

**COMPLETE ENTIRE FORM TO AVOID DELAYS**

PATIENT INFORMATION					
Name (Last, First, MI)		Date of Birth (MM/DD/YY)	Date of Death (if applicable)	Phone Number/Email	
Address	City	State	Zip	Biological Sex <input type="checkbox"/> F <input type="checkbox"/> M	Ethnicity: <input type="checkbox"/> African American <input type="checkbox"/> Asian <input type="checkbox"/> Caucasian <input type="checkbox"/> Hispanic <input type="checkbox"/> Jewish (Ashkenazi) <input type="checkbox"/> Portuguese <input type="checkbox"/> Other:
SPECIMEN INFORMATION* (For phlebotomy service, select all services you are requesting)					
Type(s) <input type="checkbox"/> Blood (EDTA preferred) <input type="checkbox"/> Saliva (Not accepted for ExomeNext and ExomeNext-Rapid probands)			<input type="checkbox"/> Personal history of allogenic bone marrow or peripheral stem cell transplant		
<input type="checkbox"/> DNA, Source: <input type="checkbox"/> Other:					
Collection Date	Specimen ID			Medical Record #	
*Blood or saliva from patients with active/recent hematological disease will undergo additional review and may not be accepted in some cases. For these, cultured fibroblasts or fresh/fresh frozen normal tissue are preferred. See <a href="http://ambrygen.com/specimen-requirements">ambrygen.com/specimen-requirements</a> for details.					
Phlebotomy Services Request: <input type="checkbox"/> Phlebotomy draw <input type="checkbox"/> Insurance preverification first <input type="checkbox"/> Send kit to patient* *As the patient's clinician, I am unaware of any potential for complication or difficulty in drawing blood for the listed patient(s). I understand that the phlebotomist has full authority to refuse to draw any patient if the safety of the phlebotomist and/or patient(s) are in question.					
ORDERING PHYSICIAN/SENDING FACILITY (Each listed person will receive a copy of the report)					
Facility Name (Facility Code)		Address	City	State/Country	Zip Phone
Ordering Licensed Provider Name (Last, First)(Code)		NPI#	Phone	Fax/Email	
ADDITIONAL RESULTS RECIPIENTS					
Genetic Counselor or Other Medical Provider Name (Last, First) (Code)			Phone/Fax/Email		
CONFIRMATION OF INFORMED CONSENT AND MEDICAL NECESSITY FOR GENETIC TESTING					
The undersigned person (or representative thereof) ensures he/she is a licensed medical professional authorized to order genetic testing and confirms that the patient has given appropriate consent. I confirm that testing is medically necessary and that test results may impact medical management for the patient. Furthermore, all information on this TRF is true to the best of my knowledge. My signature applies to the attached letter of medical necessity (unless this box is checked <input type="checkbox"/> ).					
Signature Required for Processing Medical Professional Signature:				Date:	
<input type="checkbox"/> INSURANCE BILLING (Include copy of both sides of insurance card)			<input type="checkbox"/> INSTITUTIONAL BILLING		
Patient Relation to Policy Holder? <input type="checkbox"/> Self <input type="checkbox"/> Spouse <input type="checkbox"/> Child	Name and DOB of Policy Holder (if not self)		Facility Name <input type="checkbox"/> Send invoice to facility address above		
Insurance Company	Policy #	HMO Auth #	Address		
Ambry Genetics preverifies insurance coverage and will contact the patient after the patient's sample is received if the out-of-pocket amount for testing is estimated to exceed (Nothing checked defaults to >\$100): <input type="checkbox"/> \$100 <input type="checkbox"/> Any amount <input type="checkbox"/> Other \$			Contact Name		
<input type="checkbox"/> Hold order pending patient contact and approval of payment terms regarding out-of-pocket.			Phone Number		E-mail/Fax
Patient preferred method of contact regarding out-of-pocket amount: <input type="checkbox"/> Email <input type="checkbox"/> Phone			<input type="checkbox"/> PATIENT PAYMENT		<input type="checkbox"/> Check (Payable to Ambry Genetics) <input type="checkbox"/> Credit Card (Call 949-900-5795)
<b>Patient Acknowledgement:</b> I acknowledge that the information provided by me is true and correct. For direct insurance billing: I authorize my insurance benefits to be paid directly to Ambry Genetics Corporation (Ambry), authorize Ambry to release medical information concerning my testing to my insurer, to be my designated representative for purposes of appealing any denial of benefits as needed and to request additional medical records for this purpose. I understand that I am financially responsible for any amounts not covered by my insurer and responsible for sending Ambry money received from my health insurance company. <b>For patient payment by credit card:</b> I hereby authorize Ambry Genetics Corporation to bill my credit card as indicated above. In order to expedite consideration for eligibility for Ambry's E.P.I.C. Program, please provide the total annual gross household income: \$_____ and the number of family members in the household supported by the listed income: _____. I authorize Ambry Genetics Corporation to verify the above information for the sole purpose of assessing financial need, including the right to seek supporting documentation.					
FOR NY RESIDENTS:					
<input type="checkbox"/> I am a New York resident and I give Ambry Genetics permission to store my sample for longer than 60 days. <b>NOTE:</b> If left blank, consent is interpreted as "NO".					
Signature Required For Insurance/Self-Pay Patients and NY Sample Storage Consent:				Date:	

