BIO/DATA CORPORATION

AN ISO 13485 REGISTERED COMPANY

vW ABNORMAL CONTROL PLASMA

REF 101270

IVD 2°C 8°C

INSTRUCTIONS FOR USE

ENGLISH - EN

PRODUCT DESCRIPTION
vW Abnormal Control Plasma is lyophilized citrated human plasma which has been selectively depleted of von Willebrand Factor.

vW Abnormal Control Plasma has been optimized for use with Light Transmission Aggregometers. It may also be used with other turbidometric or impedance analyzers, and flow cytometers.

INTENDED PURPOSE
vW Abnormal Control Plasma is prepared from a pool of normal infection negative human plasma which has been partially depleted of vW Factor and then lyophilized. If is used to verify the performance and sensitivity of the Ristocetin Cofactor Activity test.

DETECTION / MEASUREMENT
is used, in conjunction with other reagents, diluents and control samples, to measure changes of the light transmission in a Platelet Rich Plasma (PRP) test sample.

PRODUCT FUNCTION
vW Abnormal Control Plasma provides essential insights into the functional activity of von Willebrand Factor (vWF). This plasma is designed to aid in the evaluation of von Willebrand Syndrome (vWS), supporting the diagnosis and classification of inherited or acquired vWF-related disorders.

SPECIFIC INFORMATION PROVIDED
vW Abnormal Control Plasma is not intended for the detection of a specific disorder, condition, or risk factor.

vW Abnormal Control Plasma is essential for evaluating the functional activity of von Willebrand Factor (vWF) through the vW Cofactor Assay. vW Abnormal Control Plasma, depleted of vWF, is crucial for ensuring the accuracy and reliability of tests by providing a baseline for abnormal vWF activity. The vW Abnormal Control Plasma helps assess the ability of vWF to promote the agglutination of formalin-fixed or fresh platelets in a patient's plasma. A decrease in Ristocetin Cofactor activity, as observed with vW Abnormal Control Plasma, indicates an impairment or dysfunction of vWF.

AUTOMATION
vW Abnormal Control Plasma is intended for use in semi-automated and automated Light Transmission Platelet Aggregometers. This plasma may also be used with other turbidometric or impedance analyzers, and flow cytometers.

QUALITY / QUANTITY
There are no primary standards for vW Abnormal Control Plasma. The responses to this plasma are concentration dependent. A known normal donor should be tested with each new lot of vW Abnormal Control Plasma. Standards organizations classify Ristocetin Cofactor Activity Assays as semi-quantitative or semi-qualitative.

vW Abnormal Control Plasma comes packaged as 3 x 0.5 mL vials

SPECIMEN TYPE
The test specimen is prepared from sodium citrate anti-coagulated whole blood, and the test sample is Platelet Poor Plasma (PPP). The test blank consists of Lyophilized Platelets and TRIS Buffered Saline (TBS), providing a standardized baseline for the assay.

Ristocetin Reagent may be used with human or animal Platelet Poor Plasma (PPP). Results are based on the extent and rate of platelet agglutination, reflecting the functional activity of vWF.

Reference plasmas, lyophilized formalin-fixed platelets, control plasmas, and diluents are used to perform a Ristocetin Cofactor Activity Test. Test results are determined by interpolation from a standard curve.

TESTING POPULATION
- Human: The prevalence of von Willebrand platelet disorders is global and may vary by race, ethnicity, blood type, and other factors. The incidence is ~2%.
- Anti-Platelet Drugs: The prevalence and incidence are variable. BTK inhibitors and vancomycin are known to decrease RIPA outcomes. A recently developed anti-platelet glycoprotein (GP) Ib monoclonal antibody (moAB) labeled as OP-FI, along with a thoroughly studied anti-GBIb MoAB known as AP-1, completely eliminate platelet agglutination induced by Ristocetin.
- Inherited Platelet Disorders: The prevalence and incidence are variable. Platelets derived from individuals with Bernard-Soulier Syndrome do not agglutinate when exposed to Ristocetin. In contrast to von Willebrand Disease, the levels of von Willebrand Factor activity and von Willebrand antigen remain within normal ranges.
- Animal: The prevalence and incidence are species dependent.

