Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO Reference Reagent
EBOV RNA NP-VP35-GP
NIBSC code: 15/222
Instructions for use
(Version 2.0, Dated 17/11/2020)

1. INTENDED USE

The EBOV RNA NP-VP35-GP WHO Reference Reagent (NIBSC code 15/222) is intended to be used for the calibration of secondary references for nucleic acid amplification technique (NAT)-based assays targeting the Ebola virus NP, VP35, or GP gene. 15/222 is supplied to professional users, typically hospital laboratories, public health organisations, assay kit manufacturers and appropriate research organisations.

2. CAUTION

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

This product is a genetically modified material. It is the responsibility of the end user to seek local biosafety approval for the storage and handling of the material in their workplace. The human serum albumin used in the preparation of the universal buffer has 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

The EBOV RNA NP-VP35-GP WHO Reference Reagent has an assigned unitage of 7.5 log10 units per vial (~32,000,000 units/vial).

4. CONTENTS

Country of origin of biological material: United Kingdom.
Each vial of 15/222 contains 1 mL lyophilized, non-infectious, lentiviral vector (LVV)-based viral particles containing synthetic EBOV RNA formulated in sterile universal buffer comprising 10mM Tris-HCl (pH 7.4) containing 0.5% human serum albumin and 0.1% D-(+)-Trehalose dehydrate. The source material used to prepare 15/222 is an LVV-based construct in which the HIV-1 genes have been substituted with EBOV 2014 genes (Gire et al., 2014; Mattiuzzo et al., 2015). The sequence of the EBOV RNA NP-VP35-GP construct is available through GenBank (accession number KT186367).

5. STORAGE

Vials should be stored at –20ºC or below on receipt.
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 manufactures 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
The vial contents should be reconstituted with 1ml nuclease-free distilled water using safety precautions as described above. The product should be used to calibrate secondary reference materials, for example, by determining the equivalent concentration of secondary reference reagent being calibrated, against 15/222 in parallel. The secondary reference reagent can then be assigned a concentration in terms of the “units”. Once reconstituted for use as calibrator, 15/222 should be diluted in the matrix appropriate to the material being calibrated, and should be extracted prior to 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.
The results obtained from an accelerated thermal degradation study at 1 month indicate that 15/222 is sufficiently stable for storage at -20°C and shipment at ambient temperatures within temperate climate zones. It is recommended however that 15/222 is packed in ice packs or dry ice when shipping to hotter climates. Stability studies are ongoing.
NIBSC follows the policy of WHO with respect to its reference materials.

9. REFERENCES

Gire, S.K., et al., Genomic surveillance elucidates Ebola virus origin and transmission during the 2014 outbreak. Science, 2014. 345(6202): p. 1369-1372.
Mattiuzzo et al., Development of lentivirus-based reference materials for Ebola virus nucleic acid amplification technology-based assays. Plos One, 2015 Nov 12;10(11): e0142751.

10. ACKNOWLEDGEMENTS

We gratefully acknowledge the important contributions of the collaborative study participants. We would also like to thank NIBSC Standards Production and Development for freeze drying and distribution of the candidate material. We also thank David Wood, Micha Nuebling and Robyn Meurant of the WHO and participants of teleconferences for their support, guidance and advice. We thank Daniel Bailey, who facilitated sample shipments and data returns between NIBSC and the National Health Service (NHS)/Public Health England (PHE) Laboratories.
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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

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

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

Physical and Chemical properties	
Physical appearance: Glass vial containing freeze dried material	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: No	Irritant: No
Flammable: No	Handling:See caution, Section 2
Other (specify):	

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_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.