



**WHO International Standard
WHO 2nd International Standard von Willebrand Factor,
Concentrate
NIBSC code: 09/182
Instructions for use
(Version 4.0, Dated 05/11/2019)**

1. INTENDED USE

The WHO 2nd International Standard (IS) for von Willebrand Factor, Concentrate was established by the Expert Committee on Biological Standardisation of the World Health Organisation in October 2010. The preparation consists of glass sealed ampoules (coded 09/182) containing 1 ml aliquots of von Willebrand factor concentrate, freeze-dried. The WHO 2nd IS is intended to be used for the estimation of von Willebrand factor in therapeutic concentrates via the calibration of working standards, such as manufacturers' "in house" standards. The WHO 2nd IS has assigned values for the following analytes:

von Willebrand factor: antigen - VWF:Ag
von Willebrand factor: ristocetin cofactor - VWF:RCo
von Willebrand factor: collagen binding - VWF:CB

Further details on the preparation and the collaborative study can be found in the WHO document WHO/BS/10.2147.

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 assigned values of the WHO 2nd IS were determined by assay relative to the WHO 1st IS VWF Concentrate (00/514) and the WHO 6th IS FVIII/VWF Plasma (07/316) in an international collaborative study involving 45 laboratories in 12 countries. The overall mean values assigned to each ampoule of the WHO 2nd IS are as follows:

VWF:Ag 10.7 International Units per ampoule
VWF:RCo 9.2 International Units per ampoule
VWF:CB 10.3 International Units per ampoule

4. CONTENTS

Country of origin of biological material: United Kingdom.
The WHO 2nd IS was prepared at the National Institute for Biological Standards and Control from VWF Concentrate product used for therapy. The formulated product was kept at 4 °C throughout distribution into 10,000 glass ampoules and then freeze-dried under conditions used for international biological standards (1). The mean liquid filling weight of 461 check-weight ampoules was 1.0078 g with a coefficient of variation of 0.167%. Estimates of residual moisture after freeze-drying gave a mean value of 0.43%.

5. STORAGE

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

Dissolve the contents of each ampoule of the WHO 2nd IS by adding 1.0 ml of distilled or deionised water, using gentle shaking, then transfer the contents to a plastic tube. Although studies have shown the reconstituted standard to be stable for up to 4 hours when stored on melting ice it is recommended that assays should be carried out as soon as possible once reconstitution is complete. The use of frozen aliquots of the WHO 2nd IS is not recommended.

8. STABILITY

Reference materials are held at NIBSC within assured temperature-controlled storage facilities and they should be stored on receipt as indicated on the label. It is the policy of WHO not to assign an expiry date to their international reference materials. Accelerated degradation studies have indicated that this material is suitably stable, when stored at -20 °C or below, for the assigned values to remain valid until the material is withdrawn or replaced. These studies have also shown that the material is suitably stable for shipment at ambient temperature without any effect on the assigned values. Users who have data supporting any deterioration in the characteristics of any reference preparation are encouraged to contact NIBSC.

9. REFERENCES

1 Campbell PJ. Procedures used for the production of biological standards and reference preparations. Journal of Biological Standardization (1974) 2, 259-267.

10. ACKNOWLEDGEMENTS

Are made to the manufacturers for supplying candidate materials (Laboratoire Francais du Fractionnement et des Biotechnologies, Lille, France; Octapharma Pharmazeutika Produktionsges.m.b.H., Vienna, Austria); to the participants in the collaborative study and to the SSC/ISTH sub-committee on von Willebrand factor.

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.

establishment of international and other biological reference standards http://www.who.int/bloodproducts/publications/TRS932Annex2_Inter_biol_efstandardsrev2004.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.

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: No
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: 0.015 g
Toxicity Statement: Non-toxic
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