IN VITRO DIAGNOSTIC
vW Abnormal Control Plasma is an in vitro diagnostic reagent intended for Professional Laboratory Use Only. It is not intended for injection or ingestion.

INTENDED USER
vW Abnormal Control Plasma is intended for Professional Laboratory Use by qualified personnel.

TEST PRINCIPLE
When introduced to a 37°C Platelet Poor Plasma (PPP) test sample, the Ristocetin Reagent induces platelet agglutination by interacting with the glycoprotein Ib (GP Ib) receptor on the platelet surface, which is mediated by von Willebrand Factor (vWF). This initial aggregation, called primary aggregation, is characterized by a shape change in the platelets and is reversible. The primary aggregation may be followed by the release of endogenous ADP from platelet granules, which triggers a secondary, irreversible wave of aggregation. The extent and rate of both primary and secondary aggregation are influenced by the functional activity of vWF in the sample. The Light Transmission Platelet Aggregometer effectively captures these changes by displaying parameters such as the lag phase, shape change, and the rate and extent of aggregation over a predetermined testing period.

CALIBRATORS AND CONTROLS
There are no calibrators or controls required for vW Abnormal Control Plasma. A known donor sample should be tested with each lot of vW Abnormal Control Plasma. Responses are concentration dependent.

REAGENT LIMITATIONS
vW Abnormal Control Plasma will perform as specified when the Instructions for Use are followed. The plama must be used prior to the expiration date printed on each vial.

REAGENTS PROVIDED
REF 101270: 3 vials of vW Abnormal Control Plasma (0.5 mL)

REAGENTS AND MATERIALS REQUIRED BUT NOT PROVIDED
- Purified Water (Distilled, Deionized, Reagent Grade), pH 5.3 – 7.2 for reconstitution

⚠ *NOTE: USING BLOOD BANK SALINE WILL CAUSE ERRONEOUS RESULTS.*

MATERIALS AND ACCESSORIES
- Platelet Aggregometer *(Follow the Manufacturer's Instructions for Use)*
- Centrifuge
- Electronic Pipette
- Pipette Tips ②
- Aggregometer Test Tubes *(Siliconized)* ②
- Aggregometer Stir Bars *(Plastic Coated)* ②
- Plastic Sample Tubes and Caps *(for Dilutions)* ②
- Mechanical Specimen Rocker

⚠ *NOTE: DISPOSABLE ITEMS SUCH AS TEST TUBES, STIR BARS, SAMPLE TUBES, AND CAPS ARE FOR ONE TIME USE ONLY*

STORAGE AND STABILITY
vW Abnormal Control Plasma does not require temperature protection during shipment.

Upon receipt, store vW Abnormal Control Plasma at 2 – 8° C in its' original packaging.

Reconstituted vW Abnormal Control Plasma is stable for 8 hours, when stored in its' tightly capped, original container at 2 – 8° C.

Dilutions containing vW Abnormal Control Plasma are stable for 45 minutes at room temperature.

STERILITY

vW Abnormal Control Plasma is not a sterile products. Be careful not to contaminate the product when pipetting the reconstituted or aliquoted reagents.

WARNINGS AND PRECAUTIONS

Wear PPE in accordance with laboratory policies and practices when handling vW Abnormal Control Plasma.

Follow standard precautions when preparing test specimens and samples.

Handle vW Abnormal Control Plasma with care to avoid contamination during use.

Avoid reagent evaporation by limiting air – liquid exchange surfaces.

To ensure optimum test results, a known donor control sample should be run consecutively, without interruption.

To preserve reagent stability, store remaining plasma in its' tightly capped, original container.

Dispose of post-test materials in accordance with applicable regulations and laboratory policies.

