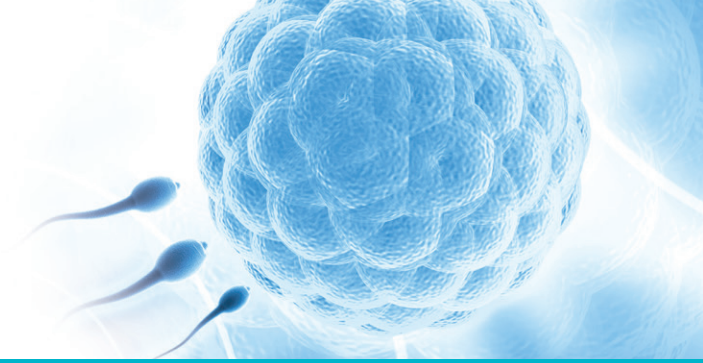


# Genetic Carrier Screen



## Carrier Screening

Carrier screening is genetic testing performed to determine whether individuals or couples have a genetic variant (mutation) that may affect their chance of having a child with a genetic condition. Genomic Diagnostics Genetic Carrier Screen, tests for three relatively common genetic conditions in general populations: Cystic Fibrosis (CF), Fragile X (FXS), and Spinal Muscular Atrophy (SMA). These conditions were chosen based on their inclusion in local and international genetic screening recommendations for patients considering conception<sup>1,3</sup>

Many children affected by these conditions are born to families with no history of disease due to the relatively rare nature of the conditions and inheritance patterns - autosomal recessive or X-linked in the included conditions. The value of carrier screening for CF and SMA has therefore been recognised for all patients in some countries such as the United States<sup>1</sup>, with the value of Fragile X also being recently recognised in Australian research<sup>2</sup>.

Importantly, if couples are found to be carriers of these conditions, they can consider several reproductive options including:

- natural pregnancy, with or without prenatal diagnosis
- preimplantation genetic diagnosis (PGD) with in vitro fertilization (IVF) to test and then transfer embryos that are free of the condition
- adoption
- the use of a sperm or egg donor

## Background:

**What is Cystic Fibrosis?** Cystic Fibrosis is an autosomal recessive genetic condition caused by a malfunction in the exocrine system responsible for producing saliva, sweat and mucus. This can result in a variety of symptoms, from mild (pancreatic sufficient) to severe (pancreatic insufficient), affecting mostly the respiratory and digestive systems.

**What is Fragile X syndrome?** Fragile X is an X-linked genetic condition causing intellectual disability, behavioural and learning challenges and various physical characteristics. It is also the most common single gene cause of autism worldwide (accounting for up to 5% of all cases) and the most common genetic cause of intellectual disability in males. Although Fragile X Syndrome occurs in both sexes, males are generally affected with greater severity than females.

**What is Spinal Muscular Atrophy:** Spinal Muscular Atrophy (SMA) is an autosomal recessive condition that results in the loss of motor neurones in the spinal cord and is classified as a motor neurone disease. The primary symptom is weakness of the voluntary muscles. In the most common form of SMA, due to mutations on chromosome 5, there is wide variability in age of onset, symptoms and progression rate.

## How Common Are These Conditions?

These three conditions combined are amongst the most commonly carried mutations in European populations.

|                         | CARRIER FREQUENCY | NUMBER OF LIVE BIRTHS                    |
|-------------------------|-------------------|--|
| Cystic Fibrosis         | 1 in 25           | 1 in 2,500                               |
| Fragile X               | 1 in 150          | 1 in 4,000 males<br>(1 in 8,000 females) |
| Spinal Muscular Atrophy | 1 in 49           | 1 in 6,000 – 10,000                      |

## Mode of Inheritance

|                         | MODE OF INHERITANCE |
|-------------------------|---------------------|
| Cystic Fibrosis         | Autosomal recessive |
| Fragile X               | X-linked            |
| Spinal Muscular Atrophy | Autosomal recessive |

**PLEASE NOTE: THIS TEST IS NOT COVERED BY PRIVATE HEALTH INSURANCE OR MEDICARE. PRE-PAYMENT FOR THIS TEST IS REQUIRED BEFORE TESTING. CALL CUSTOMER CARE TO PRE-PAY ON 1800 822 999**

## Assay performance

This assay tests for the most common genetic changes associated with FXS, CF and SMA. The assay can detect:

- 88% of Cystic Fibrosis carriers\*
- 99% of Fragile X carriers
- 95% of Spinal Muscular Atrophy carriers

The test cannot detect everyone who is a carrier as rarer mutations cannot be detected by the assay. Therefore, the use of this assay in a carrier screening setting can significantly reduce the risk of a couple having an affected child but cannot remove this risk completely.

