



HEMOPHILIA PROGRAM HEMOPHILIC GENETIC DIAGNOSTIC LABORATORY INFORMED CONSENT FOR DNA TESTING

I, _____, give permission to have blood drawn from _____
(*myself or name of child*) for hemophilia DNA testing. Removing blood from a vein carries very little risk but may occasionally cause slight discomfort, bruising or bleeding under the skin. On rare occasions an infection may develop. In addition, if prenatal diagnosis is involved, fetal cells obtained by amniocentesis or chorionic villi sampling will be used. I understand that the blood and fetal samples will be used for the purpose of attempting to determine if I and/or members of my family have a Factor VIII or Factor IX gene that causes hemophilia.

I have talked to a genetic counselor or hemophilia staff member and understand that:

1. DNA testing for hemophilia is relatively new. The tests are not considered research but they are being improved all the time. This testing is complex and uses special materials so that there is always some small chance that the test will not work properly or that an error will occur. There is a low error rate (perhaps 1 in 1000 samples) even in the best laboratories.
2. In many cases the DNA test directly finds the change in the gene (mutation) that causes the hemophilia and the results are >99.9% accurate (almost 100%)!
3. If a mutation cannot be found in my family, “markers” inside or near the Factor VIII or Factor IX gene that have nothing to do with hemophilia may be used to track the hemophilia gene through my family. Multiple family members are needed for this testing. If a useful marker is found inside the gene, this testing is at least 99% accurate. If a marker outside the gene is found, this testing can be 95% accurate. In 10-20% of hemophilia families, the markers are not informative and the testing will not be able to discover which family members carry the hemophilia gene. If this happens I will not know anymore than I knew before the testing. I also understand that when markers are used, an error in the diagnosis may occur if the true biological relationships of the family members involved in this study are not as I have stated. For example, if the biological father of an individual is not the person stated to be the father, the test results will be wrong. In some cases there will be no way of knowing an error was made but in some cases the test results will show that the person identified as the father could not possibly be the father. It will be necessary to report this finding to the individual who requested testing. For any question of sample identity or labeling, a repeat sample(s) will be run at no additional charge.
4. In some cases it may be possible for the laboratory to reanalyze leftover DNA samples in the future using new and improved methods. However, I understand that this is not a DNA banking facility and my DNA sample may not be available for future clinical studies.
5. Because of the complexity of DNA based testing and the important implications of the test results, results will be reported to me only through a genetic counselor, hemophilia staff member or other medical professional I designate. The results are confidential; they will only be released to other medical professionals or other parties with my written consent. Participation in DNA testing is completely voluntary.

Signed: _____ Date _____

Witnessed: _____

Counselor’s Statement: I have explained DNA testing to this individual. I have addressed the limitations outlined above, and I have answered this person’s questions.

Signed: _____ Date _____



HEMOPHILIA GENOTYPING GENERAL GUIDELINES

2009-2010 Fee Schedule:

3250-05	DNA Factor VIII Inversion	\$500.00
3250-02	DNA Hemophilia A Mutation Evaluation	\$500.00
3250-10	DNA Hemophilia B Mutation Evaluation	\$500.00
3250-11	Genotype for known Hemophilia/VWD mutation	\$500.00
3250-08	DNA Von Willebrand Disease Type 2A/2B 2N	\$500.00

For Hemophilia A patients (Factor VIII activity levels of $\leq 2\%$):

3250-05 DNA Factor VIII Inversion

We will screen for the Intron 22 inversion which accounts for 45% of severe hemophilia patients and the Intron 1 inversion (5% of the hemophilia patients have this mutation). If the patient is inversion “positive” then no further testing is necessary.

If an inversion is not found, then additional testing will be necessary.

3250-02 DNA Hemophilia A Mutation Evaluation

Note: Patient will be charged this second transaction code

For Hemophilia A (Factor VIII activity levels of $>2\%$):

3250-02 DNA Hemophilia A Mutation Evaluation

For Hemophilia B (Factor IX):

3250-10 DNA Hemophilia B Mutation Evaluation



HEMOPHILIA GENOTYPING GENERAL GUIDELINES - CONTINUED

For carrier typing workup:

If the sample is from a mother of an affected patient whose factor VIII level is <2% or the severity of the Hemophilia A is unknown:

3250-05 DNA Factor VIII Inversion

We will screen for the Intron 22 inversion which accounts for 45% of severe hemophilia patients and the Intron 1 inversion (5% of the hemophilia patients have this mutation). If the potential carrier is inversion “positive” then no further testing is necessary.

