Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO Reference Reagent
TUMOUR NECROSIS FACTOR-RELATED APOPTOSIS INDUCING LIGAND (TRAIL)[Human, rDNA, E. coli-derived]
NIBSC code: 04/166
Instructions for use
(Version 4.0, Dated 12/04/2013)

1. INTENDED USE

This material is the 1st WHO Reference Reagent for human TRAIL and is intended as a biological reference standard in bioassays for TRAIL.

Its activity is measured by its capacity to induce cytotoxicity in cultured cell lines, e.g. mouse L929, human KYM-1, which are normally also susceptible to TNF-mediated cytotoxicity. Metabolic inhibitors such as actinomycin D may be added to cells to augment TRAIL-mediated cytotoxicity.

Regarding the calibration of immunoassays, it is pointed out that the suitability of 04/166 for this purpose has not been tested.

2. CAUTION

This preparation is not for administration to humans or animals in the human food chain.

The preparation contains human and bovine source material. The preparation contains an excipient of human origin which has been tested and found negative for HBsAg and HIV antibody. The preparation has subsequently been tested and found negative for anti-HCV and HCV RNA by PCR. The bovine casein used as an excipient was sourced from a country where bovine spongiform encephalopathy (BSE) has not been found. 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

10,000 International units (IU).
The assigned potency is in International Units (IU) that reflect results derived from cytotoxicity assays. These IU are specific to TRAIL and are not continuous with the IU of TNF-alpha or TNF-beta.

4. CONTENTS

Country of origin of biological material: United Kingdom.
Each ampoule contains the residue after freeze-drying of 1ml of phosphate buffered saline that contained:

Approximately 1,000 nanograms of recombinant human TRAIL (see Explanatory Notes)
1.0% human serum albumin
0.3% bovine casein

The ampoule does not contain bacteriostat.

Explanatory notes

The recombinant human TRAIL was expressed in E. coli from a DNA sequence encoding the extracellular domain of human TRAIL (Val 114-Gly 281) containing 168 amino acids with a predicted molecular mass of approximately 19 kDa. This preparation contains recombinant human TRAIL as a homotrimeric protein, which is biologically active.

5. STORAGE

Unopened ampoules should be stored at -20°C.

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

For all practical purposes each ampoule contains the same quantity of the substances listed above. Dissolve the total contents of the ampoule with 0.5ml of sterile distilled water. Rinse the ampoule with 0.4ml of sterile distilled water and make up the total volume to 1ml with sterile distilled water. This solution should now be at a concentration of 10,000 IU/ml. Use carrier protein where extensive dilution is required. For economy of use, it is recommended that the solution be sub-divided into several small aliquots and stored at -40°C or below.

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. It is the policy of WHO not to assign an expiry date to their international reference materials. Accelerated degradation studies have indicated that this material 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

Meager, A. (2003). Assays for cytotoxicity. In: Methods in Molecular Biology, vol. 249: Cytokine Protocols (de Ley, M, ed.). Humana Press Inc., Totowa, NJ, USA. pp.135-51.
This reference reagent was produced under WHO guidelines cited in the WHO Technical Reports Series, no. 925, 2005.

10. ACKNOWLEDGEMENTS

N/A

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

World Health Organization

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

Physical and Chemical properties	
Classification in accordance with Directive 2000/54/EC, Regulation (EC) No 1272/2008: Not applicable or not Physical appearance: White powder	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: No	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify):	Contains material of human and bovine 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: 0.5 gram
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 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.