horizon™
natera carrier screen

Knowing Matters

Five panels plus a la carte options:

500+ MUTATIONS	for Cystic Fibrosis
DUCHENNE MUSCULAR DYSTROPHY	on every panel
ENHANCED 2+0 SCREENING	for Spinal Muscular Atrophy
HEMOGLOBINOPATHIES	on many panels
274 CONDITIONS	on the Pan-ethnic Extended Panel

natera™
Conceive. Deliver.

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.

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

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 a 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

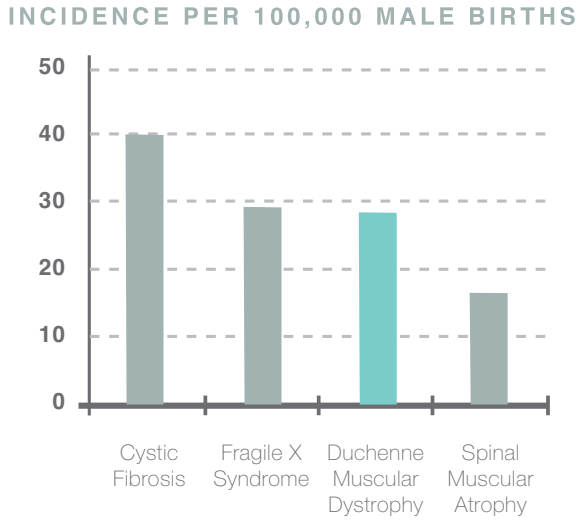
DMD carrier screening is now available on Horizon. DMD, a severe, X-linked condition, is the most common muscular dystrophy in children[1]. The incidence of DMD is approximately 1/3500 in boys[2]. It affects families of all ethnicities. Approximately 2/3 of clinically diagnosed cases of DMD are attributable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

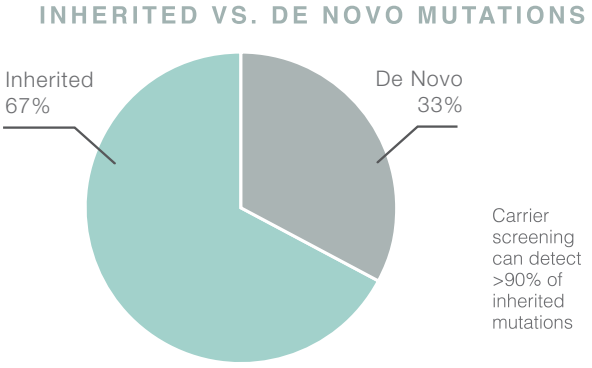
DMD has a Similar Incidence to CF, Fragile X and SMA

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 mutations[3,4]. Carrier screening can detect >90% of inherited mutations[5]. 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.

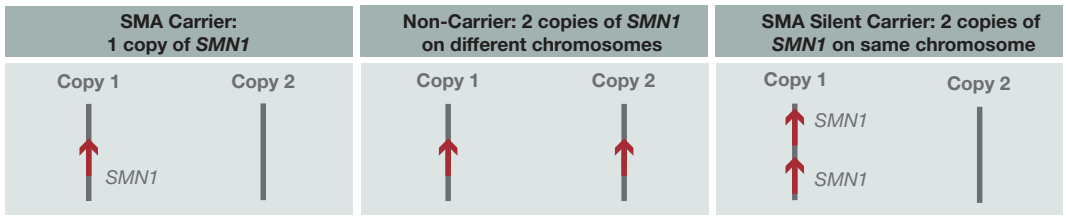
TO WATCH a brief video about DMD, text "DMD" to 67076

More Comprehensive SMA Screening Results

Enhanced (2+0) SMA Screening

SMA is a serious childhood disorder that causes progressive muscle weakness, decreased ability to breath, 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.

SCHEMATIC OF SMN1 GENE CONFIGURATION



Modified from chart provided by Mt. Sinai Genetic Testing Laboratory

RESIDUAL RISK ESTIMATES WITH ENHANCED SMA SCREENING

Ethnicity	Carrier Frequency[6,7]	Detection Rate w/out Enhanced[6,7]	Residual Risk w/ Negative Result[6,7]	Detection Rate w/ Enhanced[6,7]	Residual Risk w/ Negative[6,7]	Residual Risk w/ Positive[6,7]
Ashkenazi Jewish	1 in 41	90%	1 in 345	94%	1 in 580	Likely carrier
Asian	1 in 53	92%	1 in 628	93%	1 in 702	Likely carrier
African American	1 in 66	71%	1 in 121	>71%	1 in 396	1 in 34
Hispanic	1 in 117	91%	1 in 1061	>91%	1 in 1762	1 in 140
Caucasian	1 in 35	95%	1 in 632	>95%	1 in 769	1 in 29

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%[8,9]. 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*

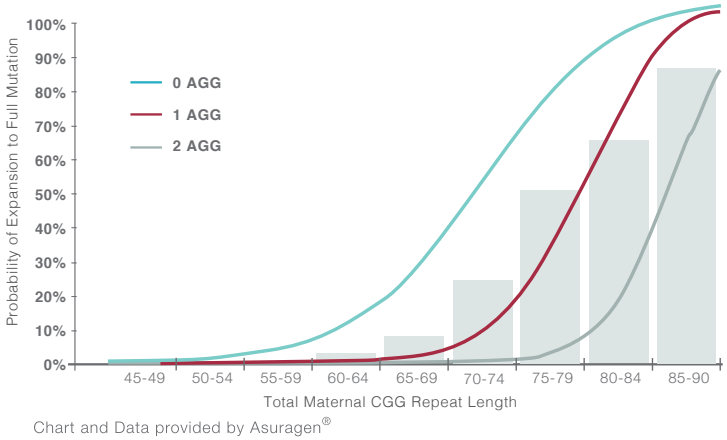


Chart and Data provided by Asuragen®

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.

