NYS Cystic Fibrosis Newborn Screening: Custom *CFTR* Variant Panel Content

Variant: Legacy | HGVS Protein (cDNA)
124del23bp | p.? (c.-9_14delCGA GAGACCATGCAGAGGTCGCC)
M1V | p.Met1Val / p.Met1? (c.1A>G)
Q2X | p.Gln2* (c.4C>T)
S4X | p.Ser4* (c.11C>A)
S13F | p.Ser13Phe (c.38C>T)
182delT | p.Phe17Serfs*8 (c.50delT)
L15P | p.Leu15Pro (c.44T>C)
185+1G->T | p.? (c.53+1G>T)
W19X | p.Trp19* (c.57G>A)
G27R | p.Gly27Arg (c.79G>A)
G27X | p.Gly27* (c.79G>T)
Q30X | p.Gln30* (c.88C>T)
Q39X | p.Gln39* (c.115C>T)
A46D | p.Ala46Asp (c.137C>A)
296+1G->A | p.? (c.164+1G>A)
296+1G->T | p.? (c.164+1G>T)
296+2T->C | p.? (c.164+2T>C)
296+3insT | p.? (c.164+4dupT)
297-3C->T | p.? (c.165-3C>T)
297-1G->A | p.? (c.165-1G>A)
E56K | p.Glu56Lys (c.166G>A)
W57G | p.Trp57Gly (c.169T>G)
W57X | p.Trp57* (c.170G>A)
W57X | p.Trp57* (c.171G>A)
306delTAGA | p.Asp58Glufs*32 (c.174_177delTAGA)
306insA | p.Arg59Lysfs*10 (c.175dupA)
E60K | p.Glu60Lys (c.178G>A)
E60X | p.Glu60* (c.178G>T)
P67L | p.Pro67Leu (c.200C>T)
R75X | p.Arg75* (c.223C>T)
365-366insT| p.Trp79Leufs*32 (c.233dupT)
G85E | p.Gly85Glu (c.254G>A)
394delTT | p.Leu88Ilefs*22 (c.262_263delTT)
L88X | p.Leu88* (c.263T>A)
L88X | p.Leu88* (c.263T>G)
G91R | p.Gly91Arg (c.271G>A)
405+1G->A | p.? (c.273+1G>A)
405+3A->C | p.? (c.273+3A>C)
406-2A->G | p.? (c.274-2A>G)
406-1G->A | p.? (c.274-1G>A)
E92K | p.Glu92Lys (c.274G>A)
E92X | p.Glu92* (c.274G>T)
Q98X | p.Gln98* (c.292C>T)
Q98R | p.Gln98Arg (c.293A>G)
P99L | p.Pro99Leu (c.296C>T)
L102R | p.Leu102Arg (c.305T>G)
442delA | p.Arg104Glufs*3 (c.310delA)
444delA | p.Ile105Serfs*2 (c.313delA)
457TAT->G | p.Tyr109Glyfs*4 (c.325_327delTATinsG)
D110H | p.Asp110His (c.328G>C)
R117C | p.Arg117Cys (c.349C>T)
R117H | p.Arg117His (c.350G>A)[J]
Y122X | p.Tyr122* (c.366T>A)
G126D | p.Gly126Asp (c.377G>A)
541delC | p.Leu137Serfs*16 (c.409delC)
L138ins | p.Leu138dup (c.413_415dupTAC)
H139R | p.His139Arg (c.416A>G)
574delA | p.Ile148Leufs*5 (c.442delA)
602del14 | p.Phe157* (c.470_483delTTAGTTTGATTTAT)
Y161D | p.Tyr161Asp (c.481T>G)
621+1G->T | p.? (c.489+1G>T)
L165S | p.Leu165Ser (c.494T>C)
663delT | p.Ile177Metfs*12 (c.531delT)
G178R | p.Gly178Arg (c.532G>A)
675del4 | p.Leu183Phefs*5 (c.543_546delTAGT)
E193X | p.Glu193* (c.577G>T)
711+1G->T | p.? (c.579+1G>T)
711+3A->G | p.? (c.579+3A>G)
711+5G->A | p.? (c.579+5G>A)
712-1G->T | p.? (c.580-1G>T)

