

**Ordered By** Physician ID: 8596 Client ID: 00618  
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Patient Name: **Testing, AmbryScreen Pos.**  
Accession #: **10-23257** Specimen#: Testing, AS  
Specimen: Blood  
Birth Date: 11/17/70 Age: 39y 5m  
Gender: F Collected: 10/01/10  
SSN: Received: 05/02/10  
MRN#: Authorized: 05/02/10  
Family#: 33956 Reported: 12/10/10  
Ethnicity: Caucasian  
Indication: Diagnostic

### The AmbryScreen™ Test

#### PANEL RESULTS

##### **BCKDHA**

Known Mutation(s): **p.Y438N**

#### INTERPRETATION

##### **BCKDHA**

The results of this test indicate the heterozygous presence of a known mutation, p.Y438N (also known as c.1312T>A), in exon 9 of the *BCKDHA* gene (Love-Gregory L et al. *Mol Gen and Met.* 2002; 75(1): 79-90). This mutation was previously known as p.Y393N.

<http://www.ncbi.nlm.nih.gov/pubmed/11825067>

Maple Syrup Urine Disease Type 1A is characterized in an infant by the presence of sweet-smelling urine, with an odor similar to that of maple syrup. Infants seem healthy at birth but if left untreated suffer severe brain damage, and eventually die. Treatment consists of a strict, lifelong special diet.

No other mutations were detected in the remainder of the genes on this panel. The list of both the mutations and the conditions can be viewed on the following pages.

This patient is a **carrier** of the **p.Y438N** mutation in the **BCKDHA** gene which is associated with **Maple Syrup Urine Disease** (MSUD).

**COMMENTS: Genetic testing of the partner is recommended in order to have a more accurate risk assessment of this disease in these individuals' offspring.**

For more information about carrier frequencies and risks related to the partner please see the chart on the following pages. Genetic counseling is a recommended option for all patients undergoing genetic testing.



Timothy Vo, PhD  
Laboratory Director



James Thompson MD, PhD  
Medical Director

**AmbryScreen NEXT GEN SEQUENCING PANEL ASSAY INFORMATION** (Supplement to Test Results)

**General Information** The AmbrySCREEN™ test screens for 78 childhood onset conditions representing only severe or common diseases. The core of the AmbrySCREEN™ test is a 100 mutation panel for Cystic Fibrosis. It was designed by utilizing Ambry's extensive database of over 25,000 patients sequenced in the last decade. Our 100 CF mutation panel includes only well defined disease causing mutations.

**Methodology** Genomic DNA is isolated from whole blood or saliva using standard methods and then quantitated via Nanodrop and/or a microgreen based assay such as Qbit (Invitrogen). The first step in the GoldenGate Assay is DNA activation (biotinylation), which enables genomic DNA samples to bind to paramagnetic particles. Three oligonucleotides are designed for each SNP locus. For each SNP site there are two allele-specific oligos (ASO). A third oligo, the locus-specific oligo (LSO), hybridizes several bases downstream from the SNP site. Because hybridization occurs prior to any amplification steps, no amplification bias is introduced into the assay. After hybridization, the BeadXpress® Reader is used for microbead code identification and fluorescent signal detection. During scanning, a laser beam penetrates the digitally inscribed VeraCode microbead to generate a unique code image, which allows for rapid and highly specific detection. Data generated using the BeadXpress Reader can be analyzed with Illumina's GenomeStudio data analysis software, which performs automated genotype clustering and calling. The performance of the entire plate and individual SNP assays is evaluated before genotypic calls for each sample. Data is first analyzed in GenomeStudio software, and then exported for downstream processing through Ambry's analysis pipeline. Positive variants are verified by Sanger sequencing, pyrosequencing or MLPA as appropriate.

**Analytical Range** The 343 known disease-causing mutations on the 74 genes that are associated with 78 conditions are analyzed and listed below.

