Hướng dẫn sử dụng bản gốc

Tài liệu được cung cấp bằng tiếng Anh

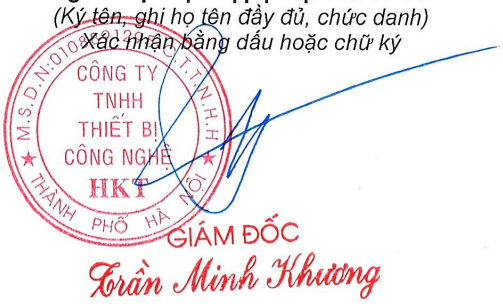
Tài liệu được xác nhận bằng chữ ký số

Tp Hà Nội ngày 15 tháng 04 năm 2022

Người đại diện hợp pháp của cơ sở

(Ký tên, ghi họ tên đầy đủ, chức danh)

Xác nhận bằng dấu hoặc chữ ký



REF **C88044** Σ **2×50Tests**

INTENDED USE

The iFlash-HBsAg assay is a paramagnetic particle chemiluminescent immunoassay (CLIA) for the quantitative determination of Hepatitis B surface antigen （HBsAg） in human serum and plasma using the iFlash Immunoassay Analyzer.

SUMMARY AND EXPLANATION

The hepatitis B surface antigen is a component of the external envelope of the hepatitis B virus particle (HBV). The HBV patient blood contains intact infectious HBV particles, smaller non-infectious “empty” envelope particles and the hepatitis B surface antigen.

The detection of HBsAg in human serum or plasma indicates an infection by the hepatitis B virus. HBsAg is the first immunological marker and is generally present some days or weeks before clinical symptoms begin to appear. HBsAg is observed in persons with acute or chronic hepatitis B infections. HBsAg tests are used within the scope of diagnostic procedures to identify persons infected with HBV and to prevent the transmission of the hepatitis B virus by blood and blood products. HBsAg tests are also used to monitor the course of the disease in persons with acute or chronic HBV infections and if necessary, to check the efficacy of an antiviral therapy. In addition, HBsAg tests are recommended as part of prenatal care, in order to be able to initiate suitable measures for preventing as far as possible the transmission of an HBV infection to the newborn child.

ASSAY PRINCIPLE

The iFlash-HBsAg assay is a sandwich immunoassay.

- 1st incubation: HBsAg in the sample and Anti-HBs-coated paramagnetic microparticles react to form a complex.
- Wash: The unbound materials are washed away from the solid phase in a magnetic field.
- 2nd incubation: Acridinium-ester-labeled anti-HBs conjugate is added to form a reaction mixture.
- Another Wash.
- Trigger of signal: The Pre-Trigger and Trigger Solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs).
- A direct relationship exists between the amount of HBsAg in the sample and the RLUs detected by the iFlash optical system.
- Results are determined via a calibration curve, which is instrument-specifically generated by 3-point calibration and a master curve provided via the reagent QR code.

REAGENTS

Reagent kit, 100 tests, 2 packs, 50 tests/pack

R1	Anti-HBs-coated paramagnetic microparticles, 3.5 mL/pack, 0.05% ProClin 300.
R2	Acridinium-ester-labeled anti-HBs conjugate; 4.0 mL/pack; 0.05% ProClin 300.
R3	Sample diluent, 4.0 mL/pack; 0.05% ProClin 300.
R4	Assay diluent, 4.0 mL/pack; 0.05% ProClin 300.
CAL1	Calibrator 1, 1 bottle, 1.0 mL, Tris buffer with protein stabilizers, 0.05% ProClin 300.
CAL2	Calibrator 2, 1 bottle, 1.0 mL, HBsAg in Tris buffer with protein stabilizers, 0.05% ProClin 300.
CAL3	Calibrator 3, 1 bottle, 1.0 mL, HBsAg in Tris buffer with protein stabilizers, 0.05% ProClin 300.

MATERIALS REQUIRED (BUT NOT PROVIDED)

REF C89999/C89959/C89949, iFlash Pre-Trigger Solution: hydrogen peroxide solution.

REF C89998/ C89958/ C89948, iFlash Trigger Solution: sodium hydroxide solution.

REF C89997, iFlash Wash Buffer: phosphate buffered saline solution with 0.05% ProClin 300.

