SIEMENS Healthineers

BC von Willebrand Reagent

BC VWF REAGENT

Revision bar indicates update to previous version.

For the determination of ristocetin cofactor activity

Intended Use

In-vitro diagnostic for the determination of ristocetin cofactor activity of von Willebrand factor in human plasma through platelet agglutination.

Summary and Explanation

BC von Willebrand Reagent is used in the determination of ristocetin cofactor activity as an aid in the diagnosis of von Willebrand Syndrome and disorders involving changes in ristocetin cofactor activity, such as lesions and inflammations of the vascular endothelium, as well as for pre-operative screening of bleeding tendencies.

Von Willebrand Syndrome is the most frequent congenital human blood disorder and is caused by a defective synthesis or functioning of von Willebrand factor multimers. Von Willebrand factor (VWF) is present in plasma in the form of a complex with factor VIII. Von Willebrand Syndrome is an autosomal dominant inherited disorder of three types, Type I (partial, quantitative decrease), Type II (partial loss of activity, several sub-types) and Type III (complete absence of VWF). These variants are differentiated on the basis of a series of laboratory tests such as ristocetin cofactor activity, VWF antigen, closure time for PFA-100®, bleeding time, partial thromboplastin time, factor VIII activity, platelet count and von Willebrand multimer analysis[1].

Principles of the Procedure

BC von Willebrand Reagent measures ristocetin cofactor activity as follows: in the presence of ristocetin, the von Willebrand factor (ristocetin cofactor) in the sample causes an agglutination of the stabilized platelets contained in the von Willebrand Reagent. The agglutination process reduces the turbidity of the reaction mixture. A coagulation analyzer measures the change in optical density and automatically determines the ristocetin cofactor activity of the sample in % of the norm.

Reagents

Note: BC von Willebrand Reagent can be used on automated coagulation analyzers.
Siemens Healthineers provides Reference Guides (Application Sheets) for several coagulation analyzers. The Reference Guides (Application Sheets) contain analyzer/assay-specific handling and performance information which may differ from that provided in these Instructions for Use. In such a case, the information contained in the Reference Guides (Application Sheets) supersedes the information in these Instructions for Use. In addition, please also consult the instruction manual of the instrument manufacturer.

Reagent	Description	Storage	Stability once opened
BC von Willebrand Reagent BC VWF REAGENT	stabilized platelets, ristocetin and EDTA in lyophilized form. sodium azide (≤ 0.25 g/L)	2–8 °C The reagent may be used up to the expiry date indicated on the label if stored unopened.	2 days at 2–8 °C or 8 hours at 15 °C (open container)

Information about on-board stability is specified in the Reference Guides (Application Sheets) for the different coagulation analyzers.

Warnings and Precautions

For *in-vitro* diagnostic use only.

For laboratory professional use.

Safety data sheets (MSDS/SDS) available on siemens-healthineers.com/sds.

CAUTION!
Federal (USA) law restricts this device to sale by or on the order of licensed healthcare professionals.

BC VWF REAGENT
Hazardous ingredient: Sodium azide (0.896 % [w/w]).
H412: Harmful to aquatic life with long lasting effects.
P273: Avoid release to the environment. **P501**: Dispose of contents and container in accordance with all local, regional, and national regulations.

CAUTION! POTENTIAL BIOHAZARD
Each donor or donor unit was tested and found to be negative for human immunodeficiency virus (HIV) 1 and 2, hepatitis B virus (HBV) and hepatitis C virus (HCV) using either tests that are CE marked or FDA approved for this purpose. Because no known test can offer complete assurance of the absence of infectious agents, all human derived products should be handled with appropriate caution.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent the buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with all government requirements.

Preparing Reagents

Resuspend the reagent with the amount of distilled water indicated on the label at 15 to 25 °C by mixing (e.g. with an automatic mixer like the Heidolph Mixer "Reax control" set in the range of 75 to 100 %, 2 x 5 seconds). The reagent is then immediately ready to use. Be sure to mix the reagent intensively and to an equal extent for each new reconstitution.

Each time before use (i.e. placement on the instrument) the reagent has to be mixed intensively equal to the initial procedure.

Specimen Collection and Handling

Collecting the Specimen

To obtain the plasma, carefully mix 1 part sodium citrate solution (0.11 mol/L) with 9 parts venous blood, avoiding the formation of foam. Centrifuge the blood specimen immediately at 1500 x g for no less than 15 minutes at 15 to 25 °C, then remove the supernatant plasma and store at 15 to 25 °C or frozen at ≤ –20 °C.

Storing the Specimen

at 15 to 25 °C	6 hours
at ≤ –20 °C	1 month

Procedure

Materials Provided

REF	Contents	Number of tests
OUBD39	BC VWF REAGENT	
	5 x → 4 mL REAGENT	dependent on the system used

Materials Required but not Provided

Item	Description
REF ORKL	Standard Human Plasma
REF ORKE	Control Plasma N
REF OUPZ	Control Plasma P
	Coagulation analyzer (Refer also to the Application Sheets)
	Distilled Water

Test Procedure

For coagulation analyzers without a stirring position, make sure that the reagent is resuspended by mixing at least every 30 minutes.

