Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

**Working Standard**
**2nd NIBSC Working Standard for FEIBA**
**NIBSC code: 13/242**
**Instructions for use**
**(Version 2.0, Dated 26/07/2016)**

**This material is not for in vitro diagnostic use.**

## 1. INTENDED USE

The 2nd NIBSC Working Standard for FEIBA Concentrate, consists of ampoules coded 13/242 and was established by National Institute for Biological Standards and Control (NIBSC) in December 2014. Each ampoule contains aliquots of freeze-dried concentrate of plasma derived human activated prothrombin complex concentrate (FEIBA). This standard is primarily intended to be used for measurement of FEIBA potency in FEIBA 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

This standard was calibrated in a collaborative study involving five expert laboratories, relative to the previous 1st NIBSC Working Standard for FEIBA (06/172), giving an assigned potency (based on DAPTTIN method) of:

**23.1 Units per ampoule**

## 4. CONTENTS

Country of origin of biological material: Austria.
The 2nd NIBSC Working Standard for FEIBA Concentrate was prepared using 4 batches of plasma-derived FEIBA concentrate bulks, which had undergone a 2 step viral reduction step performed by the manufacturer. After reconstitution and dilution using a citrate based buffer (137mM NaCl, 13.6mM Tri-sodium citrate, pH 7.0) containing 0.5% (w/v) clinical grade human albumin, the formulated material was filled and lyophilised in approximately 20,000 sealed glass ampoules at NIBSC, according to the criteria for international biological standards[1], with a mean fill weight from check weights of 1.0076g, (range of 1.0035 - 1.0145g); the coefficient of variation (CV) of fill was 0.16%. The mean residual moisture of the lyophilised material was < 0.44%. The mean oxygen content in the ampoule head space was 0.33%. All donations used to manufacture the FEIBA bulks and the human albumin were tested and found to be negative for Hepatitis B surface antigen, antibodies to HIV-1 and -2, and HCV RNA.

## 5. STORAGE

Unopened ampoules should be stored at or below -20°C. Unused material following reconstitution must be discarded and not frozen for later use.
**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.
The total contents of the ampoule should be reconstituted at room temperature with 1.0 mL distilled water, dissolved by gentle swirling, then transferred immediately to a plastic tube and should be allowed to stand for an incubation period of 35 ± 5 minutes at ambient temperature, just prior to assay.

## 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.

Accelerated degradation studies (6 months storage) have shown that this standard is extremely stable, both when stored at -20°C and at mailing temperatures. Predicted loss in FEIBA activity per year, when stored at -20°C, was found to be negligible (0.00%).

NIBSC follows the policy of WHO with respect to its reference materials.

## 9. REFERENCES

1. Campbell, PJ. International biological standards and reference preparations. II: Procedures used for the production of biological standards and reference preparations. J Biol Standardisation 1974, 2, 259-267.

## 10. ACKNOWLEDGEMENTS

We are grateful to Baxter Bioscience (Vienna, Austria) for the supply of FEIBA reagents & FEIBA-bulk concentrates used in the production of this standard, Technoclone (Vienna, Austria) for the Dapttin Reagent for the study and to the staff of Standards Division (NIBSC) for ampoule filling and freeze-drying. The participation of Paul-Ehrlich-Institut (Langen, Germany), AGES Medizinmarktaufsicht (Vienna, Austria), CBER-FDA (Bethesda, USA) and Baxter Bioscience (Vienna, Austria) in the calibration exercise is 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

## 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

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

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: | 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** |
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| 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.<br>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

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|---|
| **Country of origin for customs purposes*:** United Kingdom<br>* 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:** 0.033g |
| **Toxicity Statement:** Non-toxic |
| **Veterinary certificate or other statement** if applicable**.**<br>**Attached:** No |

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