Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
2nd International Standard for anti-SARS-CoV-2 immunoglobulin
NIBSC code: 21/340
Instructions for use
(Version 1.0, Dated 06/12/2022)

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1. INTENDED USE

The second WHO International Standard for anti-SARS-CoV-2 immunoglobulin is the freeze-dried equivalent of 0.25 mL of pooled plasma obtained from seven individuals recovered from SARS-CoV-2 in the United Kingdom between May-August 2020. The source material for the pooling was selected based on antibody titre to resemble similar levels to that of the 1st WHO International Standard 20/136 and solvent-detergent treated to minimise the risk of the presence of enveloped viruses [1]. The preparation has been evaluated in an International Collaborative study[2].

The intended use of the International Standard is for the calibration and harmonisation of neutralisation assays using SARS-CoV-2 early isolates (2020). For the calibration of secondary reagents used in neutralisation assay against variants of concerns the 1st WHO International Standard for anti-SARS-CoV-2 variants of concern immunoglobulin, NIBSC code 21/338, should be used.

The preparation can also be used as an internal reference reagent for the harmonisation of binding antibody assays.

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 2nd WHO International Standard for SARS-CoV-2 immunoglobulin is 356 IU/ampoule for neutralising antibody activity. After reconstitution in 0.25 mL of distilled water, the final concentration of the preparation is 1424 IU/mL.
The preparation has been assessed for neutralising activity against variants of concern and for binding antibody in the collaborative study [2]. The potencies reported as geometric mean of the values relative to the first WHO International Standard for anti-SARS-CoV-2 immunoglobulin, 20/136, are listed below. **These values are based on the results from the assays used in the collaborative study and are intended for guidance only.**

Method	Isolate/viral target	Potency	Units
Neutralisation	Alpha	1414	IU/mL
	Beta	843	IU/mL
	Gamma	680	IU/mL
	Delta	1663	IU/mL
	Omicron (BA.1-BA.2)	1882	IU/mL
Binding assay	Spike	652	BAU/mL
	Receptor binding domain	723	BAU/mL
	Subunit 1 of Spike	677	BAU/mL
	Nucleoprotein	563	BAU/mL

IU: international unit; BAU: binding antibody unit
For binding assays, the viral antigens were derived from an early 2020 isolates, and the assays were IgG-specific.

4. CONTENTS

Country of origin of biological material: United Kingdom. Each ampoule contains the freeze-dried equivalent of 0.25 mL pooled human plasma

5. STORAGE

International Standard 21/340 should be stored at -20°C or below upon receipt.
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
This material should be reconstituted in 0.25 mL sterile distilled water. Following addition of water, the ampoule may be left at ambient temperature for approximately 30 minutes until dissolved and then mixed thoroughly, avoiding the generation of excessive foam.

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.
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NIBSC follows the policy of WHO with respect to its reference materials.

9. REFERENCES

[1] Dichtelmüller et al. Robustness of solvent/detergent treatment of plasma derivatives: a data collection from Plasma Protein Therapeutics Association member companies. Transfusion. 2009;49:1931–43.
[2] Bentley EM et al. Establishment of the second WHO International Standard for anti-SARS-CoV-2 immunoglobulin and Reference Panel for antibodies to SARS-CoV-2 variants of concern. 2022, WHO Expert Committee on Biological Standardization. WHO/BS/2427

10. ACKNOWLEDGEMENTS

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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

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

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: freeze-dried		Corrosive:	No
Stable:	Yes	Oxidising:	No
Hygroscopic:	No	*Irritant:*	*No*
Flammable:	No	*Handling:*	*See caution, Section 2*
Other (specify):	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: 0.25 g
Toxicity Statement: Non-toxic
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.