Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

CE Marked Material
Anti-c Serum, Human
NIBSC code: 84/628
Instructions for use
(Version 11.0, Dated 30/03/2020)

This material is an 'Annex II List B' IVD and complies with the requirements of the "EU in vitro diagnostic medical device directive 98/79/EC".

1. INTENDED USE

This product is CE marked for use as an IVD within the UK, EU member states and EEA countries. In all other territories this product can be used for research purposes only.

The British Standard for anti-c is intended to be used in the assay of plasma/serum anti-c levels using automated haemagglutination (AutoAnalyzer).

The Standard is not for use as a blood grouping reagent.

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.
In the case of preparation of a replacement standard from new donations, there would be a requirement that individual donations would be tested and found negative for HBsAg, anti-HIV 1+2 and anti-HCV.

3. UNITAGE

Each ampoule contains 13 IU of Anti-c.

4. CONTENTS

Country of origin of biological material: United Kingdom.

The British Standard for anti-c consists of ampoules, coded 84/628, containing the freeze-dried residue of approximately 1 ml of pooled defibrinated human plasma. It contains no preservative.

The preparation has been calibrated by automated haemagglutination methodology (AutoAnalyzer) against the International Standard for Anti-c Incomplete Blood Typing Serum, Human, 67/160. Each ampoule contains 13 International Units of Anti-c. The preparation is intended for use as a working reference preparation for the quantitation of Anti-c by automated haemagglutination (AutoAnalyzer). Such assays may be carried out, for example, for monitoring maternal antibody levels during and after pregnancy. It is the user's responsibility to ensure the suitability of their own procedures for assay of anti-c.

Preparation 84/628 was derived from a defibrinated human plasma pool containing anti-c with a haemagglutination titre of 128-256 using papain-treated rr red cells. The lyophilized preparation was assayed, in 1987, against the WHO International Standard for incomplete anti-c blood typing serum 67/160 in a collaborative study involving 11 laboratories. The potency values ranged from 10.29-15.20 IU/ampoule; the mean value was 12.85 IU/ampoule with an inter-laboratory % coefficient of variation (% CV) of 13.8%. A value of 13 IU/ampoule was assigned.

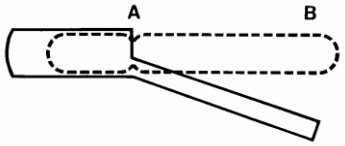
This preparation was previously dispatched from the Blood Group Reference Laboratory, Oxford.

5. STORAGE

Unopened ampoules should be stored at -20°C or below.

6. DIRECTIONS FOR OPENING

Tap the ampoule gently to collect the material at the bottom (labelled) end. Ensure ampoule is scored all round at the narrow part of the neck, with a diamond or tungsten carbide tipped glass knife file or other suitable implement before attempting to open. Place the ampoule in the ampoule opener, positioning the score at position 'A'; shown in the diagram below. Surround the ampoule with cloth or layers of tissue paper. Grip the ampoule and holder in the hand and squeeze at point 'B'. The ampoule will snap open. Take care to avoid cuts and projectile glass fragments that enter eyes. Take care that no material is lost from the ampoule and that no glass falls into the ampoule.



Side view of ampoule opening device containing an ampoule positioned ready to open. 'A' is the score mark and 'B' the point of applied pressure.

7. USE OF MATERIAL

No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution.

1. After snapping off the upper part of the glass ampoule, add about 1ml of 9g/L NaCl containing 5g/L bovine serum albumin. Leave at room temperature, with gentle intermittent mixing, until completely dissolved. Avoid frothing.
2. Using a clean pipette, transfer the dissolved materials to a 50ml volumetric flask containing some 25ml 9g/L NaCl containing 5g/L bovine serum albumin.
3. Thoroughly wash out the ampoule and the pipette in 9g/L NaC1 containing 5g/L bovine serum albumin. Transfer the washings to the volumetric flask.
4. Add 9g/L NaCl containing 5g/L bovine serum albumin to make up to 50ml and mix thoroughly. The concentration of Anti-c is now 13IU in 50ml, i.e. 0.26IU/ml.
5. Dispense in suitable aliquots and store at -40°C or below.
6. For use, make appropriate direct dilutions from an aliquot. Discard unused residue of aliquot. Use dilutions on day of preparation.

8. STABILITY

In 2005, in view of the time that had elapsed since its establishment, 84/628 was subjected to a limited collaborative study in which it was re-assayed against the International Standard for incomplete anti-c blood typing serum 67/160 by 4 laboratories. The laboratory mean value range for 84/628 was 9.9-13.8 IU/ampoule (% CV 15.9%) relative to the International Standard, with an overall mean value of 11.4 IU/ampoule. Given the large variability between laboratories, and the limited number of laboratories in the 2005 study, there was no statistically significant difference between the results of the original study and the 2005 study. The available data does not indicate any lack of stability for 84/628 and there is no evidence of significant drift in the value assignment for 84/628 from that of the International Standard. An expiry date of 31/12/2015 was assigned.
Towards the end of 2015, another collaborative study was carried out to determine the stability of 84/628 beyond 2015. Ampoules of 84/628 had been stored at a range of temperatures (-70°C, -20°C, +4°C, +20°C, +37°C and +45°C) for over 10 years for acceleration degradation studies. Preliminary testing by one laboratory showed that the contents of ampoules stored at +37°C and +45°C would not reconstitute. Two

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UK Official Medicines Control Laboratory

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ampoules of 84/628 from each of the remaining storage temperatures (i.e., -70°C, -20°C, +4°C and +20°C) were assayed by each of 3 laboratories according to a detailed protocol provided. Participants were requested to perform 2 independent assays on each of the ampoules provided to give a total of 4 estimates for each preparation and temperature. The anti-c potencies of the ampoules stored at -20°C, +4°C and +20°C were expressed as a percentage of those of ampoules stored at -70°C. The mean potencies were then used to calculate the stability at -20°C (the storage temperature of ampoule stocks for distribution to customers) from the amount of degradation at the elevated temperatures using the Arrhenius model of accelerated degradation. However, there was insufficient degradation at the elevated temperatures to fit the model. This represents excellent stability, and the shelf life was therefore extended by another 10 years to 31/12/2025.
Reference materials are held at NIBSC within assured, temperature-controlled storage facilities. This standard should be stored on receipt at -20°C or below. The expiry date of the standard is 31/12/2025.

Users who have data supporting any deterioration in the characteristics of the standard are encouraged to contact NIBSC.

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9. REFERENCES

Phillips, P.K. A preparation for calibrating the assay of the blood group antibody anti-c. Brit. J. Haemat. 1987, 65, 57-59.

10. ACKNOWLEDGEMENTS

EC REP: Advena Ltd. Tower Business Centre, 2nd Flr.,
Tower Street, Swatar, BKR 4013 Malta.

We thank the participants of the collaborative studies.

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

Classification in accordance with Directive 2000/54/EC, Regulation (EC) No 1272/2008: Not applicable or not classified

Physical and Chemical properties			
Physical appearance: Lyophilisate		Corrosive:	No
Stable:	Yes	Oxidising:	No
Hygroscopic:	No	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 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. LIABIILITY 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

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: 0.08g
Toxicity Statement: Toxicity not assessed
Veterinary certificate or other statement if applicable**.** **Attached:** No