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Rev 17NO2025 (CAN/INT'L)

Retinoblastoma
Genetic Test

1. Forms

1a Informed Consent

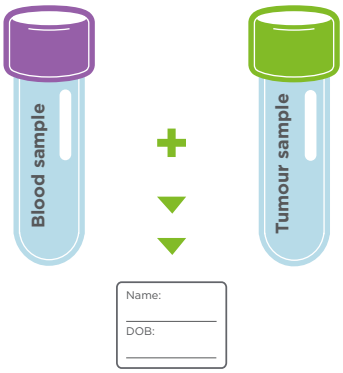
1b Requisition

1d Credit Card Authorization **if applicable**

2. Samples

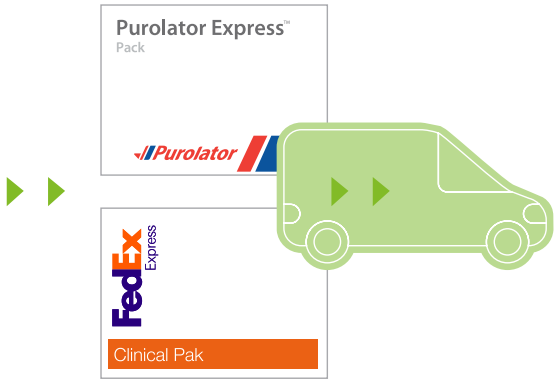
Required:

Include **if** available:
(fresh or frozen tissue only; FFPE not accepted)



Ensure samples are labelled with at least 2 patient identifiers
(name and DOB)

3. Ship



Impact Genetics, Dynacare
115 Midair Court
Brampton, ON L6T 5M3
t 877.624.9769

Results

2 to **6** weeks
sample processing to report

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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: _____

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Form 1a: Informed Consent to Perform Genetic Testing for Retinoblastoma (RB) (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: _____

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Information about the Retinoblastoma (RB) Genetic Test

What is Retinoblastoma (RB)?

Retinoblastoma *(Reh-tin-oh-blast-oma)* is a cancer of one or both eyes that occurs in young children. Retinoblastoma affects about 1 in 15,000 live births, and an estimated 9,000 children develop the cancer each year around the world. Retinoblastoma affects children of all races and both boys and girls.

The retinoblastoma tumor(s) originate in the retina, the light sensitive layer of the eye that enables the eye to see. When the tumors are present in one eye, it is referred to as unilateral retinoblastoma, and when it occurs in both eyes it is referred to as bilateral retinoblastoma. 60% of cases involve only one eye (unilateral) and the rest (40%) affect both eyes (bilateral). The majority (90%) of retinoblastoma patients have no family history of the disease. The most common early sign of retinoblastoma is a white glow in the child's eye. This cancer is easy to diagnose, and treatment is very effective when tumors are found early.

Purpose and Principle of the Test

Genetic testing for retinoblastoma searches for *RB1* gene variants in DNA obtained from patient blood and/or tumor. Results are useful to determine whether the retinoblastoma is heritable, and to estimate the probability of passing the *RB1* gene variant to subsequent family members. The results can also be useful to assess the patient's risk of other eye tumors or cancers outside the eye, affecting the patient's treatment and level of clinical surveillance that is required to discover cancers early.

Most importantly, for bilaterally affected patients and the 18% of unilaterally affected **patients who are shown to carry an *RB1* variant in blood**, identification of the *RB1* variant enables variant **testing of the patient's parents, siblings and offspring**, to determine whether they carry the patient's *RB1* variant. Offspring of the retinoblastoma patient are usually at 50% risk to inherit the *RB1* variant, and those children who inherit the *RB1* variant have a 95% risk to develop retinal tumors. Child relatives who are shown to carry o carry the *RB1* gene variant require close clinical surveillance to discover small tumors when they can be treated with minimal risks. Child relatives who do **not** carry the *RB1* variant are at population risk for retinoblastoma, and do not require close clinical surveillance. The 5% of parents who carry the *RB1* variant are at increased risk of other cancers, and their other children are at risk of inheriting the *RB1* variant.

For unilaterally affected patients who do not show a *RB1* variant in blood, clinical treatment for the patient can be modified based on the fact that no *RB1* variant is detected in blood; siblings, parents, and offspring have a much reduced risk of retinoblastoma, and clinical surveillance can be modified accordingly.

Test Method: Impact Genetics' *RB1* Variant Identification Strategy

For unilateral patients with no family history of retinoblastoma, Impact Genetics requests both blood and a fresh or frozen tumor sample. If no tumor tissue is available, blood analysis is helpful but can be less definitive. For most unilateral patients with positive family history and for bilateral patients, Impact Genetics can successfully diagnose from a blood sample only, but fresh or frozen tumor tissue is helpful for some families, so Impact strongly recommends that every retinoblastoma tumor sample be preserved by flash freezing for future analysis. Blood samples from relatives may be required to determine if family members carry the same *RB1* variant as the affected patient. Impact Genetics isolates DNA from the specimens of blood and tumor and performs a series of molecular tests to maximize efficiency in finding *RB1* variants. Testing includes screening for large deletions as well as sequencing for point mutations or small insertions or deletions.

