NGS CF Control Panel G211 v1.1

BACKGROUND:

Cystic fibrosis (CF) is the most common inherited disease in the United States today. CF is an autosomal recessive disorder, caused by the presence of mutations in both copies of the gene for the protein, cystic fibrosis transmembrane conductance regulator (CFTR). CF has a disease occurrence of approximately one out of 2,000 – 4,000 live births[1]. Although CF does not affect all people the same way, it is generally recognized as causing persistent lung infections. CF also affects other organs, including the pancreas, liver, kidneys and intestine. It is characterized by the buildup of thick, sticky mucus in the lungs, pancreas and other organs, resulting in a complex multi-organ, multisystem disease[1]. There is no cure for CF but some therapies may prolong life, therefore, a key focus of current interventional efforts is early diagnosis through newborn screening[2].

CFTR protein is involved in production of sweat, digestive fluids and mucus. The gene was first identified in 1989 on human chromosome 7 and contains 27 coding exons[3,4]. When CFTR is not functional, these secretions which are usually thin and watery instead become thick and mucus-like and ultimately lead to nutritional decline and progression of lung disease associated with morbidity and mortality[1]. Over 2,000 variants have been reported in the CFTR coding and flanking sequence, in all ethnic and racial populations at various frequencies. However, less than 10% of these reported variants have been interpreted to be clinically-relevant variants. The 190 CFTR variants listed in Table 1 are contained in the 6 tubes of **NGS CF Control Panel G211 v1.1**. The 143 asterisked (*) variants have been identified as CF-causing by The Clinical and Functional Translation of CFTR (CFTR2) international project and are listed in the CFTR2 database at http://cftr2.org (April 7, 2023 version)[5,6]. Highlighted in Table 1 are 71 of 100 mutations recommended in 2023 by the American College of Medical Genetics and Genomics (ACMG) and in 2011 by the American College of Obstetricians and Gynecologists (ACOG)[7,8,9]. These mutations have been bolded and asterisked in Table 1. Legacy nomenclature is used throughout this Package Insert. Table 2 contains the 28 ACMG variants recommended for carrier screening that are not part of the NGS CF Control Panel G211 v1.1.

INTENDED USE:

The **NGS CF Control Panel G211 v1.1** is intended for *in vitro* use as a quality control to monitor the analytical performance of library preparation, sequencing and data analysis associated with Next Generation Sequencing for identifying variants within the CFTR gene. Additionally, because the **NGS CF Control Panel G211 v1.1** carries multiple insertions, deletions and homopolymers of varying lengths and composition, this control panel can also serve as a method control to monitor the ability of any NGS test system to correctly identify these types of variants. Appropriate primers are required to amplify the areas of interest.

NGS CF Control Panel G211 v1.1 is provided for Research Use Only (RUO). It cannot be cloned, sold, or transferred without the explicit written consent of MMQCI.

PRODUCT SUMMARY AND PRINCIPLE:

Next Generation Sequencing (NGS) technology, also known as massively parallel sequencing, involves sequencing of spatially separated, clonally amplified DNA templates to generate simultaneous sequencing of thousands to millions of relatively short nucleic acid sequences in parallel. This technology allows for targeted, sequencing of the CFTR gene and includes a complex multistep procedure for library preparation, target enrichment and sequencing analysis.

NGS CF Control Panel G211 v1.1 is designed as a multiplex reference material to monitor the simultaneous detection of the CFTR mutations and variants associated with cystic fibrosis listed in Table 1, including 71 of 100 mutations recommended by ACMG and ACOG. The **NGS CF Control Panel G211 v1.1** product is intended to be analyzed routinely with each cystic fibrosis test run and provide a quality control for all aspects of library preparation, sequencing, and data analysis.

Controls should be tested routinely as a matter of Good Laboratory Practice and according to guidelines or requirements of local, state, and/or federal regulations or accrediting organizations. Best practice is to establish a quality control program for every assay performed by the laboratory. Routine use of quality controls that are consistent lot to lot assists the laboratory in identifying shifts, trends, and increased frequency of random errors caused by variations in the test system. Early investigation can prevent failed assay runs.