ACADM-K304E, ACADVL-c.1678-6G\_A, ACADVL-G441D, ACADVL-R469W, ACADVL-T260M, ACADVL-V283A, ACAT1-Q272X, ADA-L107P, ADA-P297Q, ADA-R76W, AGA-C163S, AGA-S72P, AGXT-F152I, AGXT-G170R, AGXT-I244T, ALDH3A2-c.1297\_1298delGA, ALDH3A2-P315S, ALDOB-A150P, ALDOB-A175D, ALDOB-N335K, ALPL-c.1559delT, ALPL-D361V, ALPL-E174K, ALPL-F310L, ALPL-G317D, ASL-Q116X, ASL-V178M, ASL-c.445+1G\_A (IVS5+1G\_A), ASPA-A305E, ASPA-c.433-2A\_G, ASPA-E285A, ASPA-Y231X, ASS1-G390R, ASS1-R304W, ATM-c.1561delAG, ATM-c.5712insA, ATM-7638del9TAGAATTC, ATM-c.8011-2A\_C (IVS54-2A-C), ATM-R335X, BBS10-c.271dupT, BBS1-M390R, BCKDHA-Y438N, BCKDHB-E372X, BCKDHB-G278S, BCKDHB-R183P, BCS1L-S78G, BLM-2281del6ins7, BTD-C33FfsX-del7ins3-GCGGCTG, BTD-R538C, CBS-G307S, CBS-I278T, CFTR-1078delT, CFTR-1154insTC, CFTR-1248+1G\_A, CFTR-1288insTA, CFTR-1471delA, CFTR-1717-1G\_A, CFTR-1898+1G\_A, CFTR-1898+3A\_G, CFTR-1949del84, CFTR-2143delT, CFTR-2183del2ins1, CFTR-2184delA, CFTR-2184insA, CFTR-2307insA, CFTR-2347delG, CFTR-2585delT, CFTR-2622+1G\_A, CFTR-2789+2insA, CFTR-2789+5G\_A, CFTR-3120+1G\_A, CFTR-3120G\_A, CFTR-3199del6, CFTR-3272-26A\_G, CFTR-3600G\_A, CFTR-3659delC, CFTR-3849+10kbC\_T, CFTR-3876delA, CFTR-3905insT, CFTR-394delTT, CFTR-4005+2T\_C, CFTR-405+1G\_A, CFTR-406-1G\_A, CFTR-4209delTGTTinsAA, CFTR-621+1G\_T, CFTR-663delT, CFTR-711+1G\_T, CFTR-935delA, CFTR-A455E, CFTR-D1152H, CFTR-E1371X, CFTR-E384X, CFTR-E585X, CFTR-E60X, CFTR-E92X, CFTR-G1061R, CFTR-G1244E, CFTR-G178R, CFTR-G330X, CFTR-G480C, CFTR-G542X, CFTR-G551D, CFTR-G85E, CFTR-del2-c.54-1161\_164+1603del2875, CFTR-del2,3, CFTR-DeltaF508\_delCTT, CFTR-DeltaI507\_delATC, CFTR-L1077P, CFTR-L467P, CFTR-M1101K, CFTR-N1303K, CFTR-P67L, CFTR-Q1042X, CFTR-Q220X, CFTR-Q414X, CFTR-Q493X, CFTR-Q552X, CFTR-Q98X, CFTR-R1066