BIO/DATA CORPORATION

AN ISO 13485 REGISTERED COMPANY

AGGRECETIN® REAGENT

REF 100970 REF 101241

IVD 2°C 8°C

Ristocetin A Sulfate

INSTRUCTIONS FOR USE

ENGLISH - EN

PRODUCT DESCRIPTION

AggRecetin is Ristocetin A Sulfate, a glycopeptide of unknown chemical structure isolated from Nocardia lurida. AggRecetin contains more than 90% Ristocetin A.

AggRecetin (Ristocetin) Reagent 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

AggRecetin (Ristocetin) Reagent is intended for use in performing routine Ristocetin-Induced Platelet Aggregation (RIPA) testing on Platelet-Rich Plasma (PRP) samples to assess platelet function.

DETECTION / MEASUREMENT

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

PRODUCT FUNCTION

AggRecetin (Ristocetin) Reagent provides insight into different aspects of platelet function / quality. This Reagent aids in accessing various acquired and inherited platelet disorders or the efficacy of anti-platelet therapies.

SPECIFIC INFORMATION PROVIDED

AggRecetin (Ristocetin) Reagent is not intended for the detection of a specific disorder, condition, or risk factor.

AggRecetin (Ristocetin) Reagent is a distinctive platelet reagent employed in the realm of Ristocetin Induced Platelet Aggregation (RIPA) testing. Ristocetin interacts with von Willebrand Factor (vWF), a critical plasma protein involved in platelet adhesion and aggregation processes. Ristocetin prompts a conformational shift in vWF, exposing binding sites for platelet glycoprotein Ib (GP Ib). Consequently, platelet GP Ib receptors engage with vWF, initiating platelet adhesion. This initial adherence primes platelets for aggregation. In instances lacking von Willebrand Factor (vWF) or related platelet function disorders, Ristocetin Induced Platelet Aggregation proceeds to a limited extent due to platelets' incapacity to aggregate effectively. Consequently, RIPA testing furnishes invaluable insights into platelet function / quality and vWF activity, thereby aiding in the characterization of von Willebrand Disease (vWD) and associated bleeding disorders. This testing method plays a vital role in evaluating platelet function / quality accurately.

AUTOMATION

AggRecetin (Ristocetin) Reagent is intended for use in semi-automated and automated Light Transmission Platelet Aggregometers. This reagent may also be used with other turbidometric or impedance analyzers, and flow cytometers.

QUALITY / QUANTITY

There are no primary standards for the AggRecetin (Ristocetin) Reagent. The responses to these reagents are concentration dependent. A known normal donor should be tested with each new lot of AggRecetin (Ristocetin) Reagent. Standards organizations classify Ristocetin induced platelet aggregation (RIPA) as semi-quantitative or semi-qualitative.

AggRecetin (Ristocetin) Reagent packaged as 1 x 15 mg vial, including 1 x 2.0 mL Diluent, or 1 x 100 mg. The working concentration of AggRecetin is 15 mg / mL.

SPECIMEN TYPE

The test specimen is prepared from sodium citrate anti-coagulated whole blood. The test sample is Platelet Rich Plasma (PRP). The test blank is Platelet Poor Plasma (PPP).

AggRecetin (Ristocetin) Reagent may be used with human or animal Platelet Rich Plasma (PRP) for routine platelet aggregation tests. Results are based on the concentration, extent, and rate of aggregation compared to a Platelet Poor Plasma (PPP) blank.

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 eliminating 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

AggRecetin (Ristocetin) Reagent is an in vitro diagnostic reagent intended for Professional Laboratory Use Only. This Reagent is not intended for injection or ingestion.

INTENDED USER

AggRecetin (Ristocetin) Reagent is intended for Professional Laboratory Use by qualified personnel.

TEST PRINCIPLE

When introduced to a stirred, 37°C Platelet Rich Plasma (PRP) test sample, exogenous Reagents such as AggRecetin (Ristocetin) stimulate platelets, prompting them to undergo shape change and aggregate. This initial aggregation is called primary aggregation and is reversible. However, normal platelets possess the ability to release endogenous ADP from their granules, leading to a secondary, irreversible wave of aggregation. The Light Transmission Platelet Aggregometer effectively captures these changes by displaying parameters such as 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 the AggRecetin (Ristocetin) Reagent. A known donor sample should be tested with each lot of AggRecetin (Ristocetin) Reagent. Responses are concentration dependent.