Variant: Legacy | HGVS Protein (cDNA)
H199Y | p.His199Tyr (c.595C>T)
P205S | p.Pro205Ser (c.613C>T)
L206W | p.Leu206Trp (c.617T>G)
W216X | p.Trp216* (c.647G>A)
L218X | p.Leu218* (c.653T>A)[+]
Q220X | p.Gln220* (c.658C>T)
L227R | p.Leu227Arg (c.680T>G)
V232D | p.Val232Asp (c.695T>A)
849delG | p.Leu240* (c.717delG)
852del22 | p.Gly241Glufs*13 (c.723_743+1delGAGAATGATGATGAAGTACAGG)
896delT | p.Ile255Thrfs*6 (c.764delT)[+]
935delA | p.Asn268Ilefs*17 (c.803delA)
Y275X | p.Tyr275* (c.825C>G)
C276X | p.Cys276* (c.828C>A)
977insA | p.Met284Asnfs*3 (c.850dupA)
991del5 | p.Asn287Lysfs*19 (c.861_865delCTTAA)
delF311 | p.Phe312del (c.935_937delTCT)[§]
F311L | p.Phe311Leu (c.933C>G)
1078delT | p.Phe316Leufs*12 (c.948delT)
1119delA | p.Gly330Glufs*39 (c.987delA)
G330X | p.Gly330* (c.988G>T)
R334W | p.Arg334Trp (c.1000C>T)
R334L | p.Arg334Leu (c.1001G>T)
1138insG | p.Ile336Serfs*28 (c.1006_1007insG)
I336K | p.Ile336Lys (c.1007T>A)
T338I | p.Thr338Ile (c.1013C>T)
1154insTC | p.Phe342Hisfs*28 (c.1021_1022dupTC)
S341P | p.Ser341Pro (c.1021T>C)
1161delC | p.Cys343* (c.1029delC)
L346P | p.Leu346Pro (c.1037T>C)
R347H | p.Arg347His (c.1040G>A)
R347P | p.Arg347Pro (c.1040G>C)
R352Q | p.Arg352Gln (c.1055G>A)
Q359K/T360K | p.Gln359_Thr360delinsLysLys (c.1075_1079delCAAACinsAAAAA)
1213delT | p.Trp361Glyfs*8 (c.1081delT)
1248+1G->A | p.? (c.1116+1G>A)
1249-1G->A | p.? (c.1117-1G>A)
1259insA | p.Gln378Alafs*4 (c.1130dupA)
1288insTA | p.Asn386Ilefs*3 (c.1155_1156dupTA)
W401X | p.Trp401* (c.1202G>A)
W401X | p.Trp401* (c.1203G>A)
1341+1G->A | p.? (c.1209+1G>A)
1343delG | p.Gly404Aspfs*38 (c.1211delG)
Q414X | p.Gln414* (c.1240C>T)
1429del7 | p.Ser434Leufs*6 (c.1301_1307delCACTTCT)
1461ins4 | p.Ile444Argfs*3 (c.1327_1330dupGATA)
1471delA | p.Lys447Argfs*2 (c.1340delA)
L453S | p.Leu453Ser (c.1358T>C)
A455E | p.Ala455Glu (c.1364C>A)
1497delGG | p.Val456Cysfs*25 (c.1365_1366delGG)
V456A | p.Val456Ala (c.1367T>C)
1504delG | p.Gly458Aspfs*11 (c.1373delG)
1525-2A->G | p.? (c.1393-2A>G)
1525-1G->A | p.? (c.1393-1G>A)
S466X | p.Ser466* (c.1397C>A)
S466X | p.Ser466* (c.1397C>G)
L467P | p.Leu467Pro (c.1400T>C)
1548delG | p.Gly473Glufs*54 (c.1418delG)
E474K | p.Glu474Lys (c.1420G>A)
S489X | p.Ser489* (c.1466C>A)
S492F | p.Ser492Phe (c.1475C>T)
1609delCA | p.Gln493Valfs*10 (c.1477_1478delCA)
Q493X | p.Gln493* (c.1477C>T)
W496X | p.Trp496* (c.1487G>A)
I502T | p.Ile502Thr (c.1505T>C)
I507del | p.Ile507del (c.1519_1521delATC)

