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REF 1300036383

REAGENT 12 x 2 mL

IVD CE

HORIBA ABX SAS
Parc Euromédecine
Rue du Caducée
BP 7290
34184 Montpellier Cedex 4
FRANCE

Yumizen G FIB 2

- **Yumizen G200**
- **Yumizen G400/G400 DDi/G405**
- **Yumizen G800/G800h/G850h**
- **Yumizen G1500/G1550/G1500h/G1550h**

In vitro diagnostic reagent for quantitative determination of fibrinogen level by coagulometry.

Application Release [a] [b]

	Test name
Yumizen G1500/G1550	FIB Cl
Yumizen G1500h/G1550h	FIB Cl
Yumizen G800	FIB Cl
Yumizen G800h/G850h	FIB Cl
Yumizen G405	FIB Cl
Yumizen G400/G400 DDi	Fibrinogen
Yumizen G200	Fibrinogen

Intended Use [c]

For *in vitro* diagnostic use only.
Yumizen G FIB 2 is a fibrinogen reagent used for quantitative determination of fibrinogen levels in plasma.

Clinical Interest [d]

Fibrinogen is the final plasma protein of coagulation cascade.
Its presence and intact function has a vital importance for normal blood coagulation.
Fibrinogen, produced in the liver, contains three pairs of protein chains.
This soluble fibrinogen molecule is cleaved by thrombin to fibrin monomers.
The formed fibrin monomers compose the fibrin fibers and then the insoluble fibrin net, which is stabilized by factor XIIIa.

Method (1) [e]

The method of Clauss measures the clotting time after adding a high concentration of thrombin to diluted plasma.
The fibrinogen concentration of the plasma is inversely proportional to the clotting time.

Reagents [b]

Yumizen G FIB 2 is freeze-dried.
This reagent is a highly purified human thrombin in buffered medium with calcium ion and preservative.

Human thrombin	80 - 100 NIH U/mL
$CaCl_2$*$2H_2O$	< 5 g/L
Sodium azide	< 1 g/L

Yumizen G FIB 2 should be used according to this notice.
The manufacturer cannot guarantee its performance if used otherwise.

[a] Modification: new instrument added.
[b] Modification: chapter added.
[c] Modification: new leaflet form.
[d] Modification: § "Clinical Interest" changed.
[e] Modification: § "Method" changed.

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Handling [f]

1. Allow the vial to stand for at least 5 min (20 - 25°C) before reconstitution.
2. Reconstitute the content of one vial with 2 mL of deionized or purified water.
   Be careful when opening the rubber cap as some lyophilized material may be lost.
3. Replace the cap and gently invert the bottle (8 - 10 times) to disperse the contents (avoid foaming).
4. Allow the vial to stand for at least 30 min (20 - 25°C).
5. Mix thoroughly the vial once more before use.
6. **For automated analyzers only:** place the vial in the reagent holder without cap.

For optimal performance remove the reagent from the instrument after use, close the vial and store at 2 - 8°C.
An analysis of the control must be carried out on a daily basis at the same time as the patient samples, including each time a calibration is carried out.
The frequency of the controls depends on the laboratory requirements.
Each laboratory must establish the quality assurance procedures to be followed. These must conform to the current accreditation requirements and pertinent regulations.

Care should be taken not to interchange the caps with others products.

Calibrator [b]

Calibration Information
For the calibration, use the master curve provided or the calibrator:
Yumizen G CAL (1300036416) (not included, optional)
12 x 1 mL

Calibration Procedure for Semi-Automated Analyzers
(Yumizen G400/G400 DDi, Yumizen G200)
The calibration is a calibrator dilution based process that can be used with HORIBA analyzers (Yumizen G Line).

1. Prepare a serial dilution of the calibrator **Yumizen G CAL** as follows:

	Point 1	Point 2	Point 3	Point 4
Dilution rate	1/7	1/10	1/20	1/30
Yumizen G CAL	30 µL	20 µL	20 µL	10 µL
Yumizen G IMIDAZOL	180 µL	180 µL	380 µL	290 µL
Total volume	210 µL	200 µL	400 µL	300 µL

2. Run each diluted calibrator according to the *Semi-Automated Analyzers Procedure* chapter.
   Duplicated measurement is recommended.
3. Check the target value provided in the Yumizen G CAL enclosed annex.
   This value corresponds to the 1/10 dilution (Point 2).
4. Calculate the other values, and prepare the calibration curve as follows:

Dilution rate	Second	g/L
1/7	Result 1	
1/10	Result 2	X = target value in the enclosed annex.
1/20	Result 3	
1/30	Result 4	

5. Report the g/L and Second results in the calibration menu of your instrument.
6. Enter the data by using the "points" icon.
   Refer to the user manual of your instrument.

