Carrier States



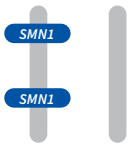
Non-Carrier

2 copies of *SMN1*, each on a different chromosome



SMA Carrier

1 copy of *SMN1* on one chromosome and 0 copies of *SMN1* on other chromosome



SMA Silent Carrier

2 copies of *SMN1* on the same chromosome

†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/SMA 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	Joubert syndrome 2
Alpha-thalassemia	Maple syrup urine disease type 1A
Alport syndrome, *COL4A3*-related	Maple syrup urine disease type 1B
Arthrogryposis, mental retardation, and seizures (AMRS)	Metachromatic leukodystrophy
Ataxia-telangiectasia	Mucolipidosis type IV
Bardet-Biedl syndrome, *BBS2*-related	Multiple sulphatase deficiency
Beta hemoglobinopathy; includes sickle cell disease, hemoglobins C, D, E, and O, and beta thalassemias	Nemaline myopathy, *NEB*-related
Bloom syndrome	Niemann-Pick disease types A and B
Canavan disease	Phenylalanine hydroxylase deficiency, includes phenylketonuria (PKU)
Carnitine palmitoyltransferase II deficiency	Phosphoglycerate dehydrogenase deficiency, *PHGDH*-related
Congenital amegakaryocytic thrombocytopenia	Polycystic kidney disease, autosomal recessive
Congenital disorder of glycosylation type 1a	Retinitis pigmentosa 59
Cystic fibrosis	Smith-Lemli-Opitz syndrome
Cystinosis	Spinal muscular atrophy
Dihydrolipoamide dehydrogenase deficiency	Tay-Sachs disease
Ehlers-Danlos syndrome type VIIC	Tyrosinemia type 1
Familial dysautonomia	Usher syndrome type IF
Familial hyperinsulinism, *ABCC8*-related	Usher syndrome type IIIA
Familial Mediterranean fever	Walker-Warburg syndrome, *FKTN*-related
Fanconi anemia group C	Wilson disease
Fragile X syndrome (females only)	Zellweger spectrum disorder, *PEX2*-related
Galactosemia, *GALT*-related	Zellweger spectrum disorder, *PEX6*-related
Gaucher disease	
Glycogen storage disease type Ia	
Glycogen storage disease type III	

Inheritest Comprehensive Panel			
Abetalipoproteinemia	Ethylmalonic encephalopathy	Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)	Pompe disease
Adenosine deaminase deficiency	Familial Mediterranean fever	Metachromatic leukodystrophy	Primary hyperoxaluria type 1
Alpha-mannosidosis	Familial dysautonomia	Methylmalonic acidemia, *MMAA*-related	Primary hyperoxaluria type 2
Alpha-thalassemia	Familial hyperinsulinism, *ABCC8*-related	Methylmalonic acidemia, *MMAB*-related	Propionic acidemia, *PCCA*-related
Alport syndrome, *COL4A3*-related	Fanconi anemia group C	Methylmalonic acidemia, *MUT*-related	Propionic acidemia, *PCCB*-related
Andermann syndrome	Fragile X syndrome (females only)	Mitochondrial acetoacetyl-CoA thiolase deficiency	Pyruvate dehydrogenase deficiency, *PDHA1*-related
Argininosuccinic aciduria	Fucosidosis	Mucolipidosis type II and III, *GNPTAB*-related	Retinitis pigmentosa 59
Arthrogryposis, mental retardation, and seizures (AMRS)	GM1 gangliosidosis and mucopolysaccharidosis type IVB	Mucolipidosis type IV	Rhizomelic chondrodysplasia punctata type 1
Aspartylglucosaminuria	GRACILE syndrome	Mucopolysaccharidosis type I	Salla disease
Ataxia with vitamin E deficiency	Galactosemia, *GALT*-related	Mucopolysaccharidosis type II	Sandhoff disease
Ataxia-telangiectasia	Galactosialidosis	Mucopolysaccharidosis type IIIA	Sialidosis
Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS)	Gaucher disease	Mucopolysaccharidosis type IIIB	Sjogren-Larsson syndrome
Bardet-Biedl syndrome, *BBS1*-related	Glutaric acidemia type 1	Mucopolysaccharidosis type IIIC	Smith-Lemli-Opitz syndrome
Bardet-Biedl syndrome, *BBS10*-related	Glutathione synthetase deficiency	Mucopolysaccharidosis type IIID	Spinal muscular atrophy
Bardet-Biedl syndrome, *BBS2*-related	Glycine encephalopathy, *AMT*-related	Mucopolysaccharidosis type IV A	*Sulfate transporter*-related osteochondrodysplasias, includes achondrogenesis type 1B, atelosteogenesis type 2, diastrophic dysplasia, and recessive multiple epiphyseal dysplasia
Beta hemoglobinopathy, includes sickle cell disease, hemoglobins C, D, E, and O, and beta thalassemias	Glycine encephalopathy, *GLDC*-related	Mucopolysaccharidosis type VI	
Beta-mannosidosis	Glycogen storage disease type III	Mucopolysaccharidosis type VII	
Bloom syndrome	Glycogen storage disease type Ia	Multiple sulphatase deficiency	Systemic primary carnitine deficiency
Canavan disease	Glycogen storage disease type Ib	Nemaline myopathy, *NEB*-related	Tay-Sachs disease
Carbamoyl phosphate synthetase I deficiency	Guanidinoacetate methyltransferase deficiency	Nephrotic syndrome, *NPHS1*-related	Tyrosinemia type 1
Carnitine palmitoyltransferase II deficiency	HMG-CoA lyase deficiency	Nephrotic syndrome, *NPHS2*-related	Usher syndrome type IF
Carnitine-acylcarnitine translocase deficiency	Hereditary fructose intolerance	Neuronal ceroid-lipofuscinosis, *CLN3*-related	Usher syndrome type IIIA
Cartilage-hair hypoplasia	Holocarboxylase synthetase deficiency	Neuronal ceroid-lipofuscinosis, *CLN5*-related	Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)
Citrullinemia type I	Homocystinuria, *CBS*-related	Neuronal ceroid-lipofuscinosis, *CLN8*-related	Walker-Warburg syndrome, *FKTN*-related
Cobalamin C disease	Hypophosphatasia, autosomal recessive	Neuronal ceroid-lipofuscinosis, *PPT1*-related	Wilson disease
Cohen syndrome	Joubert syndrome 2	Neuronal ceroid-lipofuscinosis, *TPP1*-related	X-linked severe combined Immunodeficiency (SCID)
Congenital amegakaryocytic thrombocytopenia	Junctional epidermolysis bullosa, *LAMA3*-related	Niemann-Pick disease type C, *NPC1*-related	Xeroderma pigmentosum, *ERCC5*-related
Congenital disorder of glycosylation type 1a	Junctional epidermolysis bullosa, *LAMB3*-related	Niemann-Pick disease type C, *NPC2*-related	Xeroderma pigmentosum, *XPA*-related
Cystic fibrosis	Junctional epidermolysis bullosa, *LAMC2*-related	Niemann-Pick disease types A and B	Xeroderma pigmentosum, *XPC*-related
Cystinosis	Krabbe disease	Nijmegen breakage syndrome	Zellweger spectrum disorder, *PEX1*-related
D-bifunctional protein deficiency	Leigh syndrome, French Canadian type	Ornithine transcarbamylase deficiency	Zellweger spectrum disorder, *PEX10*-related
Dihydrolipoamide dehydrogenase deficiency	Leigh syndrome, autosomal recessive, includes French Canadian type	Phenylalanine hydroxylase deficiency, includes phenylketonuria (PKU)	Zellweger spectrum disorder, *PEX12*-related
Dihydropyrimidine dehydrogenase deficiency	Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)	Phosphoglycerate dehydrogenase deficiency, *PHGDH*-related	Zellweger spectrum disorder, *PEX2*-related
Dystrophinopathies, includes Duchenne and Becker muscular dystrophies and X-linked cardiomyopathy	Maple syrup urine disease type 1A	Polycystic kidney disease, autosomal recessive	Zellweger spectrum disorder, *PEX26*-related
Ehlers-Danlos syndrome type VIIC	Maple syrup urine disease type 1B		Zellweger spectrum disorder, *PEX6*-related