NOTE TO USER: ANY SERIOUS INCIDENT THAT OCCURS IN RELATION TO THIS PRODUCT SHALL BE REPORTED TO THE MANUFACTURER AND THE COMPETENT AUTHORITY OF THE MEMBER STATE IN WHICH THE USER AND / OR PATIENT ARE ESTABLISHED.

INFECTIOUS MATERIAL STATUS

vW Abnormal Control Plasma has been screened at the source and confirmed negative for HIV-1 antigen (HIV-1Ag), anti-HIV-1/2 antibodies, Hepatitis B surface antigen (HBsAg), Hepatitis C antibodies, Human T-Lymphotropic Virus Type I and II (anti-HTLV I/II) antibodies, and Syphilis by serological testing. Nevertheless, due to their human origin, all plasma and platelets should be handled as potentially hazardous materials. Test specimens and samples must be considered infectious and should be handled as if capable of transmitting infection. After testing, test specimens and samples must be disposed of in compliance with applicable regulations and laboratory policies.

SPECIAL FACILITIES

vW Abnormal Control Plasma does not require the use of special facilities within a laboratory environment.

PREPARATION FOR USE

NOTE: vW ABNORMAL CONTROL PLASMA MUST BE AT ROOM TEMPERATURE (15 – 28° C) PRIOR TO RECONSTITUTION. STORED PLATELETS, REAGENTS, AND PLASMAS MUST BE BROUGHT TO ROOM TEMPERATURE PRIOR TO USE.

RECONSTITUTION

The working concentration of the reconstituted Ristocetin Reagent is 15 mg / mL. All final concentrations are based on adding 25 µL of Ristocetin Reagent to a 225 µL Platelet Poor Plasma (PPP) test sample.

- vW Abnormal Control Plasma with 0.5 mL of Purified Water.
- Invert gently to mix.
- Reconstituted vW Abnormal Control Plasma should be kept capped prior to use.
- After Reconstitution, allow vW Abnormal Control Plasma stand at room temperature for 20 minutes to rehydrate prior to use.

PATIENT PREPARATION

Patients should refrain from taking aspirin or using aspirin-containing medications and products, as well as other medications, supplements, or energy drinks known to affect platelet function for 7 – 10 days prior to specimen collection. Ingestion of fatty foods, dairy products, and smoking should be avoided for 12 hours before specimen collection.

NOTE: CONSULTATION WITH A PHYSICIAN IS REQUIRED PRIOR TO MAKING ANY MEDICATION CHANGES.

SPECIMEN COLLECTION

The specimen should be collected with care to avoid stasis, hemolysis, contamination by tissue fluid and exposure to glass. Specimens must be kept at room temperature. Release the tourniquet as soon as blood begins to flow into the collection device.

PRACTICE STANDARD PRECAUTIONS THROUGHOUT THE SPECIMEN COLLECTION, SAMPLE PREPARATION, AND ANALYTICAL PROCESSES. DISPOSE OF SHARPS AND BIOHAZARDOUS WASTE IN ACCORDANCE WITH APPLICABLE REGULATIONS AND LABORATORY POLICIES.

Evacuated Specimen Collection Technique

- Use a 21g or 23g winged needle collection set for specimen collection
- Draw blood into plastic evacuated specimen collection tubes containing 3.2% (0.11 M) sodium citrate anti-coagulant
- Gently mix the specimen collection tube 4 - 5 times by inversion
- Write collection time on the specimen label
- Maintain specimen collection tubes at room temperature
- Remix specimen collection tubes prior to centrifugation

Syringe Collection Technique

- Use a 21g or 23g winged needle collection set for the venipuncture
- Draw 9.0 mL of blood into a plastic syringe, avoiding excess suction
- Clamp the winged needle tubing and disconnect the syringe
- Immediately and gently dispense the blood specimen into a plastic (polypropylene) tube containing 1.0 mL of 0.11 M sodium citrate anti-coagulant. The blood to anticoagulant ratio is 9 parts blood to 1 part anti-coagulant
- Cap the plastic tube
- Gently mix the specimen collection tube 4 - 5 times by inversion
- Write collection time on the specimen label
- Maintain specimen collection tubes at room temperature
- Remix specimen collection tubes prior to centrifugation

