BIOPHEN™ LMWH Control

REF 223701 CI CII 6 x 1 mL
REF 224301 CI 12 x 1 mL
REF 224401 CII 12 x 1 mL
REF 223001 C3 C4 6 x 1 mL
REF 223801 C3 12 x 1 mL
REF 224201 C4 12 x 1 mL

CE
IVD

Human plasmas for the quality control of
Low Molecular Weight Heparin (LMWH) measurements by anti-Xa method.

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INTENDED USE:

BIOPHEN™ LMWH Control kits consist of lyophilized human plasmas, spiked with Low Molecular Weight Heparin (LMWH) at various concentrations, for the quality control of LMWH assays.
They are titrated and optimized for the assay of LMWH with anti-Xa chromogenic assay (BIOPHEN™ HEPARIN 3 and 6).

SUMMARY AND EXPLANATION:

Technical:
These control plasmas are used for the quality control of LMWH anti-Xa chromogenic assays[1] in plasma (BIOPHEN™ Heparin 3, 6).
Clinical:
Heparins (UFH and LMWH) are currently used as an anticoagulant for curative or preventive indications. Measuring the heparin concentration in patients' plasma allows monitoring the therapy and adjusting drug dosage[2].

REAGENTS:

CI **Control I:** Lyophilized human plasma containing a titrated quantity of LMWH, of approximately 0.25 IU/mL (level I).
CII **Control II:** Lyophilized human plasma containing a titrated quantity of LMWH, of approximately 0.50 IU/mL (level II).
C3 **Control 3:** Lyophilized human plasma containing a titrated quantity of LMWH, of approximately 0.80 IU/mL (level 3).
C4 **Control 4:** Lyophilized human plasma containing a titrated quantity of LMWH, of approximately 1.20 IU/mL (level 4).
Control plasmas contain an antibiotic as preservative (ciprofloxacin).
The control concentrations may vary slightly from one batch to another. For the assay, see the exact values indicated on the flyer provided with the kit used.

BIOPHEN™ LMWH Control Low
REF **223701** ➔ CI CII **6 vials of 1 mL**
BIOPHEN™ LMWH Control Low CI
REF **224301** ➔ CI **12 vials of 1 mL**
BIOPHEN™ LMWH Control Low CII
REF **224401** ➔ CII **12 vials of 1 mL**
BIOPHEN™ LMWH Control Plasma
REF **223001** ➔ C3 C4 **6 vials of 1 mL**
BIOPHEN™ LMWH Control C3
REF **223801** ➔ C3 **12 vials of 1 mL**
BIOPHEN™ LMWH Control C4
REF **224201** ➔ C4 **12 vials of 1 mL**

WARNINGS AND PRECAUTIONS:

- Some reagents provided in these kits contain materials of human origin. Whenever human plasma is required for the preparation of these reagents, approved methods are used to test the plasma for the antibodies to HIV 1, HIV 2 and HCV, and for hepatitis B surface antigen, and results are found to be negative. However, no test method can offer complete assurance that infectious agents are absent. Therefore, users of reagents of these types must exercise extreme care in full compliance with safety precautions in the manipulation of these biological materials as if they were infectious.
- Waste should be disposed of in accordance with applicable local regulations.
- Use only the reagents from the same batch of kits.
- In order to improve stability, reagents must be closed with their original screw caps following each use.
- Reagents must be handled with care, in order to avoid any contamination during use.
- It is recommended to homogenize each vial before use, in order to have a good reproducibility, all the time.
- The stability studies at 30°C show that the reagents can be shipped at room temperature without damage.
- This device of *in vitro* diagnostic use is intended for professional use in the laboratory.

REAGENT PREPARATION:

Gently remove the freeze-drying stopper, to avoid any product loss when opening the vial.

CI CII C3 C4 Reconstitute the contents of each vial with exactly **1 mL of distilled water**.
Shake vigorously until complete dissolution while avoiding formation of foam and load it directly on the analyzer following application guide instruction.
For manual method, allow to stabilize for 10 minutes at room temperature (18-25°C), homogenize before use.

This plasmatic reagent can be more or less turbid after reconstitution. This turbidity is mainly due to plasma lipids that, after freeze-drying, become "less" soluble and may form a slight deposit. If necessary, let each vial stabilize 10 minutes at room temperature and shake before use.

