Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

Working Standard
NIBSC Working Standard for Tumour Necrosis Factor - alpha (Human, rDNA derived)
NIBSC code: 17/232
Instructions for use
(Version 3.0, Dated 12/06/2020)

This material is not for in vitro diagnostic use.

1. INTENDED USE

The preparation coded 17/232, prepared using the same lot of TNF-α as the 3rd WHO International Standard for TNF-α (12/154), was established as the NIBSC Working Standard for human Tumour Necrosis Factor-alpha (TNF-α) following an assessment of its suitability in TNF-α bioassays, and assignment of unitage relative to 12/154 in a multicentre collaborative study.
This preparation is mainly intended for use as a critical reagent in bioassays for anti-TNF-α products, but can also be used for calibration of TNF-α bioassays and immunoassays as appropriate.

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 preparation has been assigned a potency of 42,607 International Units of biological activity per ampoule (expanded uncertainty 40,720 – 44,582 calculated on a log scale with coverage factor k=2.36 corresponding to a 95% level of confidence). The unitage was assigned relative to the 3rd WHO IS for TNF-α (12/154) in a multicentre collaborative study, and is therefore in continuity with the current IS.

4. CONTENTS

Country of origin of biological material: United Kingdom.
Each ampoule contains the residue after freeze-drying of 1.0 ml of Phosphate Buffered Saline containing:

TNF-α, approximately 1 microgram
1 mg Trehalose
0.6% Human Serum Albumin

The TNF-α protein was expressed in E.coli.

5. STORAGE

For economy of use, it is recommended that the solution be sub divided into several small aliquots and stored at -40ºC or below. Avoid repeated thawing/freezing. Unopened ampoules should be stored at -20ºC.
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
Dissolve the total contents of the ampoule in 1.0ml of sterile distilled water. This solution will contain TNF-α at a concentration of 42,607 International Units/ml (see section 3). Use carrier protein where extensive dilution is required.

8. STABILITY

Reference materials are held at NIBSC within assured, temperature-controlled storage facilities and they should be stored on receipt as indicated on the label. This standard has been produced according to WHO specifications and as per WHO policy an expiry date has not been assigned. Accelerated degradation studies have indicated that this material (same as 3rd IS for TNF-α) is suitably stable, when stored at -20ºC or below, for the assigned values to remain valid until the material is withdrawn or replaced. These studies have also shown that the material is suitably stable for shipment at ambient temperature without any effect on the assigned values. Once reconstituted, diluted or aliquoted, users should determine the stability of the material according to their own method of preparation, storage and use. Users who have data supporting any deterioration in the characteristics of any reference preparation are encouraged to contact NIBSC.

9. REFERENCES

This standard was produced under WHO guidelines cited in the WHO Technical Reports Series, No. 932, 2006, Annex 2.
Report on a Collaborative study for proposed NIBSC Working standard for Tumor Necrosis Factor - alpha (TNF-α) can be found here:
https://www.nibsc.org/documents/ifu/SupplementaryInformation/17-232/Human Tumor Necrosis Factor working standard.pdf

Report on a Collaborative study for proposed 3rd International standard for Tumor Necrosis Factor - alpha (TNF-α) WHO/BS/2013.2219 can be found here:
https://www.who.int/bloodproducts/catalogue/Cyto.pdf?ua=1

10. ACKNOWLEDGEMENTS

We are thankful to a manufacturer for their generous donation of the TNF-α preparation used in the collaborative study, and to the study participants for their contributions in evaluating the preparation.

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: 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 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: 4.6g
Toxicity Statement: Toxicity not assessed
Veterinary certificate or other statement if applicable**.** **Attached:** No

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