1st WHO International Reference Panel for Hepatitis B Virus (HBV) Genotypes for Hepatitis B Surface Antigen (HBsAg) Assays
PEI code 6100/09
(Version 2, 2nd Feb 2015)

1. INTENDED USE

The current WHO International Standard for HBsAg (00/588) was generated from HBV genotype A2/HBsAg subtype *adw2* (1). This HBV genotype is mainly prevalent in Western Europe and in North America and represents only 1% of the HBV-infected population worldwide. The majority of HBV-positive people living in or coming from the Mediterranean area, Africa and Asia are infected with genotypes A1, B, C, D, or E, whereas F and H originate from the Americas. The origin of genotype G is not yet known.

The 1st WHO International Reference Panel for HBV Genotypes for HBsAg assays (PEI code number 6100/09) was established by the WHO Expert Committee on Biological Standardization in October 2011. This reference panel consists of 15 different members representing subgenotypes A1 (Samples 1-2), A2 (Sample 3), B2 (Sample 4), B2 (Sample 5), C2 (Samples 6-8), D1 (Sample 9), D2 (Sample 10), D3 (Sample 11), E (Sample 12), F2 (Samples 13-14), and H (Sample 15). The panel has been evaluated in an international collaborative study with concurrent testing of the 2nd WHO International Standard for HBsAg (00/588). The reference panel is intended for the control and/or for the validation of HBsAg assays.

2. UNITAGE

No unitage is assigned to individual panel members.

3. CONTENTS

Each vial contains 0.5 ml of freeze-dried processed HBsAg positive human plasma. The amount of infectious virus particles in the HBV positive plasma samples was significantly reduced by an ultra-centrifugation step prior to dilution and lyophilisation of the individual panel members. This step resulted in an overall virus removal of >97%, with the exception of Sample 14 with 80 % elimination and Sample 10 without ultracentrifugation due to the limited source volume. Each of the processed HBV positive plasma stocks has been diluted in a negative plasma pool to a final HBsAg concentration of approx. 100 IU/ml, based on the chemiluminescent immunoassay Abbott ARCHITECT Quantitative. The collaborative study data are summarized for each panel member on page 3 (Table and Figure). The values were obtained by comparative testing with the 2nd International Standard for HBsAg (00/588). The collaborative study results are based on 24 qualitative data sets (from 21 different tests) and 6 quantitative data sets (from 2 different tests). Further details of the preparation of the reference materials and of the collaborative study are available in the report WHO/BS/11.2180 (2).

4. CAUTION

THIS PREPARATION IS NOT FOR ADMINISTRATION TO HUMANS.

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

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-20ºC. Each panel member should be **reconstituted with 0.5 ml distilled water**. If all the material is not used immediately, laboratories may aliquot the remaining material into suitable volumes which should be stored at or below -70ºC.

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. Stability of the materials is checked by PEI at regular intervals.

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

(1) Ferguson M, Heath A, Lelie N, Nübling M, Nick S, Gerlich W, Decker R, Padilla A. Report of a collaborative study to 1) assess the suitability of a candidate replacement International Standard for HBsAg and a reference panel for HBsAg and 2) to calibrate the candidate standard in IU. WHO/BS/03.1987

(2) Chudy M, Hanschmann KM, Scheiblauer H, Wend UC, Schüttler CG, Gerlich WH, Nick S, Kreß J, Nübling CM. Collaborative Study to Establish a World Health Organization International Hepatitis Genotype Panel for . WHO Report 2009, WHO/BS/11.2180

8. ACKNOWLEDGEMENTS

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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 correct name of the preparation, 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) none		
Handling:	See caution, section 4	
Toxicological properties		
Effects of inhalation: *contains infectious HBV*		Avoid –
Effects of ingestion: *contains infectious HBV*		Avoid –
Effects of skin absorption: *contains infectious HBV*		Avoid –
Suggested First Aid		
Inhalation *contains infectious HBV*	Seek medical advice –	
Ingestion *contains infectious HBV*	Seek medical advice –	
Contact with eyes	Wash thoroughly with water. Seek medical advice – *contains infectious HBV*	
Contact with skin	Wash thoroughly with water. Seek medical advice – *contains infectious HBV*	
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. 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.

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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.

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Table. Results from the Collaborative Study to Evaluate a Hepatitis B Virus Genotype Panel. Mean potencies (IU/ml) are provided relative to IS 00/588 (The lower 6 rows represent the results from the quantitative HBsAg assays).