COMPOSITION:

NGS CF Control Panel G211 v1.1 consists of synthetic CFTR DNA suspended in a non-infectious buffer with stabilizers. The synthetic DNA is composed of all 27 CFTR gene exons plus intronic borders, and contains CF associated mutations and variants divided among 6 tubes (G211Av1.1, G211Bv1.1, G211Cv1.1, G211Dv1.1, G211Ev1.1 and G211Fv1.1). The mutations and variants present in **NGS CF Control Panel G211 v1.1** are described in Table 1. This control panel is provided as a non-extractable control with copy numbers of target sequence that are similar to that of extracted human whole blood samples.

INSTRUCTIONS FOR USE:

Controls are ready to use; no extraction is needed.

1. Thaw all controls completely.
2. Allow the controls to be tested to come to room temperature (18° – 25°C).
3. Mix well by flicking the control tubes and vortex immediately before using.
4. Quick spin to remove droplets from the tube cap before opening.
5. Pipette the same volume (usually 5-10μL) pipetted for patient sample DNA for each control tube, and treat just as you would extracted genomic DNA.
6. Follow all other procedures as described by test manufacturer's product insert.
7. Opened material should be tightly capped and returned to freezer (-25°C to -15°C) immediately after use.

Note: NGS CF Control Panel G211 v1.1 cannot be quantified or measured by standard methods such as spectrophotometry (A260nm/A280nm) because synthetic DNA has significantly less mass than genomic DNA. However, the controls are manufactured to have approximately equivalent copy numbers of the target gene as genomic DNA. Please contact MMQCI if guidance on volume to add to assay is desired.

STORAGE and STABILITY:

Upon receipt and after opening, the material should be stored at -25°C to -15°C. Unopened **NGS CF Control Panel G211 v1.1** is stable through the expiration date printed on each tube when stored frozen (-25°C to -15°C). Opened material should be tightly capped and returned to the freezer (-25°C to -15°C) immediately after use. The material is stable for five freeze/thaw cycles.

PRECAUTIONS and WARNINGS:

- Do not dilute.
- Do not transfer control material to a new tube.
- Do not quantify by spectrophotometry or other standard methods.
- Do not freeze/thaw more than 5 times.
- This product does not contain any biological material of human origin and is not infectious. Universal Precautions are not required when handling this product.

EXPECTED VALUES:

The genotype for each CFTR variant found in tubes A-F of **NGS CF Control Panel G211 v1.1** is listed in Table 1. The sequence of **NGS CF Control Panel G211 v1.1** has been confirmed by bi-directional Sanger sequencing. In order for an NGS assay to detect all genotypes listed, the NGS assay primers must have sufficient control sequence on either side of the variant to anneal and amplify the area of interest. If unexpected calls are reported, or variants not detected, your laboratory's NGS primers may require sequence not present in **NGS CF Control Panel G211 v1.1**, or they may anneal poorly due to the presence of a mutation. Please contact MMQCI for interpretation assistance as needed.

The laboratory should follow Good Laboratory Practice (GLP) and establish its own performance characteristics for **NGS CF Control Panel G211 v1.1** in demonstrating adequate system performance.

ORDERING INFORMATION:
NGS CF Control Panel G211 v1.1
Part Number: G211v1.1
Kit Contains: 6 tubes x 50μL

Maine Molecular Quality Controls, Inc.
23 Mill Brook Road, Saco, ME 04072 USA
Phone: 207-885-1072, FAX: 207-885-1079
Web: www.mmqci.com, Email: info@mmqci.com

Table 1. NGS CF Control Panel G211 v1.1 Variants are listed in genomic coordinate order. **Bold** = Part of ACMG recommended panel of 100 variants.
Asterisk* = clinically relevant CFTR2 variants.

