



Form 1a: Informed Consent to Perform Genetic Testing

The purpose of my DNA test/or my child's DNA test is to look for variant(s) known to be associated with the following genetic condition or disease:______.

By signing below, I acknowledge that:

- **1.** My participation or, as applicable, my child's participation in this DNA testing is voluntary. The decision to consent to, or to refuse the above testing is entirely mine.
- 2. This testing is done on small biological samples.
- **3**. It is possible that the quantity or quality of sample submitted may be inadequate for testing or that a variant cannot be identified.
- 4. When DNA testing shows a variant, then the person is a carrier or is affected with that condition or disease, or, in the case of cancer genetic testing, the person is a carrier of a variant that may be associated with an increased risk for certain cancer(s) compared to the general population. Consulting a doctor or genetic counsellor is recommended to learn the full meaning of the results and to learn if additional testing might be necessary.
- 5. When the DNA testing does not show a variant, the chance that the person is a carrier or is affected is reduced, or, in the case of cancer genetic testing, the person's risk for certain cancer(s) compared to the general population will depend on additional personal factors. There is still a chance to be a carrier or to be affected because the current testing cannot find all the possible variants within a gene.
- 6. Impact Genetics will only collect, use, and disclose your personal health information as permitted/ designated on the requisition/order form or required by applicable laws. For example, if necessary to obtain reimbursement of test fees, Impact Genetics, its agents and legal representatives, may disclose personal health information (including test results) for such purpose.
- 7. Impact Genetics is not a DNA banking facility and patient DNA samples may not be available for future testing.
- 8. An error in diagnosis may occur if the true biological relationships of the family members are not as stated in the pedigree submitted with the requisition/order form. It is possible that the test may disclose non-paternity (someone who is not the biological father), or some other previously unknown information about family relationships, such as adoption, and I consent that this finding be reported to the referring specialist designated on the requisition/order form.
- 9. There is a chance that the test may reveal unexpected abnormalities that may be of medical value in the patient's care. Impact Genetics will inform the referring specialist designated on the requisition/order form
- **10.** Until the results of this test are reported, the patient and members of the patient's family should still undergo examinations as prescribed by the referring specialist.
- 11. I have read or have had read to me, the above information and I understand it. I have also read or had explained to me the specific disease or condition tested for, and the specific test(s) I am having, including the test descriptions, principles and limitations. I have had the opportunity to discuss the purposes and possible risks of this testing with my doctor or someone my doctor has designated.

Signature of patient:	Date:
Signature of witness:	Date

impactgenetics.com



Form 1a: Informed Consent to Perform Genetic Testing for Hereditary Hemorrhagic Telangiectasia (HHT) (NY)

By signing below, I acknowledge that:

- 1. My participation or, as applicable, my child's participation in this DNA testing is voluntary. The decision to consent to, or to refuse the above testing is entirely mine.
- 2. This testing is done on small biological samples.
- 3. It is possible that the quantity or quality of sample submitted may be inadequate for testing or that a variant cannot be identified.
- 4. No tests other than those authorized shall be performed on this biological sample.
- 5. When DNA testing shows a variant, then the person is a carrier or is affected with that condition or disease. Consulting a doctor or genetic counsellor is recommended to learn the full meaning of the results and to learn if additional testing might be necessary.
- 6. When the DNA testing does not show a variant, the chance that the person is a carrier or is affected is reduced. There is still a chance to be a carrier or to be affected because the current testing cannot find all the possible variants within a gene.
- 7. Impact Genetics will only collect, use, and disclose your personal health information as permitted/designated on the requisition/order form or required by applicable laws. For example, if necessary to obtain reimbursement of test fees, Impact Genetics, its agents and legal representatives, may disclose personal health information (including test results) for such purpose.
- 8. Impact Genetics is not a DNA banking facility and patient DNA samples may not be available for future testing.
- **9.** An error in diagnosis may occur if the true biological relationships of the family members are not as stated in the pedigree submitted with the requisition/order form. It is possible that the test may disclose non-paternity (someone who is not the biological father), or some other previously unknown information about family relationships, such as adoption, and I consent that this finding be reported to the referring specialist designated on the requisition/order form.
- **10.** There is a chance that the test may reveal unexpected abnormalities that may be of medical value in the patient's care. Impact Genetics will inform the referring specialist designated on the requisition/order form.
- 11. Until the results of this test are reported, the patient and members of the patient's family should still undergo examinations as prescribed by the referring specialist.
- 12. I have read or have had read to me, the above information and I understand it. I have also read or had explained to me the specific disease or condition tested for, and the specific test(s) I am having, including the test descriptions, principles and limitations. I have had the opportunity to discuss the purposes and possible risks of this testing with my doctor or someone my doctor has designated.

