Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
1st INTERNATIONAL STANDARD FOR BLOOD COAGULATION FACTOR V, PLASMA, HUMAN
NIBSC code: 03/116
Instructions for use
(Version 3.0, Dated 30/11/2012)

1. INTENDED USE

The 1st International Standard for Factor V, Plasma, Human consists of ampoules, coded 03/116, containing approximately 1 mL aliquots of pooled normal human plasma, freeze-dried. This preparation was established in 2005 as the 1st International Standard for Factor V, Plasma, Human by the Expert Committee on Biological Standardization (ECBS) of the World Health Organization.

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 for Factor V clotting activity in an international collaborative study involving 22 laboratories from 11 countries. It was agreed that the assigned value should be calculated as the geometric mean of the 13 estimates obtained relative to locally collected fresh normal plasma pools (total number of donors = 512). The assigned value for Factor V clotting activity is 0.74 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 +/- 0.05 %.

4. CONTENTS

Country of origin of biological material: United Kingdom.
The WHO 1st IS for Factor V, Plasma, Human was prepared from a plasma pool derived from 26 normal healthy donors (United Kingdom Blood Service, North London Blood Transfusion Centre). Blood was collected using conventional venepuncture into CPD-adenine anticoagulant at a nominal ratio of 63 mL anticoagulant to 450 mL whole blood. The donations underwent leuko-filtration followed by two centrifugation steps after which the plasma was frozen rapidly and stored at -70 ºC until the day of ampoule filling. Individual donations were tested and found negative for HBsAg, antibodies to HIV-1 and -2 and antibodies to HCV. The donations were also tested as mini-pools and found negative for the presence of HCV RNA using a PCR technique. On the morning of the fill the plasma units were thawed in a waterbath at 37 ºC and pooled. A buffering agent HEPES (N-[2-Hydroxyethyl]piperazine-N'-[2-ethanesulfonic acid) was added to the pooled plasma at a final concentration of 40 mmol/L.

The pooled plasma was distributed into glass ampoules at a mean fill weight of 1.0052 g (range 1.0038 - 1.0066 g) and coefficient of variation of 0.05%. Each ampoule underwent freeze-drying and secondary desiccation before being sealed in an atmosphere of dry nitrogen gas and placed into storage at -20 °C (1).

5. STORAGE

Unopened ampoules should be stored in the dark at -20 ºC 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
To reconstitute, allow ampoules to warm to room temperature. Open the ampoule following the directions given in section 6 taking care to ensure that all material is in the lower part, and reconstitute with 1.0 mL distilled water. Stand for 10 minutes at room temperature to allow complete disssolution of the material. It is recommended that the reconstituted standard is transferred to a stoppered plastic tube and stored on melting ice until used.

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 P J (1974) J Biol Standardization 2, 249-267.

10. ACKNOWLEDGEMENTS

The colaborative study participants are gratefully acknowledged.

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

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

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: 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: 0.084 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 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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