REF C80001, iFlash Wash Buffer (10×): phosphate buffered saline solution with 0.05% ProClin 300.

REF C89996, reaction vessels.

WARNINGS AND PRECAUTIONS

IVD For in vitro diagnostic use

- No known test method can offer the complete assurance that products derived from human sources will not transmit infection. Therefore, all humanized materials should be considered potentially infectious.
- Exercise the normal precautions required for handling all laboratory reagents.
- Disposal of all waste material should be in accordance with local guidelines.
- Wear gloves when handling specimens or reagents.
- Clean and disinfect all spills of specimens or reagents using a suitable disinfectant.
- iFlash Trigger solution contains sodium hydroxide (NaOH) and should be avoided contact with eyes.
- For further information on warnings and precautions, see Annex B.

REAGENT HANDLING

- The reagents may not be used after the stated expiration date.
- Avoid the formation of foam with all reagents.
- The reagents in the pack and calibrators are ready for use.
- Close the bottles of calibrator right after calibration and store at 2–8°C.
- Do not pool reagents within a reagent kit or between reagent kits.
- Prior to loading the iFlash-HBsAg reagent pack on the system for the first time, resuspend the microparticles by inverting the reagent pack slightly.
- For further information on reagent handling precautions during system operation, refer to the iFlash system operating instruction.

STORAGE AND STABILITY

Storage:

- Store at 2-8°C in an upright position.
- The kit may be used immediately after removal from

2-8°C storage.

Stability:

- Unopened at 2-8°C: up to the stated expiration date.
- Opened at 2-8°C: 28 days.
- Store on-board: 28 days.

SPECIMEN COLLECTION AND PREPARATION

- Serum or plasma (lithium heparin, sodium heparin potassium EDTA, and sodium citrate) are the recommended samples. Other anticoagulants have not been validated for use with the iFlash-HBsAg assay.
- Ensure that complete clot formation in serum specimens has taken place prior to centrifugation.
- Centrifuge the specimens.
- Store specimens at room temperature (20 to 25°C) for no longer than 8 hours.
- If the testing will not be completed within 8 hours, refrigerate the samples at 2 to 8°C.
- If the testing will not be completed within 14 days, or for shipment of samples, freeze at -20°C or colder.
- Frozen specimens must be mixed thoroughly after thawing.
- The samples may be frozen for maximum 3 times.
- Centrifuge specimens with a lipid layer on the top, and transfer only the clarified specimen without the lipemic material.
- Ensure that residual fibrin and cellular matter have been removed prior to analysis.
- Use with caution in handling patient specimens to prevent cross-contamination.
- Do not use heat-inactivated samples.
- Ensure that the patient samples, calibrators and controls are at ambient temperature (20-25°C) before measurement.
- Due to the possible evaporation, specimens and calibrators on the analyzers should be measured within 2 hours.

ASSAY PROCEDURE

- Refer to the system operating instruction or the online help system for detailed information on preparing the system.
- The test-specific parameters stored in barcode on the reagent pack are read in. In case the barcode cannot be read, enter the sequence numbers.
- Carry out calibration, if necessary.
- Place the calibrators CAL1, CAL2, and CAL3 in the calibrator rack in the sample zone. Only keep calibrators open during calibration.
- Test application.
- Load samples (100 µL of sample is needed for each determination in addition to the sample container and system dead volumes).
- Click RUN, the iFlash System performs all the functions automatically and calculates the results.

CALIBRATION

- Traceability: This assay has been standardized against WHO 00/588 Hepatitis B surface antigen international standard.
- Every iFlash-HBsAg reagent kit has a QR code label containing the specific information for calibration of the particular reagent lot.
- To perform an iFlash-HBsAg calibration, test CAL1. CAL2, and CAL3 in duplicate, and the predefined master curve is adapted to the analyzer.
- Once an iFlash-HBsAg calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
  - After 28 days when using the same reagent lot.
  - A reagent kit with a new lot number is used.
  - Controls are out of range.
  - Required by pertinent regulations.