Performing Calibration

A new reference curve must be calculated each time there is a change in the device used or a change in the lot of BC von Willebrand Reagent.

Internal Quality Control

Normal range: Control Plasma N

Pathological range: Control Plasma P

Two controls should be measured with each reagent vial, each calibration and at least every 8 hours during each day of testing (one in the normal range and one in the pathological range). The controls should be treated like the samples. Measurements are to be carried out as duplicates. The results obtained must lie within the range indicated for the controls in the lot-specific table of assigned values. If a control value lies outside the range, the coagulation analyzer, reagent and reference curve should be checked. Do not release patient results until the cause of deviation has been identified and corrected.

Assay Range

Information concerning assay range is specified in the Reference Guides (Application Sheets) for the different coagulation analyzers.

Results

The ristocetin cofactor activity is reported as % of the norm.

Results of this test should always be interpreted in conjunction with the patient's medical history, clinical presentation and other findings.

Limitations

Siemens Healthineers has validated use of these reagents on various analyzers to optimize product performance and meet product specifications. User defined modifications are not supported by Siemens Healthineers as they may affect performance of the system and assay results. It is the responsibility of the user to validate modifications to these instructions or use of the reagents on analyzers other than those included in Siemens Healthineers Application Sheets or these Instructions for Use.

Expected Values

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference ranges for the diagnostic evaluation of patient results.

Consider these ranges as guidelines only (For additional information on determining the reference interval, see CLSI Document C28-A3[2].)

Results below the determined reference interval can be considered an indication of von Willebrand Syndrome.

In a study carried out on ostensibly healthy subjects using the BCS®, the following data were obtained:

		% of the norm		
n	Blood group	5th Percentile	95th Percentile	Median
185	AB0	57.2	> 150	98.5
80	0	48.9	> 150	78.9
105	non-0	65.4	> 150	121

There is a connection between blood group (AB0 type), age and von Willebrand Factor concentration[3].

Performance Characteristics

Precision

Over a five day period, precision studies (one run per day in replicates of eight) were performed by assaying normal and pathological control plasmas. For normal control plasmas (n = 80), the within-run coefficient of variation (CV) ranged from 8.0 to 9.6 %, while the total CV ranged from 8.0 to 10.3 %. For pathological control plasma (n = 80), the within-run CV ranged from 6.1 to 16.2 %, while the total CV ranged from 7.6 to 16.9 %.

Method Comparison

A comparative study was carried out with BC von Willebrand Reagent and another commercially available reagent. A total of 70 patient plasma samples (35 normal and 35 pathological) were tested using both methods. The regression analysis produced a correlation coefficient of 0.94, a y-axis intercept of -4.4 % and a slope of 0.97.

Note: The values cited for specific performance characteristics of the assay represent typical results and are not to be regarded as specifications for BC von Willebrand Reagent.

Technical Assistance

For customer support, contact your local technical support provider or distributor.

siemens-healthineers.com

Current Version of Application Sheets

BC VWF REAGENT can be used in combination with various automated coagulation analyzers. Siemens Healthineers provides Reference Guides/Application Sheets for coagulation analyzers under the dedicated link below:

siemens-healthineers.com/rg

As Siemens Healthineers continuously monitors the product performance and safety, the users are required to ensure that they work with the correct revision of the instructions for the product lots in use. Please periodically review the availability of new electronic labeling revisions to ensure safe use of the product.

The IFU version number is visible on each product box label. Siemens Healthineers ensures that all products lots bearing the same IFU version number are compatible with the electronic labeling provided via siemens-healthineers.com/eIFU.

Bibliography

1. Veyradier A, Fressinaud E, Meyer D. Laboratory diagnosis of von Willebrand disease. Int J Clin Lab Res. 1998; 28:201-10.
2. Clinical and Laboratory Standards Institute (CLSI). Defining, establishing and verifying reference intervals in the clinical laboratory; Approved Guideline – Third Edition. CLSI document C28-A3. CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA 2008.
3. Gill JC, Endres-Brooks J, Bauer PJ et al. The effect of AB0 blood group on the diagnosis of von Willebrand disease. Blood 1987; 69:1691-5.

Definition of Symbols

The following symbols may appear on the product labeling:

	Do not reuse		Use By
LOT	Batch Code	REF	Catalogue Number
	Caution		Manufacturer
EC REP	Authorized representative in the European Community		Contains sufficient for <n> tests
	Biological Risks	IVD	*In Vitro* Diagnostic Medical Device
	Temperature Limitation		Consult instruction for Use
	Non-sterile	CE	CE marking of conformity
CE 0197	CE marking of conformity with notified body ID number. Notified body ID number can vary.	CONTENTS	Contents
→	Reconstitution volume	LEVEL	Level
	Keep away from sunlight and heat	WARNING	Warning
DANGER	Danger	RxOnly	Prescription device (US only)
UDI	Device Identification (UDI) barcode	REACH xx/xx/xx	REACH Authorization Number

Legal Information

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