WHO International Standard
HIV-1 RNA Genotypes, 1st International Reference Panel
NIBSC code: 01/466
Instructions for use
(Version 4.0, Dated 04/03/2008)

1. INTENDED USE

HIV-1 exhibits substantial genetic diversity and several different genotypes of HIV-1 exist. There is a major group (group M), consisting of subtypes A-K, and a more diverse collection of outliers have been referred to as groups N and O. Many of the early nucleic acid-based tests (NAT) had a fairly narrow band of specificity targeted mainly at subtype B viruses, as these predominated in the Western World. Greater awareness of the HIV genetic diversity and the desire to detect as many strains of HIV as possible has led to a number of improvements in assay design. However, it has been recognised that some assays are still poor at detecting certain subtypes, occasionally giving low or negative results for samples that are clearly positive in other assays.

The WHO agreed that there is a need for a well characterised reference panel of different HIV-1 subtypes for use in regions of the world where non-B subtypes of HIV-1 predominate and by laboratories involved in NAT diagnosis and by kit manufacturers. The 1st International Reference panel for HIV-1 RNA (Code 01/466) is provided for use in qualitative and quantitative HIV-1 RNA assays.

The Panel consists of 11 samples representing different HIV-1 Genotypes (A, B, C, D, AE, F, G, AA-GH, group N and group O) as well as a negative diluent control.

This panel has been evaluated in an international collaborative study and a report of this study has been submitted and accepted by the WHO Expert Committee on Biological Standardisation (ECBS). At the recommendation of the ECBS, this panel has been established as the 1st International Reference Panel for HIV-1 RNA Genotypes.

2. CAUTION

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

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

There is no unitage assigned to this panel.

4. CONTENTS

Country of origin of biological material: United Kingdom.

The panel contains infectious HIV-1 and must only be handled in appropriate containment facilities by fully trained and competent staff and in accordance with the local national safety guidelines (such as the UK “Protection against blood-borne infections in the workplace: HIV and hepatitis”, Advisory Committee on Dangerous Pathogens, HMSO, London).

5. STORAGE

The Biohazard container contains a panel of 10 viruses of different subtypes/groups and one negative control, following receipt all vials should be held in a freezer below -65°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 material

The vials should be rapidly thawed just before use, and well mixed by inverting or briefly vortexing (5 seconds). The subtype panel consists of 11 vials (code 01/466). The panel members should be tested in accordance with the assay protocol. We anticipate that vials will be used only once.

We do not recommend use after a freeze thaw cycle.

The materials are provided solely for the purposes described within the document. They will be discarded after use and will not be used for any other purpose.

8. STABILITY

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

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Reference materials are held at NIBSC within assured, temperature-controlled storage facilities. Reference Materials should be stored on receipt as indicated on the label.

NIBSC follows the policy of WHO with respect to its reference materials. Users who have data supporting any deterioration in the characteristics of any reference preparation are encouraged to contact NIBSC.

9. REFERENCES

ECBS report ref: WHO/BS/03.1961

10. ACKNOWLEDGEMENTS

N/A

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:
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

<table>
<thead>
<tr>
<th>Physical and Chemical properties</th>
<th>Toxicological properties</th>
<th>Suggested First Aid</th>
<th>Action on Spillage and Method of Disposal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical appearance: Liquid</td>
<td>Corrosive: No</td>
<td>Handling: See caution, Section 2</td>
<td>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.</td>
</tr>
<tr>
<td>Stable: Yes</td>
<td>Oxidising: No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hygroscopic: No</td>
<td>Irritant: No</td>
<td></td>
<td></td>
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<tr>
<td>Flammable: No</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Other (specify): Contains infectious HIV-1 and material of human origin</td>
<td></td>
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</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 inconsistences 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

<table>
<thead>
<tr>
<th>Country of origin for customs purposes*: United Kingdom</th>
</tr>
</thead>
<tbody>
<tr>
<td>* 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.</td>
</tr>
</tbody>
</table>

| Net weight: 11g |
| 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_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.