Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
Antibodies to SARS-CoV-1 for neutralisation assays (human immunoglobulin)
NIBSC code: 23/242
Instructions for use
(Version 1.0, Dated 05/11/2024)

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1. INTENDED USE

The First WHO International Standard for antibodies to SARS-CoV-1 for neutralisation assays is intended for the calibration and harmonisation of neutralisation assays detecting anti-SARS-CoV-1 antibodies.
The product is the freeze-dried equivalent of 0.25 mL of purified (3.6%) intravenous SARS-CoV-1 immunoglobulin (IVIG) which has been diluted 1:2 within normal human serum. The IVIG was manufactured using donations of plasma collected from individuals recovered from SARS from Hong Kong in 2005, following the 2002-2004 outbreak. The normal human serum used as a diluent was collected pre-2019 and thus has no sarbecovirus exposure or vaccination history.
The preparation has been evaluated in a WHO International collaborative study (1).

The product may also be used as a non-WHO status control reagent for binding assays such as ELISA, without any unit assignment.

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

The assigned potency of the WHO International Standard for antibodies to SARS-CoV-1 is 250 IU/ampoule for neutralising antibodies.
After reconstitution of the lyophilised cake in 0.25 mL of distilled water, the final concentration will be 1000 IU/mL for neutralising activity.

4. CONTENTS

Country of origin of biological material: Hong Kong.
Each ampoule contains the freeze-dried equivalent of 0.25 mL of 3.6% IVIG diluted 1:2 within normal human serum.

5. STORAGE

Ampoules should be stored at -20°C or below until 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 contents of each ampoule should be reconstituted in 0.25mL distilled water. Following addition of the distilled water, the material must be allowed to become fully reconstituted before 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.
It is the policy of WHO not to assign an expiry date to International Standards. They remain valid with the assigned potency and status until withdrawn or amended. Please note that the stability of International Standard when reconstituted has not been specifically determined. Therefore, it is recommended that the reconstituted material is for single use only. Should users wish to store reconstituted material, they should determine the stability of reconstituted material according to their own method of preparation, storage and use

9. REFERENCES

(1) Bentley et al. Establishment of the First WHO International Standard for SARS-CoV-1 Immunoglobulin G. 2024 WHO Expert Committee on Biological Standardization. WHO/BS/2023.2479

10. ACKNOWLEDGEMENTS

We would like to wholeheartedly thank the anonymous donors of the serum and plasma samples for their consent which has allowed this study to be undertaken. We express our gratitude to the teams at The National Institute of Allergy and Infectious Diseases (NIAID), Division of Microbiology and Infectious Diseases (DMID), Duke-National University of Singapore Medical School (Duke-NUS) and Tan Tock Seng Hospital (TTSH) for generously providing the samples which have facilitated this study. We gratefully acknowledge the important contributions of the collaborative study participants, particularly in meeting the tight timeframes of this study.
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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

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

World Health Organization

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: Freeze dried	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: No	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify):	
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: 0.25 g
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 https://www.who.int/publications/m/item/annex2-trs932(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.