REQUISITION

Appointment Booking: www.lifelabs.com
1-844-363-4357· Ask.Genetics@LifeLabs.com

CENTOGENE
THE RARE DISEASE COMPANY

CONTRACT #	**LL: K012-01**	**LifeLabs Demographic Label**
Report to Physician #	Physician OHIP# (Ontario): Physician MSC# (British Columbia): Other Provinces: 999	
Ordering Physician Name	Name	
Ordering Physician Address & contact info:	Address Tel: Fax:	**Additional Label** (if needed)
Physician Signature:	**Confirmation of Patient Consent:** I confirm that this patient has given consent to testing as may be required by applicable law, which indicates that: the patient has been informed about the details associated with the genetic test(s) ordered below including its risks, benefits and limitations; I/we will ensure that test results will be interpreted to the patient in an appropriate manner, and that the patient will not receive the results without accompanying counseling; and the patient was informed that s/he has the right to revoke his/her consent at any time X_____	
Copy to: ❑ Genetic Counsellor ❑ Other Healthcare Provider	Copy to name Tel: Fax:	
Bill to:	**Contract # K012-01** (patient does not pay at time of collection)	**Patient Sex:** ❑ Female ❑ Male
Patient Name (Last, First):	Name	**Patient DOB:** (MM/DD/YYYY)
Patient Address:	**Health Card #:**	**Patient Tel:**
Patient Information:	❑ African/African American ❑ Caucasian ❑ French Canadian or Acadian ❑ Middle Eastern ❑ Northern European *e.g. British, German* ❑ South Asian *e.g. Indian, Pakistani* ❑ East Asian *e.g. Chinese, Japanese* ❑ Ashkenazi Jewish ❑ Other/Mixed Caucasian ❑ Native American ❑ Hispanic ❑ Southern European *e.g. Italian, Greek* ❑ Southeast Asian *e.g. Filipino, Vietnamese* ❑ Pacific Islander	
Relevant Medical and Family History	❑ No additional information available	
Billing Status	❑ Ministry of Health Approved (Approval letter attached) ❑ Institution (Complete information below) ❑ Ministry of Health Approval Pending ❑ Private Pay (Complete additional form)	
Institution Billing ONLY	**Institution Name:** _____ **Contact Name:** _____ **Address:** **Phone: ( ) -** **Fax: ( ) -** **Email:** _____	

For samples not collected at a LifeLabs location, please ship all NON-PRENATAL samples to:
British Columbia: LifeLabs • Attn. Specimen Management • 3680 Gilmore Way • Burnaby BC • V5G 4V8
All Other Provinces: LifeLabs • Attn. Specimen Management • 37 Voyager Court N.• Toronto ON • M9W 6J2

Ordering Checklist	
Known variant **Single gene**	**Must complete pages 1, 2, & 3** □ Physician, patient, & test information (p1-2) □ Informed consent (p3)
Fx Panels **Ex Panel** **ProGx Panels**	**Must complete pages 1-5** □ Physician, patient, & test information (p1-2) □ Informed consent (p3-4) □ Clinical features checklist (p5)
Whole Exome Sequencing (WES) **Whole Genome Sequencing (WGS)**	**Must complete pages 1-8** (if applicable) □ Physician, patient, & test information (p1-2) □ Informed consent (p3-4) □ Clinical features checklist (p5) □ Parental 1 & 2 requisitions (p6-7) *(if Trio selected)* □ Additional Family Member requisition (p8) *(if TrioPlus selected OR Parental samples unavailable)*

Sample Type

	LL TC	Mnemonic
❑ **Blood-Adult** (2 x 4ml EDTA)	4005	ACG
❑ **Blood-Pediatric** (1 x 2ml EDTA)	4008	CEN
❑ **Purified DNA** (single genes: 1-10ug, Panels: 10-100ug)	4014	OCG
❑ **Filter card***	4014	OCG
❑ **Other:**** _____	4014	OCG

* Available by request. Please contact LifeLabs Genetics.
** Other sample types are permitted. Please contact LifeLabs Genetics for details.

Please contact LifeLabs Genetics before shipping prenatal samples. Samples should be shipped directly to Centogene.