REAGENT LIMITATIONS

AggRecetin (Ristocetin) Reagent will perform as specified when the Instructions for Use are followed. The reagent must be used prior to the expiration date printed on each vial.

REAGENTS PROVIDED

REF 100970: 1 vial of AggRecetin (Ristocetin) Reagent (15 mg)
1 vial of Diluent (2 mL)

REF 101241: 1 vial of AggRecetin (Ristocetin) Reagent (100 mg)

REAGENTS AND MATERIALS REQUIRED BUT NOT PROVIDED

- Purified Water (Distilled, Deionized, Reagent Grade), pH 5.3 – 7.2 for reconstitution
- TRIS Buffered Saline (TBS) or 0.85% physiological saline for dilutions

⚠ *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

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

STORAGE AND STABILITY

AggRecetin (Ristocetin) Reagent does not require temperature protection during shipment.

Upon receipt, store AggRecetin Reagent at 2 – 8° C in their original packaging.

Reconstituted AggRecetin (Ristocetin) Reagent is stable for 7 days, when stored in its tightly capped, original container at 2 – 8° C.

STERILITY

AggRecetin (Ristocetin) Reagent 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 AggRecetin (Ristocetin) Reagent.

Follow standard precautions when preparing test specimens and samples.

Handle AggRecetin (Ristocetin) Reagent 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 reagents in their tightly capped, original containers.

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

AggRecetin (Ristocetin) Reagent does not contain any infectious 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

AggRecetin (Ristocetin) Reagent does not require the use of special facilities within a laboratory environment.

PREPARATION FOR USE

NOTE: AGGRECETIN (RISTOETIN) REAGENT MUST BE AT ROOM TEMPERATURE (15 – 28° C) PRIOR TO RECONSTITUTION. STORED REAGENTS MUST BE BROUGHT TO ROOM TEMPERATURE PRIOR TO USE.

RECONSTITUTION

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

- Reconstitute AggRecetin (Ristocetin) Reagent with 0.5 mL of Purified Water
- Invert gently to mix
- Reconstituted AggRecetin (Ristocetin) Reagent should be kept capped prior to use

DILUTIONS

For RISTOCETIN INDUCED PLATELET AGGREGATION (RIPA)

Ristocetin Induced Platelet Aggregation (RIPA) is performed by using a high dose and a low dose of concentrations of AggRecetin (Ristocetin) Reagent. The Platelet Rich Plasma (PRP) may be tested with various dilutions of the reagent. The high dose is typically 1.2 or 1.0 mg / mL of Ristocetin. The low dose is either 0.6 or 0.5 mg / mL.

NOTE: FOR DILUTIONS, USE TRIS BUFFERED SALINE (TBS) OR 0.85% PHYSIOLOGICAL SALINE.

TABLE 1: AGGRECETIN (RISTOCETIN) DILUTION CHART

AGGRECETIN REAGENT	DILUENT	WORKING CONCENTRATION	FINAL CONCENTRATION
15 mg	0.50 µL	15 mg / mL	1.5 mg / mL
15 mg	0.63 µL	12 mg / mL	1.2 mg / mL
15 mg	0.75 µL	10 mg / mL	1.0 mg / mL
15 mg	1.50 µL	5 mg / mL	0.5 mg / mL

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

Routine Aggregation 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: EACH PATIENT MUST HAVE THEIR OWN BLANK. ONE PATIENT'S BLANK CANNOT BE USED FOR ANY OTHER PATIENT. THE PATIENT'S BLANK MUST BE PREPARED FROM THE PATIENT'S PLATELET POOR PLASMA (PPP) SPECIMEN. IF THE SAME PATIENT IS BEING TESTED ON MULTIPLE TEST WELLS, THE SAME PATIENT'S BLANK MAY BE USED FOR THOSE TEST WELLS.

- Label a test tube with the letter "B", test well #, and patient ID to identify the Blank
- Pipette 250 µL of Platelet Poor Plasma (PPP) into the test tube *(DO NOT ADD A STIR BAR)*
- Place Blank aside for later use
- Repeat the steps above for each patient

Prepare Test Samples

- Label one to eight new test tubes with each patient ID and test well #
- Place the labeled test tubes into the correct well # 1 - 8 of the stirred sample incubation wells