Sample / Assay	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1A	105.0	101.3	93.7	67.1	70.5	117.1	94.6	112.5	93.1	94.8	102.1	93.4	71.2	94.1	77.7
2B	102.1	109.2	97.1	62.3	63.8	137.0	125.4	147.4	91.1	104.0	93.8	103.2	75.2	87.4	73.1
2C	112.2	112.6	100.5	57.4	66.9	134.2	119.9	160.0	105.9	116.5	105.4	114.1	77.1	92.8	81.2
3D	88.1	93.0	93.2	53.3	61.8	130.5	97.3	114.7	82.6	138.8	94.2	155.1	75.5	108.1	81.5
4A	122.4	111.5	77.6	82.0	102.7	104.7	113.0	94.4	76.3	89.8	99.0	151.0	76.9	96.1	86.9
5A	82.8	73.3	63.4	57.2	66.3	66.7	72.7	57.6	62.4	72.0	64.3	80.0	73.6	90.8	80.8
6E	94.3	100.3	88.8	58.4	67.6	145.4	126.2	140.4	77.5	79.7	74.0	84.6	72.7	85.6	82.3
7A	74.8	65.6	60.3	55.4	68.1	75.1	78.8	72.1	58.1	66.8	57.7	73.4	73.1	90.9	83.2
7C	75.1	69.2	48.1	50.2	60.7	71.4	83.8	65.1	44.1	57.9	54.7	77.6	68.3	78.7	76.3
8G	81.7	81.3	58.7	48.9	60.9	84.0	86.9	79.4	47.6	64.6	56.3	70.7	54.0	63.8	60.3
8H	109.3	108.3	78.4	63.0	73.4	120.0	116.8	106.2	76.0	87.2	81.6	97.2	67.3	80.0	80.4
9A	89.7	82.6	68.4	63.2	78.0	85.5	85.5	85.0	56.0	61.4	69.8	88.8	77.2	95.8	77.1
10I	93.7	96.5	81.0	51.9	59.2	86.2	82.0	107.4	59.8	57.9	62.0	67.1	52.3	63.8	61.8
11C	54.9	40.8	19.9	44.7	48.0	35.5	37.6	23.4	15.1	35.5	19.4	82.2	58.2	66.1	58.6
12H1	102.6	98.5	81.5	67.3	78.2	95.3	95.8	92.4	82.7	88.0	82.6	87.9	77.7	89.8	98.3
13C	187.4	174.2	166.2	96.3	97.4	170.4	141.5	216.8	160.2	143.7	146.2	170.0	83.4	100.1	111.0
14C	79.1	65.1	57.6	42.6	49.9	76.1	64.6	77.8	76.9	81.5	85.0	51.1	34.1	37.4	59.3
15M	104.0	115.6	98.7	54.2	64.4	164.2	133.0	165.5	107.9	123.6	119.4	137.1	90.9	106.3	97.0
16M	115.6	127.7	104.8	52.7	64.5	195.9	161.9	204.3	124.5	151.7	140.0	161.4	98.6	115.2	107.0
17C	148.2	149.9	135.3	79.0	90.9	186.3	136.6	156.6	184.0	193.4	224.1	238.4	113.6	136.0	130.0
18C	118.8	155.0	121.3	88.7	82.3	154.5	152.9	154.1	129.8	136.0	119.2	96.6	79.5	84.9	64.5
7F	85.0	75.9	57.2	59.9	70.8	70.8	84.0	68.3	53.1	66.7	56.8	84.6	75.5	88.5	85.2
12A	93.1	85.5	80.7	62.2	70.0	91.9	88.4	93.0	81.5	82.1	83.4	86.2	82.3	99.9	86.8
12C	81.4	78.2	69.5	62.4	72.2	78.1	84.7	81.2	64.0	73.4	72.5	83.2	76.0	90.7	86.8
12J	70.0	63.6	56.1	50.5	61.9	66.5	62.3	66.2	51.5	54.6	52.6	62.1	67.8	80.7	76.8
12K	66.4	61.4	52.0	48.3	58.2	56.2	58.2	55.7	47.5	60.1	47.9	60.9	62.7	75.9	70.2
12L	80.4	78.3	69.8	56.1	64.6	71.6	68.2	70.8	59.7	67.0	65.8	72.1	69.9	83.1	72.1
19N	155.1	149.3	122.4	101.2	111.8	174.0	163.2	162.4	111.7	123.4	130.8	190.5	118.7	154.6	164.2

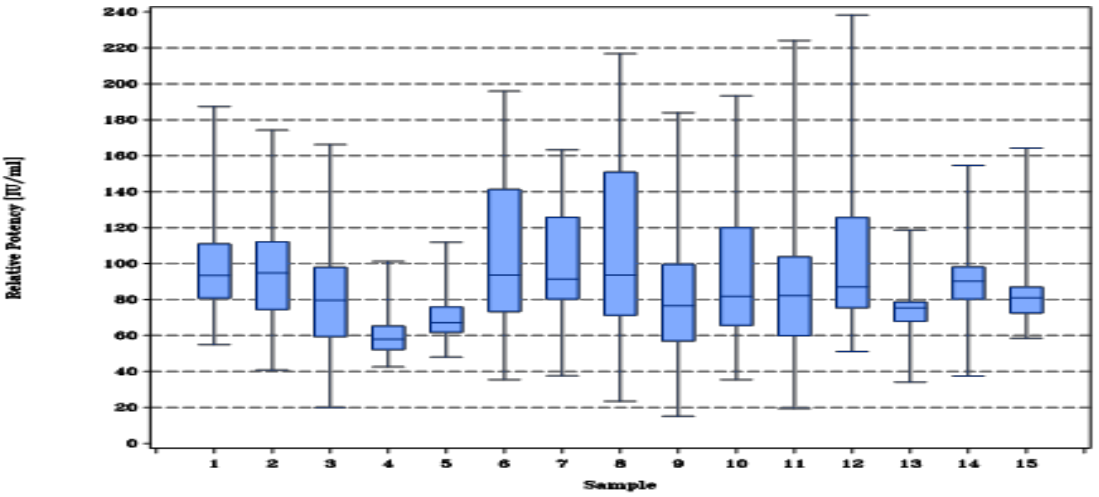

Figure. Box-plot of mean potencies (IU/ml) relative to concurrently tested IS 00/588 for all panel samples.

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