Date Sample Collected:	M M	D D	Y Y Y Y	**Time Collected:**	H H	M M	**Collector Name:**

REQUISITION

****PHOTOCOPY REQUISITION AND INCLUDE 1 COPY WITH SAMPLES****

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Patient Name:	**Patient DOB** *(MM/DD/ YYYY):*

Testing for known variants:

Gene: _____ **Mutation (HGVS) :**_____

Familial Report attached ❑ **Yes** ❑ **No**

Testing for Single Gene(s) or Fixed Panel(s):

Please use the online catalogue to find test code & names **www.lifelabsgenetics.com/hereditary-conditions**

Test Code(s): _____

Test Name(s): _____

Single Genes
- ❑ *FULL analysis *(by NGS Panel Plus+CNV)*
- ❑ Sequencing *(by NGS Panel Plus)*
- ❑ Deletion/Duplication Testing
- ❑ Repeat Expansion

Fixed Panels
- ❑ **FULL analysis *(by NGS Panel+CNV and repeat expansion, if applicable)*
- ❑ Sequencing *(by NGS Panel)*
- ❑ Deletion/Duplication Testing

**Depending on coverage optimization, sequencing may be performed via Sanger ("Full Sequencing"), if NGS Panel Plus is unavailable. Similarly, CNV analysis may be performed by MLPA of qPCR ("Deletion/Duplication Testing"), if the option of "+CNV" is unavailable.*
***Depending on coverage optimization, sequencing may be performed by NGS Panel Plus, if NGS Panel is unavailable. Similarly, CNV analysis may be performed by MLPA of qPCR ("Deletion/Duplication Testing"), if the option of "+CNV" is unavailable.*

Expanded Panel

Please contact LifeLabs Genetics if you require a Reference Number for your request

❑ **Ex Panel** *(by CentoDxPlus)*
80-100x average read depth
~95% of targeted bases covered at >20x

Test Code(s) / Reference Number(s): _____

Test Name(s): _____

❑ Sequencing + Deletion/Duplication *(by CentoDxPlus + CNV)*
❑ Sequencing only *(by CentoDxPlus)*

Progressive Panels

Please contact LifeLabs Genetics to receive a Reference Number for your request

❑ **ProGx Panels** *(by NGS Panel Genomic)*
(Reflex available – Please contact us)
30x average read depth
~99% of targeted bases covered at >10x
Deletion/Duplication is included
Repeat expansion is available as an add-on and should be requested when obtaining a Reference Number

Reference Number: _____

Whole Exome Sequencing (WES)

❑ **Gold**
100x average read depth
97-98% of targeted bases covered >10X
Turnaround time is 4-6 weeks
No prenatal testing available

❑ **Platinum**
100x average read depth
97-98% of targeted bases covered >10X
Turnaround time is 2-3 weeks
Prenatal testing is available

Whole Genome Sequencing (WGS)

❑ **WGS**
30x average read depth
~99% of targeted bases covered at >10x
Turn-around time is 4-6 weeks
Prenatal testing is available
Del/Dup included

Number of samples
select ONE of the following options:

❑ **Solo**
Solo implies analysis of index patient only; we recommend Trio analysis for enhanced diagnostic accuracy.

❑ **Trio**
Trio implies analysis of index patient, along with the parents.

❑ **Trio Plus**
"Trio plus" indicates "Trio" plus additional relatives. All Trio samples have to be received simultaneously to start testing. If not, each sample from the same family will be charged as a solo.

Additional analyses
available as add-on testing with additional cost
❑ **Del/Dup** (aCGH for proband sample only)
❑ **Repeat expansion**
❑ **Maternal Mitochondrial**
(Proband and maternal sample; >1000x read depth)
❑ **None**

Reporting and data exchange
❑ **.fastq** ❑ **.bam** ❑ **.vcf**
Raw data (.fastq and .bam files) are available only for a limited time and must be downloaded from the server within 1 month after the customer is informed of the completion of the analysis or after the final medical report has been issued.
❑ ***Data selected above with annotated and filtered variant report (Excel table)***

☑**Research Report** (Includes potential disease-causing variants in candidate genes for which there is not yet sufficient published evidence)

Additional information or instructions:

Eg: Specify genes of interest for Ex or ProGx panels

Patient Name:	**Patient DOB** *(MM/DD/ YYYY):*

INFORMED CONSENT (ALL)

(For Ex and ProGx Panels, Whole Exome, and Whole Genome analyses, please also signed consent on page 4.)

GENETIC TESTING CONSENT

A genetic test studies the inherited substance (DNA) using a molecular-genetic analysis of characteristics, which may be the cause of the disease that has occurred or is suspected in you or your family. The **study material** is usually a blood sample. Normally there are no health risks when taking a blood sample. Sometimes patients can experience bruising (hematoma) at the drawing site or, very rarely, there could be nerve damage. Another risk that cannot be fully excluded exists in the extremely unlikely possibility of the samples being swapped. Every effort is made to avoid this and other mistakes.