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INDICATIONS FOR TESTING (Check all that apply)		
ICD-10 code(s): _____		
PROBAND'S PRIMARY INDICATION FOR TESTING (Please select only one)		
<b>PLEASE SUPPLY CLINIC NOTES AND PEDIGREE</b>		
<b>Neurodevelopmental (+/- minor dysmorphic features):</b> <input type="checkbox"/> Neurodevelopmental NOS <input type="checkbox"/> Intellectual disability <input type="checkbox"/> Hypotonia <input type="checkbox"/> Seizures <input type="checkbox"/> Autism spectrum disorder <input type="checkbox"/> Psychiatric  <b>Disorder or feature primarily affecting one organ system:</b> <input type="checkbox"/> Brain <input type="checkbox"/> Cancer <input type="checkbox"/> Immune <input type="checkbox"/> Integumentary <input type="checkbox"/> Skeletal <input type="checkbox"/> Connective tissue  <b>Growth Disorder:</b> <input type="checkbox"/> Undergrowth/FTT <input type="checkbox"/> Overgrowth <input type="checkbox"/> Other _____	<b>Neuromuscular:</b> <input type="checkbox"/> Neuromuscular NOS <input type="checkbox"/> Ataxia/ spasticity <input type="checkbox"/> Muscular dystrophy <input type="checkbox"/> Neuropathy <input type="checkbox"/> Other Movement Disorder <input type="checkbox"/> Abnormal Muscle Biopsy	<b>Multiple Congenital Anomalies (+/- Neurodevelopmental symptoms):</b> <input type="checkbox"/> 2 or more major or 3 or more minor malformations
PROBAND'S CLINICAL OVERVIEW (Check all that apply)		
<input type="checkbox"/> Audiologic / Otolaryngologic <input type="checkbox"/> Cardiovascular <input type="checkbox"/> Craniofacial <input type="checkbox"/> Dental <input type="checkbox"/> Dysmorphic Features <input type="checkbox"/> Craniofacial dysmorphism <input type="checkbox"/> Dysmorphic extremities <input type="checkbox"/> Other <input type="checkbox"/> Dermatologic <input type="checkbox"/> Endocrine <input type="checkbox"/> Gastrointestinal <input type="checkbox"/> Genitourinary	<input type="checkbox"/> Hematologic <input type="checkbox"/> Immunologic/Infectious <input type="checkbox"/> Metabolic/Biochemical <input type="checkbox"/> Musculoskeletal/Structural <input type="checkbox"/> Multiple Congenital Anomalies  <input type="checkbox"/> Personal h/o allogenic bone marrow or peripheral stem cell transplant  <input type="checkbox"/> Current diagnosis of heme malignancy, Type : _____	<input type="checkbox"/> Neurologic <input type="checkbox"/> Seizures/Epilepsy <input type="checkbox"/> Autism Spectrum Disorder <input type="checkbox"/> Developmental Delay/Intellectual disability <input type="checkbox"/> Ataxia/Spasticity <input type="checkbox"/> Psychiatric <input type="checkbox"/> Abnormal brain MRI <input type="checkbox"/> Obstetric <input type="checkbox"/> Oncologic <input type="checkbox"/> Ophthalmologic <input type="checkbox"/> Pulmonary <input type="checkbox"/> Renal
ADDITIONAL CLINICAL DETAILS		
Intellectual Delay/Intellectual Disability: <input type="checkbox"/> mild <input type="checkbox"/> moderate <input type="checkbox"/> severe <input type="checkbox"/> profound    overall IQ: _____ Verbal Aptitude: <input type="checkbox"/> normal <input type="checkbox"/> mild deficiency <input type="checkbox"/> moderate deficiency <input type="checkbox"/> non-verbal Autism: <input type="checkbox"/> no autistic behaviors <input type="checkbox"/> autistic behaviors (describe): _____ Dysmorphic Features (describe): _____    Congenital Anomalies (describe): _____ History of Seizures <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> diagnosed epilepsy  <b>Previous Studies</b> MRI/CT studies (findings): _____ Chromosome analysis: _____    Microarray analysis: _____ Other molecular studies: _____ Growth Indices (current):    Head circumference: _____%    Weight: _____%    Height: _____% Differential diagnosis/Genes of interest: _____		
FAMILY HISTORY*		
*Please identify each family member available for testing below. The "Clinical Genomics Family Member Test Requisition Form" is ALSO required for each family member being tested.		
Name (Last, First)	Relationship to proband	Affected
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Partial <input type="checkbox"/> Possible
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Partial <input type="checkbox"/> Possible
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Partial <input type="checkbox"/> Possible
		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Partial <input type="checkbox"/> Possible
Is anyone in the family affected with a similar phenotype as the proband? <input type="checkbox"/> NO <input type="checkbox"/> YES, please list exact relationship to proband, symptoms and age of onset of symptoms: _____ _____ Any stillbirths or SABs? <input type="checkbox"/> NO <input type="checkbox"/> YES, please describe: _____ Is there any consanguinity (conception between blood relatives) in the family? <input type="checkbox"/> NO <input type="checkbox"/> YES    If yes please describe: _____		

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Please check the box next to the test(s) being ordered below. All tests include gene sequence and deletion/duplication analyses unless otherwise indicated. If this TRF is sent to Ambry without or ahead of the sample, it will be treated as a preverification. If test ordered is different than the test preverified, we will honor what is on the TRF order form with the sample.

For multiple test orders, testing will be run concurrently (multiple tests initiated at the same time) unless otherwise specified. To order reflexive testing (second test starts pending first test outcome), please clearly indicate the order of reflexive tests in the notes section or next to the test check box. For reflex test orders, any positive findings (pathogenic/likely pathogenic) in the first test will be reported out to the clinician, and the requested second test will be canceled; all other findings will automatically reflex (including VUS).

Check to order	Test Name	Test Code	Description/Options
<b>Clinical Genomics</b>			
<input type="checkbox"/>	Karyotype	3660	Chromosome analysis (requires green-top sodium-heparin tube)
<input type="checkbox"/>	Karyotype, rule out mosaic	3662	Chromosome analysis (requires green-top sodium-heparin tube)
<input type="checkbox"/>	SNP Array	5490	Chromosomal microarray (>2.6 million copy number probes and 750,000 SNP probes)
<input type="checkbox"/>	Follow-up parental FISH studies - ONLY available following SNP Array (5490) completed at Ambry	3750	Sodium heparin tube, submit proband sample for positive control. Name of proband tested at Ambry: _____
<input type="checkbox"/>	ExomeNext*	9999	<input type="checkbox"/> Opt-out of analysis and reporting of Candidate (novel) Genetic Etiologies
<input type="checkbox"/>	ExomeNext-Rapid**	9999R	<input type="checkbox"/> Opt-out of analysis and reporting of Candidate (novel) Genetic Etiologies
Must be ordered through AP2**	ExomeNext-Select	9500	Up to 500 gene custom exome sequencing test
*mtDNA testing cannot be performed on saliva samples. If saliva is submitted for the proband, the test will be placed on hold and the ordering physician will be contacted. **Institutional billing or patient payment only **AP2 is AmbryPort 2.0, our online portal <a href="http://ambrygen.com/ap2">ambrygen.com/ap2</a>			
If ordering ExomeNext/ExomeNext-Rapid, please complete: <b>Secondary Findings Report:</b> Check below to order the ACMG Recommended List of secondary findings. If neither box is checked secondary findings will not be reported. Secondary findings results are issued in a separate report. (For expanded secondary findings options and pricing please complete the "ExomeNext Expanded Secondary Findings Request Form" and submit with sample). Secondary findings not available for ExomeNext-Select orders. <input type="checkbox"/> Yes: I choose to receive the ACMG Recommended List of secondary findings <input type="checkbox"/> No: I choose to decline the ACMG Recommended List of secondary findings			

