



**WHO Reference Panel**  
**1st International Reference Panel for Lupus Anticoagulant**  
**NIBSC code: 13/172**  
**Instructions for use**  
**(Version 1.0, Dated 23/02/2015)**

### 1. INTENDED USE

The 1<sup>st</sup> International Reference Plasma Panel for Lupus Anticoagulant, 13/172, is a set of three freeze-dried human plasmas: Lupus Anticoagulant (LA) negative plasma (12/148), a moderate LA positive plasma (12/150) and a strong LA positive plasma (12/152). The intended use of this set of reference materials is for validation of lupus anticoagulant assay methods whenever clinical laboratories have the need to set up new methods or change in instruments and operators or for trouble shooting. This panel was established in October 2014 as the 1st International Reference Plasma Panel for Lupus anticoagulant by the Expert Committee on Biological Standardization (ECBS) of the World Health Organization.

The ECBS report is available from the WHO ([www.who.int/biologicals](http://www.who.int/biologicals)). Document number: WHO/BS/2014.2244

[http://apps.who.int/iris/bitstream/10665/137474/1/WHO\\_BS\\_2014.2244\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/137474/1/WHO_BS_2014.2244_eng.pdf?ua=1)

### 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

Values will not be assigned to this panel. The activities of the reference plasma panel were assessed by 10 laboratories using dilute Russell's Viper venom time (dRVVT), 13 laboratories using activated partial thromboplastin time (APTT), 4 laboratories using silica clotting time (SCT), 2 laboratories using dilute Prothrombin time (dPT), 1 laboratory using kaolin clotting time (KCT), activated seven lupus anticoagulant assay (ASLA) and Taipan snake venom time (TSVT). The laboratories performed screening tests and, where appropriate, confirmation and mixing studies for each method. Information on the methods used and results obtained from the evaluation study is detailed in the ECBS report.

### 4. CONTENTS

Country of origin of biological material: United Kingdom and USA. The panel consisting of 3 preparations was freshly prepared at NIBSC from frozen platelet poor normal plasma and platelet poor LA positive plasma. The LA negative pool was made using plasma from a total of 10 donors and the LA positive pool was made using plasma from a total of 17 donors. Each pool had HEPES added to a final concentration of 0.8% w/v. The LA positive pool was diluted 1:1 in LA negative plasma to generate sample C (strong positive pool) and 1:3.3 to generate sample B (moderate positive). The remaining negative plasma served as sample A (lupus negative). All 3 preparations were filled and freeze-dried into siliconised ampoules at NIBSC (1). Stocks were sufficient to generate approximately 2500 ampoules of each preparation. Each sealed, siliconised glass 3 ml DIN ampoule contains approximately 1.0 ml of freeze-dried human plasma.

### 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 the lower part, and reconstitute with 1 mL of distilled water. After reconstitution, please store the material as indicated in Section 8.

### 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. Accelerated degradation studies of 12/148, 12/150 and 12/152 have been initiated. Lupus anticoagulant tests cannot be used to assess stability as a quantitative measurement is not possible. Therefore, loss of potency of FV, FVIII and FVII is used to indicate the stability of the plasma. The stability studies are on-going and data after 1 year indicate that the materials are stable, with <0.2% loss per year at the storage temperature of -20°C.

On-bench stability was assessed using DRVVT. The results show that the status of the materials do not alter over a 3 hour period, with 12/148 remaining negative throughout, 12/150 and 12/152 remaining positive. The results for the screen and confirm clotting times and the screen/confirm ratio at all time-points assess agree well with those of the freshly reconstituted ampoules, indicating that this material is stable for at least 3 hours when kept on ice.

### 9. REFERENCES

1. Campbell PJ (1974). J Biol Standardization. 2, 249 -267

### 10. ACKNOWLEDGEMENTS

The participants of the study, Ian Jennings (UK NEQAS) and Ian Mackie (University College London) for scientific advice, Beverley Hunt and Kiran Parmar (St Thomas' Hospital, London) for collection of patient plasma.

The support of the Plasma Coagulation Inhibitors subcommittee of the SSC of the ISTH

### 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)

## 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](mailto: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](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

<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> approximately 0.08 g in each ampoule
<b>Toxicity Statement:</b> Toxicity not assessed
<b>Veterinary certificate or other statement</b> if applicable.
<b>Attached:</b> 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\\_biol\\_efstandardsrev2004.pdf](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.