The following test applies if an inversion is not found or if the factor VIII activity is >2%:

3250-02 DNA Hemophilia A Mutation Evaluation

Note: Patient will be charged this second transaction code if an inversion is not found.

For any family member that requests carrier typing for a known genotype:

3250- 11 Genotype for Known Hemophilia / VWD mutation

Only indicated if the proband has been typed and the mutation is known.

Note: Please always record the severity of the proband on the RFT. If it is not noted, we will treat the sample as a severe or “unknown” and will perform the inversion mutation which is not necessary if the patient is not severe.



DNA SAMPLES FOR HEMOPHILIA OR OTHER CONGENITAL BLEEDING DISORDERS COLLECTION AND SHIPPING INSTRUCTIONS

Draw 5-10 cc blood into purple-topped tube (EDTA). The tube should be labeled with the patient's full name and the date and time of draw.

Include the following information on the Hemostasis Laboratory Order Form:

- Patient's full name
- Social Security Number
- Date of birth
- Name of family member with bleeding disorder
- Date and time of sample collection
- Physician's name, address and phone
- **"SEND REPORT TO"** and **"BILLING INFORMATION"**
- Reason for testing
- Any additional information that affects the urgency of the sample, etc.

Samples sent from outside Washington State must be accompanied by a credit card number or a personal check plus patient billing information (see attached form) unless the facility sending the sample has an account with Puget Sound Blood Center. To set up an account with Puget Sound Blood Center, fill out the attached Facility Billing Information form or call Puget Sound Blood Center Billing Department at 206-292-6559.

Ship overnight Federal Express on Monday-Thursday to:

Ms. Colleen Engle
Hemostasis Laboratory
Puget Sound Blood Center
921 Terry Avenue – 4th Floor, Rm. 415
Seattle, Washington 98104-1256
(206) 292-6594

Call Dr. Josephson's office at (206) 292-6570 to let them know a DNA sample is coming. Please also provide the Federal Express airbill number used for tracking.

If you have any questions, please call Dr. Josephson or one of the hemophilia nurses at (206) 292-6570 weekdays.



Puget Sound Blood Center

research | medicine | blood & tissue services

FACILITY BILLING INFORMATION FORM

Invoices should be mailed to:

Department: _____

Facility Name: _____

Facility Phone Number: _____

Mailing Address: _____

Name of Contact Person: _____

Phone Number: _____

Purchase Order #: _____

PATIENT BILLING INFORMATION

Amount Enclosed: _____ Check #: _____

Card Number: _____

Visa MasterCard Exp Date: _____

Signature: _____

Name: _____

Address: _____

Day Phone: _____

REQUEST FOR TESTING HEMOSTASIS REFERENCE LABORATORY

TO REORDER FORM CALL (206) 292-6594



Puget Sound Blood Center
research | medicine | blood & tissue services
921 Terry Avenue | Seattle, WA 98104-1256

See back of this order form for sample requirements. Test descriptions, transaction codes and CPT codes may be viewed at <http://psbc.org>. Click on Laboratory Services.

HEMOSTASIS REFERENCE LABORATORY (206) 292-6594 Laboratory Staffed for Questions: 8:00 a.m. - 4:30 p.m. Monday - Friday
Samples accepted daily, 24 Hrs./Day, 7 Days/Week. Sample Info Line: (206) 292-1876

PROFILES Battery of tests in the Profiles are listed on the back of this order form.

- | | |
|---|--|
| <input type="checkbox"/> Abnormal PT or APTT Reflexive Evaluation
<i>Additional Assays will be performed as necessary</i> | <input type="checkbox"/> Intrinsic Factor Evaluation |
| <input type="checkbox"/> Bleeding Diathesis with a Normal APTT/PT | <input type="checkbox"/> Lupus Anticoagulant Screen (Reflex to Profile) |
| <input type="checkbox"/> Extrinsic Pathway Evaluation | <input type="checkbox"/> Lupus Anticoagulant |
| <input type="checkbox"/> Fibrinogen Evaluation | <input type="checkbox"/> Platelet Aggregation* |
| <input type="checkbox"/> Fibrinolysis Evaluation | <input type="checkbox"/> Platelet Function Assay (PFAs)* |
| <input type="checkbox"/> Factor VIII Inhibitor Screen | <input type="checkbox"/> Thrombosis Genetic Risk |
| <input type="checkbox"/> Factor VIII Inhibitor Bethesda Titer | <input type="checkbox"/> Thrombosis Risk |
| <input type="checkbox"/> Factor Inhibitor Screen (other than Factor VIII)
<i>Specify Factor: _____</i> | <input type="checkbox"/> Thrombosis Risk on Warfarin |
| <input type="checkbox"/> Factor Inhibitor Bethesda Titer (other than Factor VIII)
<i>Specify Factor: _____</i> | <input type="checkbox"/> Thrombosis/Hypercoagulability Risk |
| | <input type="checkbox"/> von Willebrand |

