



**WHO International Standard  
First International Standard for anti-Hepatitis B core antigen (anti-HBc), plasma, human  
NIBSC code: 95/522  
Instructions for use  
(Version 2.0, Dated 15/04/2013)**

### 1. INTENDED USE

Antibodies to hepatitis B virus core antigen (anti-HBc) are produced during acute hepatitis B virus (HBV) infection and persist lifelong so that HBV infection can be detected in chronic carriers even when negative for hepatitis B surface antigen (HBsAg) and HBV-DNA. Anti-HBc screening therefore has the potential to detect the majority of occult HBV infection. In the absence of anti-HBc testing HBV transmission occurred in blood recipients as well as after organ transplantations. This has led some countries to improve blood safety by mandatory blood screening for anti-HBc (e.g., Argentina, Brazil, France, Germany, Japan, Paraguay, Peru, Uruguay, USA and Venezuela). In addition, anti-HBc may be the only positive serological marker in chronic HBV infections.

Anti-HBc persists also in those who have cleared the virus so that isolated anti-HBc can be indistinguishable from serological profile of resolved HBV infection not easy to differentiate from potential false positive reactions in particular in low prevalence HBV countries. Therefore high quality anti-HBc tests with high sensitivity and specificity are required.

A WHO Collaborative Study organised by the Paul Ehrlich Institute was undertaken to assess the suitability of a candidate reference material (NIBSC code 95/522) for detection of antibodies to hepatitis B core antigen (anti-HBc) in diagnostic assays. Thirteen laboratories from 10 countries tested the above described materials using 20 different anti-HBc assays.

### 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. His material contains high levels of anti-HBs. It has also been tested and found negative for HBV DNA and is therefore considered non-infectious. 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 is assigned a unitage of 50IU/ampoule. (50 IU/ampoule are equivalent to the 100 PEI-U/ml of the PEI 82 anti-HBc standard)

### 4. CONTENTS

Country of origin of biological material: United Kingdom.  
This preparation contains the freeze dried residue of 1ml plasma from UK blood donors which is reactive for anti-HBc and also for anti-HBs at high levels.

### 5. STORAGE

Ampoules should be stored 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 manufacturer's 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

Each ampoule should be reconstituted in 1ml distilled water. It is recommended that human serum or defibrinated human plasma (anti-HBc negative) is used in the preparation of a series of dilutions of the IS when calibrating secondary standards as the use of diluents such as PBS/BSA may interfere with the test results.

### 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 -20°C or below, for the assigned value 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.

Users should determine the stability of reconstituted material according to their own method of preparation, storage and use. Stability studies on reconstituted material in the Collaborative Study showed that there was no loss of activity after 14 days storage at +2-8°C and after two freeze/thaw cycles. However, multiple freeze/thaw cycles should be avoided.

### 9. REFERENCES

WHO Expert Committee on Biological Standardization report WHO/BS/08.2098 available online.  
[http://apps.who.int/iris/bitstream/10665/69975/1/WHO\\_BS\\_08.2098\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/69975/1/WHO_BS_08.2098_eng.pdf)

### 10. ACKNOWLEDGEMENTS

### 11. FURTHER INFORMATION

Further information can be obtained as follows:  
This material: [enquiries@nibsc.org](mailto: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](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](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](mailto: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



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Regulatory Agency



code number, and the name and address of NIBSC are cited and cited correctly.

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WHO International Laboratory for Biological Standards,  
UK Official Medicines Control Laboratory





#### 14. MATERIAL SAFETY SHEET

Classification in accordance with Directive 2000/54/EC, Regulation (EC) No 1272/2008: Not applicable or not classified

[http://www.who.int/bloodproducts/publications/TRS932Annex2\\_Inter\\_biol\\_efstandardsrev2004.pdf](http://www.who.int/bloodproducts/publications/TRS932Annex2_Inter_biol_efstandardsrev2004.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.

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](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

<b>Country of origin for customs purposes*:</b> 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.
<b>Net weight:</b> 1.0g
<b>Toxicity Statement:</b> Non-toxic
<b>Veterinary certificate or other statement</b> if applicable. <b>Attached:</b> 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