Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
3rd International Standard for Antithrombin, Plasma
NIBSC code: 08/258
Instructions for use
(Version 2.0, Dated 31/03/2014)

1. INTENDED USE

The 3rd International Standard for Antithrombin, Plasma, consists of ampoules, coded 08/258, containing approximately 1ml aliquots of normal human plasma, freeze dried. This preparation was established in 2010 as the 3rd International Standard for Antithrombin, Plasma, by the Expert Committee on Biological Standardization of the World Health Organization, and is primarily intended for calibration of antithrombin functional activity and antigen levels in secondary plasma reference preparations.

2. CAUTION

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

The preparation contains material of human origin, and either the final product or the source materials, from which it is derived, have been tested and found negative for HBsAg, anti-HIV and HCV RNA. 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 24 laboratories in 13 countries against the 2nd IS for Antithrombin, Plasma, 93/768, using both activity (heparin co-factor) and antigen assays. It has been assigned with the following potencies: function: 0.95 IU per ampoule; antigen: 0.96 IU/ampoule. Details of the value assignment procedure are avaliable in WHO document number WHO/BS/10.2146.

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 +/- 0.16%.

4. CONTENTS

Country of origin of biological material: United Kingdom.
Plasma from 45 donors, collected in CPD-adenine from the Welsh Blood Service was buffered with HEPES to 0.05 M, pooled and distributed in 1ml quantities into ampoules, filled and freeze dried under conditions used for International Biological Standards1. Each individual donation was tested and found negative for anti-HIV 1/2, HBsAg and anti-hepatitis C.

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 manufactures 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 lower part, and reconstitute with 1.0ml distilled water using gentle agitation. Transfer the contents to a plastic tuben store on melting ice and use as soon as possible upon reconstitution (see below).

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 ammended.

Accelerated degradation studies, which involves potency estimation of ampoules stored at elevated temperatures relative to ampoules stored at below -150°C, have shown that the Standard is very stable. Using the heparin co-factor assay, the predicted loss of activity when stored at -20ºC is 0.003% per year, and using antigen measurment no loss in activity could be predicted. The accelerated degradation study and real time monitoring will continue for the lifetime of the standard. These studies have shown that when stored at -20°C or below the assigned values remain valid until the material is withdrawn or replaced.

Users who have data supporting any deterioration in the characteristics of any reference preparation are encouraged to contact NIBSC.

On bench Stability: A study in one laboratory has shown that he reconstituted Standard was stable for upto four hours when stored on melting ice. It is not recommended to freeze the standard after reconstitution for subsequent use.

9. REFERENCES

1.Campbell P J. J Biol Standardisation 1974, 2, 259 - 267.

10. ACKNOWLEDGEMENTS

All participants in the International collaborative study and the support of the Plasma Coagulation Inhibitors Sub-committee of the Interntional Society on Thrombosis and Haemostasis/ Scietnific and Standardisation Committee.

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

National Institute for Biological Standards and Control,
Potters Bar, Hertfordshire, EN6 3QG. T +44 (0)1707 641000, nibsc.org
WHO International Laboratory for Biological Standards,
UK Official Medicines Control Laboratory

World Health Organization

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: Freeze-dried powder		Corrosive:	No
Stable:	Yes	Oxidising:	No
Hygroscopic:	Yes	Irritant:	Yes
Flammable:	No	Handling:	See caution, Section 2
Other (specify):	Contains material of human 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: 0.098g
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_biolefstandardsrev2004.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.

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