NOTE: WHEN THE PATIENT'S HEMATOCRIT IS LESS THAN 30% OR GREATER THAN 55%, THE BLOOD TO ANTI-COAGULANT RATIO MUST BE ADJUSTED. BLUE TOP EVACUATED SPECIMEN COLLECTION TUBES MUST CONTAIN 3.2% (0.11 M) SODIUM CITRATE ANTICOAGULANT. WHICH IS THE RECOMMENDED CONCENTRATION FOR PLATELET FUNCTION STUDIES.

SAMPLE PREPARATION

Platelet Rich Plasma (PRP)

- Centrifuge the anti-coagulated blood at 150 x g for 10 minutes at room temperature
- Examine the plasma layer for red cells
- If red cells are present, re-centrifuge for an additional 5 minutes
- Use a Pipette to transfer the PRP to a plastic container labeled PRP
- Remove the PRP from a point just below the middle of the PRP volume for consistent platelet count *(THE TOP OF THE VOLUME HAS A LOWER PLATELET COUNT AND THE BOTTOM IS MORE CONCENTRATED)*
- Cap the container
- Allow the container to stand at room temperature

Platelet Poor Plasma (PPP)

- Centrifuge the remaining PRP blood specimen at 2500 x g for 20 minutes
- Use a Pipette to transfer the PPP to a plastic container labeled PPP
- Cap the container
- Allow the container to stand at room temperature

ASSAY PROCEDURE

Ristocetin Cofactor Assay Three Point Standard Curve Procedure

NOTE: THIS IS A GENERAL PROCEDURE. FOLLOW THE INSTRUCTIONS FOR USE PROVIDED BY THE MANUFACTURER OF THE AGGREGOMETER IN USE.

Prepare a Blank for Each Patient

NOTE: IN RISTOCETIN COFACTOR ASSAY TESTING, THE SAME BLANK MAY BE USED FOR EACH TEST WELL IN BOTH THE RISTOCETIN COFACTOR ASSAY THREE POINT STANDARD CURVE AND THE RISTOCETIN COFACTOR ASSAY THREE POINT PATIENT TESTING, PROVIDED THAT ALL TESTING IS COMPLETED WITHIN FOUR HOURS OF PREPARING THE BLANK.

- Label a test tube with the letter "B" to identify the Blank
- Pipette 125 µL of Lyophilized Platelets and 125 of TRIS Buffered Saline (TBS) into the test tube *(DO NOT ADD A STIR BAR)*
- Place Blank aside for later use

NOTE: THE PREPARED BLANK IS STABLE FOR 4 HOUS AT ROOM TEMPERATURE

Prepare Standard Curve Dilutions

NOTE: DILUTIONS SHOULD BE PREPARED INDEPENDENTLY AND NOT AS SERIAL DILUTIONS.

Use the Following Dilution Procedure for a 100%, 50%, and 25% Curve:

- Label three new test tubes: 100%, 50%, and 25%
- In the test tube labeled 100%: Pipette 200µL of vW Normal Reference Plasma (NRP) and 200µL of TRIS Buffered Saline (TBS)
- Invert gently to mix
- In the test tube labeled 50%: Pipette 100µL of vW Normal Reference Plasma (NRP) and 300µL of TRIS Buffered Saline (TBS)
- Invert gently to mix
- In the test tube labeled 25%: Pipette 50µL of vW Normal Reference Plasma (NRP) and 350µL of TRIS Buffered Saline (TBS)
- Invert gently to mix
- Place all three vW Normal Reference Plasma dilutions aside for later use