Test Results and Reporting

DNA sequencing analyzes your DNA and compares it to the reference human genome. Variations (changes) are identified by comparing data with medical databases and looking for scientific links, all of which will be reported to your physician. While there are always certain variations, depending on the individual being tested and the available data, CENTOGENE and/or LifeLabs Genetics adhere to the guidelines set out by the American College of Medical Genetics (ACMG). A medical report may include information that is considered to be of direct and immediate relevance, either to your own health or to that of family members who share part of your genetic background. Possible results of genetic testing include:

- **Positive:** Indicates a genetic variant was identified in a specific gene and that variant is pathogenic of likely pathogenic (highly likely to be causal of the disease-related condition).
- **Negative:** If no disease-causing variant is found, genetic changes responsible for the disease or a tendency to have a disease may still exist and cannot usually be fully excluded.
- **Variant of Uncertain Significance:** Sometimes, gene variants are proven but their significance is not clear. This is stated in the results and discussed with you by your physician. **This category of variant is not reported for fetal samples or samples from deceased persons.**

In addition, CENTOGENE and LifeLabs Genetics also make use of its own mutation database (CentoMD®), which encompasses over 12,000 mutations collected from a global population. Our medical colleagues may recognize other genes that might be of medical significance, and these can be reported as well. Should you not wish to receive this information in your report, it is possible to opt out of this service. A comprehensive explanation of all possible causes of diseases due to genetic reasons is not possible. It is also not possible to exclude every disease risk for you and your family members, especially your children, utilizing genetic analyses.

I consent to the carrying out of the genetic analysis indicated on these pages, on me or the person I am custodian for.

I understand that my specimen for DNA analysis will be sent to LifeLabs for genetic testing. I am aware that correct information about the relationships between my family members is important. I agree that my specimen and personal health information may be sent to Centogene AG at their laboratory in Germany (Am Strande 7, 18055 Rostock, Germany). Your personal data, medical results, and sample are subject to medical confidentiality, and can only be disclosed with your written consent, other than as permitted or required by law. To ensure accurate testing, I agree that the results of genetic testing that I have had previously completed by Centogene AG may be shared with LifeLabs. I understand that LifeLabs will contact me for a new specimen, if a test result cannot be provided from the original specimen. I agree that a copy of my results will be sent to my ordering physician. I further agree that for any test(s) performed by Centogene AG, a copy of my results will also be sent to LifeLabs. I have been comprehensively informed by my physician of the medical and psychological consequences of genetic testing. I also confirm that I will receive genetic counselling to help me understand the impact and consequences of my diagnostic results.

1. I understand that, once the requested test(s) has/have been completed, personal data and remaining sample will be stored at the testing laboratory for 20 years.
2. I agree that my de-identified sample may be used for product development or research purposes. I understand that I will not receive any royalties, resultant payments, benefits, or rights to products or discoveries.
3. I consent to the storage and use of my pseudonymized (encrypted) or de-identified test results in a statistical database for scientific purposes and to facilitate and improve the diagnosis of genetic changes and diseases in other patients.
4. I consent that my de-identified results stored in the database are being provided to physicians, scientists and researchers for the purposes of for researching genetic diseases and improving their diagnostics and treatment.

❑ I do not want my remaining sample or data from my results to be stored and/or used for product development or research purposes.

Please destroy any remaining sample once the final report has been issued. By ticking this box I disagree with points 1, 2, 3, & 4 listed above.

You can **withdraw** your consent to the analysis at any time in full or in part without stating reasons. You have the right not to be informed about test results (right not to know), to stop the testing processes that have been started at any time up to being given the results and to request the destruction of all test material and all results collected up to that time.

Patient/Substitute Decision Maker: Signature: _____; Date: _____

Printed name: _____; Relationship to person being tested: _____

OR: I certify that verbal consent was obtained from the patient /substitute decision maker for the requested genetic testing

Signature of Physician: _____; Date: _____

Patient Name:	**Patient DOB** *(MM/DD/ YYYY):*

INFORMED CONSENT
(Ex and ProGx Panels and Whole Exome and Whole Genome)

(In addition to the general informed consent on page 3)

Ex Panels and Whole Exome Sequencing

The exome is the collection of the DNA sequences of the genes that determine the production of proteins, which your body needs in order to function properly. So far, the exome is where the vast majority of causative mutations have been identified by scientific research. Whereas most genetic tests focus on a single gene or a set number of predetermined genes, WES examines thousands of genes simultaneously. **Ex Panel** focuses on approximately 6,700 genes for which scientific research has identified mutations that are directly related to the development of specific diseases or disorders. **Whole Exome Sequencing** studies the >20,000 genes that make up our genome, including those ~6,700 genes investigated by Expanded NGS Panels.