CFTR Mutation Legacy Name	cDNA Name (HGVS)	Tube A	Tube B	Tube C	Tube D	Tube E	Tube F
1. M1V*	c.1A>G	WT	WT	WT	WT	WT	HET
2. R31C	c.91C>T	WT	WT	HET	WT	WT	WT
3. CFTRdele2,3*	c.54-5940_273+10250 del21kb	HET	WT	WT	WT	WT	WT
4. Q39X*	c.115C>T	WT	WT	WT	WT	WT	HET
5. 296+2T>A	c.164+2T>A	WT	WT	WT	WT	HET	WT
6. E60X*	**c.178G>T**	WT	HET	WT	WT	WT	WT
7. P67L*	**c.200C>T**	WT	WT	WT	WT	HET	WT
8. R74W	c.220C>T	WT	WT	WT	WT	WT	HET
9. R75X*	**c.223C>T**	WT	WT	WT	HET	WT	WT
10. G85E*	**c.254G>A**	WT	HET	WT	WT	WT	WT
11. 394delTT*	**c.262_263delTT**	WT	WT	HET	WT	WT	WT
12. G91G	c.273G>A	WT	WT	WT	WT	HET	WT
13. 405+1 G>A*	c.273+1G>A	WT	WT	WT	WT	HET	WT
14. 405+3A>C*	c.273+3A>C	WT	WT	WT	HET	WT	WT
15. 406-1 G>A*	**c.274-1G>A**	WT	WT	WT	HET	WT	WT
16. E92K*	c.274G>A	WT	WT	WT	WT	WT	HET
17. E92XG>T*	c.274G>T	WT	WT	WT	WT	HET	WT
18. Q98X*	**c.292C>T**	WT	WT	HET	WT	WT	WT
19. 444delA*	**c.313delA**	WT	WT	WT	HET	WT	WT
20. 457TAT>G*	c.325_327delinsG	WT	WT	WT	WT	HET	WT
21. D110H*	**c.328G>C**	WT	WT	WT	WT	WT	HET
22. R117C*	**c.349C>T**	WT	WT	WT	HET	WT	WT
23. R117H	**c.350G>A**	WT	HET	WT	WT	WT	WT
24. Y122X*	c.366T>A	HET	WT	WT	WT	WT	WT
25. 574delA*	c.442delA	WT	WT	WT	WT	HET	WT
26. I148T	c.443T>C	WT	HET	WT	WT	WT	WT
27. 621+1 G>T*	**c.489+1G>T**	WT	HET	WT	WT	WT	HET
28. 663delT*	c.531delT	WT	WT	WT	WT	HET	WT
29. G178R*	c.532G>A	WT	WT	WT	HET	WT	WT
30. 711+1 G>T*	**c.579+1G>T**	WT	HET	WT	WT	WT	WT
31. 711+3 A>G*	**c.579+3A>G**	WT	WT	WT	WT	WT	HET
32. 711+5 G>A*	c.579+5G>A	WT	WT	HET	WT	WT	WT
33. 712-1 G>T*	c.580-1G>T	WT	WT	WT	WT	HET	WT
34. H199Y*	c.595C>T	WT	HET	WT	WT	WT	WT
35. P205S C>T*	c.613C>T	WT	WT	HET	WT	WT	WT
36. L206W*	**c.617T>G**	WT	WT	WT	HET	WT	WT
37. Q220X*	c.658C>T	WT	WT	WT	WT	WT	HET
38. L227R*	c.680T>G	WT	WT	HET	WT	WT	WT
39. 852del22*	c.723_743+1del	WT	WT	HET	WT	WT	WT
40. 935delA*	**c.803delA**	WT	WT	WT	HET	WT	WT
41. 936delTA*	c.805_806delAT	WT	WT	WT	WT	HET	WT
42. delF311	c.929TCT[2]	WT	WT	WT	HET	WT	WT
43. 1078delT*	c.948delT	WT	HET	WT	WT	WT	WT
44. G330X*	**c.988G>T**	WT	WT	WT	HET	WT	WT
45. R334W*	**c.1000C>T**	WT	HET	WT	WT	WT	WT
46. I336K*	c.1007T>A	WT	WT	WT	WT	WT	HET
47. T338I*	**c.1013C>T**	WT	WT	WT	WT	HET	WT
48. S341P*	c.1021T>C	WT	WT	HET	WT	WT	WT
49. 1154insTC*	**c.1021_1022dupTC**	HET	WT	WT	WT	WT	WT
50. R347H*	**c.1040G>A**	WT	WT	HET	WT	WT	WT
51. R347P*	**c.1040G>C**	WT	HET	WT	WT	WT	WT
52. R352Q*	**c.1055G>A**	WT	WT	WT	HET	WT	WT
53. 1213delT*	c.1081delT	WT	WT	WT	WT	WT	HET
54. S364P	c.1090T>C	WT	WT	WT	HET	WT	WT
55. 1248+1G>A*	c.1116+1G>A	HET	WT	WT	WT	WT	WT
56. 1259insA*	c.1130dupA	WT	WT	WT	WT	WT	HET
57. 1288insTA*	**c.1155_1156dupTA**	WT	WT	WT	WT	HET	WT
58. W401X (TAG)*	c.1202G>A	HET	WT	WT	WT	WT	WT
59. W401X (TGA)*	c.1203G>A	WT	WT	WT	HET	WT	WT
60. 1341+1G>A*	c.1209+1G>A	WT	WT	HET	WT	WT	WT
61. PolyT	PolyT	7T/7T	9T/9T	7T/5T	5T/9T	7T/9T	9T/9T
62. PolyTG	PolyTG	(TG)11/(TG)12	(TG)12/(TG)12	(TG)11/(TG)12	(TG)11/(TG)12	(TG)11/(TG)12	(TG)11/(TG)12
63. 1461ins4*	**c.1327_1330dupGATA**	WT	WT	WT	WT	WT	HET
64. A455E*	**c.1364C>A**	WT	HET	WT	WT	WT	WT
65. 1525-1G>A*	**c.1393-1G>A**	WT	WT	WT	WT	WT	HET
66. S466X (C>A)*	c.1397C>A	WT	WT	WT	WT	HET	WT
67. S466X (C>G)*	**c.1397C>G**	HET	WT	WT	WT	WT	WT
68. L467P*	**c.1400T>C**	WT	WT	HET	WT	WT	WT
69. M470V	c.1408G>A	HET	HOM	HET	HOM	HOM	HET
70. 1548delG*	c.1418delG	WT	WT	WT	HET	WT	WT
71. G480C	c.1438G>T	WT	WT	WT	HET	WT	WT
72. S489X*	c.1466C>A	WT	WT	HET	WT	WT	WT
73. S492F*	c.1475C>T	HET	WT	WT	WT	WT	WT
74. Q493X*	c.1477C>T	HET	WT	WT	WT	WT	WT
75. I506V	c.1516A>G	WT	WT	HET	WT	WT	WT
76. I506T (T>C)	c.1517T>C	WT	WT	WT	WT	HET	WT
77. I507V	c.1519A>G	HET	WT	WT	WT	WT	WT
78. I507del*	**c.1516ATC[1] (c.1519_1521del)**	WT	WT	HET	HET	WT	WT
79. F508del*	**c.1521_1523delCTT**	WT	HET	WT	WT	WT	WT
80. F508C	c.1523T>G	HET	WT	WT	WT	WT	WT
81. 1677delTA*	c.1545_1546delTA	WT	WT	HET	HET	WT	WT