In case of determination by any other hemostasis analyzers, please follow the instructions of the manual.

Control [b]

For internal quality control, use:

- **Yumizen G CTRL I & II** (1300036412) (not included)
  5 x 1 mL + 5 x 1 mL

The frequency of controls and the confidence intervals should correspond to laboratory guidelines and country-specific directives. You should follow federal, state and local guidelines for testing quality control materials. The results must be within the range of the defined confidence limits. Each laboratory should establish a procedure to follow if the results exceed these confidence limits.

[f]Modification: § "Handling" changed.
[b]Modification: chapter added.

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Each control should be assayed daily and/or after a calibration.

Semi-Automated Analyzers Procedure [g]

Yumizen G FIB 2 can be used on semi-automated analyzers (Yumizen G Line), according to the following procedure.
Duplicated measurement is recommended.

1	Dilute the sample with **Yumizen G IMIDAZOL**.	1:10
2	Add the diluted sample into the cuvette.	100 µL
3	Incubate at 37°C.	2 min
4	Add the **Yumizen G FIB 2**.	50 µL
7	Start immediately the measurement at 640 nm.	~1 min

In case of determination by any other hemostasis analyzers, please follow the instructions of the manual.

Materials Required but not Provided [h]

- HORIBA analyzers (Yumizen G Line) are recommended.
- Calibrator (optional): **Yumizen G CAL** (1300036416)
- Control: **Yumizen G CTRL I & II** (1300036412)
- Buffer solution: **Yumizen G IMIDAZOL** (1300036385)
- Deionized or purified water
- Standard laboratory equipment

Specimen [i]

Plasma

- 3.2% (109 mmol/L) sodium-citrate anticoagulated plasma in primary tube.
- 3.2% (109 mmol/L) sodium-citrate, theophylline, adenosine and dipyramidole (CTAD) anticoagulated plasma in primary tube.

Mix the blood carefully.

Specimen centrifugation

Speed	Time	Temperature
1500 g	15 min	room temperature

Specimen Stability (2)

- At 20 - 25°C: 4 hours
- At 2 - 8°C: 4 hours
- Between -22°C to -26°C: 18 months (only the plasma)
- Between -72°C to -76°C: 20 months (only the plasma)

To thaw plasma:

1. Place the sample in a water bath: 5 min (not more) at 37°C.
2. Centrifuge the sample.

For additional information, please refer to CLSI document H21-A5.

Reference Range (3) [b]

Each laboratory should establish its own reference ranges.
The values given here are used as guidelines only.

Normal range	Mean	From	To
g/L	3.00	2.00	4.00

The therapeutic reference range may vary depending on the clinical indication.

Storage and Stability [j]

Stability before opening

Stable up to the expiry date on the label if stored at 2 - 8°C.

Stability after reconstitution

	20 - 25°C	2 - 8°C
Yumizen G FIB 2	3 days	7 days

Stability on board

Automated Analyzers

	15 - 19°C
Yumizen G FIB 2	7 days

[g]Modification: § "Semi-Automated Analyzers Procedure" changed.
[h]Modification: § "Material Required but not Provided" changed.
[i]Modification: § "Specimen" changed.
[b]Modification: chapter added.
[j]Modification: § "Storage and Stability" changed.

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Waste Management [b]

- Please refer to local legal requirements.
- This product contains less than 0.01% of sodium azide as a preservative. Sodium azide may react with lead and copper to form explosive metal azides.

General Precautions [k]

- This product is for professional *in vitro* diagnostic use only.
  For laboratory use.
- For prescription use only.
- This reagent is classified as non-hazardous in compliance with regulation (EC) N°.1272/2008.
- **Warning:** Human source material. Treat as potentially infectious. Each donor unit used in the preparation of this product has been tested by an FDA approved method and found non-reactive for the presence of HbsAg, HCV and antibody to HIV 1/2. Because no known test method can offer complete assurance that infectious agents are absent, the product should be handled in accordance with good laboratory practices using appropriate precautions. (4, 5).
- Do not pipette by mouth.
- Do not replenish the products.
- Do not swallow. Avoid contact with skin and mucous membranes.
- Observe the standard laboratory precautions for use.
- The product vials should be discarded after use. Disposal of all waste material should be in accordance with local guidelines.
- Please refer to the SDS associated with the product.
- Do not use the product if there is visible evidence of biological, chemical or physical deterioration.
- Do not use the product if the recommended storage conditions, including temperature, are not followed.
- User must be trained by a HORIBA representative before attempting to operate the device.
- It is the user's responsibility to verify that this document is applicable to the product used.
- For technical assistance, you can call +33 (0)4 67 14 15 16.
- Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the country in which the user and/or the patient is established.
- Using of third-party hemostasis analyzers may cause a risk of system un-harmonization.
- It is the user's responsibility to evaluate the risk of using a third-party hemostasis analyzers.