ProGx Panels and Whole Genome Sequencing

Our DNA is composed of exons (studied by sequencing the exome) and introns, among other regions. Introns were previously not considered to contain important genetic information, as these regions do not directly determine the function of proteins. Recent research has provided evidence that some of these regions may be involved in the development of certain rare diseases and disorders. **Whole Genome Sequencing** analyzes all parts of the >20,000 genes that make up our genome.

Incidental or Secondary Findings

CENTOGENE and LifeLabs Genetics adhere to the guidelines set out by the American College of Medical Genetics (ACMG), which allow for reporting specific types of medically actionable or incidental findings (PMIDs: 23788249 and 25356965). Medically actionable findings may be associated to a predisposition to increased cancer risk, a carrier status of recessive diseases, or a predisposition to late-onset diseases, among others. This list of genes from the ACMG is constantly being updated to include all such instances of mutations that are seen as being relevant to patients. Patients are required to select whether or not they would like to receive information on the 59 genes or classes of genes outlined in these recommendations, which are known to be medically actionable. **Incidental findings are not reported for fetal samples or samples from deceased persons.**

Confirmation of Findings

CENTOGENE and/or LifeLabs Genetics use Sanger sequencing to confirm all pathogenic variants that do not pass the quality control parameters of next-generation sequencing. Structural variants are confirmed by orthogonal methods, such as MLPA or qPCR.

Use of Parental Samples for Large Scale Testing

Biological parental samples are used to improve the interpretation of the final results in exome and genome testing. In Trio analysis, testing and bioinformatic analyses on parental samples are done in parallel to the analysis of the index patient. We check the parents' materials only with regard to the patient´s condition and issue parental reports accordingly. If additional analyses on the parental samples are required, such as complete exome analyses or analyses of the 59 genes or classes of genes outlined in the ACMG guidelines), please contact us as additional charges may apply. If several family members are tested, accurate interpretation of the results depends on the assumed relationships being correct. If doubt is created by the genetic analysis about the apparent relationships, we will not inform you. An exception will be made if it is absolutely necessary for the completion of the requested test.

Technical Limitations

1. Exome testing does not analyze all genes in the human genome. Some genes cannot be examined because of various technical reasons. For the targeted exome and the whole exome, respectively, approximately 5% and 3% of the targeted exons may not be well covered due to various technical reasons.
2. You may have a mutation in one of the genes included in the test, but it is not always possible to detect all mutations with these methods. This means that a patient can be affected with a certain condition, but that this testing does not identify or reveal it.
3. Exome and Genome testing encompasses many different genes and looks for a variety of conditions and diseases. These tests may reveal genetic information about you or a family member that is new and is not necessarily related to your reasons for ordering such a test. Such information could reveal details about diseases that will only develop in the future or for which there is no known treatment or cure.

Consent to Exome or Genome Testing (*It is mandatory to ensure that a patient has signed his or her consent to conduct these genetic analyses)*

_____ HCP — The initials of the physician confirm **the patient has been informed of all the information on this page**.

_____ Patient — The initials of the patient confirm he/she has chosen to receive information on the **59 genes or classes of genes outlined in the ACMG recommendations** described above

_____ Patient — For private pay testing, the initials of the patient confirm, **if an exome or genome test is cancelled** prior to test set-up, he/she will be charged a processing fee and will receive a cancellation report. Once testing is initiated, the full price of the analysis will be charged.

LifeLabs GENETICS™

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CENTOGENE THE RARE DISEASE COMPANY

Patient Name:	**Patient DOB** *(MM/DD/YYYY):*

A. NEUROLOGY

1. Behavioral abnormality	
1.1 Autism	
1.2 Attention deficit disorder	
1.3 Psychiatric diseases	
2. Brain imaging	
2.1 Abnormal cortical gyration	
2.2 Abnormal myelination	
2.3 Agenesis of corpus callosum	
2.4 Brain atrophy	
2.5 Cerebellar hypoplasia	
2.6 Heterotopia	
2.7 Holoprosencephaly	
2.8 Hydrocephalus	
2.9 Leukodystrophy	
2.10 Lissencephaly	
3. Developmental delay	
3.1 Delayed language dev.	
3.2 Delayed motor dev.	
3.3 Developmental regression	
3.4 Intellectual disability	
4. Movement abnormality	
4.1 Ataxia	
4.2 Chorea	
4.3 Dystonia	
4.4 Parkinsonism	
5. Neuromuscular abnormality	
5.1 Hyperreflexia	
5.2 Muscle hypertonia	
5.3 Muscle hypotonia	
5.4 Spasticity	
6. Seizures	
6.1 Febrile seizures	
6.2 Focal seizures	
6.3 Generalized seizures	
7. Others	
7.1 Craniosynostosis	
7.2 Dementia	
7.3 Encephalopathy	
7.4 Headache	
7.5 Macrocephaly	
7.6 Microcephaly	
7.7 Migraine	
7.8 Stroke	

