Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
5th WHO International Standard for HBV DNA for NAT
NIBSC code: 22/120
Instructions for use
(Version 2.0, Dated 19/04/2023)

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1. INTENDED USE

The 5th WHO International Standard for hepatitis B virus (HBV) DNA, NIBSC code 22/120, is intended to be used for the calibration of secondary reference reagents used in HBV nucleic acid amplification techniques (NAT). The standard comprises lyophilized human plasma and HBV. The HBV was sourced from the Eurohep reference R1 (a genotype A2, HBsAg subtype adw2 virus from a single donor) [1]. The standard has been lyophilized in 0.5 mL aliquots and stored at -20°C. The material has been calibrated in International Units (IU), in parallel with the 4th WHO International Standard for HBV DNA for NAT, in a collaborative study involving 10 laboratories worldwide [2].

2. CAUTION

This preparation is not for administration to humans or animals

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 unitage of 5.69 log10 IU/vial (~489,779 IU/vial). When reconstituted in the 0.5 mL of nuclease-free water the final concentration is 5.99 log10 IU/mL (~979558 IU/mL). Uncertainty: the assigned unitage does not carry an uncertainty associated with its calibration. The uncertainty may therefore be considered to be the variance of the vial weight after filling and was determined to be +/-0.40%.

4. CONTENTS

Country of origin of biological material: United Kingdom.
Each vial contains 0.5 mL of lyophilized plasma containing infectious HBV.

5. STORAGE

Vials of lyophilized standard 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

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 material should be reconstituted with 0.5 mL of deionized, nucleasefree molecular-grade water and left for a minimum of 20 minutes with occasional agitation before use. The reconstituted material has a final concentration of 5.99 log10 IU/mL (~979558 IU/mL). Once reconstituted, the International Standard should be diluted in the matrix appropriate to the assay e.g. in HBV DNA-negative plasma, and should be extracted prior to HBV DNA measurement. 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, as described elsewhere [3]. The secondary reference reagent can then be assigned a concentration in IU.

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 material is suitably stable, when stored at -20°C, 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. Users who have data supporting any deterioration in the characteristics of any reference preparation are encouraged to contact NIBSC. The stability of the material when reconstituted has not been specifically determined. Therefore, it is recommended that the standard is for single use only.
NIBSC follows the policy of WHO with respect to its reference materials.

9. REFERENCES

1. Heermann KH, Gerlich WH, Chudy M, Schaefer S, Thomssen R. Quantitative detection of hepatitis B virus DNA in two international reference plasma preparations. Eurohep Pathobiology Group. J Clin Microbiol. 1999;37:68-73.
2. Fryer JF, Rigsby P, Morris CL and the collaborative study group. Collaborative study to evaluate the proposed 5th WHO International Standard for hepatitis B virus (HBV) DNA for nucleic acid amplification techniques (NAT). WHO ECBS Report 2023; WHO/BS/2023.2447.
3. WHO manual for the preparation of secondary reference materials for in vitro diagnostic assays designed for infectious disease nucleic acid or antigen detection: calibration to WHO International Standards. WHO Technical Report Series 2017. Geneva, Switzerland:WHO 2017; 1004,389-455.

10. ACKNOWLEDGEMENTS

We gratefully acknowledge the important contributions of the collaborative study participants.

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:

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.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: Lyophilized powder	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: No	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify):	Contains human plasma and infectious HBV
Toxicological properties	
Effects of inhalation:	Avoid, contains infectious HBV
Effects of ingestion:	Avoid, contains infectious HBV
Effects of skin absorption:	Avoid, contains infectious HBV
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 g
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.