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F508del|p.Phe508del (c.1521_1523delCTT)
D513G | p.Asp513Gly (c.1538A>G)
1677delTA | p.Tyr515* (c.1545_1546delTA)
V520F | p.Val520Phe (c.1558G>T)
C524X | p.Cys524* (c.1572C>A)
Q525X | p.Gln525* (c.1573C>T)
1716+1G->A | p.? (c.1584+1G>A)
1717-8G->A | p.? (c.1585-8G>A)
1717-1G->A | p.? (c.1585-1G>A)
G542X | p.Gly542* (c.1624G>T)
S549R | p.Ser549Arg (c.1645A>C)
S549N | p.Ser549Asn (c.1646G>A)
S549R | p.Ser549Arg (c.1647T>A)
S549R | p.Ser549Arg (c.1647T>G)
G550X | p.Gly550* (c.1648G>T)
1782delA | p.Gly551Valfs*8 (c.1650delA)
G551S | p.Gly551Ser (c.1651G>A)
G551D | p.Gly551Asp (c.1652G>A)
Q552X | p.Gln552* (c.1654C>T)
R553X | p.Arg553* (c.1657C>T)
1802delC | p.Ser557Phefs*2 (c.1670delC)
L558S | p.Leu558Ser (c.1673T>C)
A559T | p.Ala559Thr (c.1675G>A)
R560K | p.Arg560Lys (c.1679G>A)
R560T | p.Arg560Thr (c.1679G>C)
1811+1G->A | p.? (c.1679+1G>A)
1811+1G->C | p.? (c.1679+1G>C)
1811+1.6kbA->G | p.? (c.1680-886A>G)
1811+1643G->T | p.? (c.1680-877G>T)
1812-1G->A | p.? (c.1680-1G>A)
R560S | p.Arg560Ser (c.1680A>C)
A561E | p.Ala561Glu (c.1682C>A)
Y563N | p.Tyr563Asn (c.1687T>A)
Y563D | p.Tyr563Asp (c.1687T>G)
1824delA | p.Asp565Metfs*7 (c.1692delA)
1833delT | p.Leu568Cysfs*4 (c.1703delT)
Y569D | p.Tyr569Asp (c.1705T>G)
P574H | p.Pro574His (c.1721C>A)
E585X | p.Glu585* (c.1753G>T)
1898+1G->A | p.? (c.1766+1G>A)
1898+1G->C | p.? (c.1766+1G>C)
1898+1G->T | p.? (c.1766+1G>T)
1898+3A->G | p.? (c.1766+3A>G)
1898+5G->T | p.? (c.1766+5G>T)
1924del7 | p.Lys598Glyfs*11 (c.1792_1798delAAAACTA)
1949del84 | p.Met607_Gln634del (c.1820_1903del84)[+]
H609R | p.His609Arg (c.1826A>G)
A613T | p.Ala613Thr (c.1837G>A)
G628R | p.Gly628Arg (c.1882G>A)
G628R | p.Gly628Arg (c.1882G>C)
2055del9->A | p.Ser641Argfs*5 (c.1923_1931delCTCAAAACTinsA)
2075delA | p.Asp648Valfs*15 (c.1943delA)
2105-2117del13insAGAAA | p.Arg658Lysfs*4 (c.1973_1985delGAAATTCAATCCTinsAGAAA)
2118del4 | p.Thr663Argfs*8 (c.1986_1989delAACT)
2143delT | p.Leu671* (c.2012delT)
G673X | p.Gly673* (c.2017G>T)
2184delA | p.Lys684Asnfs*38 (c.2052delA)
2184insA | p.Gln685Thrfs*4 (c.2052dupA)
2183AA->G | p.Lys684Serfs*38 (c.2051_2052delAAinsG)
2185insC | p.Gln685Profs*4 (c.2053dupC)
Q685X | p.Gln685* (c.2053C>T)
R709X | p.Arg709* (c.2125C>T)
K710X | p.Lys710* (c.2128A>T)
Q715X | p.Gln715* (c.2143C>T)
Q720X | p.Gln720* (c.2158C>T)
2307insA | p.Glu726Argfs*4 (c.2175dupA)
L732X | p.Leu732* (c.2195T>G)
2347delG | p.Val739Tyrfs*16 (c.2215delG)