Consent for Storing a Sample

Impact Genetics is not a DNA banking facility and patient DNA samples may not always be available for future testing. However, Impact Genetics has my consent to store any surplus DNA samples indefinitely, for future clinical testing as requested by me. If "*No*" is checked or if neither box below is checked, the sample will be destroyed within 60 days after test completion.

🗆 Yes 🛛 🗆 No

Signature of Patient or Consenting Parent/Guardian:	Date:	
Signature of Witness:	Date:	
Statement of Referring Physician		

I reviewed this form with my Patient. I offered to answer any questions.

Signature of Referring Physician:

Date:



Information about the Hereditary Hemorrhagic Telangiectasia (HHT) Genetic Test

What is Hereditary Hemorrhagic Telangiectasia (HHT)?

Hereditary Hemorrhagic Telangiectasia (HHT) (*hr*-eh-duh-teh-ree heh-mr-a-juhk tuh-lang-jee-uhk-tay-zhuh) is a genetic disorder of the blood vessels which affects about one in 8,000 people. It affects males and females from all racial and ethnic groups. The disorder is also referred to as Osler-Weber-Rendu (OWR) syndrome. It is inherited from parent to child in an autosomal dominant mode of inheritance.

HHT causes malformed blood vessels and can affect multiple organs of the body. HHT can cause bleeding in a number of organs, the most common symptom for individuals with HHT is nosebleeds. Up to 90% of people with HHT live with persistent recurrent nosebleeds that can vary in severity from sporadic "time to time" to nosebleeds that require medical interventions. Other organs at risk for bleeding are the brain, lungs, and gastrointestinal tract.

The diagnosis of HHT can be made based on clinical criteria called "the Curaçao criteria".

The HHT diagnosis is classified as **Definite** if three criteria are present, **Possible** or **Suspected** if two criteria are present, and **Unlikely** if fewer than two criteria are present. The Curaçao criteria include the following:

- Epistaxis Spontaneous, recurrent nosebleeds
- Telangiectases Multiple at characteristic sites (lips, oral cavity, fingers, nose)
- Visceral lesions Such as Gastro-Intestinal telangiectasia (with or without bleeding), pulmonary AVM (PAVM), hepatic AVM, cerebral AVM, spinal AVM
- Family history A first-degree relative with HHT

Purpose and Principle of the Test

Genetic testing for HHT searches for gene variants in DNA from patient blood. Three genes are currently associated with HHT which are *ENG*, *ACVRL1* and *SMAD4*. Variants in the endoglin (*ENG*) gene (HHT type 1) are more often associated with PAVMs. Variants in the *ACVRL1* gene (HHT type 2) lead to a lower frequency of PAVMs than HHT type 1 and show a higher incidence of liver involvement. Clinical features of the disease do not reliably indicate whether the gene mutated is *ENG* or *ACVRL1*. Variants in the *SMAD4* gene (most often in exons 8 through 11) have been associated with Juvenile Polyposis HHT (JP- HHT).

A positive result provides a conclusive answer that the individual is definitively affected with HHT. Most families with HHT have their own unique variant. The position of the variant does not influence the severity of disease, as it is loss of one functional copy of the gene and the consequential deficiency of a key signaling protein (i.e. reduced endoglin) that is believed to lead to the disorder. The spectrum of variants spans all types of pathogenic variants and there are no known "hot spots" on the three genes: *ENG*, *ACVRL1*, and *SMAD4*.