C, CFTR-R1070W, CFTR-R1158X, CFTR-R1162X, CFTR-R117C, CFTR-R117H, CFTR-R334W, CFTR-R347H, CFTR-R347P, CFTR-R553X, CFTR-R560T, CFTR-R709X, CFTR-R75X, CFTR-R764X, CFTR-S1196X, CFTR-S1251N, CFTR-S466X\_1529C\_A, CFTR-S466X\_1529C\_G, CFTR-S489X, CFTR-S549N, CFTR-S912X, CFTR-S945L, CFTR-T1053I, CFTR-T338I, CFTR-T351I, CFTR-V520F, CFTR-W1089X, CFTR-W1204X\_3744G\_A, CFTR-W1282X, CFTR-Y1032C, CFTR-Y1092X\_3408C\_A, CFTR-Y1092X\_3408C\_G, CFTR-Y563N, CLN3-1.02kbbdel, CLN5-W75X, CLN5-Y342X, CLN8-R24G, CPS1-c.1529delG, CPS1-G982D, CPS1-K280N, CPS1-Q44X, CPS1-R787X, CPT2-D328G, CPT2-G549D, CPT2-K414TfsX7 delGA, CPT2-M214T, CPT2-P227L, CPT2-P50H, CPT2-R151Q, CPT2-R382K, CPT2-R503C, CPT2-R631C, CPT2-S113L, CPT2-Y120C, CPT2-Y628S, DHCR7-F302L, DHCR7-R242C, DHCR7-R242H, DHCR7-R352W, DHCR7-R404C, DHCR7-S169L, DHCR7-T93M, DHCR7-V326L, DHCR7-W151X, DPYD-c.1905+1G\_A (IVS14+1G\_A), ETHE1-R163Q, ETHE1-R163W, FAH-D233V, FAH-c.1062+5G\_A (IVS12+5G\_A), FAH-c.554-1G\_T (IVS6-1G\_T), FAH-P261L, FAH-W262X, FANCC-c.322delG, FANCC-c.711+4A\_T, FANCC-L554P, FANCC-R548X, G6PC-Q347X, G6PC-R83C, GAA-c.\*-32-13T\_G, GAA-D645G, GAA-c.525delT, GAA-EXON18DEL, GAA-R854X, GALT-c.1424delA, GALT-c.30kbbdel, GALT-c.635\_646del12ins3, GALT-G270D, GALT-I289V, GALT-I66M, GALT-T513M, GALT-T652P, GALT-Y551S, GALK1-G349S, GALK1-P28T, GALK1-Q832X, GALK1-T344M, GALT-K285N, GALT-L218L, GALT-N314D, GALT-Q188R, GALT-S135L, GCDH-A421V, GCDH-c.1083-2A\_C (IVS10-2A\_C), GCDH-R402W, GLDC-G761R, GLDC-M1T, GLDC-R151S, GLDC-S564I, GRHPR-c.103delG, GRHPR-c.403+3\_403+6delAAGT, GSS-c.129+1663A\_G, GSS-c.