impact genetics inc.

Step 1a: *Informed Consent To Perform Genetic Testing For Retinoblastoma (RB) [NY]*

I, _____, consent to participate, or as applicable, to have my child _____ participate, in a DNA-based test to identify a genetic abnormality believed to cause retinoblastoma. I understand this test requires a blood sample from the person to be tested and may require blood samples from blood relatives. I understand that the blood samples will be used to determine if the patient and members of the patient's family carry a genetic abnormality. Supplemental disease and test method information is available from Impact Genetics at **www.impactgenetics.com.**

By signing below, I acknowledge that:

1. My participation and as applicable, my child's participation, in this DNA testing is voluntary.
2. The removal of up to 10 ml of blood *(5 ml for infants)* required for the test carries a low risk of discomfort and infection.
3. It is possible that the quantity or quality of sample submitted may be inadequate for testing or that a mutation cannot be identified.
4. A person whose DNA contains a genetic abnormality associated with retinoblastoma does not necessarily develop the disease. A negative test result does not imply that the subject has no chance to develop retinoblastoma.
5. All test results are ***confidential***. Except as described in point 11 below, no information will be printed or released that discloses the patient's identity without my additional written permission. Only the referring specialist designated on the Retinoblastoma Requisition Form will receive a written report of test results.
6. Impact Genetics is not a DNA banking facility and patient DNA samples may not be available for future testing.
7. 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 Retinoblastoma Requisition Form. It is possible that the test may disclose paternity and I consent that this finding be reported to the specialist designated on the Retinoblastoma Requisition Form.
8. 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 Retinoblastoma Requisition Form of such a result..
9. The referring specialist reviewed this consent form with me and explained the implications of the test results to me. Any questions that I asked have been answered to my satisfaction. I know that my family and I may continue to ask questions about the collection, use and disclosure of our personal genetic information.
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. If necessary to obtain reimbursement of test fees, Impact Genetics, its agents and legal representatives may disclose information that identifies the patient who is subject to retinoblastoma genetic testing.
12. I received a copy of this consent form and the referring specialist whom I designate on the Retinoblastoma Requisition Form received a copy of this consent form.

Consent for Future Research:

After all analysis required to reach a genetic diagnosis is complete, Impact Genetics has my consent to use any surplus DNA or RNA in an ***anonymous*** fashion for research. Future research is only possible if 'Consent for Banking Sample' is also marked ***'Yes'***.

☐ YES ☐ NO

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Consent for Banking of 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 bank any DNA samples indefinitely, for clinical use to test other family members. 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: _____ 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 (RB1) Genetic Test

What is Retinoblastoma?

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 mutations in DNA from patient blood or tumor. Results are useful to determine whether the retinoblastoma is heritable, and to estimate the probability of passing the defective gene 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 15% of unilaterally affected patients who are **shown to carry an *RB1* mutation in blood**, identification of the *RB1* mutation enables mutation **testing of the patient's parents, siblings and offspring**, to determine whether they carry the patient's *RB1* mutation. Offspring are usually at 50% risk to inherit the mutation, and those children who inherit the mutation have a 95% risk to develop retinal tumors. Child relatives who are shown to carry the mutant gene require close clinical surveillance to discover small tumors when they can be treated with minimal risks. Child relatives who do **not** carry the proband's mutation are at population risk of retinoblastoma, and do not require close clinical surveillance. The 5% of parents who carry the mutant gene are at increased risk of other cancers, and their other children are at risk of inheriting the mutation.

For unilaterally affected patients who do not show a mutation in blood, clinical treatment for the patient can be modified based on the fact that no *RB1* mutation 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 Genetic's Mutation 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 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* mutation 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* mutations. 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.