Some individuals with a clinical diagnosis of HHT can have negative genetic testing results. A negative result does not entirely exclude the diagnosis of HHT since it is possible that that individual could be a carrier of a variant not detectable in one of the genes tested or a variant in a gene that is still unknown and not tested for.

Test Method: Impact Genetics' Variant Identification Strategy

Impact Genetics requests a blood sample and isolates DNA from which a series of molecular tests are performed to maximize efficiency in finding *ENG*, *ACVRL1* or *SMAD4* variants. Testing includes screening for large deletions as well as sequencing for single nucleotide changes or small insertions or deletions.

Blood samples from relatives may be required to determine if family members carry the same HHT gene variant as the affected patient. Blood samples from relatives may be required to determine if family members carry the same HHT gene variant as the affected patient.

Impact Genetics is certified under the US Clinical Laboratory Improvement Amendments of 1988 (CLIA-88) as qualified to perform high complexity clinical laboratory testing. Impact Genetics' tests were developed, and their performance characteristics determined, by Impact Genetics. They have not been cleared or approved by the US Food and Drug Administration, which has determined that such approval is not necessary. Impact Genetics does not perform linkage analysis.



LabCorp Account #:__ **U.S patients only**

Form 1b: HHT Genetic Test Requisition LabCorp test #480074, #480192 and #480216

Dynacare^{*}

Ordering Options

- □ Comprehensive proband HHT genetic testing LabCorp test #480074 (variant not found previously in family)
- □ Known genetic variant in family LabCorp test #480192 (must provide the familial genetic report)
- Prenatal diagnosis for known genetic variant in family LabCorp test #480216 (must provide the familial genetic report)

Patient

Legal last name:			
Legal first name:			
Preferred first name (if app	olicable):		
Date of birth: Y	М	D	
Sex at birth: 🗌 Male	🗌 Female	Other specify:	
Gender identity: 🗌 Same as sex at birth			
Differ	ent than sex	at birth specify:	
Address:			
		'State:	
Postal/Zip code:	Coun	try:	
Phone:			

Patient History

- Confirmed clinical diagnosis
- □ Suspected clinical diagnosis □ Unaffected

Symptoms:

PAVM	Rare nose bleeds	Liver shunts
CAVM	Frequent nose bleeds	Stroke
Telangiectasia	Other specify:	

Family History

Isolated case	
No family history	

Positive family history Please complete pedigree

Family member previously tested:

- **Yes** Family member's name:
- 🗌 No

Variant identified: 🗌 Yes 🗌 No

If variant identified at a lab other than Impact Genetics please provide the genetic testing report and/or list the variant below.

Variant:

Specimen Information

Sample:

- Blood sample for DNA (EDTA or ACD tube)
- DNA from blood (provide extraction method):
- **Buccal swab** (only for select cases please contact lab prior to submitting)
- Other (refer to Accepted Samples Reference Sheet):

Date Collected: Y Μ D

Lab Use Only. Do not fill out.

Date received: Y M D

Specimen type:_

Condition:

Lab #:

Tech:

Pedigree

If unable to draw the family history please write in below how your patient is related to the other family member(s) who have HHT.

Referring Specialist

Name:	
Contact:	
Phone:	_ Fax:
City:	Prov/State:
	_ Country:

Billing

Institution Provide details:

Patient pay

Complete Form 1d: Credit Card Authorization for Non-Covered Services (Canada and international patients only).

□ Third party insurance (U.S. patients only) Complete Form 1c: U.S. Insurance Information.

impact genetics

115 Midair Court, Brampton, ON L6T 5M3

 $t \; 647.478.4902 \; \text{or} \; 877.624.9769 \; \; f \; 905.697.9786$ e impactgenetics@dynacare.ca

Please ensure to use secure email.



Form 1c: U.S. Insurance Information (U.S. patients only)

Impact Genetics is committed to providing the highest quality genetic testing to all patients. In many situations, genetic testing improves outcomes and quality of life and decreases total costs to the patient and healthcare system.