-9+5G\_A, GSS-R283C, HADHA-E510Q, HEXA-c.1274\_1277dupTATC, HEXA-G269S, HEXA-7.6del, HEXA-c.1421+1G\_C (IVS12+1G\_C), HEXA-c.1073+1G\_A (IVS9+1G\_A), HEXA-R247W, HEXA-R249W, HLCS-R508W, HLCS-V550M, HMGCL-E37X, HMGCL-R41Q, IDUA-c.613\_617dupTGCTC, IDUA-A327P, IDUA-G51D, IDUA-L346R, IDUA-P533R, IDUA-Q70X, IDUA-R89Q, IDUA-W402X, IKBKAP-c.2204+6T\_C (IVS20+6T\_C), IKBKAP-R696P, IL2RG-R226C, IL2RG-R289X, LRPPRC-A354V, MCOLN1-c.406-2A\_G (IVS3-2A\_G), MCOLN1-6.4kbbdel(g.511\_6493DEL), MEFV-M680I(c.2040G\_A), MEFV-M680I(c.2040G\_C), MEFV-M694I, MEFV-M694V, MEFV-V726A, MAAA-R145X, MMAB-R186W, MMACHC-c.271dupA, MMACHC-R111X, MMACHC-R132X, MUT-G717V, MUT-N219Y, MUT-R108C, NPHS1-121delCT, NPHS1-c.2335-1G\_A, NPHS1-R1109X, NPHS1-R1160X, NPHS1-R408Q, NPHS2-A284V, NPHS2-L316X (c.948delT), NPHS2-P118L, NPHS2-R138Q, NPHS2-R229Q, NPHS2-V165X, NPHS2-V290M, OTC-R26Q, OTC-R92X, OTC-T178M, PAH-E280K, PAH-F299C, PAH-F39L, PAH-I65T, PAH-c.1066-11G\_A (IVS10-11G\_A), PAH-c.1315+1G\_A (IVS12+1G\_A), PAH-P281L, PAH-R408W, PAH-Y414C, PEX-c.2097\_2098insT (1700YfsX42), PEX1-G843D, PEX1-c.2916delA, PEX7-A218V, PEX7-G217R, PEX7-c.903+1G\_C (IVS9+1G\_C), PEX7-L292X, PKHD1-A1254fs delG, PKHD1-D3230fs (c.9689delA), PKHD1-I222V, PKHD1-I2957T, PKHD1-I3177T, PKHD1-L1966fs (c.5896\_5897insA), PKHD1-L1966fs (c.5896\_5897insC), PKHD1-Q3392X, PKHD1-R496X, PKHD1-T36M, PKHD1-V3471G, PPT1-R122W, PPT1-R151X, PPT1-T75P, RMRP-nt70-A, SLC12A6-T813fsX813 (c.2436delG), SLC17A5-R39C, SLC22A5-R254X, SLC22A5-R282X, SLC22A5-Y211C, SLC25A15-F188\_delITTC (c.562\_564del3), SLC25A15-G27R, SLC25A15-R179X, SLC25A20-Q238R, SLC26A2-C653S, SLC26A2-c.699+2T\_C (IVS1+2T\_C), SLC26A2-R178X, SLC26A2-R279W, SLC26A2-V340del (c.1020\_1022delGTT), SLC37A4-c.1042\_10343delICT, SLC37A4-G339C, SLC37A4-W118R, SLC6A8-F107delCTT (c.319\_321del3), SLC6A8-F408delITTC (c.1222\_1224del3), SMPD1-c.996delC, SMPD1-H423Y (H421Y), SMPD1-K578N (K576N), SMPD1-L304P (L302P), SMPD1-R498L (R496L), TPP1-R208X