**Single Site Analysis (Please include a copy of relative's report)**

Gene(s): \_\_\_\_\_ Mutation(s): \_\_\_\_\_

Relative Name: \_\_\_\_\_

Relationship to Relative: \_\_\_\_\_

Accession #: \_\_\_\_\_

Positive control sample:  will be provided  already at Ambry  not available

**Other Order**

Please visit [ambrygen.com/tests](http://ambrygen.com/tests) for details.

Test Code: \_\_\_\_\_ Test Name: \_\_\_\_\_

Notes:

**ORDERING CHECKLIST (Required\*)**

Proband specimen

Clinical Genomics TRF with patient & clinician signatures

Clinical history (attach clinic notes)

Insurance orders only:

- Letter of Medical Necessity (LMN)
- Copy of Insurance Card

*\*Orders with missing requirements will be placed on hold until all requirements are received.*

**ORDERING CHECKLIST (Highly Recommended)**

Family member specimens\*\* (1 family member TRF required per individual)

Family history or pedigree

Previous test results

*\*\*Please complete a "Clinical Genomics Family Member TRF" for each family member submitted for testing. Please send all 1st degree relatives and informative relatives at the beginning of testing.*

**CONTACT INFORMATION**

For ExomeNext preverification requests please send the LMN and Clinical Genomics TRF to [preverification@ambrygen.com](mailto:preverification@ambrygen.com) or fax to 949-900-5501.

All other documents can be secure uploaded at [ambrygen.com/secure-upload](http://ambrygen.com/secure-upload), or faxed to 949-900-5501.

AmbryPort 2.0 is a new secure client portal that allows order submission, test status updates, insurance authorization status and report downloads. All required documents can be completed and directly uploaded through AmbryPort2.0 during the ordering process or after order submission. Please visit [portal.ambrygen.com/signup](http://portal.ambrygen.com/signup) to sign up.

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## SNP ARRAY PATIENT GUIDE

Proband Initials \_\_\_\_\_

### 1. THE GENOME, CHROMOSOMES, AND DNA

The human genome contains a complete set of genetic information for humans. This information is packaged as DNA sequences into 23 pairs of chromosomes. Each parent contributes one chromosome to each of the 23 pairs, so that half of the person's genetic material is inherited from each parent. Each chromosome contains many genes that are responsible for producing the proteins that are the building blocks of our bodies. Genomic imbalances, such as gains or losses of chromosomes or portions of chromosomes, are a known underlying cause of developmental delay, intellectual disability, autism spectrum disorders (ASD), dysmorphic features, birth defects or other congenital anomalies, and numerous genetic syndromes.

### 2. THE SNP ARRAY

The SNP Array assesses patient DNA for gains or losses of genomic material on all 23 chromosome pairs in a single test at a superior resolution compared to traditional chromosome analysis (karyotyping). Ambry's SNP array detects genetic losses of ~100 kb (100,000 base pairs) and genetic gains of ~300kb (300,000 base pairs) while the resolution of traditional chromosome analysis is ~4Mb (4,000,000 base pairs). SNP Array also detects regions of homozygosity. Regions of homozygosity (ROH) may indicate a familial relationship between parents of the individual being tested and raises the possibility of a recessive disorder. ROH may also indicate uniparental disomy (UPD); UPD is associated with conditions such as Beckwith-Wiedemann and Prader-Willi/Angelman syndromes. ROH greater than 10.0Mb in size are reported, though this threshold may vary depending on the location of the ROH.

