Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO Reference Reagent
EBOV RNA NP-VP35-GP in-run control
NIBSC code: 15/136
Instructions for use
(Version 1.0, Dated 03/11/2015)

1. INTENDED USE

The EBOV RNA NP-VP35-GP in-run control (NIBSC code 15/136) is intended to be used as a control for nucleic acid amplification technique (NAT) assays targeting the Ebola virus NP, VP35 or GP gene. The control should be extracted and amplified alongside unknown samples as part of a continuing quality control programme used to monitor assay performance. 15/136 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.

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 in-run control (NIBSC code 15/136) has been calibrated against the EBOV RNA NP-VP35-GP WHO Reference Reagent (NIBSC code 15/222).
15/136 has a unitage of 3.5 log10 units/mL i.e ~3200 units/mL (95% CL 3.3 - 3.7; n=5) when reconstituted in 1 mL molecular-grade water.

4. CONTENTS

Country of origin of biological material: United Kingdom.
Each vial of 15/136 contains 1 mL lyophilized, non-infectious, synthetic EBOV RNA formulated in sterile universal buffer comprising 10mM Tris-HCl (pH 7.4), 0.5% human serum albumin and 0.1% D-(+)-Trehalose dehydrate. The source material used to prepare 15/136 is a lentiviral vector-based construct in which the HIV-1 genes have been substituted with EBOV 2014 genes (Gire et al., 2014; Mattiuzzo et al., manuscript accepted). The sequence of the EBOV RNA NP-VP35-GP construct is available through GenBank (accession number KT186367).

5. STORAGE

The lyophilised product should be stored at -20°C or below upon 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.
Din ampoules have an “easy-open” coloured stress point, where the narrow ampoule stem joins the wider ampoule body. Tap the ampoule gently to collect the material at the bottom (labeled) end. Ensure that the disposable ampoule safety breaker provided is pushed down on the stem of the ampoule and against the shoulder of the ampoule body. Hold the body of the ampoule in one hand and the disposable ampoule breaker covering the ampoule stem between the thumb and first finger of the other hand. Apply a bending force to open the ampoule at the coloured stress point, primarily using the hand holding the plastic collar. Care should be taken to avoid cuts and projectile glass fragments that might enter the eyes, for example, by the use of suitable gloves and an eye shield. Take care that no material is lost from the ampoule and no glass falls into the ampoule. Within the ampoule is dry nitrogen gas at slightly less than atmospheric pressure. A new disposable ampoule breaker is provided with each ampoule.

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 the vial should be reconstituted with 1mL molecular grade water using safety precautions as described above.
The EBOV RNA NP-VP35-GP in-run control should be used as an aid to assessing the analytical sensitivity of assays for the detection of EBOV NP, VP35 or GP. 15/136 should be used following reconstitution without further dilution, other than as required in individual test procedures.

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 15/136 is sufficiently stable for storage at -20°C and shipment at ambient temperatures within temperate climate zones. It is recommended however that 15/136 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 (manuscript accepted)

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

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

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: Glass ampoules with freeze-dried material		Corrosive:	No
Stable:	Yes	Oxidising:	No
Hygroscopic:	No	Irritant:	No
Flammable:	No	Handling:See caution, Section 2	
Other (specify):	N/A		

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.

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WHO International Laboratory for Biological Standards,
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