Table 1. Cont'd: NGS CF Control Panel G211 v1.1 Variants are listed in genomic coordinate order. **Bold** = Part of ACMG recommended panel of 100 variants. Asterisk* = clinically relevant CFTR2 variants.

CFTR Mutation Legacy Name	cDNA Name (HGVS)	Tube A	Tube B	Tube C	Tube D	Tube E	Tube F
82. V520F*	c.1558G>T	WT	HET	WT	WT	WT	WT
83. Q525X*	c.1573C>T	WT	WT	WT	WT	WT	HET
84. 1717-1G>A*	**c.1585-1G>A**	WT	HET	WT	WT	WT	WT
85. 1717-8G>A*	c.1585-8G>A	WT	WT	WT	WT	WT	HET
86. G542X*	**c.1624G>T**	WT	HET	WT	WT	WT	WT
87. S549R*	c.1645A>C	WT	WT	HET	WT	WT	WT
88. S549N*	**c.1646G>A**	WT	WT	WT	HET	WT	WT
89. S549R*	**c.1647T>G**	HET	WT	WT	WT	WT	WT
90. G551D*	**c.1652G>A**	WT	HET	WT	WT	WT	WT
91. Q552XC>T*	c.1654C>T	WT	WT	WT	WT	HET	WT
92. R553X*	**c.1657C>T**	WT	WT	HET	WT	WT	WT
93. L558S*	**c.1673T>C**	WT	WT	WT	WT	WT	HET
94. A559T*	**c.1675G>A**	HET	WT	WT	WT	WT	WT
95. R560T*	**c.1679G>C**	WT	HET	WT	WT	WT	WT
96. R560K*	c.1679G>A	WT	WT	WT	HET	WT	WT
97. 1811+1.6 kb*	c.1680-886A>G	WT	WT	WT	WT	WT	HET
98. 1812-1 G>A*	c.1680-1G>A	WT	WT	WT	HET	WT	WT
99. Y569D*	**c.1705T>G**	WT	WT	WT	WT	WT	HET
100. G576A	c.1727G>C	WT	WT	WT	HET	WT	WT
101. D579G	c.1736A>G	WT	WT	WT	WT	HET	WT
102. E585X*	**c.1753G>T**	WT	WT	HET	WT	WT	WT
103. 1898+1 G>A*	**c.1766+1G>A**	WT	HET	WT	WT	WT	WT
104. 1898+3 A>G*	c.1766+3A>G	WT	WT	WT	WT	HET	WT
105. 1898+5G>T*	**c.1766+5G>T**	HET	WT	WT	WT	WT	WT
106. 1949del84*	c.1820_1903del84	HET	WT	WT	WT	WT	WT
107. D614G	c.1841A>G	WT	WT	WT	WT	WT	HET
108. G622D	c.1865G>A	WT	WT	WT	HET	WT	WT
109. 2055del9>A*	c.1923_1931delinsA	WT	WT	WT	HET	WT	WT
110. 2108delA*	c.1976delA	WT	WT	WT	WT	HET	WT
111. R668C	c.2002C>T	WT	WT	WT	WT	WT	HET
112. 2143delT*	c.2012delT	WT	HET	WT	WT	WT	WT
113. 2183AA>G*	c.2051_2052delinsG	WT	WT	HET	WT	WT	WT
114. 2184insA*	**c.2052dupA**	WT	WT	WT	WT	HET	WT
115. 2184delA*	**c.2052delA**	WT	HET	WT	WT	WT	WT
116. R709XC>T*	**c.2125C>T**	WT	WT	WT	WT	HET	WT
117. K710X*	c.2128A>T	WT	WT	WT	HET	WT	WT
118. 2307insA*	**c.2175dupA**	HET	WT	WT	WT	WT	WT
119. L732X*	c.2195T>G	WT	WT	WT	WT	WT	HET