### 3. TECHNICAL LIMITATIONS

The SNP Array will only detect net gains or losses of genomic material and regions of homozygosity, and therefore is not intended to detect the following types of chromosomal aberrations; balanced translocations, Robertsonian translocations, balanced insertions, inversions, point mutations, low level mosaicism, epigenetic abnormalities, heterodisomic or mosaic UPD or any microdeletions and duplications that are below the resolution of the array or not represented on the array. A negative result from the analysis cannot rule out the possibility that an individual carries an abnormality in one of these categories.

### 4. RESULTS AND INTERPRETATION

SNP Array analysis is typically completed in 14-21 days. If copy number variations (gains or losses of genomic material) are found, they will be classified into categories according to their likelihood of causing disease. When appropriate, a clear statement of clinical significance will be included in the interpretation section of the report. Some variants may be classified as variants of uncertain significance (VUS). If certain conditions are met, Ambry will provide complimentary parental analysis. The inheritance of a copy number variation from an apparently unaffected parent may indicate that the likelihood that the alteration relates to the patient's clinical symptoms is reduced. However, a causal relationship between the alteration and the proband's clinical presentation cannot be excluded due to reduced penetrance, variable expressivity, and multifactorial inheritance.

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## EXOMENEXT PATIENT GUIDE

Proband Initials \_\_\_\_\_

### 1. TEST PROCESS

ExomeNext involves sequencing and analysis of the ~20,000 nuclear genes in addition to sequencing and screening for proven mutations in the mitochondrial genome (mtDNA). This process includes genes that have been previously associated with human disease (characterized) and those that have not been previously described to underline a Mendelian condition (novel). Whole exome sequencing differs from whole genome sequencing as it targets the ~1-2% of the protein coding regions (exons) of the genome. Whole exome sequencing provides a time and cost effective method of sequencing all of an individual's genes since ~85% of known diseases-causing mutations are expected to occur within the exons. The goal of ExomeNext is to identify the underlying molecular cause of an affected individual's condition.

### 2. TECHNICAL LIMITATIONS

Not all exons in the genome are targeted. Approximately, 5% of the exons that are targeted may not be well covered. The empirical coverage data for specific genes can be found on the Ambry Genetics website. Certain mutation types may not be detectable (eg. large copy number variants, methylation abnormalities, mutations in genes with highly homologous pseudogenes, and expansions of trinucleotide repeats) and exome sequencing is also limited in the detection of alterations confounded by various non-Mendelian factors (penetrance, variable expressivity, multifactorial disease, epigenetic factors, phenocopies and uniparental disomy (UPD)).

### 3. TESTING & ANALYSIS PIPELINE

Several hundred thousand variants will be identified through whole exome sequencing, and all variants will be filtered through an in-house developed pipeline, Ambry variant analyzer (AVA), based on types of alterations, minor allele frequencies, and various mutation databases. Next, a thorough clinical and medical review is performed by our medical team to identify candidate alterations with overlapping features consistent with the patient's reported phenotype. Analysis begins with characterized genetic etiologies and if no candidate alterations are identified among characterized genetic etiologies the case may then move to the second step for analysis of novel genetic etiologies. Variants that are considered "candidates" thought to be involved in the syndrome being investigated will undergo further analysis and interpretation by an ABMG-certified laboratory director and will be included in the Primary Report.

### 4. TESTING OF FAMILY SAMPLES

ExomeNext is a family-centered approach to whole exome sequencing and involves the sequencing of three individuals (trio): the patient/fetus (proband) and two other family members, preferentially parents or other first-degree relatives. If an informative trio is not available, analysis of novel genetic etiologies will not be performed. Co-segregation analysis (family studies) is performed for candidate alterations on the trio, and additional family members submitted at the time of testing. Providing family member samples improves the likelihood of a more definitive diagnosis.

Confirmation of candidate alterations by Sanger sequencing will be performed for all candidate alterations. De-identified co-segregation results for the family members will be included in the primary report. For candidate mitochondrial DNA alterations, only mutations in the proband with apparently >15% mutant load by NGS will be confirmed using an alternate method. If no candidate alterations are identified, additional family member samples beyond the trio will not be tested. Testing of family members after testing is completed and starts at \$400 per sample.