INDIVIDUAL TESTS

- | | |
|---|---|
| 3260-01 <input type="checkbox"/> ADAMTS 13 Activity (Performed by Platelet Lab) | 3210-16 <input type="checkbox"/> Factor XI Activity |
| 3260-02 <input type="checkbox"/> ADAMTS 13 Inhibitor (Performed by Platelet Lab) | 3210-17 <input type="checkbox"/> Factor XII Activity |
| 3230-04 <input type="checkbox"/> Antiplasmin | 3200-07 <input type="checkbox"/> Factor XIII Screen |
| 3230-01 <input type="checkbox"/> Antithrombin III Activity | 3210-06 <input type="checkbox"/> FDP in Plasma (semi-quantitative) |
| 3230-08 <input type="checkbox"/> APC Resistance Activity Ratio for Factor V Leiden | 3200-08 <input type="checkbox"/> Fibrinogen Activity |
| 3200-05 <input type="checkbox"/> APTT (Abnormals reflex to 1:1 mix) | 3210-19 <input type="checkbox"/> Heparin by anti-Xa |
| 3200-10 <input type="checkbox"/> APTT 1:1 Mix | 3230-06 <input type="checkbox"/> Plasminogen Activity |
| 3200-05 <input type="checkbox"/> APTT (Post-Heparin Removal)* | 3245-01 <input type="checkbox"/> Platelet Function Assay (PFA) Epinephrine/Collagen* |
| 3200-01 <input type="checkbox"/> Bleeding Time Surgicutt | 3245-02 <input type="checkbox"/> Platelet Function Assay (PFA) ADP/Collagen* |
| 3210-05 <input type="checkbox"/> D-dimer (semi-quantitative) | 3230-02 <input type="checkbox"/> Protein C Activity |
| 3250-04 <input type="checkbox"/> DNA/Factor II (Prothrombin) Mutation | 3230-03 <input type="checkbox"/> Protein S Activity |
| 3250-03 <input type="checkbox"/> DNA/Factor V Leiden (APC Resistance) Mutation | 3200-04 <input type="checkbox"/> Prothrombin Time (Abnormals reflex to 1:1 mix) |
| 3250-07 <input type="checkbox"/> DNA MTHFR C677T Mutation | 3200-04 <input type="checkbox"/> Prothrombin Time 1:1 Mix |
| 3250-05 <input type="checkbox"/> DNA/Factor VIII Inversion | 3200-11 <input type="checkbox"/> Reptilase Time |
| 3250-02 <input type="checkbox"/> DNA Hemophilic Mutation Screen <i>Specify Factor: _____</i> | 3210-03 <input type="checkbox"/> Ristocetin Cofactor (VWF Activity) |
| 3250-08 <input type="checkbox"/> DNA von Willebrand Disease Type 2A/2B | 3220-06 <input type="checkbox"/> STACLOT-LA (Hexagonal PL) |
| 3210-10 <input type="checkbox"/> Factor II Activity | 3200-02 <input type="checkbox"/> Thrombin Time |
| 3210-11 <input type="checkbox"/> Factor V Activity | 3200-02 <input type="checkbox"/> Thrombin Time 1:1 Mix |
| 3210-12 <input type="checkbox"/> Factor VII Activity | 3220-03 <input type="checkbox"/> Tissue Thromboplastin Inhibition Time (TTIT) |
| 3210-13 <input type="checkbox"/> Factor VIII Activity | 3210-20 <input type="checkbox"/> von Willebrand Antigen ** |
| 3210-18 <input type="checkbox"/> Factor VIII Activity Chromogenic | 3210-24 <input type="checkbox"/> von Willebrand Multimers** (sent out) |
| 3210-14 <input type="checkbox"/> Factor IX Activity | <input type="checkbox"/> OTHER _____ |
| 3210-15 <input type="checkbox"/> Factor X Activity | |

*NOTE: See Specimen Collection Information - reverse side.
** All Antigen testing must be accompanied by ordering the corresponding activity/screen.

PLEASE PRINT:

Note: Information in BOLD must be complete.