120. 2347delG*	c.2215delG	WT	WT	WT	HET	WT	WT
121. V754M	c.2260G>A	WT	WT	WT	WT	WT	HET
122. R764XC>T*	**c.2290C>T**	WT	WT	WT	WT	HET	WT
123. 2585delT*	c.2453delT	WT	WT	WT	WT	WT	HET
124. E822X*	c.2464G>T	WT	WT	WT	HET	WT	WT
125. 2622+1G>A*	**c.2490+1G>A**	WT	HET	WT	WT	WT	WT
126. E831X*	c.2491G>T	WT	WT	WT	WT	WT	HET
127. W846X*	c.2537G>A	HET	WT	WT	WT	WT	WT
128. W846X(2670)*	c.2538G>A	WT	HET	WT	WT	WT	WT
129. R851X*	c.2551C>T	WT	WT	WT	WT	WT	HET
130. 2711delT*	c.2583delT	WT	WT	WT	HET	WT	WT
131. 2789+2insA	c.2657+2_2657+3insA	WT	WT	WT	WT	WT	HET
132. 2789+5G>A*	**c.2657+5G>A**	WT	HET	WT	WT	WT	WT
133. Q890X*	**c.2668C>T**	WT	WT	WT	HET	WT	HET
134. 2869insG*	c.2737_2738insG	WT	WT	WT	HET	WT	WT
135. L927P*	c.2780T>C	WT	WT	WT	WT	WT	HET
136. S945L*	**c.2834C>T**	WT	WT	WT	WT	WT	HET
137. 3007delG*	c.2875delG	WT	HET	WT	WT	WT	WT
138. G970R*	c.2908G>C	WT	WT	WT	WT	WT	HET
139. S977F	c.2930C>T	WT	WT	WT	WT	WT	HET
140. 3120G>A*	**c.2988G>A**	WT	WT	WT	HET	WT	WT
141. 3120+1G>A*	**c.2988+1G>A**	WT	HET	WT	WT	WT	WT
142. 3121-1G>A*	c.2989-1G>A	WT	WT	WT	WT	WT	HET
143. L997F (G>C)	c.2991G>C	WT	WT	WT	WT	HET	WT
144. 3171delC*	c.3039delC	WT	WT	WT	WT	HET	WT
145. 3199del6*	**c.3067_3072delATAGTG**	WT	HET	WT	WT	WT	WT
146. I1027T	c.3080T>C	WT	WT	WT	WT	WT	HET
147. 3272-26A>G*	**c.3140-26A>G**	WT	WT	HET	WT	WT	WT
148. F1052V	c.3154T>G	WT	WT	WT	WT	WT	HET
149. L1065P*	c.3194T>C	WT	WT	WT	WT	HET	WT
150. R1066C*	**c.3196C>T**	WT	WT	WT	HET	WT	WT
151. R1066H*	**c.3197G>A**	WT	WT	HET	WT	WT	WT
152. G1069R	c.3205G>A	WT	WT	WT	WT	WT	HET
153. R1070W	c.3208C>T	WT	HET	WT	WT	WT	WT
154. R1070Q	c.3209G>A	HET	WT	WT	WT	WT	WT
155. L1077P*	c.3230T>C	WT	HET	WT	WT	HET	WT
156. W1089X*	**c.3266G>A**	WT	WT	WT	HET	WT	WT
157. Y1092X (C>A)*	c.3276C>A	HET	WT	WT	WT	WT	WT
158. Y1092X (C>G)*	c.3276C>G	WT	WT	HET	WT	WT	WT
159. M1101K*	c.3302T>A	HET	WT	WT	WT	WT	WT
160. E1104X*	c.3310G>T	WT	WT	WT	WT	WT	HET
161. D1152H	c.3454G>C	WT	HET	WT	WT	WT	WT
162. R1158X*	**c.3472C>T**	WT	WT	HET	WT	WT	WT
163. R1162X*	**c.3484C>T**	WT	HET	WT	WT	WT	WT
164. R1162L	c.3485G>T	WT	WT	WT	WT	WT	HET