### 5. FAMILY MEMBER DISCREPANCIES

As with any family-centered genetic testing, there is a possibility that the family genetic relationships do not align with what is reported by your family. If relationship confirmation results are not as reported to Ambry, your clinicians will be contacted to determine how to proceed with testing.

### 6. CLINICAL INFORMATION AND RESULTS INTERPRETATION

ExomeNext interpretation and analysis is significantly enhanced by the provision of a full and complete clinical history. For informative results and the best likelihood of a conclusive diagnosis, it is critical to provide all relevant clinical and family history information to the ordering clinician and to Ambry Genetics. Testing will not begin until the laboratory has received the required paperwork and specimens.

### 7. RESULTS AND INTERPRETATION

The Primary Report will contain results related to the proband's primary indication for testing. All candidate alterations will undergo Sanger confirmation and co-segregation analysis. Overall result categories will be dependent on the pathogenicity of the alteration along with the phenotypic overlap of the gene with the proband's symptoms. Additional findings (aka notable findings) with limited clinical overlap do not routinely undergo co-segregation analysis or confirmation via Sanger sequencing. Results will be released to the ordering clinician, and the final clinical interpretation of ExomeNext results will be made by the ordering clinician and NOT Ambry Genetics.

Analysis of novel genetic etiologies may allow for the discovery of genes not currently reported in association with a known genetic condition, and this may be a pathway toward diagnosing a previously undescribed genetic defect. However, under certain circumstances a diagnosis will not be readily available. Since new scientific information becomes available on a regular basis, this could alter the interpretation of previously reported results. In the event of a change in interpretation, an unsolicited re-classification/amended report may be issued to the ordering clinician. Re-analysis may also be performed by request. Please contact the laboratory for re-analysis options.

Secondary findings, pathogenic mutations unrelated to the current clinical presentation, will be reported in a separate Secondary Findings Report (See "Secondary Findings" below). This report will be separate from the Primary Report.

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Proband Initials \_\_\_\_\_

**8. CLINICAL COURSE/PROGNOSIS OF DISEASE**

Identification of a specific genetic variant does not predict the onset, severity, or spectrum of human disease with any degree of certainty. Similarly, the absence of a sequence variant may reduce, but will not eliminate the possibility of being affected with a specific condition.

**9. STANDARD LABORATORY LIMITATIONS**

Standard laboratory limitations apply to each specimen drawn for testing, including but not limited to: sample mix-up, samples unavailable from critical family members, inaccurate reporting of family relationships, mosaicism, low-level heteroplasmy or technical limitations, under these potential, yet rare circumstances, exome sequencing may not be capable of generating an accurate result.

**10. SECONDARY FINDINGS**

Exome sequencing of a single individual for a clinical indication may result in the identification of other incidental mutations unrelated to the indication for testing (aka "secondary findings"). The patient undergoing testing along with family members sequenced as part of the trio may or may not want to be informed of these potential secondary findings (see "Technical Limitations"). Secondary findings results are also available for each family member chosen to be sequenced as part of the trio. The family members chosen as the ExomeNext trio are at the discretion of the laboratory. Thus, not all consented member may receive secondary findings reports. Each trio family member opting-in will undergo an individual secondary findings analysis. Please note, pathogenic mutations that may be present in a family member but not in the proband may be detected and reported. Secondary findings reports are issued in a separate report and available for the proband and each family member sequenced as part of the trio. Secondary findings will not be reported for ExomeNext-Select test orders.

**ACMG SECONDARY FINDINGS RECOMMENDED LIST\* (OPTIONAL-NO COST)**

In 2013, the American College of Medical Genetics and Genomics (ACMG) released "Recommendations on Incidental Findings in Clinical Exome and Genome Sequencing." The group recommends that laboratories performing diagnostic exome sequencing (DES) actively search and report alterations in genes from among a provided "minimum list" of genes. The list was updated in 2016 and includes 59 genes associated with roughly 28 genetic conditions determined by ACMG to be well-recognized and known to have a strong link of causation. The conditions were chosen if preventative measures and treatments exist. Among the condition types are cancer predisposition risk, later-onset cardiac syndromes, connective tissue syndromes (Marfan Syndrome, Loeys-Dietz Syndrome), and one childhood-onset disease (familial hypercholesterolemia). Secondary findings results are available for all probands and members of the trio, regardless of age. These results may include the conditions listed above. Family members may be able to infer carrier status based on the proband's results.

