Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

Working Standard
Panel of recombinant antibody controls for Cytokine Release Assays
NIBSC code: 19/156
Instructions for use
(Version 2.0, Dated 10/02/2021)

This material is not for in vitro diagnostic use.

1. INTENDED USE

The lyophilised recombinant antibodies included in the panel are intended for used as controls in in vitro cytokine release assays (CRAs). CRAs are key for hazard ID of antibodies such as cytokine release syndrome, and the choice of CRA platform (e.g. whole blood versus peripheral blood mononuclear cell) should be optimized for the expected MoA of the antibody (Vessillier at al,2015). The panel consists of three positive (anti-CD52, anti-CD3 and anti-CD28 remanufactured according to the respective published sequences of Campath-1H (Riechmann et al., 1988), OKT-3 muromonab (Kung et al., 1979) and TGN1412 (Ball et al., 2012)) controls known to induce mild, moderate and severe cytokine release syndrome in the clinic and three isotype matched negative controls (IgG1, IgG2a and IgG4). The relative potency of these positive controls to stimulate cytokine release was evaluated in an international collaborative study involving eleven laboratories (Vessillier et al, 2020).

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

There is no unitage assigned to these preparations.

4. CONTENTS

Country of origin of biological material: United Kingdom.
Recombinant antibodies produced in HEK293 cells or CHO cells in a custom-made formulation.
The panel contains 7 individually coded ampoules.
2 ampoules of 15/144, each containing 100 µg of anti-CD28SA recombinant antibody.
1 ampoule of 15/162 contains 200 µg of anti-CD3 recombinant antibody.
1 ampoule of 15/178 contains 200 µg of anti-CD52 recombinant antibody
1 ampoule of 15/198 contains 200 µg of IgG1K isotype control
1 ampoule of 15/218 contains 200 µg of IgG2a isotype control
1 ampoule of 15/232 contains 200 µg of IgG4 isotype control

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.

Care should be taken on opening to prevent loss of contents.

7. USE OF MATERIAL

No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution
Take ampoule out of storage, place in a tube holder and allow to adjust to room temperature. Break ampoule seal.

Reconstitute the contents of the ampoule with 1 ml of sterile distilled water. Allow 5-10 min for rehydration. Mix the antibody solution and transfer to a capped tube. After reconstitution in 1 ml of water the stock concentration of recombinant antibodies 15/162, 15/178, 15/198, 15/218 and 15/232 will be 200 µg/ml. After reconstitution in 1 ml of water the stock concentration of 15/144 will be 100 µg/ml.

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.
For short term storage up to 7 days, transfer the reconstituted material in a capped tube to 4°C. For longer storage, users should determine the stability of the reconstituted material according to their own storage facilities.

9. REFERENCES

1. Vessillier, S., et al., Cytokine release assays for the prediction of therapeutic mAb safety in first-in man trials — Whole blood cytokine release assays are poorly predictive for TGN1412 cytokine storm. Journal of Immunological Methods, 2015. 424: p. 43-52.
2. Kung, P., et al., Monoclonal antibodies defining distinctive human T cell surface antigens. Science, 1979. 206(4416): p. 347-9.
3. Riechmann, L., et al., Reshaping human antibodies for therapy. Nature, 1988. 332(6162): p. 323-327.
4. Ball, C., et al., Antibody C region influences TGN1412-like functional activity in vitro. J Immunol, 2012. 189(12): p. 5831-40.
5. Vessillier, S., M. Fort, L. O'Donnell, H. Hinton, K. Nadwodny, J. Piccotti, P. Rigsby, K. Staflin, R. Stebbings and D. Mekala, Willingham, A. and B. Wolf (2020). "Development of the first reference antibody panel for qualification and validation of cytokine release assay platforms-Report of an international collaborative study." Cytokine: X: 100042. https://doi.org/10.1016/j.cytox.2020.100042

10. ACKNOWLEDGEMENTS

We are deeply thankful to the participants in this collaborative study who have dedicated their time to the project.

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

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

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 powder		Corrosive:	No
Stable:	Yes	Oxidising:	No
Hygroscopic:	Yes	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 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: 25.2 g
Toxicity Statement: Toxicity not assessed
Veterinary certificate or other statement if applicable**.** **Attached:** No

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