WHO International Standard
5th WHO International Standard for HCV NAT
NIBSC code: 14/150
Instructions for use
(Version 2.0, Dated 08/07/2016)

1. INTENDED USE

PLEASE NOTE RECONSTITUTION VOLUME.

NEW: USER NOTICE

This material was formulated from a donation of window period plasma, in order to obtain a suitable concentration the window period donation was then further diluted into negative human plasma. Prior to dilution, the window period donation was seen to contain some very small white lipid particles that could not be removed by centrifugation. In our experience, this is a frequent occurrence in human plasma especially when the material is exposed to freeze thaw cycles which was the case for this donated material. The severity of the particulate presence is also influenced by the diet of the donor, in the case of negative plasma used for diluting purposes, there is a plentiful supply we can be selective and exclude any pack that shows lipid presence, however due to the rarity of the window period donation we could not do this. The final bulk material was mixed thoroughly before and during the dispensing process. The material was then assessed by multiple laboratories in the collaborative study to establish the standard and in accelerated thermal degradation studies in house, in the data sets associated with this work, we have not seen any evidence to suggest that these lipid particles have caused any detriment to the results given in any assay when the material is fully mixed immediately prior to use and particules are included in the assay sample.

The 5th WHO International Standard for hepatitis C virus (HCV), NIBSC code 14/150, is intended to be used for the calibration of HCV secondary standards. The standard comprises genotype 1a HCV antibody-negative, HCV RNA-positive plasma, diluted in pooled human plasma. The virus stock was tested and found negative for HIV-1 RNA, HBV DNA, HAV RNA and parvovirus B19 DNA.

The pooled human plasma diluent was sourced from blood donations and had been tested and found negative for HIV antibody, HCV antibody, HBsAg, syphilis antibody, HTLV antibody, as well as HIV and HCV RNA. The standard has been lyophilized in 1.1 mL aliquots and stored at -20 °C. The material has been calibrated in International Units (IU) against the 2nd WHO International Standard for HCV.

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 unitage of 100,000 IU/mL (~5.00 log10 IU/mL) when reconstituted in 1.1 mL of nuclease-free water. This unit is derived from the combined quantitative and qualitative data obtained in the collaborative study.

4. CONTENTS

Country of origin of biological material: United Kingdom.
Each vial, when reconstituted, will contain 1.1ml of infectious HCV

5. STORAGE

Vials of lyophilised material should be stored at -20°C. 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 material should be reconstituted with 1.1 mL of deionized, nuclease-free molecular-grade water and left for a minimum of 20 minutes with occasional agitation before use. The reconstituted material has a final concentration of 100,000 IU/mL.

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. Once reconstituted, the International Standard should be diluted in human plasma and should be extracted prior to HCV RNA measurement.

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. This material has under gone accelerated thermal degradation studies, data has been reviewed and approved by the WHO Expert Committee on Biological Standardisation and concluded with data to date this material is stable. Real time stability studies are on going.

All stability assessments are in line with the policy of WHO with respect to its reference materials.

9. REFERENCES


3. World Health Organization collaborative study to calibrate the 3rd International Standard for Hepatitis C virus RNA nucleic acid amplification
4. Proposed 5th WHO International Standard for Hepatitis C Virus (HCV) for Nucleic Acid Amplification Technology (NAT)-Based Assays

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:
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

<table>
<thead>
<tr>
<th>Physical and Chemical properties</th>
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</thead>
<tbody>
<tr>
<td>Physical appearance:</td>
<td>Lyophilised</td>
</tr>
<tr>
<td>Corrosive:</td>
<td>No</td>
</tr>
<tr>
<td>Stable:</td>
<td>Yes</td>
</tr>
<tr>
<td>Oxidising:</td>
<td>No</td>
</tr>
<tr>
<td>Hygroscopic:</td>
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</tr>
<tr>
<td>Irritating:</td>
<td>No</td>
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<tr>
<td>Flammable:</td>
<td>No</td>
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<tr>
<td>Handling:</td>
<td>See caution, Section 2</td>
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<tr>
<td>Other (specify):</td>
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<table>
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<th>Toxicological properties</th>
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<tbody>
<tr>
<td>Effects of inhalation:</td>
<td>Not established, avoid inhalation</td>
</tr>
<tr>
<td>Effects of ingestion:</td>
<td>Not established, avoid ingestion</td>
</tr>
<tr>
<td>Effects of skin absorption:</td>
<td>Not established, avoid contact with skin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Suggested First Aid</th>
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</thead>
<tbody>
<tr>
<td>Inhalation:</td>
<td>Seek medical advice</td>
</tr>
<tr>
<td>Ingestion:</td>
<td>Seek medical advice</td>
</tr>
<tr>
<td>Contact with eyes:</td>
<td>Wash with copious amounts of water. Seek medical advice</td>
</tr>
<tr>
<td>Contact with skin:</td>
<td>Wash thoroughly with water.</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Net weight:</th>
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<td>Toxicity not assessed</td>
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<tr>
<td>Veterinary certificate or other statement if applicable</td>
<td>Attached: No</td>
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</table>

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_biol_eftstandardsrev2004.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.