Test/Panel Name	Test No.
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
1. Henneman U: Responsible Implementation of expanded carrier screening. Journal of Human Genetics 2016.
2. American College of Obstetrics and Gynecologists. Carrier screening in the age of genomic medicine. Committee opinion no. 690. Obstet Gynecol, March 2017.
3. Genomics and World Health. Report of The Advisory Committee on Health Research. World Health Organization, Geneva, 2002.
4. Gregg, et al. Screening for autosomal recessive and X-linked conditions during pregnancy and preconception: a practice resource of the American College of Medical Genetics and Genomics (ACMG). Genetics in Medicine 2021; https://doi.org/10.1038/s41436-021-01203-z.
5. Genetic and Rare Diseases Information Center (GARD). https://rarediseases.info.nih.gov. Accessed August 8, 2017.
6. Genetics Home Reference. https://ghr.nlm.nih.gov. Accessed August 8, 2017.
7. Wildhagen MF, et al. Screening for cystic fibrosis and its evaluation. British Medical Bulletin 1998;54 (No. 4): 857-875.
8. Chong JX, et al. A population-based study of autosomal-recessive disease-causing mutations in a founder population. Am J Hum Genet. 2012 Oct 5; 91(4): 608-Q20.
9. American College of Obstetricians and Gynecologists. Carrier screening for genetic conditions. Committee opinion no. 691. Obstet Gynecol 2017;129:e41–55
10. American College of Obstetricians and Gynecologists. Update on carrier screening for cystic fibrosis. Committee Opinion No. 486. April 2011.
11. Sugarman EA, et al. Pan-ethnic carrier screening and prenatal diagnosis for spinal muscular atrophy: clinical laboratory analysis of >72,400 specimens. Eur J Hum Genet 2012; 20:27-32.
12. Dombrowski C, et al. Premutation and intermediate-size FMR1 alleles in 10572 males from the general population: loss of an AGG interruption is a late event in the generation of fragile x syndrome alleles. Hum Mol Genet 2002; 11 (4): 371-8.
13. Luo M, Liu L, Peter I, et al. An Ashkenazi Jewish SMN1 haplotype specific to duplication alleles improves pan-ethnic carrier screening for spinal muscular atrophy. American College of Medical Genetics and Genomics. Submitted 2 February 2013; accepted 2 May 2013; advance online publication 20 June 2013. Doi:10.1038/gim.2013.84.

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