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# Cystic Fibrosis Testing: Information for Ordering Providers

Cystic fibrosis (CF) is a multisystem disease caused by variants in the *CFTR* gene. CF may affect the respiratory tract, pancreas, sweat glands, and male reproductive tract. Pulmonary disease is the major cause of morbidity and mortality in CF. CF is a complex disease with significant clinical variability in the type and severity of symptoms. Many factors, including the combination of genetic variants, contribute to this clinical variability.[1]

## Testing Approach

Testing should begin with the panel of the most common *CFTR* variants. A negative result *reduces but does not eliminate* the chance that an individual is a CF carrier/is affected by CF. Complete sequencing of the CF gene is available for certain clinical indications. Additional information about sequencing the *CFTR* gene is available by contacting the laboratory genetic counsellors.

## *CFTR* Variants on Panel

| | | | | |
|---|---|---|---|---|
| G85E* (c.254G>A) | R117H* (c.350G>A) | 394delTT (c.262_263delTT) | 621+1G>T* (c.489+1G>T) | 711+1G>T* (c.579+1G>T) |
| R334W* (c.1000C>T) | R347P* (c.1040G>C) | R347H* (c.1040G>A) | A455E* (c.1364C>A) | delI507* (c.1519_1521delATC) |
| 1717-1G>A* (c.1585–1G>A) | G542X* (c.1624G>T) | S549R (c.1647T>G) | S549N (c.1646G>A) | G551D* (c.1652G>A) |
| R560T* (c.1679G>C) | 1898+1G>A* (c.1766+1G>A) | 2184delA* (c.2052delA) | 2789+5G>A* (c.2657+5G>A) | 3120+1G>A* (c.2988+1G>A) |
| 3876delA (c.3744delA) | R1162X* (c.3484C>T) | 3659delC* (c.3528delC) | 3905insT (c.3773dupT) | W1282X* (c.3846G>A) |
| N1303K* (c.3909C>G) | R553X* (c.1657C>T) | delF508* (c.1521_1523delCTT) | 3849+10kbC>T* (c.3718–2477C>T) | 1078delT (c.948delT) |
| Y122X (c.366T>A) | V520F (c.1558G>T) | A559T (c.1675G>A) | 1898+5G>T (c.1766+5G>T) | 2183AA>G (c.2051_2052delAAinsG) |
| Y1092X (c.3276C>G, c.3276C>A) | M1101K (c.3302T>A) | S1255X (c.3764C>A) | 2307insA (c.2175dupA) | IVS8-5/7/9T (c.1210-12T[5,7,9]) |

*mutations currently recommended by the American College of Medical Genetics

## Panel Detection Rates

North American Caucasian: 90.5%
African Americans: 67.5%
Ashkenazi Jewish: 94%
Hispanic Americans: 73.8%
Asian Americans: 48.9%

## Newborn Screening

- CF is one of the disorders on the newborn screening panel (https://www.ahs.ca/info/Page9024.aspx). In the context of newborn screening, the IVS8 T tract length is only reported in the presence of R117H.

## Indications for Testing

- Confirmation of a clinical diagnosis of CF or *CFTR*-related disorder
- Carrier testing for individuals with a confirmed family history of a *CFTR* variant or a partner with one or more *CFTR* variants
- Male factor infertility due to congenital absence of the vas deferens (CAVD)
- Prenatal diagnosis when the fetus is at increased risk for CF
- Parental carrier testing or prenatal diagnosis when fetus has echogenic bowel
- Confirmation of molecular results following an inconclusive or probable newborn screen result

**Familial Variants**
If your patient has a family history of CF or a relative who is a CF carrier, please provide the name of the relative and a copy of the molecular report. This will ensure that your patient has the appropriate testing.

**When can I expect results?**
CF panel testing may take up to 8 weeks.

**How are results reported?**
Results are sent to the ordering provider and available in Netcare and Connect Care.

**Requisition forms, contact information and other resources can be found at:**
**http://ahsweb.ca/lab/if-lab-genetics-and-genomics**

**Contact Information**
Genetic Counsellors, Genetics & Genomics
Edmonton: 780-407-1015

**References**
1. Adam MP, Mirzaa GM, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2018. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1116/ (accessed [2022 August])