\*Based on Caucasian population data

## Which Cystic Fibrosis mutations are tested for by the assay?

Since the discovery of the CFTR gene in 1989, more than 1900 mutations and variants have been described. Many of these mutations have been described only in one patient and/or family. Routine testing for all possible mutations is not cost effective and therefore testing is confined to the most common mutations.

Genomic Diagnostics' carrier screening test identifies 50 of the most common mutations in European populations. This exceeds both Human Genetics Society of Australasia (HGSA) and American College of Medical Genetics and Genomics (ACMG) guideline recommendations for the 29 most frequently occurring mutations.

## How to Order

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### Step 1

#### Consider Genetic Testing

Discuss with your patient as recommended by clinical guidelines

### Step 2

#### Request Test

Order test using standard request form. **Ask for 'Genetic Carrier Screen' noting any family history or pregnancy**

### Step 3

#### Patient Pays for the Test

**The patient calls our customer care team on 1800 822 999 to pre-pay for the test and is given a receipt number**

### Step 4

#### Patient Attends a Dorevitch Collection Centre

The patient attends a Dorevitch collection centre where the sample is collected and

### Step 5

#### Results Returned

The results will be returned using your preferred method

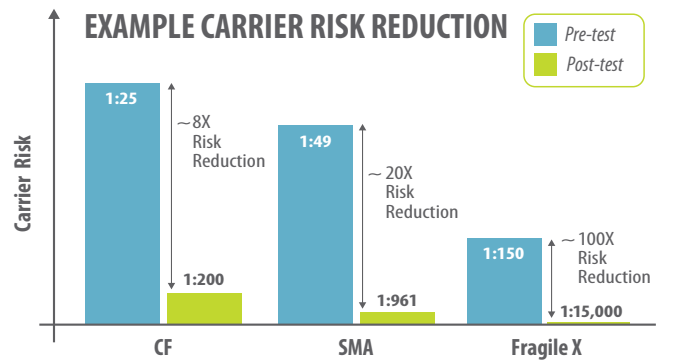
**ENQUIRIES: CALL 1800 822 999 or EMAIL: [info@genomicdiagnostics.com.au](mailto:info@genomicdiagnostics.com.au)**

**Autosomal recessive inheritance:** A mode of inheritance such that an individual must have a mutation in both copies of the specific disease gene, usually one inherited from each parent, to express the genetic condition.

**X-linked inheritance:** A mode of inheritance in which a mutation on the X chromosome causes the expression of the genetic condition. Males are typically affected, as they only have one X chromosome, whereas females may show variable expression of the condition due to differences in X chromosome inactivation: As Fragile X is a dominant mutation, females can be affected, but at approximately half the rate of males (50% chance of female receiving normal allele from mother). Mutations are typically inherited from a mother who is an unaffected carrier.

#### References:

1. ACOG Committee Opinion, No. 690, March 2017. "Carrier Screening in the Age of Genomic Medicine".
2. Metcalfe, S.A. Genetics In Medicine, 2017. "Informed decision making and psychosocial outcomes in pregnant and non-pregnant women offered population fragile X carrier screening".
3. Prenatal screening and diagnosis of chromosomal and genetic abnormalities in the fetus in Pregnancy. RANZCOG. C-obs 59.



#### Assumptions:

1. Caucasian population - frequencies will vary for other ethnic groups.
2. Calculations are based on reported test sensitivity CF: 90% SMA: 95% and Fragile X: 99%

## When should patients be tested?

The ideal setting for carrier screening is preconception, in order to have the most time to deal with all possible testing outcomes. However, testing can also be used in an antenatal setting.

## Genetic counselling

If the couple are shown to be carriers for any of these conditions, then genetic counselling is recommended so that they can get more information and discuss in detail their options and potential impacts of their situation.

## How can I get my patient tested?

The two testing options are to either initially test the **female partner**, and to only test her partner if she is found to be a carrier or, for fastest results, test both partners at the same time. **Please note details on the request form if the patient has a family history of any of these conditions or is pregnant.**