Table 1. Cont'd: NGS CF Control Panel G211 v1.1 Variants are listed in genomic coordinate order. **Bold** = Part of ACMG recommended panel of 100 variants. Asterisk* = clinically relevant CFTR2 variants.

CFTR Mutation Legacy Name	cDNA Name (HGVS)	Tube A	Tube B	Tube C	Tube D	Tube E	Tube F
165. 3659delC*	**c.3528delC**	WT	HET	WT	WT	WT	WT
166. 3667del4*	c.3536_3539delCCAA	WT	WT	WT	WT	HET	WT
167. S1196X*	c.3587C>G	WT	WT	WT	HET	WT	WT
168. W1204X (3743G>A)*	c.3611G>A	WT	WT	WT	WT	HET	WT
169. W1204X (3744G>A)*	**c.3612G>A**	WT	WT	WT	WT	WT	HET
170. 3791delC*	**c.3659delC**	WT	WT	WT	HET	WT	WT
171. I1234V*	c.3700A>G	WT	WT	WT	WT	WT	HET
172. S1235R	c.3705T>G	WT	HET	WT	WT	WT	WT
173. Q1238XC>T	c.3712C>T	WT	WT	WT	WT	HET	WT
174. 3849+10kb C>T*	**c.3718-2477C>T**	WT	HET	WT	WT	WT	WT
175. 3849+4A>G*	c.3717+4A>G	HET	WT	WT	WT	WT	WT
176. G1244E*	c.3731G>A	WT	WT	WT	WT	HET	HET
177. 3876delA*	**c.3744delA**	WT	HET	WT	WT	WT	WT
178. S1251N*	c.3752G>A	HET	WT	WT	WT	HET	WT
179. S1255XA>G	c.3607A>G	WT	WT	HET	WT	WT	WT
180. S1255XC>A*	**c.3764C>A**	WT	WT	HET	WT	WT	WT
181. 3905insT*	c.3773dupT	WT	HET	WT	WT	WT	WT
182. D1270N	c.3808G>A	WT	WT	WT	HET	WT	WT
183. W1282X*	**c.3846G>A**	WT	HET	WT	WT	WT	WT
184. 4005+1G>A*	c.3873+1G>A	WT	WT	WT	WT	WT	HET
185. 4016insT*	**c.3889dupT**	WT	WT	WT	WT	HET	WT
186. N1303K*	**c.3909C>G**	WT	HET	WT	WT	WT	HET
187. Q1313X*	c.3937C>T	HET	WT	WT	WT	WT	WT
188. CFTRdel22,23*	c.3964-78_4242+577del	WT	WT	WT	WT	WT	HET
189. 4209TGTT>AA*	c.4077_4080delinsAA	HET	WT	WT	WT	WT	WT
190. 4382delA*	c.4251delA	HET	WT	WT	WT	WT	WT