FIGURE 1: RISTOCETIN-INDUCED PLATELET AGGREGATION (RIPA) NORMAL AGGREGATION

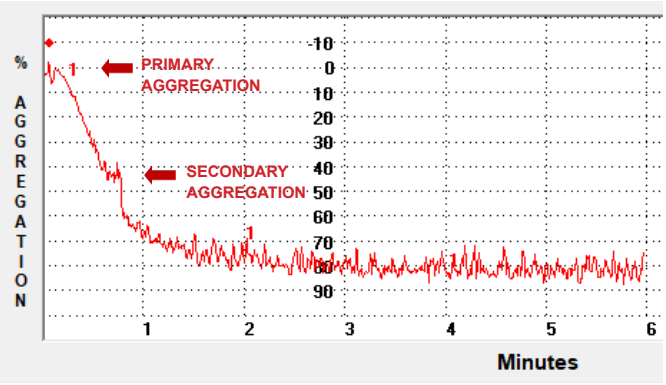
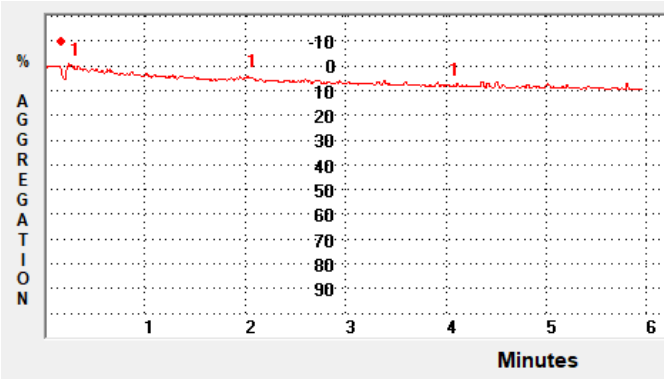


FIGURE 2: RISTOCETIN-INDUCED PLATELET AGGREGATION (RIPA) ABNORMAL AGGREGATION



- Add a stir bar to each test tube
- Pipette 225 µL of Platelet Rich Plasma (PRP) sample 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 well in use and the warming count down will start
- The samples will incubate at 37° C for the pre-set time
- Set the 100% baseline (Blank)
- Place the appropriate previously prepared patient's Blank test tube into test well # 1
- Select BLANK to activate the test well
- The BLANK button will change to START
- Repeat the steps above 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 well
- 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 25 µL of reagent directly into the Platelet Rich Plasma (PRP) test tube in test well # 1 *(DO NOT ALLOW REAGENT TO RUN DOWN THE WALL OF THE TEST TUBE OR PERMIT PIPETTE TIP TO BREAK THE SURFACE OF THE SAMPLE)*
- Select INJECT for test well # 1
- Repeat the steps above 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.

RESULTS

The aggregation patterns for AggRecetin (Ristocetin) Reagent are depicted in Figures 1 and 2. These typical aggregation patterns provide a detailed view of the reagent's effects on Platelet-Rich Plasma (PRP). Ristocetin-induced aggregation can manifest as either a biphasic response or a single large wave of aggregation. The primary wave of aggregation results from the agglutination of platelets mediated by the von Willebrand Factor in the presence of Ristocetin. Following this, a secondary wave may occur due to the release of endogenous ADP from the platelets, which further contributes to the aggregation process. In patients without a bleeding disorder, the administration of a high dose of Ristocetin typically results in a strong, single wave of aggregation. This robust response is indicative of normal platelet function and von Willebrand Factor activity. Conversely, a low dose of Ristocetin generally elicits no response in these patients, as the lower concentration is insufficient to induce significant platelet aggregation.

However, a strong response to a low dose of Ristocetin suggests the presence of certain types of von Willebrand Disease. In contrast, normal individuals with no bleeding disorders typically exhibit little or no response to low doses of Ristocetin.

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.

TABLE 2: AGGRECETIN (RISTOCETIN) RESULTS OBSERVED IN PLATELET FUNCTION DEFECTS

DEFECT	AGGRECETIN REAGENT
ASPIRIN-LIKE	↓ or N
THROMBASTHENIA	N
STORAGE POOL DISEASE	↓ or N
VON WILLEBRAND SYNDROME	↓ ↓
BERNARD-SOULIER SYNDROME	↓ ↓

↓ = *Reduced Aggregation Resulting From a Decrease or Absence of Secondary Wave*

↓ ↓ = *Reduced Aggregation Resulting From a Decrease or Absence of Primary and Secondary Wave*

N = *Normal Response*

EXPECTED VALUES

Each laboratory should establish expected ranges for each reagent at various concentrations used to induce aggregation (Table 3).