Processing medical insurance claims is usually challenging and time consuming. Many insurance companies require pre-authorization prior to testing. Impact Genetics supports insurance billing via LabCorp, completing coverage checks and pre-authorization.

It is important for patients to understand that insurance may not cover 100% of the cost of genetic testing and they may be financially responsible for some of all of the cost of testing. The patient is responsible for any portion of the test fee not covered by insurance for any reason, including but not limited to, co-payments, unmet deductibles, co-insurance and non-covered services. Prior determinations do not guarantee payment and the amount paid by insurance when the claim is submitted may be different from the coverage indicated during the pre-verification or pre-authorization process.

Pre-authorizations can take time to obtain depending on each individual insurance plan's policy and documentation requirements. Turnaround time for test results begins after the pre-authorization has been processed and approved.

Insurance process

- 1. Send Form 1c: U.S. Insurance Information as soon as possible.
- 2. Insurance coverage will be investigated and the patient will be contacted to provide coverage estimate if the patient's out-of-pocket costs are over \$300.00.
- 3. Insurance claim will be submitted upon completion of testing.
- 4. After insurance payment is received patient will be billed for non-covered services.

Note: Timely and complete submissions will enable faster insurance checks.



Form 1c: U.S. Insurance Information

HHT Genetic Test

Disease/Genetic Test

	Proband	(LabCorp	test #480344)
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ICD-10 Code • provide code here ▶___ CPT Codes: 81405, 81406, 81479

HHT Familial Mutation Analysis (LabCorp test #480192) ICD-10 Code • provide code here •

- **CPT Codes:** D ENG del/dup mutation 81405
 - ENG point mutation 81403
 - □ ACVRL1/SMAD4 del/dup or point mutation - 81479

□ Prenatal HHT Test (LabCorp test #480216) ICD-10 Code • provide code here •

- **CPT Codes:**
 □ ENG del/dup mutation 81405 □ ENG point mutation - 81403
 - □ ACVRL1/SMAD4 del/dup or point mutation - 81479
 - □ Maternal cell contamination 81265

Insurance Information

Primary insurance □ Secondary insurance

If patient has secondary insurance, include the information on an additional copy of this form with the secondary insurance box checked.

Name of insured (if not patient):

Insurance company:

Claims address:

City:	
State:	Zip code:

Country:

Group #:

Subscriber/member #:

Physician Information

Physician's name:		
NPI:		
Practice name:		
Practice address:		
Phone:		
Fax:		

Patient Information

Last name:		
First name:		
Date of birth: \vee		
Address:		
City:		
State:		
Country:		
Phone:		

Contact Information

Details of insurance coverage will be communicated directly to patient. Please provide patient contact info:

Phone:	
Alternate phone:	
Email:	

□ In the event Patient cannot be reached a voice message related to HHT genetic testing may be left at the above phone number(s).

Please Attach All of the Following

- Copies of both the front and back of insurance membership card(s)
- Letter of Medical Necessity, signed by Referring Specialist (contact Impact Genetics for template if needed)
- Clinic notes demonstrating the Patient's need for testing and confirmation of diagnosis
- Insurance approval details if prior authorization already completed

Performing lab:

impact genetics 115 Midair Court, Brampton, ON L6T 5M3 t 647.478.4902 or 877.624.9769 f 905.697.9786 e impactgenetics@dynacare.ca Please ensure to use secure email.

Page 2 of 2. Please retain a copy for your own reference. Rev 12May2024 (US/LabCorp)



Please do not send form with sample: Send this form to Impact Genetics by fax to 905.697.9786 or call 647.478.4902/1.877.624.9769 For patient pay, testing will be held pending receipt of this completed form.

Form 1d: Credit Card Authorization for Non-Covered Services (Canada and international patients only)

To be completed by and returned to Impact Genetics directly by the cardholder.

