Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

Non WHO Reference Material
1st British Reference Plasma Panel for Lupus Anticoagulant
NIBSC code: 96/522; 96/554 & 96/560
Instructions for use
(Version 6.0, Dated 08/08/2013)

This material is not for in vitro diagnostic use.

1. INTENDED USE

The Reference Plasma Panel
The 1st British Reference Plasma Panel for Lupus Anticoagulant (LA) consists of a set of three freeze-dried human plasmas: a LA negative (96/522), a LA weakly positive (96/560) and a LA moderately positive (96/554) preparation.

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

See Biological activities table on page 2

4. CONTENTS

Country of origin of biological material: United Kingdom.

a. The LA negative plasma, 96/522: Pooled platelet poor plasma was prepared from 19 donations of blood collected at the North London Blood Transfusion Centre. After the first centrifugation step, the plasma was buffered by the addition of 0.5 M HEPES, pH7.4 to a give final concentration of 20mM. The units of plasma were then centrifuged again before freezing and stored below –70°C. On the day of fill, the plasmas were thawed and pooled before filling or dilution with lupus positive plasmas. The platelet counts of the plasma were all less than 1×10^9/L.

b. Weak positive plasma, 96/560: Frozen LA positive plasmas from two patients, obtained from University College Hospital (UCH) London and Thrombosis Reference Centre (TRC) Manchester, were thawed and diluted 1 in 3 with pooled negative plasma (prepared as described above).

c. Moderate positive plasma, 96/554: Prepared as described for the weak positive plasma, except the LA positive patient plasmas were thawed and diluted 1 in 2 with pooled negative plasma.

All reference plasmas were filled into glass sealed ampoules at a volume of 1.1 ml per ampoule. The ampoules of plasma were then freeze-dried according to the conditions used for International Biological Standards (Campbell, 1974).

5. STORAGE

Unopened ampoules should be stored 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
It is recommended that this panel of plasmas should be used as a set of three. Allow ampoules to warm to room temperature. Open ampoule, taking care to ensure that all material is in lower part. Dissolve the total contents of each ampoule by adding 1.0 ml of distilled water, using gentle shaking, then transfer the contents into a plastic tube. Although the reconstituted material is stable for up to 2 hours when kept at +4°C, it should be used as soon as possible. Used material must be discarded and not frozen for later use.

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

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

10. ACKNOWLEDGEMENTS

We are grateful for Professor S Machin and Dr D Taberner for collection of LA containing patient plasmas and to the participants of the study.

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.

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WHO International Laboratory for Biological Standards,
UK Official Medicines Control Laboratory

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:	Unknown
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: ~80 mg
Toxicity Statement: Toxicity not assessed
Veterinary certificate or other statement if applicable**.** **Attached:** No

The Biological Activities Continued

The biological activities of the reference plasma panel were assessed by 5 expert laboratories of the UK Haemostasis and Thrombosis Task Force. The overall geometric mean ratios and the range of the weak and moderate LA positive plasmas against the LA negative plasma in the lupus anticoagulant tests are as follows:

Tests	96/560 LA weak positive	96/554 LA moderate positive
KCT	1.17 (1.08 – 1.34)	1.48 (1.33 – 1.76)
KCT 80:20 mix	1.05 (0.98 – 1.20)	1.32 (1.14 – 1.73)
DRVVT	1.18 (1.00 – 1.37)	1.50 (1.27 – 1.72)
DRVVT high phospholipid/platelets	1.04 (0.94 – 1.12)	1.09 (0.94 – 1.25
DRVVT 50:50 mix	1.09 (0.98 – 1.22)	1.37 (1.18 – 1.56)
DRVVT high phospholipid/platelets 50:50 mix	1.02 (0.93 – 1.22)	1.06 (0.96 – 1.19)

For tests such as the KCT 80:20 mix and the DRVVT 50:50 mix, local normal pooled plasmas were used for mixing studies

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