



**WHO International Standard  
5th INTERNATIONAL STANDARD FACTOR VIII AND VON  
WILLEBRAND FACTOR IN PLASMA  
NIBSC code: 02/150  
Instructions for use  
(Version 3.0, Dated 17/03/2008)**

### 1. INTENDED USE

The WHO 5th International Standard for Factor VIII and von Willebrand Factor in plasma was established by the Expert Committee on Biological Standardization of the World Health Organization in November 2003. The preparation consists of ampoules (coded 02/150) containing 1 ml aliquots of pooled fresh human plasma, freeze-dried. The International Standard (IS) is calibrated for the following activities:

Factor VIII Clotting activity	- FVIII:C
Factor VIII Antigen	- FVIII:Ag
von Willebrand Factor Ristocetin Co-factor function	- VWF:RCo
von Willebrand Factor Antigen	- VWF:Ag
von Willebrand Factor Collagen Binding function	- VWF:CB

The standard is intended to be used for the estimation of the above parameters in human plasma. For the estimation of FVIII:C in therapeutic concentrates it is recommended that the current WHO International Standard Factor VIII Concentrate is used. For the estimation of VWF:Ag and VWF:RCo in therapeutic concentrates it is recommended that the WHO 1st International Standard von Willebrand Factor Concentrate (00/514) is used. The WHO 5th International Standard Factor VIII / von Willebrand Factor, Plasma (02/150) should not be used for the estimation of VWF:CB in therapeutic concentrates.

### 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 for FVIII:C, FVIII:Ag, VWF:Ag and VWF:RCo were determined by comparison against the 4th International Standard Factor VIII / von Willebrand Factor in Plasma (97/586) in an international collaborative study involving 37 laboratories in 13 countries. The overall mean values assigned to each ampoule of the 5th IS are as follows:

FVIII:C	0.68 IU/ampoule
FVIII:Ag	0.94 IU/ampoule
VWF:RCo	0.78 IU/ampoule
VWF:Ag	0.91 IU/ampoule
VWF:CB	0.94 IU/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 +/- 0.07%.

### 4. CONTENTS

Country of origin of biological material: United Kingdom.  
The International Standard was prepared at the National Institute for Biological Standards and Control in June 2002 from a pool of 5.8 litres of plasma collected from 22 donors. Blood was collected into CPD-A

anticoagulant (63 ml CPD-A + 420 ml blood) and each unit underwent leuco-depletion by filtration. After the first centrifugation, the individual plasma donations were buffered by addition of HEPES to a final concentration of 0.04 mol/l. The plasmas were then centrifuged again and stored overnight at 2-8 °C before being pooled. The pooled plasma was kept at 4 °C throughout distribution into approximately 5,500 ampoules, then freeze-dried under conditions used for international biological standards (1). The mean liquid filling weight was 1.0068 g (range 1.0052 - 1.0087 g) with a coefficient of variation of 0.07 %. Estimates of residual moisture after freeze-drying and secondary desiccation gave a mean value of 0.76 %.

### 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 total contents of each ampoule of the standard by adding 1.0 ml of distilled water, using gentle shaking, then transfer contents to a plastic tube. Although studies have shown the reconstituted standard to be stable for up to 2 hours when kept at 4 °C or at room temperature (20 °C), it is recommended that assays of FVIII:C and VWF:RCo be carried out as soon as possible after reconstitution. Unused material may be frozen and thawed once only, for subsequent measurements of FVIII:Ag and VWF:Ag subject to validation by the user. It is not recommended that frozen aliquots are used for FVIII:C, VWF:RCo and VWF:CB measurements.

### 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.

### 9. REFERENCES

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

### 10. ACKNOWLEDGEMENTS

Are made to Mr M Haines, North London Blood Transfusion Centre, Colindale, for arranging the supply of plasma, and to all the participants in the collaborative study.

### 11. FURTHER INFORMATION

Further information can be obtained as follows;

This material: [enquiries@nibsc.org](mailto: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](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](http://www.nibsc.org/terms_and_conditions.aspx)



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**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: Solid	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: No adverse effects reported for this material	
Effects of ingestion: No adverse effects reported for this material	
Effects of skin absorption: No adverse effects reported for this material	
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.

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**16. INFORMATION FOR CUSTOMS USE ONLY**

<b>Country of origin for customs purposes*:</b> 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.
<b>Net weight:</b> 0.085 g
<b>Toxicity Statement:</b> Non-toxic
<b>Veterinary certificate or other statement</b> if applicable.
<b>Attached:</b> No