Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
1st International Standard for Human Papillomavirus (HPV) Type 31 DNA
NIBSC code: 14/258
Instructions for use
(Version 1.0, Dated 21/11/2019)

1. INTENDED USE

The 1st International Standard for HPV Type 31 (HPV31) DNA for use in nucleic acid-based assays consists of a freeze-dried preparation of recombinant plasmid pT713 containing full-length HPV31 DNA cloned via EcoRI at nt position 3361 (located in the E4 gene) (Lorincz et al.,1986; Eklund et al., 2018). The standard has been formulated in a background of purified human genomic DNA, lyophilized in 0.5 ml aliquots and stored at -20 °C. The material was characterised in an international collaborative study involving 15 laboratories (WHO/BS/2019.2360).

2. CAUTION

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

The material contains DNA from human placenta (Sigma, D7011) . 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 1st International Standard for HPV31 DNA (NIBSC code 14/258) has an assigned unitage of 1.6 x 10^7 International Units (IU) per ampoule.

4. CONTENTS

Country of origin of biological material: United Kingdom.
Each ampoule contains the lyophilized equivalent of 0.5 mL HPV31 plasmid DNA diluted in 10mM Tris buffer pH7.4 containing 1mM EDTA, 5 mg/mL trehalose and human DNA (~1 x 10^6 GEq/mL) derived from placenta.

5. STORAGE

The ampoule should be stored at -20 °C 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 1st International Standard for HPV31 DNA contains high copy number template. There is a high risk of HPV31 plasmid DNA contamination via aerosolization upon opening of the glass ampoule. The material must be opened and handled in a separate laboratory environment, away from other pre-amplification components such as reagents, labware and samples.

The material is supplied lyophilized and, before use, should be reconstituted in 0.5 ml sterile nuclease-free water. Ensure that the inside surface of the ampoule is wetted with the added water so that any particles of freeze-dried material adhering to the glass are reconstituted. The reconstituted material has a final concentration of 3.2 x 10^7 IU/mL. The reconstituted material is suitable for calibration of in-house or working standards for the amplification and detection of HPV31 DNA (WHO/BS/2019.2360). The material should NOT be used to calibrate or assess extraction, precipitation or centrifugation procedures. NIBSC can provide guidance for the use of 14/258 in assays where the extraction step cannot be separated from the amplification step (e.g. sample-in, answer-out platforms). This material has NOT been calibrated for human DNA nucleic acid amplification techniques.

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.
Degradation studies on 14/258 indicate that the freeze-dried material is extremely stable and suitable for long-term storage (WHO/BS/2019.2360). Users should determine the stability of the reconstituted material according to their own method of preparation, storage and use.

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

9. REFERENCES

Lorincz AT, Lancaster WD, Temple GF. Cloning and Characterization of the DNA of a New Human Papillomavirus from a Woman with Dysplasia of the Uterine Cervix. Journal of Virology. 1986;58(1):225-9.

Eklund C, Forslund O, Wallin KL, Dillner J. Continuing global improvement in human papillomavirus DNA genotyping services: The 2013 and 2014 HPV LabNet international proficiency studies. J Clin Virol. 2018;101:74-85.

Mattiuzzo G, Onyekwuluje J, Eklund C, Bentley E, Unger ER, Dillner J, Hockley J, Rigsby P, Wilkinson DE. WHO International Standards for Human Papillomavirus (HPV) DNA for Low-Risk Types HPV6 & HPV11 and High-Risk Types HPV31, HPV33, HPV45, HPV52 & HPV58. Expert Committee on Biological Standardization. 2019. WHO/BS/2019.2360.

10. ACKNOWLEDGEMENTS

We gratefully acknowledge the important contributions of the collaborative study participants and external reference laboratories. This project was funded in part by the World Health Organization.

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

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

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: Lyophilized powder		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: 0.5 g
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.