NOTE: DILUTIONS ARE STABLE FOR 40 MINUTES AT ROOM TEMPERATURE

Prepare Samples

- Label three new test tubes with 100% Well #1, 50% Well # 2, and 25% Well # 3

- Place the labeled test tubes into the corresponding well # 1 - 3 of the Stirred Sample Incubation Wells
- Add a Stir Bar to Each Test Tube
- Pipette 200µL of Lyophilized Platelets into each Test tube in the stirred sample incubation wells (MAKE SURE THERE ARE NO BUBBLES)
- Pipette 25µL of Ristocetin Reagent into each test tube in the stirred sample incubation wells (MAKE SURE THERE ARE NO BUBBLES)
- Select the on-screen timer for each stirred sample incubation wells and the warming countdown will start
- The samples will incubate at 37ºC for the pre-set time

Set the 100% Baseline (Blank)

- Locate the previously prepared Blank test tube labeled "B"
- Place the test tube into test well # 1
- Select BLANK to activate the test well
- The BLANK button will change to START
- Repeat the above process for test wells # 2 and # 3

Begin Testing

- Once the countdown timer reaches 0:00, press the timer button to stop each stirred sample incubation wells
- Transfer the test tube in the stirred sample incubation well #1 to test well # 1
- Repeat the step above for each test well, making sure all test tubes remain with their corresponding well #'s during transfer
- Close the pipette guides
- Select START for test well # 1
- Pipette 25µL of the previously prepared dilution labeled 100% into test well # 1
  (DO NOT ALLOW REAGENT TO RUN DOWN THE WALL OF THE TEST TUBE OR PERMIT THE PIPETTE TIP TO BREAK THE SURFACE OF THE SAMPLE)
- Select INJECT for test well # 1
- Select START for test well # 2
- Pipette 25µL of the previously prepared dilution labeled 50% into test well # 2
  (DO NOT ALLOW REAGENT TO RUN DOWN THE WALL OF THE TEST TUBE OR PERMIT THE PIPETTE TIP TO BREAK THE SURFACE OF THE SAMPLE)
- Select INJECT for test well # 2
- Select START for test well# 3
- Pipette 25µL of the previously prepared dilution labeled 25% into test well# 3
  (DO NOT ALLOW REAGENT TO RUN DOWN THE WALL OF THE TEST TUBE OR PERMIT THE PIPETTE TIP TO BREAK THE SURFACE OF THE SAMPLE)
- Select INJECT for test well # 3
- The test will now run for the pre-set time
  (OTHER MANUFACTURER'S TEST PROCEDURES MAY SPECIFY DIFFERENT TIMES OR VOLUMES)

Ristocetin Cofactor Assay Three Point Patient Test Procedure

⚠ *NOTE: THIS IS A GENERAL PROCEDURE. FOLLOW THE INSTRUCTIONS FOR USE PROVIDED BY THE MANUFACTURER OF THE AGGREGOMETER IN USE.*

Prepare a Blank for Each Patient

⚠ *NOTE: IN RISTOCETIN COFACTOR ASSAY TESTING, THE SAME BLANK MAY BE USED FOR EACH TEST WELL IN BOTH THE RISTOCETIN COFACTOR ASSAY THREE POINT CURVE AND THE RISTOCETIN COFACTOR ASSAY THREE POINT PATIENT TESTING, PROVIDED THAT ALL TESTING IS COMPLETED WITHIN FOUR HOURS OF PREPARING THE BLANK.*

- Use the Blank previously prepared for the Ristocetin Cofactor Assay Three Point Curve
- If the Blank was prepared more than 4 hours ago, it is no longer stable, and a new Blank must be prepared
- To prepare a new Blank, follow the blank preparation instructions located in this IFU under Ristocetin Cofactor Assay Three Point Standard Curve Procedure

Prepare Dilutions

- Label one to eight new test tubes with each patient's ID and well #
- Pipette 100µL of the patient sample into the corresponding labeled test tube for each patient being tested
- Pipette 100µL of TRIS Buffered Saline (TBS) into each test tube
- Place dilutions aside for later use

