Batroxobin Reagent
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Revision bar indicates update to previous version.

CE 0197

Intended Use

Batroxobin REAGENT is an in vitro diagnostic reagent for the quantitative determination of batroxobin time as an aid to diagnosis of fibrinogen related hemostasis disorders in patients with signs or at risk of bleeding disorders in human sodium citrated plasma by means of automated, semi-automated and/or manual coagulometric methods.

For batroxobin time testing no international reference preparation or method is available.

Summary and Explanation

Batroxobin is a proteolytic snake venom enzyme which causes cleavage of fibrinopeptide A from fibrinogen, thereby inducing coagulation. Batroxobin time is a coagulation assay performed to investigate fibrinogen-related bleeding disorders. Batroxobin time is correlated to fibrinogen concentration and function; congenital and acquired defects in fibrinogen and fibrin polymerization (including elevated levels of fibrin(ogen) degradation products) result in in prolongation of batroxobin time[1–3].

The combination of the heparin insensitive batroxobin time and the heparin-sensitive thrombin time can be used to identify the presence of heparin in the sample, either due to heparin therapy, or due to heparin contamination during sampling.

Determination of batroxobin time can aid in

- monitoring fibrin(ogen) degradation products, e.g. under fibrinolytic therapy,
- diagnosis of severe fibrinogen deficiency and dysfibrinogenaemia,
- clarification of prolonged thrombin times in case of suspected presence of heparin.

Principles of the Procedure

Batroxobin REAGENT is added to citrated plasma and the time it takes for a clot to form is measured.

Reagents

Note: Batroxobin REAGENT can be used manually or on automated coagulation analyzers. Sysmex 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 this case, the information contained in the Reference Guides (Application Sheets) supersedes the information in these Instructions for Use. Please also consult the instruction manual of the instrument manufacturer!

Reagent	Description	Storage	Stability
Batroxobin Reagent Batroxobin REAGENT	Lyophilized reagent containing: • Batroxobin[a] (reconstituted: ~5.5 BU/mL) • BSA • HEPES • Preservatives: • reaction mass of 5-chloro-2-methyl-2H-isothiazol-3-one / 2-methyl-2H-isothiazol-3-one (3:1) (reconstituted: 10 mg/L)	2–8 °C May be used up to the expiry date indicated on the label if stored unopened.	≤ –20 °C: reconstituted, 3 months; 2–8 °C: reconstituted, 14 days; 15–25 °C: reconstituted, 24 hours; 37 °C: reconstituted, 24 hours

[a] an enzyme from the venom of Bothrops atrox

Reconstituted reagent can be frozen and thawed up to three times.

On-board stability
Information regarding 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.

According to EU regulation 2017/746, any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the EU Member State through your local distribution representative in which the user and/or patient is established.

Safety data sheets (MSDS/SDS) available upon request.

Warning! Batroxobin REAGENT
Hazardous ingredient: reaction mass of 5-chloro-2-methyl-2H-isothiazol-3-one / 2-methyl-2H-isothiazol-3-one (3:1) (0.0426 % [w/w]).
H317: May cause an allergic skin reaction. **H411**: Toxic to aquatic life with long lasting effects. **P280**: Wear protective gloves/protective clothing/eye protection/face protection. **P261**: Avoid breathing dust. **P273**: Avoid release to the environment. **P302 + P352**: IF ON SKIN: Wash with plenty of soap and water. **P333 + P313**: If skin irritation or rash occurs: Get medical advice/ attention. **P362 + P364**: Take off contaminated clothing and wash it before reuse. **P391**: Collect spillage. **P501**: Dispose of contents and container in accordance with all local, regional, and national regulations.

Caution
This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

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.

Summary of Safety and Performance (SSP) is available in the European database on medical devices (see Eudamed public website: https://ec.europa.eu/tools/eudamed). In case Eudamed is not available, SSP can be delivered by the manufacturer on request.

Preparing Reagents

Reconstitute a vial of Batroxobin REAGENT with 5 mL of distilled or deionized water and warm to 37 °C prior to assay.

Before use the reagent should be mixed carefully.

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. An evacuated tube system or syringe may be used. Please refer to CLSI document H21-A5 for further details. Centrifuge immediately at 1 500 × g for no less than 15 minutes at room temperature[4], remove the supernatant plasma and keep at 15 to 25 °C until required in the test (max. 4 hours).