Variant: Legacy | HGVS Protein (cDNA)
2372del8 | p.Ile748Serfs*28 (c.2241_2248delGATACTGC)
R764X | p.Arg764* (c.2290C>T)
R785X | p.Arg785* (c.2353C>T)
R792X | p.Arg792* (c.2374C>T)
2556insAT | p.Ser809Ilefs*13 (c.2423_2424dupAT)
2585delT | p.Leu818Trpfs*3 (c.2453delT)
2594delGT | p.Ser821Argfs*4 (c.2463_2464delTG)
E822X | p.Glu822* (c.2464G>T)
2622+1G->A | p.? (c.2490+1G>A)
E831X | p.Glu831* (c.2491G>T)
W846X | p.Trp846* (c.2537G>A)
W846X | p.Trp846* (c.2538G>A)
Y849X | p.Tyr849* (c.2547C>A)
R851X | p.Arg851* (c.2551C>T)
2711delT | p.Phe861Leufs*3 (c.2583delT)
2721del11 | p.Ile864Serfs*28 (c.2589_2599delAATTTGGTGCT)
2732insA | p.Val868Serfs*28 (c.2601dupA)
W882X | p.Trp882* (c.2645G>A)
2789+5G->A | p.? (c.2657+5G>A)
2790-1G->C | p.? (c.2658-1G>C)
Q890X | p.Gln890* (c.2668C>T)
S912X | p.Ser912* (c.2735C>A)
2869insG | p.Tyr913* (c.2737_2738insG)
Y913X | p.Tyr913* (c.2739T>A)
2896insAG | p.Val922Glufs*2 (c.2763_2764dupAG)
L927P | p.Leu927Pro (c.2780T>C)
2942insT | p.Val938Glyfs*37 (c.2810dupT)
2957delT | p.Ile942Thrfs*26 (c.2825delT)
S945L | p.Ser945Leu (c.2834C>T)
2991del32 | p.Leu953Phefs*11 (c.2859_2890delACATTCTGTTCTTCAAG CACCTATGTCAACCC)
3007delG | p.Ala959Hisfs*9 (c.2875delG)
3028delA | p.Thr966Argfs*2 (c.2896delA)
G970R | p.Gly970Arg (c.2908G>C)
G970D | p.Gly970Asp (c.2909G>A)
D979V | p.Asp979Val (c.2936A>T)
3120G->A | p.Gln996= / p.? (c.2988G>A)
3120+1G->A | p.? (c.2988+1G>A)
3121-2A->G | p.? (c.2989-2A>G)
3121-1G->A | p.? (c.2989-1G>A)
3132delTG | p.Val1001Aspfs*45 (c.3002_3003delTG)
3143del9 | p.Ala1004_Ala1006del (c.3011_3019delCTATAGCAG)
A1006E | p.Ala1006Glu (c.3017C>A)
3171delC | p.Tyr1014Thrfs*9 (c.3039delC)
3171insC | p.Tyr1014Leufs*33 (c.3039dupC)
T1036N | p.Thr1036Asn (c.3107C>A)
Q1042X | p.Gln1042* (c.3124C>T)
3271delGG | p.? (c.3139_3139+1delGG)
3272-26A->G | p.? (c.3140-26A>G)
H1054D | p.His1054Asp (c.3160C>G)
G1061R | p.Gly1061Arg (c.3181G>C)
L1065P | p.Leu1065Pro (c.3194T>C)
R1066C | p.Arg1066Cys (c.3196C>T)
R1066H | p.Arg1066His (c.3197G>A)
3349insT | p.Tyr1073Leufs*3 (c.3217dupT)
L1077P | p.Leu1077Pro (c.3230T>C)
W1089X | p.Trp1089* (c.3266G>A)
Y1092X | p.Tyr1092* (c.3276C>A)
Y1092X | p.Tyr1092* (c.3276C>G)
W1098R | p.Trp1098Arg (c.3292T>C)
W1098X | p.Trp1098* (c.3293G>A)
W1098X | p.Trp1098* (c.3294G>A)
W1098C | p.Trp1098Cys (c.3294G>C)
W1098C | p.Trp1098Cys (c.3294G>T)
M1101K | p.Met1101Lys (c.3302T>A)
M1101R | p.Met1101Arg (c.3302T>G)
R1102X | p.Arg1102* (c.3304A>T)
E1104X | p.Glu1104* (c.3310G>T)