STORAGE AND STABILIY:

Unopened reagents should be stored at 2-8°C in their original packaging. Under these conditions, they can be used until the expiry date printed on the kit.

CI CII C3 C4 Reagent stability after reconstitution, free from any contamination or evaporation, and stored closed, is of:

- **7 days** at 2-8°C.
- **48 hours** at room temperature (18-25°C).
- **Do not freeze.**
- **Stability on board of the analyzer: see the specific application.**

REAGENTS AND MATERIALS REQUIRED BUT NOT PROVIDED:

Reagents:
- Distilled water.

Materials:
- Calibrated pipettes.

TRACEABILITY:

The value assignment of controls is related to the corresponding International Standard for LMWH from NIBSC in force.

QUALITY CONTROL:

BIOPHEN™ LMWH Control (levels I, II, 3 and 4) kits are used for the quality control of LMWH assays in plasma by anti-Xa chromogenic methods, such as BIOPHEN™ Heparin 3, 6 (221003/221006).
The target values are determined using BIOPHEN™ Heparin 3, 6 and multi-instruments tests.
The use of quality controls serves to validate method compliance, along with between-series assay homogeneity for a given batch of reagents.
Include the quality controls with each series, as per good laboratory practice, to validate the test.
If the controls fall outside of the acceptable range, the series of assays must be invalidated, and the analyses repeated. Check all system parameters before repeating the series.

The following example shows the Low Molecular Weight Heparin (LMWH) concentrations indicated for one lot of BIOPHEN LMWH Control Low (obtained on water bath, ACL and/or STA):

LMWH Control Low	LMWH (IU/ml)	Acceptance range (IU/ml)	Intra assay		Inter assay	
			N	CV	N	SD
Level I	0.25	0.17-0.33	10	1.9	43	0.02
Level II	0.50	0.40-0.60	10	0.9	43	0.03
Level 3	0.79	0.69-0.89	38	1.9	69	0.03
Level 4	1.25	1.10-1.40	38	1.5	69	0.05

The control C3 has usually a concentration of 0.80 ± 0.10 IU/mL.
The control C4 has usually a concentration of 1.20 ± 0.15 IU/mL.
The control CI has usually a concentration of 0.25 ± 0.10 IU/mL.
The control CII has usually a concentration of 0.50 ± 0.15 IU/mL.

The currently available anti-Xa methods, used for the measurement of heparins and their analogues in plasma, offer a sensitivity threshold of about 0.05 IU/mL.

LIMITATIONS:

- If the controls are used under measurement conditions other than those validated by HYPHEN BioMed, the test results may vary. The laboratory is responsible for validating the use of these controls in its own analytical system.
- Any reagent presenting an unusual appearance or showing signs of contamination must be rejected.

REFERENCES:

1. "Heparin activity", UW Medicine, Clinical assay interference and limitations.
2. Wood, Weitz, Low molecular weight heparins, New England Journal of Medicine, 337:10, 688-698 (1997).
3. Gray E. *et al.* Heparin and low-molecular-weight heparin. Thromb Haemost. 2008, 99:807-818.
4. Richardson J.H. and Backley W.E. Eds. Bios. Microbiological and Biomedical laboratories. US. Dept. and Human Services, Public Health Service, HHS publication (CDC) 84-8395, Washington, D.C. (1984).
5. National Committee for Clinical Laboratory St Specifications for reagent water used in the clinical lab NCCLS Approved Standard: ASC-3.
6. Westgard J.O., Barry P.L. Cost effective Quality Managing for managing the quality and the Productivity of Analytical AACC Press (1986).
7. Leirozovicz A., Hought M.C, Chapuis FX, Samama, Boissel JP Low molecular weight heparin in prevention of perioperative thrombosis. Br Med. J 305, 913 (1992).
8. Hemker H.C., Beguin S., The mode of action of heparin in vitro and in vivo. In; heparin platelet polysaccharides Plenum Press. New York 221-230 (1992).

SYMBOLS:

Symbols used, and signs listed in the ISO 15223-1 standard, see Symbol definitions document.

Changes compared to the previous version.