**Residual Risk Chart**

| CONDITION (S)  | GENE    | Detection Rate | Carrier Risk | Residual Risk | Ethnic Background |
|--|---------|----------------|--------------|---------------|-------------------|
| 3-Hydroxy-3-methylglutaric aciduria, HMG-CoA lyase deficiency                  | HMGCL   | 87%            | 1 in 158     | 1 in 1209     | Saudi Arabian     |
|  |         | 97%            | 1 in 158     | 1 in 5234     | Spanish/Portugese |
| Achondrogenesis type 1B  | SLC26A2 | 75%            | 1 in 71      | 1 in 468      | General           |
| Andermann Syndrome (Agenesis of the Corpus Colosum with Peripheral Neuropathy) | SLC12A6 | 99%            | 1 in 23      | 1 in 2201     | French Canadian   |
|  |         | 48%            | 1 in 76      | 1 in 145      | General           |

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| CONDITION (S)   | GENE     | Detection Rate | Carrier Risk      | Residual Risk       | Ethnic Background |
|---|----------|----------------|-------------------|---------------------|-------------------|
| Argininosuccinate aciduria  | ASL      | 30%            | 1 in 132          | 1 in 188            | General           |
| Aspartylglucosaminuria  | AGA      | 98%            | 1 in 68           | 1 in 3351           | Finnish           |
| Ataxia Telangiectasia   | ATM      | 99%            | 1 in 100          | 1 in 9901           | Amish             |
|   |          | 97%            | 1 in 100          | 1 in 3234           | N. African Jews   |
|   |          | 24%            | 1 in 100          | 1 in 133            | General           |
| Atelosteogenesis type 2   | SLC26A2  | 75%            | 1 in 71           | 1 in 281            | General           |
| Bardet-Biedl syndrome 1   | BBS1     | 80%            | <1 in 187         | <1 in 931           | General           |
| Bardet-Biedl syndrome 10  | BBS10    | 46%            | <1 in 187         | <1 in 345           | General           |
| Batten Disease, Juvenile Neuronal Ceroid Lipofuscinosis                                       | CLN3     | 81%            | 1 in 79           | 1 in 412            | Icelandic         |
| Beta ketothiolase deficiency  | ACAT1    | 17%            | <1 in 500         | <1 in 600           | General           |
| Biotinidase Deficiency; Multiple Carboxylase Deficiency                                       | BTD      | 53%            | 1 in 120          | 1 in 254            | General           |
| Bloom Syndrome  | BLM      | 97%            | 1 in 107          | 1 in 3534           | Ashkenazi         |
| Carnitine-acylcarnitine Translocase Deficiency (CACT)   | SLC25A20 | 20%            | 1 in 350          | 1 in 437            | Saudi Arabian     |
| Carnitin Palmitoyltransferase II Deficiency   | CPT2     | 90%            | <1 in 500         | 1 in 4991           | General           |
| Carnitine Uptake Defect   | SLC22A5  | 83%            | 1 in 125          | 1 in 730            | Chinese           |
| Canavan   | ASPA     | 99%            | 1 in 41           | 1 in 2001           | Ashkenazi         |
|   |          | 60%            | <1 in 100         | <1 in 250           | General           |
| Carbamoylphosphate synthetase (CPS)   | CPS1     | 34%            | 1 in 447          | 1 in 677            | Japanese          |
| Cartilage-Hair Hypoplasia   | RMRP     | 92%            | 1 in 76           | 1 in 938            | Finnish           |
| Ceroid Lipofuscinosis, Neuronal 2; CLN2   | TPP1     | 60-90%         | 1 in 53           | 1 in 209            | Newfoundland      |
|   |          | 60-90%         | <1 in 80          | <1 in 159           | General           |
| Ceroid Lipofuscinosis, Neuronal 1; CLN1   | PPT1     | 98%            | <1 in 80          | 1 in 3951           | Finnish           |
|   |          | 75%            | <1 in 80          | <1 in 159           | General           |
| Citrullinemia type I  | ASS1     | 58%            | 1 in 119          | 1 in 237            | Japanese          |
|   |          | 31%            | 1 in 119          | 1 in 172            | General           |
| Creatine transporter defect, X-linked MR with seizures, short stature, and midface hypoplasia | SLC6A8   | 20%            | 1 in 8500 females | 1 in 10,625 females | General           |
| Cystic Fibrosis   | CFTR     | 91%            | 1 in 27           | 1 in 290            | Caucasian         |
|   |          | 96%            | 1 in 27           | 1 in 651            | Ashkenazi         |
|   |          | 81%            | 1 in 46           | 1 in 156            | Hispanic          |
|   |          | 78%            | 1 in 65           | 1 in 292            | African American  |
|   |          | 49%            | 1 in 94           | 1 in 182            | Asian American    |
| Diastrophic Dysplasia   | SLC26A2  | 75%            | 1 in 71           | 1 in 281            | General           |
|   |          | 90%            | 1 in 28           | 1 in 271            | Finnish           |
| Dihydropyrimidine Dehydrogenase Deficiency  | DPYD     | 52%            | -1 in 50          | -1 in 103           | General           |
| Ethylmalonic Encephalopathy   | ETHE1    | 49%            | <1 in 150         | <1 in 293           | Mediterranean     |
| Familial Dysautonomia   | IKBKAP   | 99%            | 1 in 32           | 1 in 3101           | Ashkenazi         |
| Familial Mediterranean Fever  | MEFV     | 51%            | 1 in 5            | 1 in 9              | Turkish           |
|   |          | 89%            | 1 in 6            | 1 in 46             | Syrian            |
|   |          | 90%            | 1 in 6            | 1 in 51             | Armenian          |