The ACMG and AAP offer the following precautions when performing genetic testing in minors: 1) Parents or guardians may authorize predictive genetic testing for asymptomatic children at risk of childhood-onset conditions. Ideally, the assent of the child should be obtained; 2) Predictive genetic testing for adult-onset conditions generally should be deferred unless an intervention initiated in childhood may reduce morbidity or mortality; 3) For ethical and legal reasons, health care providers should be cautious about providing predictive genetic testing to minors without the involvement of their parents or guardians, even if a minor is mature. Results of such tests may have significant medical, psychological, and social implications, not only for the minor but also for other family members.

\*A list of the ACMG recommended genes and diseases can be found at: [ambrygen.com/exomenext-forms](http://ambrygen.com/exomenext-forms)

**AMBRY'S EXPANDED SECONDARY FINDINGS\*\* (OPTIONAL)**

For an additional cost, patients and family members chosen as the trio may also order an expanded secondary findings report. In addition to the ACMG recommended list, each patient/family member can choose from an expanded set of reportable secondary findings including recessive carrier status, cancer predisposition, adult onset disease and childhood onset disease. Please note, DNA variants associated with drug metabolism and risk of common multifactorial diseases (i.e. coronary artery disease, obesity, asthma, etc.) are not analyzed and reported as part of the expanded secondary findings report.

Please complete and submit the Expanded Secondary Findings Request Form to request this option.

[ambrygen.com/exomenext-forms](http://ambrygen.com/exomenext-forms)

\*\*A complete list of genes from the four Expanded Secondary Findings categories described above can be found at:

[ambrygen.com/exomenext-forms](http://ambrygen.com/exomenext-forms)

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## FILTERED VARIANT CONSENT FORM

PROBAND NAME : \_\_\_\_\_

PROBAND DOB : \_\_\_\_\_

Ambry Genetics provides the list of raw filtered variants including candidate (novel) genes when requested, with the understanding that the data will be used strictly on a research basis, and not for clinical purposes. Other than those described in the final report, the variants have not undergone thorough interpretation and/or may represent sequencing artifacts as most have not been confirmed by a second laboratory method. In the case that additional important findings related to the phenotype in question are identified, clinicians should immediately contact the laboratory for verification, and possibly, generation of an amended report. This list of variants may include secondary findings. All patients undergoing diagnostic exome sequencing (DES) have completed a consent form which includes the opportunity to opt-out of secondary findings disclosure.

Filtered variant list (*provided in excel format at no charge*)

### PHYSICIAN CONSENT:

I understand that the receipt of the raw filtered variant list may include secondary findings, potential sequencing artifacts, and variants which have not undergone interpretation and the patients/family members listed below are aware that I am requesting this data. I also understand that any information gleaned from review of this data, outside that which is described in the patient's final report, is strictly for research purposes and shall not be used for clinical decision-making purposes. I understand that Ambry Genetics recommends against the delivery of these data to patients.

Signature : \_\_\_\_\_

Date : \_\_\_\_\_

Printed Name : \_\_\_\_\_

Phone : \_\_\_\_\_

Institution : \_\_\_\_\_

Email Address : \_\_\_\_\_

### PATIENT/GUARDIAN CONSENT:

I understand that my doctor has requested receipt of the raw filtered variant list resulting from the diagnostic exome sequencing (DES) performed for me/the person for whom I am the caregiver. I acknowledge that the information included in the data files may include secondary findings, potential sequencing artifacts, and variants which have not undergone interpretation. I also understand that these data are for research purposes only and shall not be used for clinical decision-making purposes. I understand that Ambry Genetics recommends against the delivery of these data to patients.

**NAME AND DOB OF EACH PATIENT/FAMILY MEMBER FROM WHOM YOU ARE REQUESTING THE RAW FILTERED VARIANT LIST:  
(ONE LIST WILL BE PROVIDED PER FAMILY)**

NAME	DOB	PATIENT/FAMILY MEMBER SIGNATURE	DATE