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Variant: Legacy | HGVS Protein (cDNA)
S1118F | p.Ser1118Phe (c.3353C>T)
3500-2A->G | p.? (c.3368-2A>G)
W1145X | p.Trp1145* (c.3435G>A)
3600G->A | p.Leu1156= / p.? (c.3468G>A)
3600+2insT | p.? (c.3468+2dupT)
3600+5G->A | p.? (c.3468+5G>A)
R1158X | p.Arg1158* (c.3472C>T)
S1159P | p.Ser1159Pro (c.3475T>C)
S1159F | p.Ser1159Phe (c.3476C>T)
R1162X | p.Arg1162* (c.3484C>T)
3659delC | p.Lys1177Serfs*15 (c.3528delC)
3667ins4 | p.Thr1179Ilefs*17 (c.3532_3535dupTCAA)
S1196X | p.Ser1196* (c.3587C>G)
3737delA | p.Asp1202Alafs*9 (c.3605delA)
W1204X | p.Trp1204* (c.3611G>A)
W1204X | p.Trp1204* (c.3612G>A)
3791delC | p.Thr1220Lysfs*8 (c.3659delC)
3821delT | p.Ser1231Profs*4 (c.3691delT)

Variant: Legacy | HGVS Protein (cDNA)
I1234V | p.Ile1234Val (c.3700A>G)
3849G->A | p.Arg1239= / p.? (c.3717G>A)
3849+4A->G | p.? (c.3717+4A>G)
3849+5G->A | p.? (c.3717+5G>A)
3849+40A->G | p.? (c.3717+40A>G)
3849+10kbC->T | p.? (c.3718-2477C>T)
3850-3T->G | p.? (c.3718-3T>G)
3850-1G->A | p.? (c.3718-1G>A)
V1240G | p.Val1240Gly (c.3719T>G)
G1244E | p.Gly1244Glu (c.3731G>A)
3876delA | p.Lys1250Argfs*9 (c.3744delA)
3878delG | p.Lys1250Argfs*9 (c.3747delG)
G1249R | p.Gly1249Arg (c.3745G>A)
S1251N | p.Ser1251Asn (c.3752G>A)
L1254X | p.Leu1254* (c.3761T>G)
S1255P | p.Ser1255Pro (c.3763T>C)
S1255X | p.Ser1255* (c.3764C>A)
3905insT | p.Leu1258Phefs*7 (c.3773dupT)
I1269N | p.Ile1269Asn (c.3806T>A)