Performance

The performance data listed below are representative of performance on HORIBA systems.

Lot to Lot Variability [b]

The comparison of plasma samples tested consecutive lots of reagent shows that the lot to lot variability is within specification.

Sample Volume [b]

Instrument	Volume
Yumizen G1500/G1550	100 µL (of diluted sample)
Yumizen G1500h/G1550h	100 µL (of diluted sample)
Yumizen G800	100 µL (of diluted sample)
Yumizen G800h/G850h	100 µL (of diluted sample)
Yumizen G405	100 µL (of diluted sample)
Yumizen G400/G400 DDi	100 µL (of diluted sample)
Yumizen G200	100 µL (of diluted sample)

Precision

Repeatability (on automated analyzers) [l]

Repeatability according to the recommendations found in the CLSI (NCCLS), EP15-A3 (6), EP05-A3 (7), H30-A2 (8) (data obtained on internal study).

- 2 controls (10 runs)
- 1 specimen (20 runs)

	Mean value	CV %
Control specimen 1	2.54	2.106
Control specimen 2	1.26	1.292
Specimen	3.40	3.539

Maximum acceptance criteria (CV %): < 5%

[b]Modification: chapter added.
[k]Modification: § "General Precautions" changed.
[l]Modification: modification of repeatability.

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Reproducibility (on automated analyzers) [m]

Reproducibility according to the recommendations found in the CLSI (NCCLS), EP05-A3 (7), H30-A2 (8) (data obtained on internal study).

- 2 controls (10 runs)

	Mean value	CV %
Control specimen 1	2.19	4.276
Control specimen 2	1.22	4.358

Maximum acceptance criteria (CV %): < 10%

Measuring Range [b]

The measuring range is 1.0 - 5.0 g/L on the Yumizen G Line instruments.

Linearity [b]

The linearity range without extra dilution on HORIBA analyzers (Yumizen G Line) is 1.00 - 5.00 g/L.
In case of higher value (5.0 g/L) it is recommended to retest the sample with the dilution 1:20.
In case of lower value (1.0 g/L) it is recommended to retest the sample with the dilution 1:5.

Correlation [b]

Specimens are correlated with a commercial reagent taken as reference on HORIBA analyzers (Yumizen G Line).
Number of samples: 40

- Passing-Bablok regression: 1.000 (slope)
- Bland et Altman plot procedure: 0.006 (g/L difference)

Interferences (9) [b]

Haemoglobin: No significant influence is observed up to 6.80 g/L.
Triglycerides: No significant influence is observed up to an Intralipid® concentration (representative of lipemia) of 10.0 mmol/L.
Bilirubin: No significant influence is observed up to 340 µmol/L.
Heparin: No significant influence is observed up to 2.00 IU/mL.

Clinical Performance [b]

Clinical sensitivity and specificity, positive predictive value and negative predictive value are not commonly reported for this test.
This is largely attributed to the fact that this test is used for quantitative determination of fibrinogen levels in plasma for screening purposes.
To arrive at a diagnosis and a course of treatment, results from others routine coagulation tests should be used in conjunction with other diagnostic information and the attending health-care professional's evaluation of the patient's condition.

Precautions of Characteristics

The measurement data was generated during a performance evaluation and is not recommended as an acceptance criterion.

Reference

1. Clauss A. Gerinnungsphysiologische Schnellmethode zur Bestimmung des Fibrinogens. Acta Haematol (1957) **17** (4): 237-246.
2. Collection, Transport, and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Hemostasis Assays. Approved Guideline, 5th ed., CLSI (NCCLS) document H21-A5 (2008).
3. Samama M, Conard J, Horrelou MH, Lecompte T. Physiologie et exploration de l'hémostase. Ed.: Paris: Doin (1990), 123-137, 153-155.
4. Occupational Safety and Health Standards: bloodborne pathogens. (29 CFR 1910. 1030). Federal Register July 1, 1998; **6**: 267-280.
5. Council Directive (2000/54/EC). Official Journal of the European Communities. No. L262 from October 17, 2000: 21-45.
6. User Verification of Precision and Estimation of Bias. Approved Guideline, 3rd ed., CLSI (NCCLS) document EP15-A3 (2014).
7. Evaluation of Precision of Quantitative Measurement Procedures. Approved Guideline, 3rd ed., CLSI (NCCLS) document EP05-A3 (2014).
8. Procedure for the Determination of Fibrinogen in Plasma. Approved Guideline, 2nd ed., CLSI (NCCLS) document H30-A2 (2001).
9. Interference Testing in Clinical Chemistry. Approved Guideline, 2nd ed., CLSI (NCCLS) document EP07-A2 (2005).

[m]Modification: modification of reproducibility.
[b]Modification: chapter added.