TABLE 3: EXPECTED RESULTS FOR PLATELET AGGREGATION RESPONSES IN NORMAL DONORS

Final Aggregation at 6 Minutes

Parameter	Units	AGGRECETIN REAGENT	
		1.0 mg / mL	1.5 mg / mL
Final Concentration		Diluent Dependent	Diluent Dependent
Primary Aggregation	%	83	89
Primary Slope		63	68
Secondary (Biphasic) Aggregation	%	Occasionally	Occasionally
Secondary Slope		Variable	Variable
Area Under The Curve	Minutes	N / A	N / A
Lag Phase	Seconds	N / A	N / A
Disaggregation	%	No	No
Maximum Aggregation	%	≥ 96	≥ 101
Final Aggregation	%	82 - 96	54 - 101

⚠ *NOTE: ADJUSTING PLATELET COUNTS IS NOT RECOMMENDED*

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 AggRecetin (Ristocetin) Reagent, is a non-linear test system. Responses are based on the difference between the patient's Platelet Rich Plasma (PRP) and Platelet Poor Plasma (PPP) 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 AggRecetin (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%

SYMBOLS


Bio-Hazardous

Catalog Number


Caution


CE Marked & Registered Product


Consult Instructions For Use

European Union Representative

In Vitro Diagnostic Device


Manufacturer


Must Read

Non-Sterile


Single Use Only


Temperature Limitations

United Kingdom Marked & Registered Product

United Kingdom Representative

REFERENCES

- Allain JP, Cooper HA, Wagner RH, Brinkhous KM. Platelets fixed with paraformaldehyde: a new reagent for assay of von Willebrand factor and platelet aggregating factor. J Lab Clin Med. 1975 Feb;85(2):318-28.
- Angiolillo DJ, Ueno M, Goto S. Basic principles of platelet biology and clinical implications. Circ J. 2010 Apr;74(4):597-607.
- Born GV, Cross MJ. The Aggregation of Blood Platelets. J Physiol. 1963 Aug; 168(1):178-95.
- Brinkhous KM, Graham JE, Cooper HA, Allain JP, Wagner RH. Assay of von Willebrand factor in von Willebrand's disease and hemophilia: use of a macroscopic platelet aggregation test. Thromb Res. 1975 Mar;6(3):267-72.
- Brinkhous KM, Read MS. Preservation of platelet receptors for platelet aggregating factor/von Willebrand factor by air drying, freezing, or lyophilization: new stable platelet preparations for von Willebrand factor assays. Thromb Res. 1978 Oct;13(4):591-7.
- Bye A, Lewis Y, O'Grady J. Effect of a single oral dose of aspirin on the platelet aggregation response to arachidonic acid. Br J Clin Pharmacol. 1979 Mar; 7(3):283-6.
- Cattaneo M, Cerletti C, Harrison P, Hayward CP, Kenny D, Nugent D, Nurden P, Rao AK, Schmaier AH, Watson SP, Lussana F, Pugliano MT, Michelson AD. Recommendations for the Standardization of Light Transmission Aggregometry: A Consensus of the Working Party from the Platelet Physiology Subcommittee of SSC/ISTH. J Thromb Haemost. 2013 Apr 10.
- CLSI. Procedures for the Handling and Processing of Blood Specimens for Common Laboratory Tests; Approved Guideline—Fourth Edition. CLSI document H18-A4. Wayne, PA: Clinical and Laboratory Standards Institute; 2010.
- CLSI. Protection of Laboratory Workers from Occupationally Acquired Infections, Approved Guideline - Fourth Edition. CLSI document M29-A4. Wayne, PA: Clinical and Laboratory Standards Institute; 2010.
- CLSI. Platelet Function Testing by Aggregometry, Approved Guideline - Fourth Edition. CLSI document H58-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.
- CLSI. Collection, Transport and Processing for Plasma Based Coagulation Assays and Molecular Hemostasis Assays, Approved Guideline - Fifth Edition. CLSI document H21-A5. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.
- CLSI. Clinical Laboratory Safety, Approved Guideline - Third Edition. CLSI document GP17-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.
- Day HJ, Holmsen H. Laboratory tests of platelet function. Ann Clin Lab Sci (1971). 1972 Jan-Feb; 2(1):63-74.
- Day HJ, Rao AK. Evaluation of platelet function. Semin Hematol. 1986 Apr;23(2):89-101.
- Eichelberger, JW. Kinetic (Slope) Measurement of Platelet Aggregation. Bio/ Data Corporation, Horsham, PA; 1984.
- Favaloro EJ, Gosselin RC, Pasalic L, Lippi G. Post-analytical issues in hemostasis and thrombosis testing: An update. In EJF, RCG, editors, Hemostasis and Thrombosis: Methods and Protocols. 2nd ed. New York: Humana Press. 2023. p. 787-811. (Methods in Molecular Biology).
- Federici AB, Lee CA, Berntorp EE, Lillicrap D, Montgomery RR. Von Willebrand Disease: Basic and Clinical Aspects. 2011.