Laboratory Test

- Retinoblastoma Genetic Test
- Uveal Melanoma Prognostic Genetic Test
- HHT Genetic Test
- □ *MLH1/MSH2/MSH6/PMS2/EPCAM* Somatic Tumour MMR Sequencing and Deletion/Duplication Test

Billing Information

Patient name:	Date of birth:	Μ	D	
Visa MasterCard				
Name on card:				
Billing address:				
City:	Province/State:			
Postal/Zip code:	Country:			
Card #:	Expiration date:			
CVC # (3-digit Card Verification Code on back of card):				

Contact Information

Please provide at least 2 contact methods and check preferred:

Phone:	

- Email:
- □ Fax:_____

Statement of Financial Responsibility

Box below must be checked for testing to proceed.

□ I understand that my health coverage plan is not expected to pay for these test(s) at 100% and I agree to be personally and fully responsible for payment.

Cardholder's signature:	D	Date:	



Step 2: Sample Preparation **Accepted Samples Reference Sheet** – HHT and Retinoblastoma Genetic Tests

All samples **must** be labelled with **at least 2** patient identifiers (e.g. full name and DOB).

Sample Type for Germline Analysis	Sample Requirements	Shipment Instructions
Blood for DNA analysis	 5 mL in lavender top (EDTA) tube, or 10 mL in yellow top (ACD) tube 2-5 mL in pediatric/small tubes for infants 	 Ship at room temperature To be received within 5 days of blood draw
Blood for RNA analysis	 5 mL in lavender top (EDTA) tube 2-5 mL in pediatric/small tubes for infants 	 Ship on 4°C cool pack Must be received within 48 hours of blood draw
DNA from blood (provide DNA extraction method)	 DNA concentration: 100 ng/μL DNA Quantity: 150 μL 	Ship at room temperature
Buccal swab	 Select cases only Contact us for collection kit See Buccal Swab Collection Instructions sheet for details 	• Ship at room temperature
Direct CVS	• Send CVS tissue in a sterile tissue culture medium	Ship at room temperature
DNA extracted from CVS (provide DNA extraction method)	 DNA concentration: 100 ng/μL DNA Quantity: minimum 20 μL 	Ship at room temperature
Direct amniotic fluid	As much volume as possible in conical tube	 Ship at room temperature Must be received within 48 hours of collection
Cultured amniocytes/CVS	• Two T25 flasks of cultured amniotic cells	Ship at room temperature
DNA extracted from amniocytes (provide DNA extraction method)	 DNA concentration: 100 ng/μL DNA Quantity: minimum 20 μL 	Ship at room temperature
Maternal blood for MCC	• 5 mL in lavender top (EDTA) tube, or 10 mL in yellow top (ACD) tube	Ship at room temperature
Maternal DNA extracted from blood for MCC (provide DNA extraction method)	 DNA concentration: 100 ng/μL DNA Quantity: 150 μL 	Ship at room temperature
Other	• For alternative collection methods please contact us for confirmation	Ship according to method instructions



Buccal Swab Collection Instructions

- 1. The person providing the buccal cell samples should not eat, drink, smoke, clean their teeth or use mouthwash 1 hour before sample collection.
- 2. The person taking the samples should thoroughly wash their hands prior to collecting the sample.
- 3. Open the OmniSwab packaging at the handle end and carefully remove the swab. Do not touch the collection pad (soft side) of the swab.

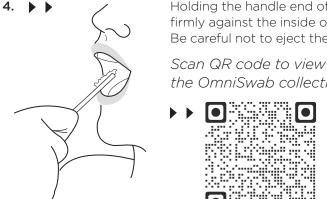


Figure 1

Holding the handle end of the OmniSwab, scrape the collection pad (soft side) firmly against the inside of the cheek 5-6 times (for around 10 seconds). Be careful not to eject the tip. See Figure 1.

Scan QR code to view a short video demonstrating the OmniSwab collection method.



- 5. After taking the sample, eject the tip into the tube labelled "Buccal" (provided) by firmly pressing the plunger at the end of the handle. After ejecting the tip into the lysis tube, dispose of buccal swab handle according to local regulations.
- 6. Once the buccal sample is in the tube, place the twist top cap on the tube and firmly tighten to close.
- 7. Label the buccal tube with one of the stickers (provided) with full name (first and last) and date of birth of the patient from whom the buccal sample has been collected.
- 8. Place the tube inside the plastic biohazard bag and seal the bag.
- 9. Complete the Buccal Swab Patient Information Form. Fold and place in the external pouch of the plastic biohazard specimen bag. Then place specimen biohazard bag into rigid container (provided).
- 10. Once collected, the buccal sample tube is stable when stored at room temperature or refrigerated (2-8 °C) for several days. However we recommend sending the buccal sample as soon as possible to ensure specimen integrity and to expedite your test results.