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| CONDITION (S)  | GENE     | Detection Rate | Carrier Risk | Residual Risk | Ethnic Background  |
|--|----------|----------------|--------------|---------------|--------------------|
| Fanconi Type C   | FANCC    | 99%            | 1 in 89      | 1 in 8801     | Ashkenazi          |
| Galactokinase Deficiency, Galactosemia II, GALK deficiency                 | GALK1    | 99%            | 1 in 47      | 1 in 4601     | Romani (gypsies)   |
|  |          | 60%            | 1 in 500     | 1 in 1248     | Japanese           |
| Galactosemia   | GALT     | 75%            | 1 in 122     | 1 in 485      | General            |
| Glutaric Acidemia type 1 (GA-1)  | GCDH     | 99%            | 1 in 94      | 1 in 9301     | Amish              |
|  |          | 40%            | 1 in 94      | 1 in 156      | German             |
| Glutathione Synthetase Deficiency  | GSS      | 46%            | 1 in 3700    | 1 in 6851     | General            |
| Glycogen Storage Disease type 1a   | G6PC     | 99%            | 1 in 71      | 1 in 7001     | Ashkenazi          |
|  |          | 45%            | 1 in 71      | 1 in 128      | General            |
| Glycogen Storage Disease type 1b   | SLC37A4  | 50%            | 1 in 112     | 1 in 223      | General            |
| GRACILE syndrome   | BCS1L    | 99%            | 1 in 120     | 1 in 11,901   | Finnish            |
| Guanidinoacetate Methyltransferase Deficiency                              | GAMT     | 85%            | ~1 in 100    | 1 in 661      | Portuguese         |
|  |          | 53%            | ~1 in 150    | 1 in 318      | General            |
| Hereditary Fructose Intolerance, Fructosemia                               | ALDOB    | 85%            | 1 in 71      | 1 in 468      | General            |
| Holocarboxylase Synthetase Deficiency                                      | HLCS     | 43%            | 1 in 148     | 1 in 259      | General            |
| Homocystinuria   | CBS      | 50%            | 1 in 112     | 1 in 223      | General            |
| Hurler, Scheie, Hurler-Scheie disease (MPS1)                               | IDUA     | 72%            | 1 in 160     | 1 in 569      | European           |
|  |          | 79%            | 1 in 160     | 1 in 590      | Scandinavian       |
|  |          | 92%            | 1 in 160     | 1 in 1989     | Moroccan           |
|  |          | 50%            | 1 in 160     | 1 in 319      | Italian            |
|  |          | 50%            | 1 in 160     | 1 in 319      | Korean             |
| Hyperoxaluria type 1   | AGXT     | 74%            | 1 in 155     | 1 in 209      | General            |
| Hyperoxaluria type 2   | GRHPR    | 50%            | <1 in 150    | <1 in 210     | Asian              |
| Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome (HHH syndrome) | SLC25A15 | 95%            | <1 in 500    | <1 in 10,000  | French Canadian    |
| Hypophosphatasia, AR   | ALPL     | >35%           | 1 in 150     | <1 in 230     | Caucasian/European |
|  |          | >90%           | 1 in 25      | 1 in 241      | Mennonite          |
| Krabbe disease, GALC Deficiency  | GALC     | 66%            | 1 in 150     | 1 in 439      | General            |
| Leigh Syndrome, French-Canadian Type                                       | LRPPRC   | 98%            | 1 in 22      | 1 in 1051     | French Canadian    |
| Long-chain L-3- hydroxyacyl-CoA dehydrogenase (LCHAD)                      | HADHA    | 87%            | 1 in 125     | 1 in 955      | General            |
| Maple Syrup Urine Disease  | BCKDHA   | 99%            | 1 in 12      | 1 in 1101     | Mennonite          |
|  |          | 95%            | 1 in 80      | 1 in 1581     | Ashkenazi          |
| Medium-chain acyl-coenzyme A dehydrogenase (MCAD)                          | ACADM    | 90%            | 1 in 50      | 1 in 491      | General            |
| Methylmalonic Aciduria and Homocystinuria, cblC Type                       | MMACH    | 67%            | 1 in 141     | 1 in 442      | General            |
| Methylmalonic Aciduria - MUT related                                       | MUT      | 41%            | 1 in 141     | 1 in 287      | African American   |
|  |          | 20%            | 1 in 141     | 1 in 176      | Caucasian          |
|  |          | 60%            | 1 in 141     | 1 in 234      | Hispanic           |
| Methylmalonic Aciduria (cobalamin deficiency) cblA type                    | MMAA     | 43%            | 1 in 141     | 1 in 247      | General            |
| Methylmalonic Aciduria (cobalamin deficiency) cblB type                    | MMAB     | 58%            | 1 in 141     | 1 in 334      | General            |
| Mucopolipidosis type IV  | MCOLN1   | 95%            | 1 in 96      | 1 in 1901     | Ashkenazi          |