Collection: DATE ____ / ____ / ____ TIME _____ am/pm

Drawn By: _____

Specimen / Accession No: _____

Diagnosis/Purpose of Testing: _____

Medications: _____

_____ Heparin _____ Coumadin _____ Aspirin **ICD-9** _____

History / Comments / Special Instructions: _____

Physician or authorized person ordering test:

(First) (Last)

<i>Name on Sample</i>	<i>LAST</i>	<i>FIRST</i>	<i>M.I.</i>
<i>Hospital Identification Number</i>			
<i>Hospital/Institution</i>			
<i>Social Security Number</i>	<i>Sex (M/F)</i>	<i>Date of Birth (mm/dd/yyyy)</i>	

Sample ID / HC #

place label here

Shaded areas for Blood Center use only.

Contact Information: _____
Name Number

SEND REPORT TO:

Name: _____

Street: _____

City, State, Zip: _____

Fax number: _____

SEND BILL TO (if different than above):

Name: _____

Street: _____

City, State, Zip: _____

Bill to: Institution Insurance Medicare Medicaid Patient Study
Attach insurance information if applicable

If sample is for carrier detection/family study, complete the following:

Affected Member(s): _____

Relationship to Patient: _____

TESTS IN THE HEMOSTASIS PROFILES

Order only those tests that are medically necessary. Tests may be ordered individually.
Any profile may be customized to meet client needs and expedite the ordering process.

Abnormal PT or APTT Reflexive Evaluation Profile

APTT (3200-05)
PT (3200-04)
Thrombin Time (3200-02)
Fibrinogen Activity (3200-08)
Additional assays will be performed as necessary

Bleeding Diathesis with a Normal APTT/PT Profile

APTT (3200-05)
PT (3200-04)
Factor VIII Activity (3210-13)
Factor IX Activity (3210-14)
Factor XI Activity (3210-16)
von Willebrand Antigen (3210-20)
Ristocetin Cofactor (vWF) Activity (3210-03)
Factor XIII Screen (3200-07)
D-Dimer Semi-quantitative (3210-05)
Fibrinogen Degradation Prod. (3210-06)
Antiplasmin (3230-04)
Fibrinogen Activity (3200-08)

Extrinsic Pathway Evaluation Profile

PT (3200-04)
PT 1:1 Mix (3200-04)
APTT (3200-05)
APTT 1:1 Mix (3200-10)
Factor II Activity (3210-10)
Factor V Activity (3210-11)
Factor VII Activity (3210-12)
Factor X Activity (3210-15)

Factor VIII Inhibitor Screen Profile

APTT (3200-05)
APTT 1:1 Mix (3200-10)
Factor VIII Activity (3210-13)
Factor VIII Inhibitor Screen (3220-04)
(Reflex to Bethesda titer if positive)

Factor VIII Inhibitor Bethesda Titer Profile

APTT (3200-05)
APTT 1:1 Mix (3200-10)
Factor VIII Activity (3210-13)
Factor VIII Inhibitor Titer (3220-02)

Factor Inhibitor Screen other than

Factor VIII Profile. Specify Factor: _____
PT (3200-04)
PT 1:1 Mix (3200-04)
APTT (3200-05)
APTT 1:1 Mix (3200-10)
Factor Inhibitor Screen (3220-04)
(Reflex to Bethesda titer if positive)

Factor Inhibitor Bethesda Titer other than Factor VIII.

Specify Factor: _____
PT (3200-04)
PT 1:1 Mix (3200-04)
APTT (3200-05)
APTT 1:1 Mix (3200-10)
Other Factor Inhibitor Titer (3220-02)

Fibrinogen Evaluation Profile

Fibrinogen Activity (3200-08)
Reptilase Time (3200-11)
Thrombin Time (3200-02)
Thrombin 1:1 Mix (3200-02)

Fibrinolysis Evaluation Profile

Abnormal PT or APTT Reflexive Evaluation Profile
Antiplasmin (3230-04)
D-dimer Semi-quantitative (3210-05)
Fibrinogen Degradation Prod. (FDP) (3210-06)
Plasminogen Activity (3230-06)

Thrombosis Genetic Risk Profile

Factor V Leiden (3250-03)
Factor II Prothrombin Mutation (3250-04)

Thrombosis/Hypercoagulability Profile

Factor VIII Activity (3210-13)
Lupus Anticoagulant Screen Profile
Thrombosis Genetic Risk Profile
Thrombosis Risk Profile