Table 2. 28 ACMG variants recommended for carrier screening that are <u>not</u> included in NGS CF Control Panel G211 v1.1.

CFTR Mutation Legacy Name	cDNA Name (HGVS)	CFTR Mutation Legacy Name	cDNA Name (HGVS)
1. Q2X*	**c.4C>T**	**15. R560S***	**c.1680A>C**
2. G91R*	**c.271G>A**	**16. A561E***	**c.1682C>A**
3. Q98R*	**c.293A>G**	**17. 1824delA***	**c.1692del**
4. F191V*	**c.571T>G**	**18. A613T***	**c.1837G>A**
5. L218X*	**c.653T>A**	**19. G628R***	**c.1882G>A**
6. V232D*	**c.695T>A**	**20. R785X***	**c.2353C>T**
7. Q290X*	**c.868C>T**	**21. R792X***	**c.2374C>T**
8. 1161delC*	**c.1029del**	**22. Y913X***	**c.2739T>A**
9. V456A*	**c.1367T>C**	**23. G970D***	**c.2909G>A**
10. 1504delG*	**c.1373del**	**24. T1036N***	**c.3107C>A**
11. C524X*	**c.1572C>A**	**25. W1098C***	**c.3294G>C**
12. 1716+1G->A*	**c.1584+1G>A**	**26. S1118F***	**c.3353C>T**
13. G551S*	**c.1651G>A**	**27. 3849+5G->A***	**c.3717+5G>A**
14. 1811+1G->A*	**c.1679+1G>A**	**28. 3940delG***	**c.3808del**

References:

1. Moskowitz SM, Chmiel JF, Sternan DL, Cheng E, Gibson RL et al. Clinical practice and genetic counseling for cystic fibrosis and CFTR-related disorders. Genet Med. 2008;10:851–868
2. Screening newborn infants for Cystic Fibrosis [online]. The Leeds Method of Management. April, 2008. Leeds Regional Adult and Paediatric Cystic Fibrosis Units, St James's University Hospital, Leeds, UK; available from http://www.cysticfibrosismedicine.com.
3. Rommens JM, Iannuzzi MC, Kerem B, Drumm ML, Melmer G et al. Identification of the cystic fibrosis gene: chromosome walking and jumping. Science 1989;245:1059-1065
4. Riordan JR, Rommens JM, Kerem B, Alon N et al. Identification of the cystic fibrosis gene: cloning and characterization of complementary DNA. Science 1989;245:1066-1072
5. The Clinical and Functional TRanslation of CFTR (CFTR2); available at http://cftr2.org
6. Sosnay PR, Siklosi Kr, Van Goor F, Kaniecki K, Yu H, et al. Defining the disease liability of variants in the cystic fibrosis transmembrane conductance regulator gene. Nat Genet. 2013;45:1160-1167.
7. Deignan, Joshua L et al. "Updated recommendations for CFTR carrier screening: A position statement of the American College of Medical Genetics and Genomics (ACMG)." Genetics in medicine: official journal of the American College of Medical Genetics vol. 25,8 (2023): 100867. doi:10.1016/j.gim.2023.100867
8. Update on Carrier Screening for Cystic Fibrosis. Committee Opinion Number 486. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117:1028-31
9. Bobadilla JL, Macek M, Fine JP, and Farrell PM. Cystic fibrosis: A worldwide analysis of CFTR mutations correlation with incidence data and application to screening. Human Mutation 2002;19(6):575-606