Ethnicity	Detection Rate (ACOG/ACMG mutations)[10]	Detection Rate (Horizon 500+ mutations)[11,12,13]
Caucasian	>88%	>94%
African American	>64%	>87%
Hispanic	>71%	>87%
Asian	>48%	>65%
Ashkenazi Jewish	>94%	>97%
General Population	>84%	>86%

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

1. Punnoose, AR, Golub, RM MD. Muscular Dystrophy. JAMA. 2011;306(22):2526.
2. Rodino-Klapac LR, Chicoine LG, Kaspar BK, Mendell JR. Gene therapy for Duchenne muscular dystrophy. Arch Neurol 2007;64:1236–1241
3. Dent KM, Dunn DM, von Niederhausern AC, Aoyagi AT, Kerr L, Bromberg MB, Hart KJ, Tuohy T, White S, den Dunnen JT, Weiss RB, Flanigan KM. Improved molecular diagnosis of dystrophinopathies in an unselected clinical cohort. Am J Med Genet A. 2005;134:295–8.
4. Flanigan KM, Dunn DM, von Niederhausern A, Soltanzadeh P, Gappmaier E, Howard MT, Sampson JB, Mendell JR, Wall C, King WM, Pestronk A, Florence JM, Connolly AM, Mathews KD, Stephan CM, Laubenthal KS, Wong BL, Morehart PJ, Meyer A, Finkel RS, Bonnemann CG, Hinton VJ, De Vivo DC, Nereo NE, Goldstein E, Stern Y. Selective deficits in verbal working memory associated with a known genetic etiology: the neuropsychological profile of duchenne muscular dystrophy. J Int Neuropsychol Soc. 2001; 7: 45–54.
5. Data on file.
6. Hendrickson BC et al. Differences in SMN1 allele frequencies among ethnic groups within North America. J Med Genet. 2009;46:641-644.
7. Luo M et al. An Ashkenazi Jewish SMN1 haplotype specific to duplication alleles improves pan-ethnic carrier screening for spinal muscular atrophy. Genet Med. 2014 Feb;16(2):149-56.
8. Nolin, S.L. et al., Fragile X AGG Analysis Provides New Risk Predictions for 45–69 Repeat AllelesExpansion of the fragile X CGG repeat in females with premutation or intermediate alleles. Am J Med Genet Part A 2013; 161A:771-778.
9. Internal data courtesy of Asuragen, Inc. Austin, TX
10. Watson M, Cutting G, Desnick R et al. Cystic fibrosis population carrier screening: 2004 revision of American College of Medical Genetics mutation panel. Genet Med. 2004;6(5):387-391.
11. American College of Obstetricians and Gynecologists Committee on Genetics. ACOG Committee Opinion No. 486: Update on carrier screening for cystic fibrosis. Obstet Gynecol. 2011 Apr;117(4):1028-31.
12. Scott SA, Edelmann L, Liu L, Luo M, Desnick RJ, Kornreich R. Experience with carrier screening and prenatal diagnosis for 16 Ashkenazi Jewish genetic diseases. Hum Mutat. 2010 Nov;31(11):1240-50.
13. Data on file.

Natera's Horizon Support Services

Genetic Counseling Support. More than 20 Board Certified Genetic Counselors who are experts on Horizon and are here to support your clinic at no additional cost.

Patient Counseling Materials. Pre-counseling fact sheets are available to help explain conditions to your patients. Post-test disease supplements and counseling videos for specific positive results are also available.

Natera Connect Portal. Natera Connect provides a secure, central access point for all results for any Natera test you have ordered.

EMR Integration. Integration through HL7 provides connectivity to your Electronic Medical Records (EMR) / Electronic Health Records (EHR) system for ordering and receiving test results.

Phlebotomy Services. If you do not have a phlebotomist in your office, patients can get their blood drawn at one of the more than 2500 locations with which we are contracted or through one of our mobile phlebotomists.

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.**

ANORA™, a miscarriage (products of conception) test, helps determine if a miscarriage was caused by a chromosomal abnormality in the fetus.

SPECTRUM™, a preimplantation screening (PGS) and diagnosis (PGD) product, screens IVF-created embryos for chromosome abnormalities before implantation.

TO WATCH a brief video about the Horizon and Panorama combination collection kits, text **"COMBO"** to **67076**

Ordering Information

Collection kits are provided directly to the clinic at no charge and can be stored on site.

To order a Horizon Carrier Screen Collection Kit

SIMPLY CALL: +1(650) 249-9090

OR EMAIL: customersupport@natera.com

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panorama™ natera prenatal screen

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spectrum™ natera preimplantation genetics (PGS/PGD)

anora™ natera miscarriage test (POC)

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