- Garner JS. Guideline for isolation precautions in hospitals. The Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol. 1996 Jan;17(1):53-80.
- Gralnick HR, Sultan Y, Coller BS. Von Willebrand's disease: combined qualitative and quantitative abnormalities. N Engl J Med. 1977 May 5;296(18):1024-30.
- Harmening, D. M. Clinical Hematology and Fundamentals of Hemostasis. Fifth Edition. F. A. Davis Company. 2009.
- Hoffbrand, A. V., Moss, P. A. H., & Pettit, J. E. Hoffbrand's Essential Haematology. Seventh Edition. John Wiley & Sons Ltd. 2016.
- Howard MA, Firkin BG. Ristocetin--a new tool in the investigation of platelet aggregation. Thromb Diath Haemorrh. 1971 Oct 31; 26(2): 362-9.
- Israels SJ, El-Ekiaby M, Quiroga T, Mezzano D. Inherited disorders of platelet function and challenges to diagnosis of mucocutaneous bleeding. Haemophilia. 2010 Jul;16 Suppl 5:152-9.
- Kambayashi J, Shinoki N, Nakamura T, Ariyoshi H, Kawasaki T, Sakon M, Monden M. Prevalence of impaired responsiveness to epinephrine in platelets among Japanese. Thromb Res. 1996 Jan 1;81(1):85-90.
- Kaushansky K, Lichtman MA, Prchal JT, Levi MM, Press OW, Burns LJ, Caligiuri M. eds. Williams Hematology, 9e. McGraw-Hill Education. 2015.
- Keohane, E. M., Smith, L. J., Walenga, J. M., & Block, D. R. Rodak's Hematology: Clinical Principles and Applications. Fifth Edition. Saunders, an imprint of Elsevier Inc. 2016.
- Levine PH. The effect of thrombocytopenia on the determination of platelet aggregation. Am J Clin Pathol. 1976 Jan;65(1):79–82
- Linnemann B, Schwonberg J, Mani H, Prochnow S, Lindhoff-Last E. Standardization of light transmittance aggregometry for monitoring antiplatelet therapy: an adjustment for platelet count is not necessary. J Thromb Haemost. 2008 Apr;6(4):677-83.
- Marcus AJ, Coleman RW, Hirsh J, Ivarder VJ, Salzman EW. Hemostasis and thrombosis: Basic Principles and Clinical Practice. Vol. 472. Philadelphia: JB Lippincott Company; 1982.
- Michelson, AD. Platelets. Third Edition. Amsterdam: Academic Press; 2013.
- Miller CH, Graham JB, Goldin LR, Elston RC. Genetics of classic von Willebrand's disease. I. Phenotypic variation within families. Blood. 1979 Jul;54(1):117-36.
- Mills DC, Robb IA, Roberts GC. The release of nucleotides, 5-hydroxytryptamine and enzymes from human blood platelets during aggregation. J Physiol. 1968 Apr;195(3):715-29.
- Moncada S, Vane JR. Arachidonic acid metabolites and the interactions between platelets and blood-vessel walls. N Engl J Med. 1979 May 17;300(20):1142-7.
- NCCLS. Assays of von Willebrand Factor Antigen and Ristocetin Cofactor Activity; Approved Guideline. NCCLS document H51-A. NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2002.
- Nilsson, I. M. and Holmberg, L.: von Willebrand's Disease Today. Clin. Hematol., 8:276, 1979.
- O'Donnell CJ, Larson MG, Feng D, Sutherland PA, Lindpaintner K, Myers RH, D'Agostino RA, Levy D, Tofler GH; Framingham Heart Study. Genetic and environmental contributions to platelet aggregation: the Framingham heart study. Circulation. 2001 Jun 26;103(25):3051-6.
- Olson JD, Brockway WJ, Fass DN, Magnuson MA, Bowie EJ. Evaluation of ristocetin-Willebrand factor assay and ristocetin-induced platelet aggregation. Am J Clin Pathol. 1975 Feb;63(2):210-8.
- Owen CA Jr, Bowie EJW, Thompson JH Jr. The Diagnosis of Bleeding Disorders. 2nd ed. Little, Brown, and Company; 1975.
- Palma-Barqueros V, Revilla N, Sánchez A, Zamora Cánovas A, Rodriguez-Alén A, Marín-Quílez A, González-Porras JR, Vicente V, Lozano ML, Bastida JM, Rivera J. Inherited Platelet Disorders: An Updated Overview. Int J Mol Sci. 2021 Apr 26;22(9):4521.
- Ramsey R, Evatt BL. Rapid assay for von Willebrand factor activity using formalin-fixed platelets and microtitration technic. Am J Clin Pathol. 1979 Dec;72(6):996-9.
- Siegel JD, Rhinehart E, Jackson M, Chiarello L; Health Care Infection Control Practices Advisory Committee. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Health Care Settings. Am J Infect Control. 2007 Dec;35(10 Suppl 2):S65-164.
- The Hospital Infection Control Practices Advisory Committee, Centers for disease Control and Prevention, Public Health Service, U.S. Department of Health and Human Services. Guideline for isolation precautions in hospitals Part II.