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| CONDITION (S)  | GENE    | Detection Rate | Carrier Risk | Residual Risk | Ethnic Background   |
|--|---------|----------------|--------------|---------------|---------------------|
| Nephrosis 1, congenital, Finnish type  | NPHS1   | 81%            | 1 in 45      | 1 in 233      | Finnish             |
|  |         | 99%            | 1 in 113     | 1 in 11,201   | Maltese             |
|  |         | 31%            | 1 in 113     | 1 in 163      | General             |
| Nieman Pick Type A   | SMPD1   | 90%            | 1 in 90      | 1 in 891      | Ashkenazi           |
| Nieman Pick Type B   | SMPD1   | 90%            | 1 in 250     | 1 in 2491     | North African       |
| Nonketotic hyperglycinemia (NKH); GLYCINE DECARBOXYLASE                            | GLDC    | 78%            | 1 in 55      | 1 in 246      | Finnish             |
| Ornithine Transcarbamylase Deficiency  | OTC     | 14%            | 1 in 142     | 1 in 165      | General             |
| Phenylketonuria (PKU)  | PAH     | 48%            | 1 in 50      | 1 in 93       | Caucasian           |
| Polycystic kidney and hepatic disease; Congenital Hepatic Fibrosis; Caroli Disease | PKHD1   | 39%            | 1 in 70      | 1 in 114      | General             |
| Pompe disease (Glycogen storage disease type II)                                   | GAA     | 67%            | 1 in 100     | 1 in 301      | Dutch               |
|  |         | 42%            | 1 in 100     | 1 in 172      | Italian             |
|  |         | 85%            | 1 in 100     | 1 in 661      | Chinese             |
|  |         | 60%            | 1 in 100     | 1 in 249      | African American    |
| Progressive Epilepsy with Mental Retardation (EPMR)                                | CLN8    | 99%            | 1 in 210     | 1 in 20,801   | Finnish             |
| Recessive multiple epiphyseal dysplasia  | SLC26A2 | 75%            | 1 in 71      | 1 in 281      | General             |
| Rhizomelic Chondrodysplasia Punctata Type 1  | PEX7    | 68%            | 1 in 167     | 1 in 520      | General             |
| Salla Disease  | SLC17A5 | 95%            | 1 in 40      | 1 in 976      | Finnish             |
| Severe Combined Immunodeficiency (AR), Adenosine deaminase deficiency              | ADA     | 64%            | 1 in 224     | 1 in 620      | African - Caribbean |
| Sjogren-Larsson syndrome   | FALDH   | 83%            | 1 in 50      | 1 in 328      | Swedish             |
|  |         | 56%            | 1 in 250     | 1 in 567      | General             |
| Smith-Lemli-Opitz Syndrome   | DHCR7   | 35%            | 1 in 70      | 1 in 112      | General             |
| Steroid-Resistant Nephrotic Syndrome   | NPHS2   | 73%            | 1 in 400     | 1 in 1479     | General             |
| Tay-Sachs Disease  | HEXA    | 96%            | 1 in 28      | 1 in 696      | Ashkenazi           |
| Tyrosinemia Type 1   | FAH     | 88%            | 1 in 66      | 1 in 543      | French Canadian     |
|  |         | 50%            | 1 in 100     | 1 in 199      | General             |
|  |         | 99%            | 1 in 100     | 1 in 9901     | Ashkenazi           |
| Variant late infantile Neuronal Ceroid Lipofuscinosis CLN5                         | CLN5    | 94%            | <1 in 80     | 1 in 1318     | Finnish             |
| Very long-chain acyl-CoA dehydrogenase (VLCAD)                                     | ACADVL  | 20%            | 1 in 89      | 1 in 111      | General             |
| X-linked Severe Combined Immunodeficiency  | IL2RG   | 21%            | 1 in 112     | 1 in 141      | General             |
| Zellweger, Neonatal Adrenoleukodystrophy, Infantile Refsum disease                 | PEX1    | 81%            | 1 in 112     | 1 in 585      | General             |

**Expected (Normal) Value** Family History/Carrier Testing: 0 or 1 mutation detected for each individual gene.

**Test Reports** Known mutations detected by the 343 mutation panel for the 78 conditions will be reported. Polymorphisms are not specifically analyzed or reported. Definitions: Mutations (previously described variants leading to clinical manifestations), novel variants (variants not previously reported, unknown genotype-phenotype correlation), polymorphisms (previously described variants without a phenotype impact).

**Disclaimer** This test was developed and its performance characteristics were determined by Ambry Genetics Corporation. The laboratory is regulated under the Clinical Laboratory Improvement Amendments 2003 as qualified to perform non-waived testing. The AmbryScreen Panel, analyzes the specific mutations listed above. A negative result from the analysis cannot rule out the possibility that the tested individual carries an unexamined mutation. The AmbryScreen Panel is designed and validated to be capable of detecting >99% of the previously described 343 mutations on the 74 genes listed above. Although molecular tests are highly accurate, rare diagnostic errors may occur. Possible diagnostic errors include sample mix-up, erroneous paternity identification, technical errors, and genotyping errors. Genotyping errors can result from trace contamination of PCR reactions, from maternal cell contamination in fetal samples, from rare genetic variants, which interfere with analysis, or from other sources. This report does not represent medical advice. Any questions, suggestions, or concerns regarding interpretation of results should be forwarded to a genetic counselor, medical geneticist, or physician skilled in interpretation of the relevant medical literature. References are available upon request.

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