Prepare Samples

- Label one to eight new test tubes with each patient's ID and well #
- Place the labeled test tubes into the corresponding wells # 1 - 8 of the stirred sample incubation wells
- Add a Stir Bar to each test tube
- Pipette 200µL of Lyophilized Platelets into each test tube in the stirred sample incubation wells (MAKE SURE THERE ARE NO BUBBLES)
- Pipette 25µL of Ristocetin into each test tube in the stirred sample incubation wells (MAKE SURE THERE ARE NO BUBBLES)
- Select the on-screen timer for each stirred sample incubation wells and the warming countdown will start
- The samples will incubate at 37ºC for the pre-set time

Set the 100% Baseline (Blank)

- Locate the previously prepared Blank test tube labeled "B"
- Place the test tube into test well # 1
- Select BLANK to activate the test well
- The BLANK button will change to START
- Repeat the above process for each test well being used for testing

Begin Testing

- Once the countdown timer reaches 0:00, press the timer button to stop each stirred sample incubation wells
- Transfer the test tube from the stirred sample incubation wells # 1 to test well # 1
- Repeat the step above for each test well, making sure all test tubes remain with their corresponding cell #'s during transfer
- Close the pipette guides
- Select START for test well # 1
- Pipette 25µL of the previously prepared patient dilution directly into the test tube in test well # 1
- VERIFY THE CORRECT PATIENT DILUTIONS ARE BEING TRANSFERRED TO THE CORRECT PATIENT TEST WELL
  (DO NOT ALLOW REAGENT TO RUN DOWN THE WALL OF THE TEST TUBE OR PERMIT THE PIPETTE TIP TO BREAK THE SURFACE OF THE SAMPLE)
- Select INJECT for test well # 1
- Repeat the above procedure for each test well being used for testing
- The test will now run for the pre-set time
  (OTHER MANUFACTURER'S TEST PROCEDURES MAY SPECIFY DIFFERENT TIMES OR VOLUMES)

⚠ *NOTE: USE A KNOWN DONOR AS A CONTROL SAMPLE. EACH LABORATORY SHOULD ESTABLISH AND VALIDATE ITS OWN TEST PROTOCOL AND VERIFY THE RESULTING PERFORMANCE OF ITS TEST SYSTEM (REAGENTS, INSTRUMENT, AND TEST PROTOCOL).*

QUALITY CONTROL

For platelet aggregation studies, a known donor should be tested in the same manner as the patient to ensure test system performance and consistency. A new control should be included with each test series, and preferably with each new reagent lot or after instrument maintenance. Each laboratory must define its acceptable ranges for its patient population and verify the expected performance of the test system.

A von Willebrand Factor deficient plasma serves as an abnormal control and should be assayed as a test plasma with an expected result of ≤ 45% activity. This control ensures that the assay system is specific for the von Willebrand Factor and that agglutination will not be influenced by other normal plasma proteins. Additionally, it is suggested to run vW Normal Reference Plasma and vW Abnormal Control Plasma to validate standard curves.

RESULTS

When testing vW Abnormal Control Plasma, the expected von Willebrand Factor (vWF) activity level should be ≤ 45%. This threshold serves as a critical benchmark for identifying deficiencies in vWF activity, thereby aiding in the evaluation of von Willebrand factor-related disorders. If the results exceed this expected limit, it may suggest potential issues with the assay procedure, reagent performance, or the control plasma itself. Consistent results within this defined range across multiple assays reinforce the reliability and specificity of the testing system. Furthermore, th ese results should be interpreted alongside those from vW Normal Control Plasma and other reference controls to ensure comprehensive assay validation and accuracy.

The von Willebrand Factor (vWF) Assay utilizes a three-point standard curve to determine the percent activity of vWF in a patient's plasma. As illustrated in Figure 1, the standard curve is generated using three known dilutions of vWF, typically representing 100%, 50%, and 25% activity. The assay measures the response at these concentrations and plots the values to establish a reference curve.

When the patient's sample is analyzed, its response is interpolated against the standard curve to determine vWF activity as a percentage of normal plasma (100% activity). Clinically, vWF activity levels within the normal range (45–150%) indicate typical function, while values below 45% may suggest von Willebrand Disease (vWD). Conversely, elevated vWF activity may be associated with conditions or disorders. disorders.