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's 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.

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Lab Use Only. Do not fill out.

Date received: Y M D

Specimen type:

Condition:

Lab #: Tech:

Form 1b: Retinoblastoma Genetic Test Requisition

Ordering Options

☐ **Bilateral Retinoblastoma Proband**
Date diagnosed: Y M D

☐ **Unilateral Retinoblastoma Proband**
Date diagnosed: Y M D

☐ **Known *RB1* Familial Variant**
(**must** provide the familial genetic report)

☐ **Affected** ☐ **Unaffected**

☐ **Prenatal diagnosis for known *RB1* Familial Variant**
(**must** provide familial variant report and maternal sample for MCC)

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 retinoblastoma.

Patient

Legal last name:

Legal first name:

Preferred first name (if applicable):

Date of birth: Y M D

Sex at birth: ☐ **Male** ☐ **Female** ☐ **Other** specify:

Gender identity: ☐ **Same as sex at birth**
☐ **Different than sex at birth** specify:

Address:

City: Prov/State:

Postal/Zip code: Country:

Phone:

Specimen Information

Refer to *Accepted Samples Reference Sheet.*

Germline sample **(required)**:

☐ **Blood sample for DNA** (EDTA or ACD tube)
☐ **DNA from blood**
☐ **Buccal swab** (only for select cases please contact lab prior to submitting)
☐ **Other** (refer to *Accepted Germline Samples Reference Sheet*):
Date collected: Y M D

Tumour sample:
Note: **not** able to accept FFPE tumour samples

☐ **Fresh RB tumour** ☐ **Frozen RB tumour**
☐ **Tumour to follow** ☐ **No tumour to follow**
☐ **DNA from tumour***
Date collected: Y M D

Prenatal sample:

☐ **Cord Blood** ☐ **Chorionic Villus (CVS)**
☐ **Direct Amniotic Fluid** ☐ **Cultured Amniocytes**
☐ **Extracted DNA***, Source:
Date collected: Y M D

* **Must** provide extraction method, **must be performed** by a CLIA-accredited laboratory

Referring Specialist

Name:

Specialty:

Contact:

Phone: Fax:

Email:

Signature:

Institution:

Address:

City: Prov/State:

Postal/Zip code: Country:

Additional copies to:

Email:

Fax:

Billing

☐ **Institution**
Provide details:

☐ **Patient pay**
Complete **Form 1d:** Credit Card Authorization for Non-Covered Services

Ordering Specialist: By submitting this form, I confirm that this test is being ordered for the purpose of prognosis as per the **Laboratory and Specimen Collection Centre Licensing Act** (Ontario, Canada).

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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

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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

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: Y ____ M ____ 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: _____ Date: _____

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Step 2: Sample Preparation
Accepted Somatic/Tumour Samples Reference Sheet—Retinoblastoma

All samples **must** be labelled with **at least 2** patient identifiers (e.g. full name and DOB).
We do not accept formalin-fixed (FFPE) tissue.

Sample Preparation Instructions (instructions for enucleating surgeon or pathology lab)

Fresh tumour in medium:

After removal of an eye containing retinoblastoma,

- Cut off optic nerve and retain as separate specimen for pathology lab.
- Open globe by pupillary-optic nerve section as in routine eye pathology.
- Excise or scoop the bulk of the tumour from inside the eye, leaving tumour-optic nerve and tumour-choroidal relationship undisturbed for pathological evaluation.
- Place fresh retinoblastoma tumour in a sterile tissue culture media, such as RPMI or Alpha MEM with antibiotic added (100 U/mL penicillin and 100 ug/mL streptomycin) and seal container securely with parafilm.
- Tumour may be kept at room temperature until it is ready to be shipped. **Do not freeze** tumour in tissue culture.
- Retain the remainder of the eye for pathology.
- Send tumour sample at room temperature.

Frozen tumour sample preparation:

- Flash freeze tumour sample and ship on enough dry ice to keep frozen for maximum transit time.
- Detailed tumour extraction information available on our website:
  http://impactgenetics.com/testing-services/retinoblastoma/info-for-rb-clinicians

DNA extracted from fresh or frozen RB tumour:

- Extracted DNA **must** be performed by a CLIA-accredited laboratory.
- Extraction method **must** be provided
- DNA concentration: 100 ng/µL
- DNA Quantity: 150 µL
- Ship at room temperature

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Step 2: Sample Preparation
Accepted Germline Samples Reference Sheet

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. **Must be performed** at a CLIA-accredited lab.	• 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. **Must be performed** at a CLIA-accredited lab.	• 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. **Must be performed** at a CLIA-accredited lab.	• 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. **Must be performed** at a CLIA-accredited lab.	• 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

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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: _____

Date of birth: Y M D _____ Date of collection: Y M 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**

   If *Yes*, please describe: _____

Signature: _____ Date: _____

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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.
4. 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.*

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**

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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.*

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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)*"