Intrinsic Factor Evaluation Profile

PT (3200-04)
PT 1:1 Mix (3200-04)
APTT (3200-05)
APTT 1:1 Mix (3200-10)
Factor VIII Activity (3210-13)
Factor IX Activity (3210-14)
Factor XI Activity (3210-16)
Factor XII Activity (3210-17)

Lupus Anticoagulant Screen Profile

PT (3200-04)
APTT (3200-05)
APTT 1:1 Mix (3200-10)
Tissue Thromboplastin Inhibition (3220-03)
(Reflex to Profile)

Lupus Anticoagulant Profile

Lupus Anticoagulant Screen Profile
Thrombin Time (3200-02)
STACLOT-LA (Hexagonal PL) (3220-06)

Platelet Aggregation Profile

Platelet Function Assay (PFA) Profile
Platelet Aggregation Study (3240-01)
(each agent)

Platelet Function Assay (PFA) Profile

Platelet Count (3200-06)
PFA Epinephrine/Collagen (3245-01)
PFA ADP/Collagen (3245-02)

Thrombosis Risk Profile

PT (3200-04)
PT 1:1 Mix (3200-04)
APTT (3200-05)
Antithrombin III Activity (3230-01)
Protein C Activity (3230-02)
Protein S Activity (3230-03)

Thrombosis Risk on Warfarin Profile

PT (3200-04)
APTT (3200-05)
APTT 1:1 Mix (3200-10)
Antithrombin III Activity (3230-01)
Protein C Activity (3230-02)
Protein S Activity (3230-03)
Factor VII Activity (3210-12)
Factor X Activity (3210-15)

von Willebrand Profile

APTT (3200-05)
Factor VIII Activity (3210-13)
Ristocetin Cofactor (vWF) Activity (3210-03)
Von Willebrand Factor (vWF) Antigen (3210-20)

HEMOSTASIS REFERENCE LABORATORY

(206) 292-6594

The Puget Sound Blood Center's Hemostasis Reference Laboratory has over 25 years of experience in providing quality hemostatic evaluations including testing, interpretation of results and patient evaluations. The laboratory features considerable technical experience in a wide variety of instrumentation, reagents and available specialty testing with extensive Quality Assurance and CLIA approved procedures. Puget Sound Blood Center's blood component therapy, hemophilia care and apheresis programs are supported by the Hemostasis Reference Laboratory and testing is also available for various research protocols.

SPECIMEN COLLECTION INFORMATION

(206) 292-1876

Hemostasis Reference Laboratory Samples:

- All coagulation testing is done in sodium citrate plasma. This is the traditional "blue top tube."
- Send two 5 ml or three 3 ml tubes. The sample should be kept at Room Temperature (15-25°C) and received by the Blood Center, Terry and Madison location, within three hours after collection between the hours of 8am to 3pm Monday through Friday (excluding holidays).
- Where appropriate sample integrity testing will be performed. This involves running APTT and possibly PT on Factor levels.

If this is not possible:

- The tubes are centrifuged at 1500g for 15-20 minutes and the plasma removed. For best results the plasma should be centrifuged a second time at 1500g for 15-20 minutes. Then place a minimum of 1 ml of plasma into four (4) plastic tubes, freeze and send on dry ice.
- The minimum requirements are two (2) plasma tubes with at least 0.5 ml of plasma in each tube for each two (2) tests ordered. Do not send more than 6 aliquots.

Notes: (1) Insufficient sample tubes will negatively affect turn-around time. (2) Therapeutic anticoagulation interferes with most kinetic (but not DNA) tests. Care should be taken to obtain samples on the opposite arm from the IV site or from an adequately flushed port site. If a sample is found to contain Heparin, it may be necessary to remove it and charge for an APTT Post-Heparin Removal.

Bleeding Time, PFA, and Platelet Aggregation:

Bleeding times and Platelet Aggregations cannot be collected outside our facility and require the patient to visit the Puget Sound Blood Center, where the samples will be drawn. PFAs only, may be sent if prior arrangements have been made. Call the Hemostasis Reference Laboratory at (206) 292-6594 for details on how to send a PFA or to schedule an appointment with the technologist.

DNA Laboratory Samples:

DNA mutation testing requires at least 10 ml EDTA whole blood (purple top). The sample must arrive at the Blood Center within 48 hrs. after collection shipped preferably with a "cool pack." Samples may be sent via overnight express, addressed to Puget Sound Blood Center, ATTN: Hemostasis Reference Laboratory, 921 Terry Avenue, Seattle WA 98104-1256. Send samples so they arrive Monday - Thursday only (no holidays).