Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO Reference Reagent
IVIG + anti-D and Negative control IVIG to standardise haemagglutination tests for anti-D in IVIG
NIBSC code: 02/228 & 02/226
Instructions for use
(Version 7.0, Dated 01/04/2008)

1. INTENDED USE

These materials are reference preparations for haemagglutination tests performed to control the level of anti-D in normal intravenous immunoglobulin (IVIG) products. Preparation 02/228 has a nominal titre of 8 using direct haemagglutination of papain-treated OR_2R_2 erythrocytes. Preparation 02/226 is the negative control. An international collaborative study has shown that use of the reference reagents would help overcome interlaboratory variability in haemagglutination tests and ensure that such tests are sufficiently sensitive to detect anti-D in IVIG products [1]. It is also proposed that the level of anti-D in 02/228 defines the maximum permissible titre of anti-D in IVIG products [1, 2].
Preparations 02/228 and 02/226 were established as WHO International Reference Reagents in 2004. Stocks were shared with the Center for Biologics Evaluation and Research of the United States Food and Drug Administration, Bethesda, MD, USA for distribution as Immune Globulin Intravenous (Human) containing anti-D (anti-Rho), Lot 1A, (02/228) and a negative control, Lot 1N-a, (02/226) for use with this material.

2. CAUTION

These preparations are 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

N/A

4. CONTENTS

Country of origin of biological material: United Kingdom.
Both 02/228 and 02/226 contain the lyophilized residue of approximately 1 ml normal IVIG (5% IgG, w/v; kindly donated by the Bio Products Laboratory, Elstree, UK); 02/228 was 'spiked' with anti-D (reconstituted 2nd International Standard for anti-D immunoglobulin, 01/572 at 1/6000).

5. STORAGE

Store unopened ampoules at -20°C 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

RECONSTITUTE THE CONTENTS OF THE AMPOULE WITH 1.0 ML DISTILLED OR DEIONIZED WATER CONTAINING 0.02% SODIUM AZIDE

Allow several minutes, with occasional vortexing, for reconstitution. Transfer the reconstituted contents to a capped tube and store at 4°C. Users should determine the stability of the reconstituted material according to their own storage facilities but tests at NIBSC indicate that the reconstituted material is stable for at least 1 week at 4°C.

The reconstituted contents are 5% (w/v) IgG.

The reconstituted material is to be used in direct haemagglutination tests using papain-treated erythrocytes for anti-D activity in IVIG products [1,2].

8. STABILITY

NIBSC and CBER follow the policy of WHO with respect to their reference materials.

It is the policy of WHO not to assign an expiry date to their international reference materials. They remain valid with the assigned potency and status until withdrawn or amended.

Reference materials are held at NIBSC and CBER within assured, temperature-controlled storage facilities. Reference Materials should be stored on receipt as indicated on the label. For information specific to this particular biological standard, contact NIBSC or CBER.

Users who have data supporting any deterioration in the characteristics of these reference preparations are encouraged to contact NIBSC or CBER.

9. REFERENCES

1. SJ Thorpe, B Fox, A Heath, C Dolman, ML Virata, M-Y W Yu and R Thorpe. International collaborative study to evaluate a candidate reference preparation to define an appropriate specified limit of anti-D in IVIG products. Vox Sang 2005; 88:278-287.
2. Anon: Human normal immunoglobulin for intravenous administration. 2.6.26. Test for anti-D antibodies in intravenous immunoglobulin. Pharmeuropa 2004; 16:119-121.

10. ACKNOWLEDGEMENTS

IVIG was donated by the Bio Products Laboratory, Elstree, UK.

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

World Health Organization

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. 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: 0.1g
Toxicity Statement: Toxicity not assessed
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.