



**1st World Health Organization International Standard
for Hepatitis E Virus RNA Nucleic Acid Amplification
Techniques (NAT)-Based Assays**

PEI code 6329/10

(Version 2.0, 17th April 2018)

1. INTENDED USE

The 1st World Health Organization International Standard for hepatitis E virus (HEV) is intended to be used in the standardization of nucleic acid amplification technique (NAT)-based assays for HEV. The need to develop a standard was demonstrated in an initial study investigating performance of HEV NAT assays (Baylis *et al.*, J. Clin. Microbiol. 2011). The standard has been prepared using a genotype 3a strain of HEV, derived from the plasma of a blood donor and further diluted in human plasma. 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 23 laboratories performing a wide range of HEV NAT assays. Further details of the collaborative study are available in the report WHO/BS/2011.2175.

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 250,000 International Units/ml.

3. CONTENTS

Each vial contains 0.5 ml of lyophilized plasma containing infectious HEV.

4. CAUTION

THIS PREPARATION IS NOT FOR ADMINISTRATION TO HUMANS.

The preparation contains material of human origin, and contains infectious HEV. The reference materials has been diluted in human plasma negative for HIV-1 RNA, HCV RNA, HBV DNA, HBsAg, anti-HBs, anti-HBc, anti-HIV-1/2, anti-HCV and anti-HEV (IgM and IgG).

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 HEV 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

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.

The reference materials are held at PEI within assured, temperature-controlled storage facilities. 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

Baylis, S. A., K. M. Hanschmann, J. Blümel, and C. M. Nübling; on behalf of the HEV Collaborative Study Group. 2011. Standardization of hepatitis E virus (HEV) nucleic acid amplification technique (NAT)-based assays: an initial study to evaluate a panel of HEV strains and investigate laboratory performance. J. Clin. Microbiol. 49:1234-1239.

Baylis, S.A., S. Mizusawa, Y. Okada, and K.M.O Hanschmann. Collaborative Study to Establish a World Health Organization International Standard for Hepatitis E Virus RNA for Nucleic Acid Amplification Technology (NAT)-Based Assays. WHO Report 2011, WHO/BS/2011.2175.

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

8. ACKNOWLEDGEMENTS

We are grateful to the Japanese Red Cross Hokkaido Blood Center for supplying the candidate materials, the Japanese National Institute of Infectious Diseases for their collaboration and to the study participants.

9. FURTHER INFORMATION

This material: whoccivd@pei.de
WHO Biological Reference Preparations:
<http://www.who.int/biologicals/en/>

10. 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 whoccivd@pei.de



11. CITATION

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

12. MATERIAL SAFETY SHEET

Physical properties (at room temperature)		
Physical appearance	Lyophilized powder	
Fire hazard	None	
Chemical properties		
Stable	Yes	Corrosive: No
Hygroscopic	No	Oxidising: No
Flammable	No	Irritant: No
Other (specify)	CONTAINS HUMAN PLASMA & INFECTIOUS HEPATITIS E	
Handling:	See caution, section 4	
Toxicological properties		
Effects of inhalation: <i>contains infectious HEV</i>	Avoid –	
Effects of ingestion: <i>contains infectious HEV</i>	Avoid –	
Effects of skin absorption: <i>contains infectious HEV</i>	Avoid –	
Suggested First Aid		
Inhalation <i>contains infectious HEV</i>	Seek medical advice -	
Ingestion <i>contains infectious HEV</i>	Seek medical advice -	
Contact with eyes Seek medical advice – <i>contains infectious HEV</i>	Wash thoroughly with water.	
Contact with skin Seek medical advice – <i>contains infectious HEV</i>	Wash thoroughly with water.	
Action on Spillage and Method of Disposal		
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.

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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.