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AFIAS D-Dimer

INTENDED USE

AFIAS D-Dimer is a fluorescence immunoassay (FIA) for the quantitative determination of D-Dimer in human whole blood/plasma. It is useful as an aid in management and monitoring of therapeutic evaluation of thromboembolic disease patients.

For *in vitro* diagnostic use only.

INTRODUCTION

D-dimer, a degradation product of cross-linked fibrin formed during activation of the coagulation system, is commonly used to exclude thromboembolic disease in outpatients suspected of having deep venous thrombosis (DVT) and pulmonary embolism (PE).[1] DVT and PE is relatively common and can cause sudden, fatal embolic events in the pulmonary arteries and other regions.[2-3]

Measurement of the D-Dimer level in plasma has been used as a screening strategy for subclinical DVT. A systematic review reported that a normal range of a highly sensitive D-dimer level accurately ruled out DVT in patients classified as having a low or moderate clinical probability of DVT. The DVT is a high-risk factor for the stroke because of advanced age, hemiplegia, and coagulation disorders, and DVT can cause paradoxical embolic stroke via a right-to-left shunt. Thus, it is important to monitor the level of D-Dimer the incidence and characteristics of DVT in acute stroke patients.[4-7] The Plasma D-dimer level has proven to be useful for DVT screening in chronic stroke patients undergoing rehabilitation.[8-10] National and international scientific organizations have suggested the use of these markers when implementing new diagnostic strategies in patients with coronary syndrome. Since D-Dimer is well known to be an important prognostic indicator of heart diseases, its most definitive role is on monitoring post-treatment clinical status and the post therapeutic evaluation of patients.

PRINCIPLE

The test uses a sandwich immunodetection method.

The detector antibodies in buffer bind to antigens in the sample, forming antigen-antibody complexes, and migrate onto nitrocellulose matrix to be captured by the other immobilized antibodies on a test strip.

More antigens in sample will form more antigen-antibody complexes which lead to stronger fluorescence signal by detector antibodies, which is processed by the instrument for AFIAS tests to show D-Dimer concentration in sample.

COMPONENTS

AFIAS D-Dimer consists of 'cartridges'.

- Each sealed aluminum pouch contains two cartridges.
- Each cartridge packaged in an aluminum pouch has two components including a cartridge part and a detector part.
- The cartridge part contains the membrane called a test strip which has anti-D-Dimer at the test line and streptavidin at the control line.
- The detector part contains anti-D-Dimer-fluorescence conjugate, biotin-BSA-fluorescence conjugate, and sodium azide as a preservative in phosphate buffered saline (PBS).

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow instructions and procedures described in this 'Instructions for use'.
- Use only fresh samples and avoid direct sunlight.
- Lot numbers of all the test components (cartridge and ID chip) must match each other.
- Do not interchange the test components between different lots or use the test components after the expiration date, either of which might yield incorrect test result(s).
- Do not reuse cartridges. A cartridge should be used for testing one sample only.
- The cartridge should remain sealed in its original pouch until just before use. Do not use the cartridge if pouch is damaged or has already been opened.
- Frozen sample should be thawed only once. For shipping, samples must be packed in accordance with local regulations. Sample with severe hemolysis and/or hyperlipidemia must not be used.
- If test components and/or sample are stored in refrigerator, then allow cartridge and sample to be at room temperature for approximately 30 minutes before use.
- The instrument for AFIAS tests may generate slight vibration during use.
- Used cartridges and pipette tips should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- The cartridge contains sodium azide (NaN_3), and it may cause certain health issues like convulsions, low blood pressure, low heart rate, loss of consciousness, lung injury and respiratory failure. Avoid contact with skin, eyes, and clothing. In case of contact, rinse immediately with running water.
- No Biotin interference was observed in **AFIAS D-Dimer** when biotin concentration in the sample was below 250 ng/mL. If a patient has been taking biotin at dosage of more than 0.03 mg a day, it is recommended to test again 24 hours after discontinuation of biotin intake.
- **AFIAS D-Dimer** will provide accurate and reliable results subject to the below conditions.
  - **AFIAS D-Dimer** should be used only in conjunction with the instrument for AFIAS tests.
  - Have to use recommended anticoagulant.

Recommended anticoagulant
Sodium citrate

LIMITATIONS OF THE TEST SYSTEM

- The test may yield false positive result(s) due to the cross-reactions and/or non-specific adhesion of certain sample components to the capture/detector antibodies.
- The test may yield false negative result(s) due to the non-responsiveness of the antigens to the antibodies which is the most common if the epitope is masked by some unknown components, so therefore not being able to be detected or captured by the antibodies. The instability or degradation of the antigens with time and/or temperature may also cause false negative result as it makes the antigens unrecognizable by the antibodies.
- Other factors may interfere with the test and cause erroneous results, such as technical/procedural errors, degradation of the test components/reagents or presence of interfering substances in the test samples.
- Any clinical diagnosis based on the test result must be supported by a comprehensive judgment of the concerned physician in conjunction with clinical symptoms and other relevant test results.