MEASURING RANGE

- 0.1-250 IU/mL (for Adr and Adw subtype of HBsAg)
- 0.2-250 IU/mL (for Ay subtype of HBsAg)

QUALITY CONTROL

Quality control materials should be run as single determinations at least once every 24 hours when the test is in use, once per reagent kit and after every calibration. Include commercially available quality control materials that cover at least two levels of analyte. Follow manufacturer's instructions for reconstitution and storage. Each laboratory should establish mean values and acceptable ranges to assure proper performance. Quality control results that do not fall within acceptable ranges may indicate invalid test results.

RESULT

Calculation:

The iFlash system automatically calculates the analyte concentration of each sample. The results are given in IU/mL.

Interpretation of Results

- Nonreactive: <0.05 IU/mL
- Reactive: ≥ 0.05 IU/mL

A nonreactive result indicates the sample is considered negative for HBsAg.

A reactive result indicates the sample is considered positive for HBsAg.

LIMITATIONS

- The iFlash-HBsAg assay is limited to the determination of HBsAg in human serum or plasma (lithium heparin, sodium heparin, potassium EDTA, and sodium citrate). It has not been validated for use with other types of plasma.
- The use of serum separator (gel) blood collection tubes has been validated for use with this assay. However, it is not possible to survey all manufacturers or tube types.
- If the results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- For diagnostic purposes, the results should be interpreted in light of the total clinical presentation of the patient, including symptoms, clinical history results.

- Specimens from heparinized patients may be partially coagulated and erroneous results could occur due to the presence of fibrin.
- The results from an alternative assays (i.e. EIA or RIA) may not be equivalent and cannot be used interchangeably.
- The assay is unaffected by icterus (bilirubin <30 mg/dL), hemolysis (Hb <1,500mg/dL), lipemia (Intralipid< 1,500 mg/dL) and total serum protein(<10 g/dL).
- No interference was observed from rheumatoid factors up to a concentration of 2,000 IU/mL.
- No interference was observed from anti-nuclear antibodies up to a concentration of 500 U/mL.
- No interference was observed from HAMA up to a concentration of 600 ng/mL.

PERFORMANCE CHARACTERISTICS

Below are the representative performance data, and the results obtained in individual laboratories may differ.

Precision

The iFlash-HBsAg is designed to have a precision of ⩽10% total CV.

The precision of iFlash-HBsAg was determined using HBsAg reagents, samples and controls.

The within run precision was determined by testing each sample in replicates of 10 (n = 10), and calculating percent coefficient of variation (%CV). The results of the study are shown below:

Sample	Mean (IU/mL)	SD	%CV
1	0.94	0.04	4.26

The between run precision was determined by testing each sample in duplicate, two separate runs daily for20 days (n = 80), and calculating percent coefficient of variation (%CV). The results of the study are shown below:

Sample	Mean (IU/mL)	SD	%CV
1	0.50	0.03	6.00
2	100.56	6.54	6.50

Analytical Sensitivity

The detection limit representing the lowest measurable analyte level is 0.1 IU/mL for Adr and Adw subtype and 0.2 IU/mL for Ay subtype, which can be distinguished from zero. It is calculated as the value lying two standard deviations above that of the lowest standard of the master curve (standard 1 + 2 SD, n = 20).

Method comparison

A comparison of the iFlash-HBsAg assay (y) with a commercially available HBsAg assay (x) using clinical samples was performed, and the curve is fitted with Linear regression).

y = 1.0317x + 0.5174

r = 0.9972

Sample concentration: 0.2-216.86 IU/mL

Number of samples measured: 100

Analytical Specificity

The analytical specificity of iFlash-HBsAg assay was evaluated with viral antibody specimens. The nonreactive HBsAg status of each specimen was verified using a commercially available HBsAg assay.

Clinical Category	Number of Specimens	iFlash HBsAg Nonreactive
HAV antibody	5	5
HCV antibody	5	5
HIV-1/2 antibody	8	8
Toxo antibody	7	7
Rubella antibody	10	10
CMV antibody	20	20
HSV antibody	6	6
Epstein-Barr Virus (EBV)	10	6
Total Samples Tested	71	71

Relative Sensitivity

The relative sensitivity of iFlash-HBsAg assay was determined by testing samples that were found reactive in a commercially available HBsAg assay. A total of 306 samples including sequential and single samples were tested with iFlash-HBsAg assay.

Clinical Category	Number of Specimens	Reactive Specimens	Relative Sensitivity
Expected positive	306	306	100%

Relative Specificity

The relative specificity of iFlash-HBsAg assay was determined by testing samples that were found nonreactive in a commercially available HBsAg assay. A total of 802 samples including blood donors and hospitalized patients were tested with iFlash-HBsAg assay.