B. METABOLISM

1. Abnormal creatine kinase	
2. Decreased plasma carnitine	
3. Hyperalaninemia	
4. Hypoglycemia	
5. Increased CSF lactate	
6. Increased serum pyruvate	
7. Ketosis	
8. Lactic acidosis	
9. Organic aciduria	

C. EYE

1. Blepharospasm	
2. Cataract	
3. Coloboma	
4. Glaucoma	
5. Microphthalmos	
6. Nystagmus	
7. Ophthalmoplegia	
8. Optic atrophy	
9. Ptosis	
10. Retinitis pigmentosa	
11. Retinoblastoma	
12. Strabismus	
13. Visual impairment	

D. MOUTH, THROAT AND EAR

1. Abnormality of dental color	
2. Cleft lip / palate	
3. Conductive hearing impair.	
4. External ear malformation	
5. Hypodontia	
6. Sensoneural hearing impair.	

E. SKIN, INTEGUMENT AND SKELETAL

1. Skeletal	
1.1 Abnormal limb morphology	
1.2 Abnormal vertebral column	
1.3 Abnorm. of the skeletal system	
1.4 Joint hypermobility	
1.5 Multiple joint contractures	
1.6 Polydactyly	
1.7 Scoliosis	
1.8 Syndactyly	
1.9 Talipes equinovarus	
2. Skin and integument	
2.1 Abnormal hair	
2.2 Abnormal nail	
2.3 Abnormal skin pigmenta.	
2.4 Hyperextensible skin	
2.5 Ichthyosis	

F. CARDIOVASCULAR

1. Angioedema	
2. Aortic dilatation	
3. Arrhythmia	
4. Atrial septal defect	
5. Coarctation of aorta	
6. Dilated cardiomyopathy	
7. Hypertension	
8. Hypertrophic cardiomyopathy	
9. Hypotension	
10. Lymphedema	
11. Malf. of heart and great vessels	
12. Myocardial infarction	
13. Stroke	
14. Tetralogy of Fallot	
15. Vasculitis	
16. Ventricular septal defect	

G. GASTROINTESTINAL, GENITOURINARY, ENDOCRINE

1. Gastrointestinal	
1.1 Aganglionic megacolon	
1.2 Constipation	
1.3 Diarrhea	
1.4 Gastroschisis	
1.5 Hepatic failure	
1.6 Hepatomegaly	
1.7 High hepatic transaminases	
1.8 Obesity	
1.9 Pyloric stenosis	
1.10 Vomiting	
2. Genitourinary	
2.1 Abnormal renal morphology	
2.2 Abnormal urinary system	
2.3 Hydronephrosis	
2.4 Renal agenesis	
2.5 Renal cyst	
2.6 Renal tubular dysfunction	
3. Endocrine	
3.1 Diabetes mellitus	
3.2 Hyperparathyroidism	
3.3 Hyperthyroidism	
3.4 Hypoparathyroidism	
3.5 Hypothyroidism	

H. REPRODUCTION

1. Abnormal external genitalia	
2. Abnormal internal genitalia	
3. Hypogonadism	
4. Hypospadias	
5. Infertility	

I. ONCOLOGY

1. Adenomatous colonic polyposis	
2. Breast carcinoma	
3. Colorectal carcinoma	
4. Leukemia	
5. Myelofibrosis	
6. Neoplasm of the lung	
7. Neoplasm of the skin	
8. Paraganglioma	
9. Pheochromocytoma	

J. HEMATOLOGY AND IMMUNOLOGY

1. Abnormal hemoglobin	
2. Abnormality of coagulation	
3. Anemia	
4. Immunodeficiency	
5. Neutropenia	
6. Pancytopenia	
7. Splenomegaly	
8. Thrombocytopenia	

K. PRENATAL AND DEVELOPMENT

1. Abnormal facial shape	
2. Failure to thrive	
3. Hemihypertrophy	
4. Hydrops fetalis	
5. IUGR	
6. Oligohydramnios	
7. Overgrowth	
8. Polyhydramnios	
9. Premature birth	
10. Short stature	
11. Tall stature	

****PHOTOCOPY REQUISITION AND INCLUDE 1 COPY WITH SAMPLES****