STORAGE AND STABILITY

Storage condition			
Component	Storage Temperature	Shelf life	Note
Cartridge	2 - 8°C	20 months	Unopened
		1 month	Resealed

- Return an unused cartridge to the spare cartridge zipper bag containing the desiccant pack. Reseal along entire edge of zip-seal.

MATERIALS SUPPLIED

REF SMFP-4

Components of **AFIAS D-Dimer**

- Cartridge box :
  - Cartridge 24
  - Pipette tip (zipper bag) 24
  - Spare cartridge zipper bag 1
  - ID chip 1
  - Instructions for use 1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately with **AFIAS D-Dimer.**

Please contact our sales division for more information.

- Instrument for AFIAS tests
  - **AFIAS-1** REF FPRR019
  - **AFIAS-3** REF FPRR040
  - **AFIAS-6** REF FPRR020
  - **AFIAS-10** REF FPRR038
- **Boditech D-Dimer Control** REF CFPO-101
- **Boditech D-Dimer Calibrator** REF CFPO-113

SAMPLE COLLECTION AND PROCESSING

The sample type for **AFIAS D-Dimer** is human whole blood/plasma.

- It is recommended to test the sample within 24 hours after collection when collected sample is stored at room temperature.
- The sample (plasma) should be separated from the clot by centrifugation within 3 hours after the collection of whole blood.
- If testing will be delayed more than 1 day, sample (plasma) should be frozen at -20 °C.
- The sample (plasma) stored frozen at -20 °C for 3 months showed no performance difference.
- However, the whole blood sample should not be kept in a freezer in any case.
- As a repeated freeze-thaw cycle may affect the test result, do not refreeze previously frozen samples.

TEST SETUP

- Check the components of the **AFIAS D-Dimer** as described below: Cartridges, pipette tips, an ID chip, a spare cartridge zipper bag and an instructions for use.
- Ensure that the lot number of the cartridge matches that of the ID chip.
- If the sealed cartridge has been stored in a refrigerator, place them on a clean and flat surface at room temperature for at least 30 minutes before testing.
- Turn on the instrument for AFIAS tests.
- Empty the tip box.
- Insert the ID chip into the 'ID chip port'.

※ **Please refer to the instrument for AFIAS tests operation manual for complete information and operating instructions.**

TEST PROCEDURE

▶ **AFIAS-1, AFIAS-3, AFIAS-6**

General mode

1) Insert the cartridge into the cartridge holder.
2) Insert a tip into the tip hole of the cartridge.
3) Select the 'General mode' in the instrument for AFIAS tests.
4) Take 100 µL of sample (whole blood/plasma/control) using a pipette and dispense it into the sample well of the cartridge.
5) Tap the 'Start' button on the screen.
6) The test result will be displayed on the screen after 12 minutes.

▶ **AFIAS-10**

Normal mode

1) Insert a cartridge into the cartridge holder.
2) Insert a tip into the tip hole of the cartridge.
3) Tap the 'Load' button of the bay that holds the cartridge with the tip to read the barcode of the cartridge and please confirm the item name written on the cartridge.
4) Insert the sample tube into the tube rack.
5) Insert the tube rack into the loading part of the sampling station.
6) Tap the 'Start' button on the screen.
7) The test result will be displayed on the screen after 12 minutes.

Emergency mode – General tip

1) The test procedure is same with the 'Normal mode 1) – 3)'.
2) Convert the 'Emergency mode' in AFIAS-10.
3) Select the tip type (general tip) on the screen.
4) Select the sample type (whole blood/plasma) on the screen.
5) Take 100 µL of the sample using a pipette and dispense it into the sample well of the cartridge.
6) Tap the 'Start' button on the screen.
7) The test result will be displayed on the screen after 12 minutes.

Commented [A1]: 검체 보관, 취급상의 조건설정 시험 시험자료 TF에 누락되어 있음. TF Rev.05 개정시 추가 필요.

Commented [A2]: Check with PM about sample refrigerator storage and she said this part should be eliminated.

INTERPRETATION OF TEST RESULT

- The instrument for AFIAS tests calculates the test result automatically and displays D-Dimer concentration of the test sample in terms of ng/mL (FEU, Fibrinogen equivalent units).
- Working range: 50 - 10,000 ng/mL
- Unit Conversion: DDU x 2 = FEU
  ex) 1 ng/mL (DDU) = 2 ng/mL (FEU)
- Cut-off Value: 500 ng/mL

QUALITY CONTROL

- Quality control tests are a part of the good testing practice to confirm the expected results and validity of the assay and should be performed at regular intervals.
- Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control materials are provided on demand with **AFIAS D-Dimer**. For more information regarding obtaining the control materials, contact Boditech Med Inc.'s Sales Division for assistance.
  (Please refer to the instructions for use of control material.)