Recommendations for isolation precautions in hospitals. American Journal of Infection Control. 1996; Vol 24, Issue 1: 32-52.
- Triplett DA, et al. Platelet function: laboratory evaluation and clinical application. Chicago, IL: American Society for Clinical Pathology 1978.
- Weiss HJ. Aspirin and Platelets in Drugs and Hematologic Reactions. New York, NY: Dimittov and Nodine, eds. Grune and Stratton. 1974.
- White, M.M., and Jennings, L.K. Platelet Protocols: Research and Clinical Laboratory Procedures, Academic Press, Inc.; 1999.
- Williams WJ, Beutler E, Erslev AJ, Rundles RW. Hematology. New York, NY: McGraw-Hill. 1977.
- Zimmerman TS, Abildgaard CF, Meyer D. The factor VIII abnormality in severe von Willebrand's disease. N Engl J Med. 1979 Dec 13;301(24):1307-10.
- Zuzel M, Nilsson IM, Aberg M. A method for measuring plasma ristocetin cofactor activity. Normal distribution and stability during storage. Thromb Res. 1978 May;12(5):745-54.
- Zimmerman TS, Abildgaard CF, Meyer D. The factor VIII abnormality in severe von Willebrand's disease. N Engl J Med. 1979 Dec 13;301(24):1307-10.
- Zuzel M, Nilsson IM, Aberg M. A method for measuring plasma ristocetin cofactor activity. Normal distribution and stability during storage. Thromb Res. 1978 May;12(5):745-54.

REVISION HISTORY

Document No: 101242 Revision: AA, 04/2025

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

For a complete product catalog, please visit our website at www.biodatacorp.com or contact our Customer Service Department.

THE BIO/DATA CORPORATION PRODUCT LINE INCLUDES GENERAL PURPOSE, PROFESSIONAL LABORATORY USE REAGENTS INTENDED TO INDUCE AND REPORT PLATELET FUNCTION ACTIVITY AND RESPONSES. THIS PRODUCT IS WARRANTED TO PERFORM AS DESCRIBED IN ITS LABELING INCLUDING THE INSTRUCTIONS FOR USE. BIO/DATA CORPORATION MAKES NO CLAIM OR WARRANTY, EXPRESSED OR IMPLIED, OF THE CAPABILITY, FITNESS, OR MERCHANTABILITY FOR ANY OTHER PURPOSE. IN NO EVENT SHALL BIO/DATA CORPORATION BE LIABLE FOR ANY CONSEQUENTIAL DAMAGES ARISING OUT OF AFORESAID EXPRESSED WARRANTY.

155 Gibraltar Road
Horsham, PA 19044 USA

Worldwide: +1 215-441-4000
USA: 1-800-257-3282
FAX Worldwide: +1 215-443-8820
customer.service@biodatacorp.com

REF
100970
101241

BIO/DATA CORPORATION
AN ISO 13485 REGISTERED COMPANY
www.biodatacorp.com

EU REP
mdi Europa GmbH
Langenhagener Str. 71
D-30855 Langenhagen GERMANY

UK REP
Alpha Laboratories
40 Parham Drive Eastleigh
S050 4NU Hampshire UNITED KINGDOM

PROUDLY MANUFACTURED IN THE USA