Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
1st WHO International Standard for HHV-6B virus DNA
NIBSC code: 15/266
Instructions for use
(Version 3.0, Dated 23/11/2017)

1. INTENDED USE

The 1st WHO International Standard for Human Herpes virus 6B (HHV-6B) DNA, NIBSC code 15/266, is intended for the standardisation of nuclieic amplification technique-based assays for HHV-6B. It should be used primarily for the calibration of secondary reference standards. The material has been evaluated in a worldwide collaborative study involving 26 laboratories using a range of HHV-6 NAT-based assays, and was subsequently established by the World Health Organisation Expert Committee on Biological Standardization (ECBS) in October 2017. Details of the prepartion and value assignment are available in document WHO/BS/2017.2321 [1].

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

This material has been assigned a concentration of 7.75 log10 International Units (IU) per vial when reconstituted in 1 mL of nuclease-free water, based on on the combined quantitative mean estimate values from a worldwide collaborative study [1].The assigned untiage does not carry an uncertainty associated with its calibration. The uncertainty may therefore be considered to be the variance of the vial contents which was determined to be +/-0.24%.

4. CONTENTS

Country of origin of biological material: United Kingdom.

The reference preparation comprises of lyophilised whole virus of HHV-6B Z-29 strain, formulated in a universal buffer (10mM Tris-HCl pH 7.4, 0.5% Human serum albumin (HSA), 2.0% D-(+)-Trehalose dehydrate). Each vial contains the lyophilised equivalent of 1 mL of HHV-6B in 10mM Tris-HCl pH 7.4, 0.5% Human serum albumin (HSA), 2.0% D-(+)-Trehalose dehydrate.

5. STORAGE

Vials of lyophilised material should be stored at -20^{0}C. Once reconsituted, contents are for single use only. This material has not been assessed for in use stability of reconstituted material. Reconstituted material should not be stored without in house validation studies performed by the end user.
Please note: because of the inherent stability of lyophilized material, NIBSC may ship these materials at ambient temperature.

6. DIRECTIONS FOR OPENING

Vials have a screw cap; an internal stopper may also be present. The cap should be removed by turning anti-clockwise. Care should be taken to prevent loss of the contents. Please note: If a stopper is present on removal of the cap, the stopper should remain in the vial or be removed with the cap.

7. USE OF MATERIAL

No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution.
The total contents of the ampoule should be reconstituted at room temperature with 1 mL nuclease-free molecular-grade water, and left for a minimum of 20 minutes with occasional gentle agitation before use. Recommended for single use only.

Once reconstituted, the International Standard should be further diluted into a matrix comparable to the clinical samples being tested for the diagnosis of HHV-6B DNA.The material is designed to be used in conjunction with the extraction step of the NAT procedure.

The International Standard should be used to calibrate secondary reference materials, for example, by determining the equivalent concentration of secondary reference reagent being calibrated, against the International Standard, in parallel. The secondary reference reagent can then be assigned a concentration in IU [2].

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. It is the policy of WHO not to assign an expiry date to their International reference materials.

Accelerated degradation studies have indicated that this lyophilised material is suitably stable, when stored at -20^{0}C, for the assigned values to remain valid until the material is withdrawn or replaced. This material has under gone accelerated thermal degradation studies. The data have been reviewed and approved by the WHO Expert Committee on Biological Standardisation and concluded with data to date that this material is stable. Real time stability studies are on going.

Users who have data supporting any deterioration in the characteristics of this reference preparation are encouraged to contact NIBSC.

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

9. REFERENCES

[1] Sheila Govind, Jason Hockley, Clare Morris and the Collaborative Study Group. Collaborative Study to establish the 1st WHO International Standard for Human Herpes Virus 6B (HHV-6B) DNA for nucleic acid amplification technique (NAT)-based assays. WHOECBS Report 2017; WHO/BS/2017.2321
http://www.who.int/biologicals/expert_committee/BS2321_HHV-6_WHO_ECBS_report_v5.pdf?ua (accessed October 2017)

[2] Manual for the preparartion of secondary reference materials for in vitro diagnostic assays designed for infectious disease nucleic acid or antigen detection: Calibration to WHO International Standards.
http://www.who.int/biologicals/expert_committee/WHO_Manual_Calibration_of_secondary_standards_final_mn.pdf?ua=1 (accessed November 2017)

10. ACKNOWLEDGEMENTS

We gratefully acknowledge the important contributions of the collaborative study participants [1].

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:

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

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: Lyophilised		Corrosive:	No
Stable:	Yes	Oxidising:	No
Hygroscopic:	Yes	Irritant:	No
Flammable:	No	Handling:See caution, Section 2	
Other (specify):	Contains infectious HHV-6B		
Toxicological properties			
Effects of inhalation:	Avoid - contains infectious HHV-6B		
Effects of ingestion:	Avoid - contains infectious HHV-6B		
Effects of skin absorption:	Avoid - contains infectious HHV-6B		
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: 1.0g
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.