Type 1 von Willebrand disease (VWD) is an inherited bleeding disorder caused by a partial quantitative deficiency in von Willebrand factor (VWF). Decreased survival (increased clearance) is one mechanism that can cause autosomal dominant type 1 VWD. A classification of type 1C has been proposed for this type of VWD. VWD Vicenza (c.3614G>A encoding for p.R1205H) is one example of a type 1C variant.

Typical laboratory findings in patients with this phenotype include low VWF antigen and proportionately low VWF ristocetin cofactor activity; factor VIII levels may be low. Further evaluation of these patients might reveal an elevated VWF propeptide to VWF antigen ratio and occasionally a persistence of larger than normal size multimers. An increased rate of VWF clearance can be documented by a DDAVP trial. In patients with a clinical phenotype of type 1C VWD, molecular testing is useful for confirming the diagnosis and identifying affected family members.

VWD TYPE 1C (Clearance) SEQUENCE ANALYSIS
VWF Exon 27, 28, 34 and 37 Sequence Analysis

REASONS FOR REFERRAL:
Confirmation of a diagnosis of type 1C VWD
Evaluation of family members

METHOD:
Assay Principle:
PCR amplification and bi-directional DNA sequence analysis are performed. Complete coding regions and splice junctions of VWF exons 27, 28, 34 and 37 are compared to the NM_000552 reference sequence. Functional implications are classified using data from the HGMD and the ISTH VWD database (http://www.vwf.group.shef.ac.uk). Sequence variations are reported using standard nomenclature recommendations of the Human Variation Society. Sequence variations designated as benign are not reported, but those results are available upon request.

Assay Sensitivity/Specificity:
Analytical sensitivity is >99% for sequence variations in the exons examined. Rare polymorphisms within primer or probe regions may interfere with detection of gene variants. Mutations that are outside the regions sequenced will not be detected. Large deletions and duplications are not detected. Clinical sensitivity is >99% for reported mutations.

LIMITATIONS:
Analytical sensitivity is >99%. Rare polymorphisms within primer or probe regions may interfere with detection of gene variants. Mutations that are outside the regions sequenced will not be detected. Clinical sensitivity is >99% for reported mutations.
REPORTABLE RANGE:
Sequence variations are reported as heterozygous or homozygous and are classified according to the following system:

I. Sequence variation is previously reported and is a recognized cause of the disorder
II. Sequence variation is previously unreported and is of the type which is expected to cause the disorder.
III. Sequence variation is previously unreported and is of the type which may or may not be causative of the disorder
IV. Sequence variation is previously unreported and is probably not causative of disease.
V. Sequence variation is previously reported and is a recognized neutral variant.
VI. Sequence variations that are not known or expected to be causative of disease, but have been found to be associated with a clinical presentation.

Known polymorphisms are not reported but are available upon request.

SPECIMEN REQUIREMENTS:
Sample must be less than 1 month old when received by our laboratory.
Parental/Patient: 3-5 ml EDTA (lavender top) whole blood.
Fetal: 7-15 ml Amniotic Fluid or 5-10 mg CVS, backup culture of Amniocytes or CVS is highly recommended; Two T25 flasks Cultured Amniocytes or CVS (2x10^6 minimum).

SHIPPING REQUIREMENTS:
Ship on an ice pack or at room temperature. Place the specimen and the requisition into plastic bags and seal. Insert into a Styrofoam container; seal and place into a sturdy cardboard box, and tape securely. Ship the package in compliance with your overnight carrier guidelines. Label with the following address:

Client Services/Hemostasis Reference Laboratory
BloodCenter of Wisconsin
638 N. 18th St.
Milwaukee, WI 53233
Phone: 800-245-3117, ext. 6250

TURNAROUND TIME: 21 days
CPT CODES: 81404

REFERENCES: