Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO Reference Panel
First International Reference Panel for antibodies to SARS-CoV-2 variants of concern
NIBSC code: 22/270
Instructions for use
(Version 1.0, Dated 20/04/2023)

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1. INTENDED USE

The First WHO International Reference Panel of antibodies to SARS-CoV-2 variants of concern (VOC) consists of the equivalent of 0.25 mL of freeze-dried pool of plasma or serum from individuals recovered from Coronavirus Disease 2019 (COVID-19). The panel was evaluated in two WHO International Collaborative studies (1, 2). Individual panel members are NIBSC code 21/296 (pre-VOC), 21/300 (Alpha), 21/312 (Delta), 22/126 (Gamma) and 22/128 (Omicron BA.1). It is intended that the panel is used in the assessment and development of assays used in the detection and quantitation of anti-SARS-CoV-2 antibodies. The preparation has been solvent-detergent treated to minimise the risk of presence of enveloped viruses (3).

2. CAUTION

The preparation contains material of human origin, and either the final product or the source material from which it is derived have been tested and found negative for HBsAg, anti-HIV and HCV RNA. Sample 21/312 was found positive for anti-HIV antibodies and HBsAg. The product has been solvent-detergent treated and deemed not infectious for shipping.

This preparation is not for administration to humans or animals.

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

No unitage has been assigned to the panel members. The potencies, reported as geometric means of the values relative to the second WHO International Standard for anti-SARS-CoV-2 immunoglobulin, 21/340 or for Omicron, to the First WHO International Standard to antibodies to SARS-CoV-2 variants of concern, 21/338, were obtained during the collaborative study (1) for 21/296, 21/300 and 21/312 or (2) for 22/126 and 22/128. These values are provided to the end users as guidance only. Actual values may vary between assays.

	21/296	21/300	21/312	22/126	22/128	
Neutralising Ab						
Early 2020	373	1814	399	746	203	IU/mL
Alpha	599	3872	708	891	380	IU/mL
Beta	1075	2953	1190	1601	1498	IU/mL
Gamma	1110	3333	887	1315	1155	IU/mL
Delta	261	1020	504	368	442	IU/mL
Omicron	498	1386	831	1599	3840	IU/mL
Binding Ab						
anti-Spike IgG	479	3278	532	972	624	BAU/mL
anti-RBD IgG	355	2164	428	408	261	BAU/mL
anti-S1 IgG	397	2666	507	nt	nt	BAU/mL
anti-N IgG	132	756	105	157	122	BAU/mL

Ab: antibody; IU: International Unit; BAU:binding antibody unit; RBD: receptor binding domain; S1: subunit 1 of the spike protein; N:nucleoprotein; IgG: immunoglobulin G; nt: not tested

4. CONTENTS

Country of origin of biological material: Brazil, Kenya, South Africa, United Kingdom and United States of America.
Each ampoule contains the equivalent of 0.25 mL of human plasma or serum.

5. STORAGE

The ampoules should be stored at t -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.
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7. USE OF MATERIAL

No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution
Each ampoule should be reconstituted in 0.25 mL distilled water. Following addition of water, the ampoules should 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.

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

9. REFERENCES

(1) Bentley EM et al. Establishment of the 2nd WHO International Standard for anti-SARS-CoV-2 immunoglobulin and Reference Panel for antibodied to SARS-CoV-2 variants of concern. 2022. WHO Expert Committee on Biological Standardization. WHO/BS/2022.2428
(2) Bentley et al. Expansion of WHO Reference Panel for antibodies to SARS-CoV-2 variants of concern. 2023. WHO Expert Committee on Biological Standardization. WHO/BS/2023.2450.
(3) 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

10. ACKNOWLEDGEMENTS

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UK Official Medicines Control Laboratory

World Health Organization

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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

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):	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.