Notes:

- To ensure a safe experience during buccal sample collection, follow instructions above.
- If the swab becomes contaminated through touch or contact with an unclean surface do **not** proceed to use the swab for sample collection. Contact us directly to request an additional buccal collection kit.
- If the contents of the tube are spilled prior to or after buccal collection continue with sample collection steps above and add this information to the Buccal Swab Patient Information Form.
- The tube provided for buccal collection contains "Cell Lysis Solution" provided by Qiagen GmbH. This cell lysis solution is considered non-hazardous. For more information, visit: https://www.qiagen.com/de-us/knowledge-and-support/product-and-technical-support/quality-and-safety-data/sds-search.



Buccal Swab Patient Information Form

This form is to be completed by the person who has performed the buccal swab collection. Once completed, fold and place this form in the outside pouch of the biohazard plastic bag containing the buccal sample.

Patient Information

First name:			Last name:	Last name:			
Date of birth:_	Y M	D	Date of collection:_ Y	М	D		

Sample Collection Comments

1. Did the buccal swab collection pad (soft side) potentially come in contact with hands or other surfaces?

🗆 Yes 🛛 No

If Yes, please describe:

2. Was any cell lysis solution lost from the specimen tube provided?

□ Yes □ No

Signature:_____ Date:_____





Step 3: Shipping Instructions

For shipping inquiries and notifications, please contact:

impact genetics

email: info@impactgenetics.com phone: 647.478.4902 or 877.624.9769 fax: 905.697.9786

General Shipping Instructions

- If you have more than one patient request to submit, multiple patients can be sent in the same shipment.
- Submit specimen(s) for each patient in a biohazard specimen bag, **only one patient's specimen(s) per bag**. Refer to **Step 2:** *Sample Preparation Instructions* for shipping conditions.
- Include informed consent and requisition forms (Form 1a and 1b) as well as any required clinical documents along with the samples. Place documents in a separate pouch or bag. Do not place documents inside the biohazard bag with specimens.
- Samples coming from the U.S. must also include U.S. insurance information (Form 1c) if required and not provided previously.
- Provide us with the parcel tracking number by phone or email shortly after courier pickup.
- For emailed PDF FedEx waybills and customs forms, please contact us directly.

Instructions for Specimens from Outside of Canada

- DNA studies: select FedEx International Priority
- RNA studies for *RB1*, or prenatal studies on direct amniotic fluid or CVS sample,: select FedEx International Priority Express (contact Impact Genetics before sending)
 - Samples **must** be received within 48 hours of collection
- Samples coming from outside of Canada **must** submit a waybill and commercial invoice:
 - Print **one** copy of the waybill and **three** copies of the commercial invoice
 - Sign each commercial invoice and place with the waybill in the external document pouch
- When preparing documentation:
 - Declare a value of \$10.00
 - Declare as "Exempt Human Diagnostic Specimen(s)"
 - Description of Goods: Human (blood/tissue) specimen for testing in a clinical laboratory. The enclosed material(s) are not zoonotic, are not of tissue culture origin, and are not known or suspected to contain an etiological agent, host, or vector of human disease.





Step 3: Shipping Instructions (continued)

Instructions for Specimens from Within Canada

- DNA studies: select **Purolator Express** (next-day) or **FedEx Priority** (overnight)
- RNA studies for *RB1*, **or** prenatal studies on direct amniotic fluid or CVS sample: select **FedEx First Overnight** (contact Impact Genetics before sending)
 - Samples **must** be received within 48 hours of collection
- When preparing documentation:
 - Declare a value of \$10.00
 - If required, declare as "Exempt Human Diagnostic Specimen(s)"