Procedure

Materials Provided

REF	Contents	
OUOV21	Batroxobin Reagent Batroxobin REAGENT	2 × → 5 mL

Materials Required but not Provided

Item	Description
REF ORKE41	CONTROL N, Control Plasma N, or
REF 291070	Dade® Ci-Trol® 1, or
REF B4244-10	Ci-Trol CONTROL 1, Dade® Ci-Trol® Coagulation Control Level 1, as control for the normal range
Coagulation analyzers[b], such as:	• Automated Blood Coagulation Analyzer CA-600 series (CA-600 series) • AUTOMATED BLOOD COAGULATION ANALYZER CS-2500 (CS-2500 System) • AUTOMATED BLOOD COAGULATION ANALYZER CS-5100 (CS-5100 System)

[b] Availability of analyzers may vary by country.

Please note that the applications on other analyzers can be validated by the instrument manufacturer in accordance with the requirements of the REGULATION (EU) 2017/746 under their responsibility as long as the intended purpose and performance are not modified.

Test Procedure

Pipette into a test tube prewarmed to 37 °C:

Citrated plasma	100 µL
Incubate at 37 °C for 1 minute.	
Batroxobin REAGENT (37 °C!)	200 µL
On addition of Batroxobin REAGENT start stop-watch or timer on the coagulation analyzer and determine the coagulation time.	

Internal Quality Control

Normal range: CONTROL N, Control Plasma N, or
Dade® Ci-Trol® 1, or
Ci-Trol CONTROL 1, Dade® Ci-Trol® Coagulation Control Level 1

A control has to be measured at start of the test run, upon reagent vial changes and at least every eight hours on each day of testing. The controls should be processed like the samples. Each laboratory should determine its own quality control range, either by means of the target values and ranges provided by the manufacturer of the controls or by means of its own confidence level established in the laboratory. If the measured control value lies outside the confidence level previously established, then the reagent and the coagulation analyzer should be examined.

Results

Results are given in seconds.

Limitations

The manufacturer has validated use of these reagents on various analyzers to optimize product performance and meet product specifications. Please note that the applications on other analyzers can be validated by the instrument manufacturer in accordance with the requirements of the REGULATION (EU) 2017/746 under their responsibility as long as the intended purpose and performance are not modified. User defined modifications are not supported by the manufacturer 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 Application Sheets or these Instructions for Use.

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

Expected Values

16 to 22 s

Reference intervals vary from laboratory to laboratory depending on the population served and the technique, method, equipment and reagent lot used. Therefore, each laboratory must establish its own reference intervals or verify them whenever one or more of the aforementioned variables are changed.

Performance Characteristics

Measuring Range

The measuring range depends on the individual application of the assay due to instrument related conditions. Application specific performance data is listed in the respective Reference Guides of the instruments.

Precision

In a precision study performed by the manufacturer the coefficient of variation for repeatability was between 1.5 and 3.9 %, and from day to day between 0.3 and 3.6 %.

Other system specific results are given in the respective Reference Guides (Application Sheets).

The reproducibility was assessed by the manufacturer for batroxobin time with Batroxobin REAGENT based on internal studies. The reproducibility CV% was found to be <5 % under consideration of the site-to-site variability.

Method Comparison

A comparison of the Batroxobin REAGENT with reagents from other manufacturers yielded correlation coefficients of 0.918 and 0.986.

Technical Assistance

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

Current Version of Application Sheets

Batroxobin REAGENT can be used in combination with various automated coagulation analyzers. Sysmex provides Reference Guides/Application Sheets for the coagulation analyzers listed in section "Materials Required but not Provided", page 3 under the dedicated link below:

sysmex-ifu.com/ag

As the manufacturer 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. Sysmex ensures that all products lots bearing the same IFU version number are compatible with the electronic labeling provided via sysmex-ifu.com.

References

1. Karapetian H. Reptilase time (RT). Methods Mol Biol 2013; 992:273-7.
2. Verhovsek M, Moffat KA, Hayward CP. Laboratory testing for fibrinogen abnormalities. Am J Hematol. 2008; 83:928-31.
3. Cunningham MT, Brandt JT, Laposata M, et al. Laboratory diagnosis of dysfibrinogenemia. Arch Pathol Lab Med 2002; 126:499-505.
4. CLSI. Collection, Transport, and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Hemostasis Assays. Approved Guideline – Fifth Edition. CLSI document **H21-A5** [ISBN 1-56238-657-3]. CLSI, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA, 2008.

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	CH REP	Authorized representative in Switzerland
	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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