



WHO International Standard
The 3rd International Standard for Low Molecular Weight Heparin
NIBSC code: 11/176
Instructions for use
(Version 1.0, Dated 27/06/2013)

1. INTENDED USE

The 3rd International Standard for Low Molecular Weight Heparin, consists of ampoules, coded 11/176, containing aliquots of a freeze-dried material prepared from porcine mucosa. This preparation was established as the 3rd International Standard for Low Molecular Weight Heparin by the Expert Committee on Biological Standardisation of the World Health Organisation in 2012. It is intended for anti-Xa and anti-IIa potency estimation of low molecular weight heparin.

2. CAUTION

This preparation is not for administration to humans or animals in the human food chain.

The material is not of human or bovine origin. As with all materials of biological origin, this preparation should be regarded as potentially hazardous to health. It should be used and discarded according to your own laboratory's safety procedures. Such safety procedures should include the wearing of protective gloves and avoiding the generation of aerosols. Care should be exercised in opening ampoules or vials, to avoid cuts.

3. UNITAGE

The standard was calibrated by 22 laboratories from 13 countries against the 2nd International Standard for Low Molecular Weight Heparin (01/608). Anti-Xa and anti-IIa chromogenic methods were used in the study. Twenty-two laboratories performed anti-Xa assays (100 assays in total) and anti-IIa assays (80 assays in total). The following potencies were assigned based on the geometric mean of all the valid assay results:

1068 International Units of anti-Xa activity per ampoule
342 International Units of anti-IIa activity per ampoule

Uncertainty: the assigned unitage does not carry an uncertainty associated with its calibration. The uncertainty may therefore be considered to be the variance of the ampoule content and was determined to be +/- 0.1%.

4. CONTENTS

Country of origin of biological material: France

The mean weight of liquid content of 879 check weight ampoules was 1.0068g, with a coefficient of variation of 0.097%. The mean weight of the freeze-dried plug was 9.22mg, with a coefficient of variation of 1.39%. The mean residual moisture was 3.41%.

5. STORAGE

Unopened ampoules should be stored in the dark at or below -20°C.

Please note: because of the inherent stability of lyophilized material, NIBSC may ship these materials at ambient temperature.

6. DIRECTIONS FOR OPENING

DIN ampoules have an 'easy-open' coloured stress point, where the narrow ampoule stem joins the wider ampoule body. Various types of ampoule breaker are available commercially. To open the ampoule, tap the ampoule gently to collect material at the bottom (labelled) end and follow manufacturers instructions provided with the ampoule breaker.

7. USE OF MATERIAL

No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution

Allow ampoules to warm to room temperature. Open ampoule, taking care to ensure that all material is in the lower part, and reconstitute with 1.0 mL of distilled water.

Low molecular weight heparin is reasonably stable and aliquots of the reconstituted solution, at a suitable concentration (eg 100 anti-Xa IU/mL) could be stored frozen at -40°C or below for up to 6 months. Once reconstituted, diluted and/or aliquoted, users should determine the stability of the material according to their own method of preparation, storage and use.

8. STABILITY

Reference materials are held at NIBSC within assured, temperature-controlled storage facilities. Reference Materials should be stored on receipt as indicated on the label.

NIBSC follows the policy of WHO with respect to its reference materials. It is the policy of the WHO not to assign an expiry date to their international reference materials. They remain valid with the assigned potency and status until withdrawn or amended. Accelerated degradation studies for this preparation have, to date shown no loss in activity.

9. REFERENCES

N/A

10. ACKNOWLEDGEMENTS

All participants in the international collaborative study. We are also grateful to the following manufacturers for their kind donation of low molecular weight heparin samples, two of which were used as candidates for the collaborative study:

Leo Pharmaceutical Products Ltd
Laboratories Rovi SA
Opocrin SpA
Sanofi Aventis
Pfizer
Glaxo Smith Kline

11. FURTHER INFORMATION

Further information can be obtained as follows;

This material: enquiries@nibsc.org

WHO Biological Standards:

<http://www.who.int/biologicals/en/>

JCTLM Higher order reference materials:

<http://www.bipm.org/en/committees/jc/jctlm/>

Derivation of International Units:

http://www.nibsc.org/standardisation/international_standards.aspx

Ordering standards from NIBSC:

<http://www.nibsc.org/products/ordering.aspx>

NIBSC Terms & Conditions:

http://www.nibsc.org/terms_and_conditions.aspx

12. CUSTOMER FEEDBACK

Customers are encouraged to provide feedback on the suitability or use of the material provided or other aspects of our service. Please send any comments to enquiries@nibsc.org

13. CITATION

In all publications, including data sheets, in which this material is referenced, it is important that the preparation's title, its status, the NIBSC code number, and the name and address of NIBSC are cited and cited correctly.

14. MATERIAL SAFETY SHEET



Classification in accordance with Directive 2000/54/EC, Regulation (EC) No 1272/2008: Not applicable or not classified

Physical and Chemical properties	
Physical appearance: White freeze-dried solid	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: Yes	Irritant: Yes
Flammable: No	Handling: See caution, Section 2
Other (specify): Contains material of porcine origin	
Toxicological properties	
Effects of inhalation:	Not established, avoid inhalation
Effects of ingestion:	Not established, avoid ingestion
Effects of skin absorption:	Not established, avoid contact with skin
Suggested First Aid	
Inhalation:	Seek medical advice
Ingestion:	Seek medical advice
Contact with eyes:	Wash with copious amounts of water. Seek medical advice
Contact with skin:	Wash thoroughly with water.
Action on Spillage and Method of Disposal	
Spillage of ampoule contents should be taken up with absorbent material wetted with an appropriate disinfectant. Rinse area with an appropriate disinfectant followed by water. Absorbent materials used to treat spillage should be treated as biological waste.	

15. LIABILITY AND LOSS

In the event that this document is translated into another language, the English language version shall prevail in the event of any inconsistencies between the documents.

Unless expressly stated otherwise by NIBSC, NIBSC's Standard Terms and Conditions for the Supply of Materials (available at http://www.nibsc.org/About_Us/Terms_and_Conditions.aspx or upon request by the Recipient) ("Conditions") apply to the exclusion of all other terms and are hereby incorporated into this document by reference. The Recipient's attention is drawn in particular to the provisions of clause 11 of the Conditions.

16. INFORMATION FOR CUSTOMS USE ONLY

Country of origin for customs purposes*: United Kingdom * Defined as the country where the goods have been produced and/or sufficiently processed to be classed as originating from the country of supply, for example a change of state such as freeze-drying.
Net weight: 9.22 mg
Toxicity Statement: Toxicity not assessed
Veterinary certificate or other statement if applicable. Attached: No

17. CERTIFICATE OF ANALYSIS

NIBSC does not provide a Certificate of Analysis for WHO Biological Reference Materials because they are internationally recognised primary reference materials fully described in the instructions for use. The reference materials are established according to the WHO Recommendations for the preparation, characterization and establishment of international and other biological reference standards http://www.who.int/bloodproducts/publications/TRS932Annex2_Inter_bi_olefstandardsrev2004.pdf (revised 2004). They are officially endorsed by the WHO Expert Committee on Biological Standardization (ECBS) based on the report of the international collaborative study which established their suitability for the intended use.