Figure 2 illustrates key phases of platelet aggregation over time, providing insights into platelet function. The initial downward deflection observed in each curve represents shape change, where platelets respond to the agonist by undergoing morphological alterations without immediate aggregation. This is followed by the primary aggregation phase, characterized by an upward trend as platelets begin to clump together, increasing light transmission. The maximum aggregation point varies across the curves, reflecting differences in platelet responsiveness. Certain tracings, such as those in channels 6, 7, and 8, exhibit a decline after reaching maximum aggregation, indicating a reversible aggregation pattern, whereas others sustain aggregation, signifying a strong response. Variations in lag time before aggregation initiation highlight differences in platelet activation kinetics. These characteristics help assess platelet function and identify potential abnormalities in aggregation response.

The von Willebrand Factor (vWF) Assay tracing shown in Figure 3, illustrates an abnormal vWF activity response, with results measuring below 45% activity. This reduced activity suggests a potential von Willebrand Disease (vWD). The tracing demonstrates a weaker-than-expected response compared to the standard curve, indicating impaired vWF function or decreased factor levels. Such abnormal results may be associated with vWD Type 1 or Type 2 variants, acquired vWF deficiency, or other coagulation disorders. These findings underscore the need for further diagnostic testing to accurately characterize the nature and severity of the deficiency.

It is essential to interpret these aggregation results within the broader context of the patient's clinical condition. A definitive diagnosis should only be made after further testing and comprehensive evaluation. The figures include spike marks that indicate the precise points of reagent addition, providing clear reference points for understanding the timing of reagent introduction and its immediate effects on the aggregation process.

FIGURE 1: VW RISTOCETIN COFACTOR ASSAY THREE POINT PERCENT ACTIVITY

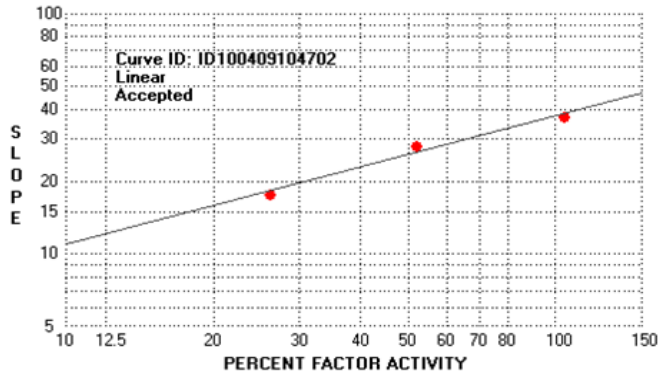


FIGURE 2: NORMAL VW RISTOCETIN COFACTOR ASSAY THREE POINT PATIENT TESTING

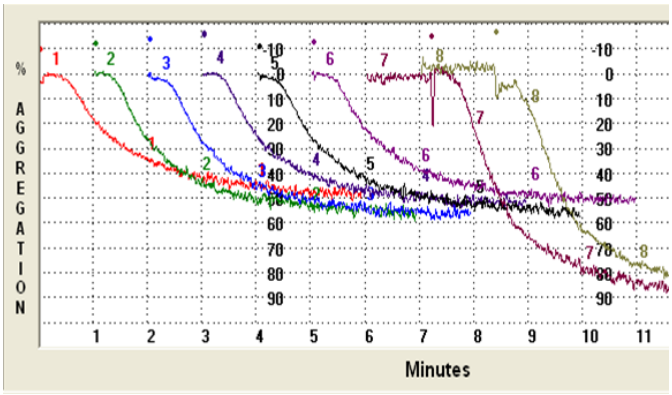
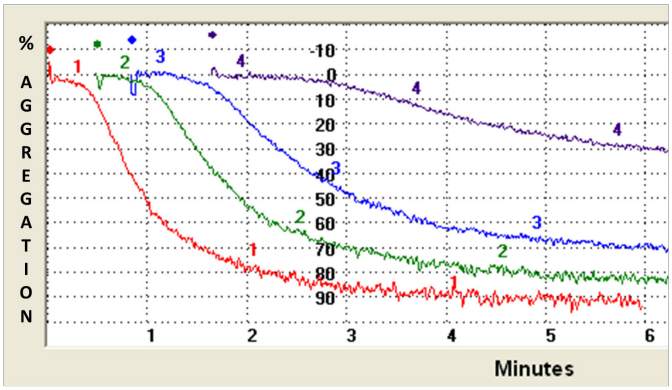


