



**1<sup>st</sup> World Health Organization International Standard for  
Zika virus RNA for Nucleic Acid Amplification Techniques  
(NAT)-Based Assays**

**PEI code 11468/16**

**(Version 1.3, February 2018)**

**1. INTENDED USE**

The World Health Organization (WHO) International Standard for Zika virus (ZIKV) RNA is intended to be used in the standardization of nucleic acid amplification technique (NAT)-based assays for ZIKV. The standard has been prepared using an Asian strain of ZIKV (PF13/251013-18), isolated from a patient serum in French Polynesia in 2013 (1). The material has been lyophilized in 0.5 ml aliquots and stored at -20°C. The material has been evaluated in an international collaborative study involving 24 laboratories performing a wide range of ZIKV NAT assays. Further details of the collaborative study are available in the report (2).

The standard is intended for calibration of secondary reference materials and for definition critical assay attributes such as analytical sensitivities in International Units (IU).

**2. UNITAGE**

This reagent has been assigned a unitage of 50,000,000 IU/ml.

**3. CONTENTS**

Each vial contains 0.5 ml of lyophilized material containing inactivated ZIKV. The virus has been diluted in a solution of hydroxyectoin (0.6 M) and lyophilized. The material is intended for dilution in a diluent appropriate for the assay matrix being tested e.g. plasma, urine etc.

**4. CAUTION**

**THIS PREPARATION IS NOT FOR ADMINISTRATION TO HUMANS.**

The preparation contains heat inactivated ZIKV.

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 probably will include the wearing of protective gloves and avoiding the generation of aerosols. Care should be exercised in opening ampoules or vials, to avoid cuts.

**5. USE OF MATERIAL**

No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution.

The material is supplied lyophilized and should be stored at or below -20°C. Each vial should be reconstituted in 0.5 ml of sterile nuclease-free water. The product should be reconstituted just prior to use. The international standard should be used for the calibration of secondary reference preparations for ZIKV RNA, in parallel. The secondary reference preparations can then be assigned a concentration in IU (3). If not all the material is used immediately, laboratories may aliquot the remaining material into suitable single use volumes which should be stored at or below -70°C.

**6. STABILITY**

*Paul-Ehrlich-Institut  
Paul-Ehrlich-Str. 51-59  
63225 Langen, Germany*

As the stability studies with accelerated conditions indicate high stability of the lyophilized reference material under the recommended storage conditions (at or below -20°C), there is no expiry date assigned to the International Standard. This approach complies with the recommendations for the preparation, characterization and establishment of international and other biological reference standards (4). The reference material is held at the Paul-Ehrlich-Institut (PEI) within assured, temperature-controlled storage facilities. During its life cycle the stability is monitored at regular intervals. The international standard remains valid with the assigned potency and status until withdrawn or amended.

Reference materials should be stored on receipt as indicated on the label. Once, diluted or aliquoted, users should determine the stability of the material according to their own method of preparation, storage and use.

Users who have data supporting any deterioration in the characteristics of any reference preparation are encouraged to contact PEI.

**7. REFERENCES**

The accession number for the ZIKV virus strain is KX369547 (1).

1. Trösemeier J-H, Musso D, Blümel J, Thézé J, Pybus OG, Baylis SA. Genome Sequence of a Candidate World Health Organization Reference Strain for Zika Virus for Nucleic Acid Testing. *Genome Announcements*, 2016;4(5). pii: e00917-16.

2. Baylis SA, Hanschmann KO, Schnierle BS, Trösemeier JH, Blümel J; Zika Virus Collaborative Study Group. Harmonization of nucleic acid testing for Zika virus: development of the 1st World Health Organization International Standard. *Transfusion* 2017; 57:748-761.

3. Manual for the preparation of secondary reference materials for in vitro diagnostic assays designed for infectious disease nucleic acid or antigen detection: Calibration to WHO International Standards.

[http://www.who.int/biologicals/expert\\_committee/WHO\\_Manual\\_Calibration\\_of\\_secondary\\_standards\\_final\\_mn.pdf?ua=1](http://www.who.int/biologicals/expert_committee/WHO_Manual_Calibration_of_secondary_standards_final_mn.pdf?ua=1)

4. World Health Organization. Recommendations for the preparation, characterization and establishment of international and other biological reference standards (revised 2004). WHO Technical Report Series 2006. 932, 73-131.

**8. ACKNOWLEDGEMENTS**

We are grateful to the Didier Musso at the Institut Louis Malardé for supplying the virus strain used to develop the International Standard and to all study participants.

**9. FURTHER INFORMATION**

Further information for this material can be obtained as follows: [whoccivd@pei.de](mailto:whoccivd@pei.de) or WHO Biological Reference Preparations: <http://www.who.int/biologicals/en/>

**10. CUSTOMER FEEDBACK**

Email: [whoccivd@pei.de](mailto:whoccivd@pei.de)  
Web: <http://www.pei.de>



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 [whoccivd@pei.de](mailto:whoccivd@pei.de)

**11. CITATION**

In any circumstance where the recipient publishes a reference to PEI materials, it is important that the correct name of the preparation, the PEI code number, the name and the address of PEI are cited correctly.

**12. MATERIAL SAFETY SHEET**

<b>Physical properties (at room temperature)</b>		
Physical appearance	Lyophilized powder	
Fire hazard	None	
<b>Chemical properties</b>		
Stable	Yes	Corrosive: No
Hygroscopic	No	Oxidising: No
Flammable	No	Irritant: No
Other (specify)	Contains inactivated ZIKV	
Handling:	See caution, section 4	
<b>Toxicological properties</b>		
Effects of inhalation:	Not established - avoid	
Effects of ingestion:	Not established - avoid	
Effects of skin absorption:	Not established - avoid	
<b>Suggested First Aid</b>		
Inhalation	Seek medical advice	
Ingestion	Seek medical advice	
Contact with eyes	Wash thoroughly with water. Seek medical advice	
Contact with skin	Wash thoroughly with water. Seek medical advice	
<b>Action on Spillage and Method of Disposal</b>		
Spillage of vial 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.		

**13. LIABILITY AND LOSS**

Information provided by the Institute is given after the exercise of all reasonable care and skill in its compilation, preparation and issue, but it is provided without liability to the Recipient in its application and use.

It is the responsibility of the Recipient to determine the appropriateness of the materials supplied by the Institute to the Recipient ("the Goods") for the proposed application and ensure that it has the necessary technical skills to determine that they are appropriate. Results obtained from the Goods are likely to be dependent on conditions of use by the Recipient and the variability of materials beyond the control of the Institute.

All warranties are excluded to the fullest extent permitted by law, including without limitation that the Goods are free from

infectious agents or that the supply of Goods will not infringe any rights of any third party.

The Institute shall not be liable to the Recipient for any economic loss whether direct or indirect, which arise in connection with this agreement.

The total liability of the Institute in connection with this agreement, whether for negligence or breach of agreement or otherwise, shall in no event exceed 120% of any price paid or payable by the Recipient for the supply of the Goods.

If any of the Goods supplied by the Institute should prove not to meet their specification when stored and used correctly (and provided that the Recipient has returned the Goods to the Institute together with written notification of such alleged defect within seven days of the time when the Recipient discovers or ought to have discovered the defect), the Institute shall either replace the Goods or, at its sole option, refund the handling charge provided that performance of either one of the above options shall constitute an entire discharge of the Institute's liability under this Condition.