



**WHO International Standard
The 1st International Standard for ANTI-CANINE HEPATITIS
SERUM**

**NIBSC code: CHS
Instructions for use
(Version 5.0, Dated 26/04/2013)**

1. INTENDED USE

This material has been prepared and characterised by the Veterinary Laboratories Agency, Weybridge, Surrey, UK. With effect from 1st June 1998, the National Institute for Biological Standards and Control (NIBSC), Potters Bar, UK is the custodian and distributor of this material.

Relevant factors

For details of this International Standard, please refer to the enclosed package insert from the Veterinary Laboratories Agency. The Distribution statement in the package insert is no longer valid.

The package insert from VLA is attached.

2. CAUTION

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

The material is not of human or bovine origin. 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

Each ampoule contains 1000 International Units

4. CONTENTS

Country of origin of biological material: United Kingdom.
Each ampoule contains the freeze-dried residue of 1ml horse serum containing antibodies to Canine Hepatitis Virus

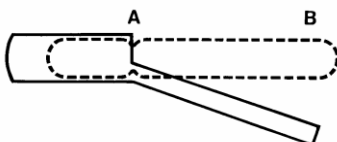
5. STORAGE

Ampoules should be stored at -20°C on receipt.

Please note: because of the inherent stability of lyophilized material, NIBSC may ship these materials at ambient temperature.

6. DIRECTIONS FOR OPENING

Tap the ampoule gently to collect the material at the bottom (labelled) end. Ensure ampoule is scored all round at the narrow part of the neck, with a diamond or tungsten carbide tipped glass knife file or other suitable implement before attempting to open. Place the ampoule in the ampoule opener, positioning the score at position 'A'; shown in the diagram below. Surround the ampoule with cloth or layers of tissue paper. Grip the ampoule and holder in the hand and squeeze at point 'B'. The ampoule will snap open. Take care to avoid cuts and projectile glass fragments that enter eyes. Take care that no material is lost from the ampoule and that no glass falls into the ampoule.



Side view of ampoule opening device containing an ampoule positioned ready to open. 'A' is the score mark and 'B' the point of applied pressure.

7. USE OF MATERIAL

No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution

The contents of each ampoules should be reconstituted as described in the package insert from VLA (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. They remain valid with the assigned potency and status until withdrawn or amended.

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

9. REFERENCES

10. ACKNOWLEDGEMENTS

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

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 solid	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: No	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify):	Contains horse serum



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: 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_biologicalstandardsrev2004.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.



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**Veterinary
Laboratories
Agency**

**INTERNATIONAL STANDARD FOR ANTI-CANINE-HEPATITIS SERUM
(CHS)**

Description

The International Standard for Anti-Canine-Hepatitis Serum is intended for the standardization of anti-canine-hepatitis sera for clinical use and for measuring the antibody content of sera from vaccinated and infected dogs.

The International Standard was established in 1967. It was prepared from serum from a horse inoculated with hepatitis virus. The serum was dispensed in 1ml amounts into ampoules and freeze-dried. The ampoules were sealed in an atmosphere of dry nitrogen at approximately atmospheric pressure. The average weight of dry material per ampoule has been determined as 0.0796g with a standard deviation of 1.7%.

International Unit

The International Unit is defined as the activity contained in 0.0796mg of the International Standard. Each ampoule contains 1000 International Units.

Distribution

The International Standard is distributed by the International Laboratory for Biological Standards, Ministry of Agriculture, Fisheries and Food, New Haw, Addlestone, Surrey, England, on behalf of the World Health Organisation. It is available free of charge in limited amounts. If a laboratory needs more than 1 ampoule every 6 months, it is expected to prepare its own standard and to calibrate it against the International Standard. A quantity of the latter sufficient for this purpose will be supplied on request.

Reconstitution of the International Standard

The Standard should be reconstituted immediately before it is to be used.

Ampoules may be opened by scoring with a small saw specifically designed for the purpose, or a hard mineral edge, for approximately one third of the circumference. Application of a piece of red hot glass rod to this scratch will give a clean line of fracture.

If the scoring is made firmly and the glass rod is hot enough, it is possible to produce a fine crack without disturbing the ampoule top until needed. Then slight pressure will complete the separation.

The freeze-dried material in each ampoule may be reconstituted in any convenient volume of a suitable diluent, which will not alter the final pH.

Care should be taken to ensure that the entire contents of the ampoule are completely resuspended.

*An Executive Agency of the
Ministry of Agriculture,
Fisheries and Food*

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This can be achieved by suspending the bulk of the contents of the ampoule in some of the fluid and using the remainder of the diluent to rinse out the ampoule three times.

National and Laboratory Standards

National and laboratory standards should be prepared in a stable form. This may be achieved by freeze-drying aliquots of the standard in neutral-glass ampoules and sealing them in an oxygen-free atmosphere by fusion of the glass. The ampoules should be stored in the dark at a low temperature e.g. -20°C .

The potency of such a standard relative to that of the International Standard should be determined by performing a series of comparative neutralization tests. Series of dilutions of the two preparations should be compared in the same tissue culture system. Two-fold dilutions of serum should be titrated against a uniform amount of virus, covering the range from complete neutralization to no neutralization. The dilutions needed to achieve this should be determined by carrying out a preliminary titration e.g., using five-fold dilutions ranging from 1/200 to 1/125,000. At least six tissue culture tubes should be used for each dilution. The amount of virus used varies from laboratory to laboratory but is usually between 100 and 500 TCID₅₀ per tube.

The relative potencies of the two preparations should be estimated by the standard statistical methods. The number of International Units per ampoule of the proposed standard can thus be calculated. This calculation should be based on a series of at least three tests.

It is suggested that the potency of a national or laboratory standard should be checked against that of a fresh sample of the International Standard about once a year.

The International Laboratory for Biological Standards at Weybridge is willing to advise and assist laboratories in providing their own standards.

Assaying Batches of Serum intended for Clinical Use

Once a national or laboratory standard has been prepared, it can be used to assay routine batches of serum, thus defining their potencies in International Units. This can be done by performing a comparative test as described in the previous section.

Although no international requirements for anti-canine-hepatitis serum have yet been formulated, the potencies of a number of sera known to be satisfactory were determined in the international collaborative assay which was carried out to test the suitability of the International Standard. The potencies of these sera ranged from 300 to 1000 International Units per ml.

Measuring the Antibody Content of Sera from Vaccinated and Infected Dogs

A standard can also be used in the same way as described above, for standardizing the measurement of the antibody content of sera obtained in clinical and vaccination studies. This enables the antibody content of such sera to be expressed in International Units and facilitates the comparison of results obtained by different laboratories.