Physician Insert: MiSeqDx® Cystic Fibrosis Clinical Sequencing Assay

FOR IN VITRO DIAGNOSTIC USE

Test Indication

This test is indicated to aid in the diagnosis of patients with suspected cystic fibrosis (CF). This test is most appropriate when a patient has an atypical presentation of CF or when other mutation variant panels have failed to identify both causative variants. The results of the test should be used in conjunction with clinical symptoms, other diagnostic tests, and family history.

CAUTION

This test is not intended for newborn screening, carrier screening, or population screening or for stand-alone diagnostic purposes.

This test is not intended for fetal diagnostic testing or pre-implantation testing.

What the Test Detects

- This test performs targeted sequencing at 5206 genomic positions/regions in the Cystic Fibrosis Transmembrane Conductance Regulator (*CFTR*) gene in DNA isolated from whole blood collected in K_2EDTA.
- All protein coding regions in the *CFTR* gene including 10 nt of flanking intronic sequence are detected for all exons with the exception of three (exons 7, 10, and 20).
  - For exon 7 and exon 10, only 5 nt of flanking intronic sequence is included at the 5' end of the exon to avoid proximal homopolymeric InDels.
  - For exon 20, 30nt of flanking intronic sequence is included at the 5' end of the exon to enable detection of the mutation 3272-26A>G.
- In addition, the assay also detects ~100 nt of flanking sequence at the 5' and 3' UTRs, 2 deep intronic mutations (1811+1.6kbA>G, 3489+10kbC>T), 2 large deletions (CFTRdele2,3, CFTRdele22,23) and the PolyTG/PolyT region.
- The test detects single base changes and small insertions and deletions within the *CFTR* gene region sequenced.
- The test has not been validated for any other deletions or insertions greater than 3 bp in size.

Test Interpretation and Limitations

- Test results should be interpreted by board-certified clinical molecular geneticist or equivalent.
- Variants in *CFTR* identified by this test may be CF-disease causing, non-disease causing, or of unknown significance.
- There is substantial variability in phenotype among patients, even those with the same genotype. Expected disease presentation associated with certain variants may be based on a few clinical cases and may range from benign to severe. Rare *CFTR* variants may be poorly characterized and clinical significance may not have been assessed.
- If more than one variant is detected in a sample, the assay cannot determine phase or haplotype of the variants.
- It is recommended that patients consult with a genetic counselor regarding their results.
- It was not possible to validate all rare and novel variants that could be detected in the *CFTR* gene by this test. Therefore, it is highly recommended that novel or rare variants be confirmed by a reference method, such as Sanger sequencing. Please discuss variant detection validation with the testing laboratory.

- This test sequences specific regions of the *CFTR* gene including all coding regions and certain other areas deemed clinically relevant. However, some regions of the gene are not covered. Thus an overall "wild-type" result does not guarantee that *CFTR* variants are not present in the sample.
- Variants which could be identified by this test vary in frequency in the population. Please be aware that for very rare *CFTR* variants, the possibility of false positive findings is increased.

NOTE
For more information about the clinical significance of a large number of *CFTR* variants that may be detected by this test, please refer to the *MiSeqDx Cystic Fibrosis 139-Variant Assay Physician Insert (part # 15052172)*.

Patents and Trademarks

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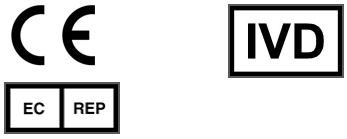

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