Variant: Legacy | HGVS Protein (cDNA)
W1282X | p.Trp1282* (c.3846G>A)
R1283M | p.Arg1283Met (c.3848G>T)
4005+1G->A | p.? (c.3873+1G>A)
4005+2T->C | p.? (c.3873+2T>C)
4010del4 | p.Ile1295Phefs*32 (c.3883_3886delATTT)
4015delA | p.Ile1295Phefs*33 (c.3883delA)
4016insT | p.Ser1297Phefs*5 (c.3889dupT)
4022insT | p.Gly1298Trpfs*4 (c.3891dupT)
4040delA | p.Asn1303Thrfs*25 (c.3908delA)
N1303K | p.Asn1303Lys (c.3909C>G)
Q1313X | p.Gln1313* (c.3937C>T)
L1324P | p.Leu1324Pro (c.3971T>C)
Q1330X | p.Gln1330* (c.3988C>T)
L1335P | p.Leu1335Pro (c.4004T>C)
4168delCTAAGCC | p.Leu1346Metfs*6 (c.4036_4042delCTAAGCC)

Variant: Legacy | HGVS Protein (cDNA)
G1349D | p.Gly1349Asp (c.4046G>A)
4209TGTT->AA | p.Val1360Thrfs*3 (c.4077_4080delTGTTinsAA)
4218insT | p.Lys1363* (c.4086dupT)
E1371X | p.Glu1371* (c.4111G>T)
H1375P | p.His1375Pro (c.4124A>C)
4259del5 | p.Leu1376Serfs*8 (c.4127_4131delTGGAT)
4279insA | p.Ile1383Asnfs*3 (c.4147dupA)
Q1382X | p.Gln1382* (c.4144C>T)
4326delTC | p.Cys1400* (c.4197_4198delCT)
Q1411X | p.Gln1411* (c.4231C>T)
Q1412X | p.Gln1412* (c.4234C>T)
4374+1G->A | p.? (c.4242+1G>A)
4374+1G->T | p.? (c.4242+1G>T)
4382delA | p.Glu1418Argfs*14 (c.4251delA)
4428insGA | p.Ser1435Glyfs*14 (c.4300_4301dupAG)

Cystic Fibrosis (CF) is screened in NYS infants at birth using a three-tier IRT-DNA-SEQ algorithm. ***Tier 1***: Immunoreactive trypsinogen (IRT) is tested in all infants. ***Tier 2***: A custom second-tier panel targeting 338 clinically-relevant *CFTR* variants is screened in infants with elevated IRT (top 5%). Variants included on the panel are listed in the table. Each is described using legacy[1] and Human Genome Variation Society (HGVS) nomenclature,[2] with cDNA nucleotide changes with respect to NCBI transcript NM_000492.3, and amino acid changes with respect to NCBI amino acid reference sequence NP_000483.3. 334 of 338 targeted variants have been classified as CF-causing by The Clinical and Functional Translation of CFTR database (CFTR2),[3,4] with the exception of R117H, a varying clinical consequence variant,[∫] and three classified as pathogenic[+] and 1 classified as likely pathogenic[§] using American College of Medical Genetics and Genomics (ACMG) standards.[5] Large deletion/duplications defined as CF-causing by CFTR2 are not included on the second-tier panel. ***Tier 3:*** Other *CFTR* variants, including pathogenic and likely pathogenic variants[5] not catalogued in CFTR2; variants of varying clinical consequence;[4] and variants of unknown[4] or uncertain significance (VOUS)[5] may be detected via expanded third-tier analysis, in which the complete *CFTR* coding sequence and other relevant regions are analyzed. Third-tier analysis is only conducted for infants with one second-tier panel variant or ultra-high IRT and no panel variants. Large deletions and duplications may be detected via third-tier analysis.

Variants recommended for population-based CF carrier screening[6] are shown in bold.

Most variants with protein effects listed as p.? represent variants that alter splicing.

[∫]Defined as a variant of varying clinical consequence by CFTR2. If R117H is detected, intron 8 polyT/TG status at c.1210-12T/c.1210-34TG is unmasked.

References

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