FIGURE 3: ABNORMAL VW RISTOCETIN COFACTOR ASSAY THREE POINT PATIENT TESTING



EXPECTED VALUES

Each laboratory should establish expected ranges for each reagent at various concentrations used to induce aggregation.

A result of less than 40% von Willebrand Factor is considered abnormal and suggestive of von Willebrand Syndrome. However, other properties of the von Willebrand molecule must be considered for diagnosis of the variant forms of von Willebrand Syndrome. Since reference ranges for von Willebrand Factor are dependent on blood type, each laboratory should establish blood type specific reference ranges for its patient population.

vW Abnormal Control Plasma will yield von Willebrand Factor Assay results of ≤ 45%. The ability to generate a quantitative value in this range is dependent upon the sensitivity of the assay system in use.

Unexpected assay values should be carefully assessed to identify the source of deviation, as several factors may contribute to erroneous results. These include non-specific agglutination of reagent platelets, incorrect ristocetin concentration, improper reconstitution of normal control plasma, instrument malfunctions, and procedural errors.

LIMITATIONS

In Light Transmission Aggregometry, the presence of red blood cells in the PRP will cause the observed aggregation to be reduced. The presence of platelets in the PPP will cause final aggregation to be increased. Spurious results may occur if the PRP platelet count is less than 75,000 platelets / cumm. PRP platelet counts can only be performed using the hemocytometer method. Compromised samples must be rejected. If the results are abnormal, the test should be repeated on another occasion. Each laboratory must establish reference ranges tailored to the population it serves, and the specific reagent concentrations used.

ANALYTICAL PERFORMANCE

Platelet aggregation, induced by commonly used reagents like Ristocetin Reagent, is a non-linear test system. Responses are based on the difference between the patient's Platelet Rich Plasma and Platelet Poor Plasma light transmission and therefore, results are unique to that patient. Certain parameters are more prone to non-linearity than others. These include lag phase, primary slope, secondary slope, biphasic response and disaggregation. The non-linearity is caused by many factors such as the reaction chemistry and instrumentation. Platelet aggregation displays the response rate or activity and does not quantify the reactants or their concentrations.

In platelet aggregation, accuracy is a relative parameter and is dependent on the test system. The limitations of platelet aggregation make it difficult to provide typical precision or reproducibility ranges.

The variability in linearity, precision and reproducibility of results in Ristocetin Reagent-based test systems is acknowledged by multiple standards organizations. The commonly accepted CV is ± 15%.

Test to Test Reproducibility:	less than ± 7.5%
Instrument to Instrument Reproducibility:	less than ± 15.0%
Reagent Lot to Lot Variability:	less than ± 10.5%
Laboratory to Laboratory (System to System)	less than ± 12.5%

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SYMBOLS

	Bio-Hazardous
REF	**Catalog Number**
	Caution
CE	**CE Marked & Registered Product**
	Consult Instructions For Use
EU REP	**European Union Representative**
IVD	**In Vitro Diagnostic Device**
	Manufacturer
	Must Read
NON STERILE	**Non-Sterile**
2	**Single Use Only**
	Temperature Limitations
UK CA	**United Kingdom Marked & Registered Product**
UK REP	**United Kingdom Representative**

REVISION HISTORY

Document No: 101276 Revision: AA, August 2025

- Modified Testing Instructions
- Implemented IVDR Regulatory Requirements
- Reformatted and Reconfigured to Enhance Operator Use

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