PERFORMANCE CHARACTERISTICS

- **Analytical sensitivity**
  - Limit of Blank (LoB) 0.7 ng/mL
  - Limit of Detection (LoD) 10.6 ng/mL
  - Limit of Quantitation (LoQ) 50.0 ng/mL
- **Analytical Specificity**
  - **Cross-reactivity**

Biomolecules such as below the ones in the table were added to the test sample(s) at concentrations much higher than their normal physiological levels in the blood. **AFIAS D-Dimer** test results did not show any significant cross-reactivity with these biomolecules.

Cross-reactants	Concentration
Fibrinogen	10 g/L
Troponin Complex	1,000 ng/mL
CK-MB	1,000 ng/mL
NT-proBNP	100 ng/mL
Myoglobin	3,000 ng/mL

  - **Interference**

Interferents listed in the following table were added to the test sample at the concentration mentioned below. **AFIAS D-Dimer** test results did not show any significant interference with these materials.

Interferents	Concentration
Bilirubin (unconjugated)	700 µmol/L
Cholesterol	13 mmol/L
Glucose	60 mmol/L
Hemoglobin	10 g/L
Ascorbic acid	300 µmol/L
Triglyceride, total	37 mmol/L
Sodium citrate	2 mg/mL

- **Precision**
  - **Single-site study**

Repeatability (within-run precision)
within-laboratory precision (Total precision)
Lot to lot precision

3 Lots of **AFIAS D-Dimer** were tested for 20 days. Each standard material was tested 2 times per day. For each test, each material was duplicated

Single-site study						
D-Dimer [ng/mL]	Repeatability			Within-laboratory precision		
	Mean [ng/mL]	SD	CV (%)	Mean [ng/mL]	SD	CV (%)
100	98.48	6.28	6.4	99.67	5.83	5.9
680	680.30	37.04	5.4	678.42	36.77	5.4
4700	4722.44	291.79	6.2	4713.79	280.07	5.9

D-Dimer [ng/mL]	Lot to Lot precision		
	Mean [ng/mL]	SD	CV (%)
100	99.46	5.48	5.5
680	678.37	39.58	5.8
4700	4698.96	268.65	5.7

  - **Multi-site study**

Reproducibility

1 Lot of **AFIAS D-Dimer** was tested for 5 days in 3 different sites (1 person per 1 site, 1 instrument per 1 site). Each standard material was tested 1 time per and 5 replicates per day.

Multi-site study			
D-Dimer [ng/mL]	Reproducibility		
	Mean [ng/mL]	SD	CV (%)
100	100.59	7.17	7.1
680	673.34	40.77	6.1
4700	4688.72	301.15	6.4

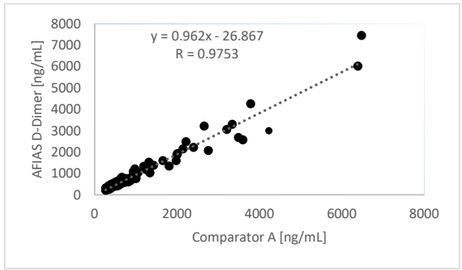
- **Accuracy**

The accuracy was confirmed by testing with 3 different lots of **AFIAS D-Dimer**. The tests were repeated 10 times at each concentration of the control standard.

D-Dimer [ng/mL]	Lot 1	Lot 2	Lot 3	AVG	Recovery (%)
4700	4994.44	4933.36	5055.04	4994.28	106.3
3550	3632.04	3807.59	3625.81	3700.15	104.2
1633	1704.08	1647.64	1719.69	1687.67	103.3
1020	1073.10	1055.31	1047.54	1058.65	103.8
560	560.55	599.14	578.51	580.25	103.6
100	102.92	103.82	107.18	104.89	104.9

- **Comparability**

D-Dimer concentration of 100 clinical samples were quantified independently with **AFIAS D-Dimer (AFIAS-6)** and **comparator A** as per prescribed test procedures. Test results were compared, and their comparability was investigated with linear regression and correlation coefficient (R). The regression equation and correlation coefficient are as follows.



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Note: Please refer to the table below to identify various symbols.

	Sufficient for <n> tests
	Read instruction for use
	Use by Date
LOT	Batch code
REF	Catalog number
	Caution
	Manufacturer
EC REP	Authorized representative of the European Community
IVD	In vitro diagnostic medical device
	Temperature limit
	Do not reuse
CE	This product fulfills the requirements of the Directive 98/79/EC on in vitro diagnostic medical devices

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