Clinical Category	Number of Specimens	Non-reactive Specimens	Relative Specificity
Expected negative	802	796	99.46%

REFERENCES

1. F Gavilanes, J M Gonzalez-Ros, D L Peterson. Structure of hepatitis B surface antigen. Characterization of the lipid components and their association with the viral proteins. The Journal of Biological Chemistry 1982;257:7770-7777.
2. Satoh O, Imai H, Yoneyama, Membrane structure of the hepatitis B virus surface antigen particle. J Biochem 2000;127(4):543-50.
3. Jack R. Wands, M. Anthony Wongt, James Shoreyt, et al. Hepatitis B viral antigenic structure: Signature analysis by monoclonal radioimmunoassays. Medical Sciences1984;81:2237-2241.
4. H Delius, N M Gough, C H Cameron et al. Structure of the hepatitis B virus genome. J Virol 1983;47(2): 337–343.
5. D. Robert Dufour. Hepatitis B Surface Antigen (HBsAg) Assays—Are They Good Enough for Their Current Uses. Clinical Chemistry 2006;52(8):

1457-1459.
6. Blumberg B, Alter H. A “new” antigen in leukemia sera. JAMA 1965;191:101-106.
7. Chulanov VP, Shipulin GA, Schaefer S, et al, Kinetics of HBV DNA and HBsAg in acute hepatitis B patients with and without co-infection by other hepatitis viruses. J Med Virol2003;69(3):313-23.
8. Villeneuve JP, Desrochers M, Infante-Rivard C, et al. A long-term follow-up study of asymptomatic hepatitis B surface antigen-positive carriers in Montreal. Gastroenterology 1994;106:1000-1005.
9. Liaw YF, Chu CM. Hepatits B virus infection. Lancet 2009;373:582-592.
10. Evaluation of Precision Performance of Quantitative Measurement. Methods. Approved guideline-Second Edition. Volume 24 Number 25.ISBN 1-56238-542-9 ISSN 0273-3099.
11. Protocols for Determination of Limits of Detection and Limits of Quantitation. Approved Guideline, EP17-A Vol24 No10.ISBN 1-56238-551-8,ISSN 0273-3099.

SHENZHEN YHLO BIOTECH CO., LTD.

Building 1, YHLO Biopark, Baolong 2nd Road, Baolong Subdistrict, Longgang District, 518116 Shenzhen, PEOPLE’S REPUBLIC OF CHINA

ANNEX A:

Explanation of abbreviation

Abbreviation	Explanation
REF	Product No.
CAL	Calibrator
R	Reagent
Σ	Number of tests
	Manufactured by
EC REP	EU Representative
	Caution
	Instructions for use
IVD	In vitro diagnostic medical device
LOT	Lot No.
	Date of manufacture
	Expiry date
	Biohazard Symbol
GHS07	Pictograms for Caution
GHS09	Pictograms for Hazardous to the aquatic environment

ANNEX B:

WARNINGS AND PRECAUTIONS (Proclin 300)

- Hazardous Component: 0.05% Proclin 300

  (Reaction mass of: 5-chloro-2-methyl-4-isothiazolin

  [EC no. 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC no. 200-239-6] (3:1))
- Hazard Statement:

  H317: May cause an allergic skin reaction.

  H319: Causes serious eye irritation.

  H410: Very toxic to aquatic life with long-lasting effects.
- Precautionary Statement:

  P261: Avoid breathing dust/fume/gas/mist/vapours/ spray.

  P264: Wash hands thoroughly after handling.

  P272: Contaminated work clothing should not be allowed out of the workplace.

  P280: Wear protective gloves/protective clothing/eye protection/face protection.

  P305+P351+P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

  P337+P313: If eye irritation persists: Get medical advice/attention.

  P333+P313: If skin irritation or rash occurs: Get medical advice/attention.

  P302+P352: IF ON SKIN: Wash with plenty of soap and water.

  P321: Seek immediate care from a doctor.

  P363: Wash contaminated clothing before reuse.

  P273: Avoid release to the environment.

  P391: Collect spillage.

  P501: Dispose of contents/container in a safe way.