OPERATOR'S MANUAL

NIHON KOHDEN

Celltac chemi D-dimer
DD-421W

General

Intended Purpose

For in vitro diagnostic use only.

Celltac chemi D-dimer is for in vitro diagnostic use in the automated quantitative measurement of cross-linked fibrin degradation products (D-dimer) in EDTA treated human whole blood / plasma or citrated plasma, as an aid to diagnosis in the detection and evaluation of thrombotic disorders.

Celltac chemi D-dimer is intended for use in conjunction with a clinical pretest probability (PTP) assessment model to exclusion of the diagnosis of venous thromboembolism (VTE) [deep vein thrombosis (DVT) and pulmonary embolism (PE)].

For use with MEK-1303 automated hematology and clinical chemistry analyzer (only when software Ver.04-01 or later is installed). Celltac chemi D-dimer is intended for laboratory professional use only. Testing population are non-pediatric general population patients undergoing evaluation for the associated conditions.

NOTE
- Nihon Kohden representative will replace a product which proves to be defective until the expiration date shown on the package, provided that the product is used as prescribed by the operating instructions in the operator's manuals.
- Overall judgement must be performed by the physician, referring to the analysis result, clinical findings and other examination results.
- Use a test cartridge for a single test. Do not reuse it.
- Use the product with the specified analyzers only.
- Read the SDS (Safety Data Sheet) carefully before use. The SDS is available from your Nihon Kohden representative.
- The SSP (Summary of Safety and Performance) for the Celltac chemi D-dimer can be obtained from the following URL: https://ec.europa.eu/tools/eudamed

Devices Intended for Use in Combination with

- MEK-1303 automated hematology and clinical chemistry analyzer (software Ver.04-01 or later)

0614-908216

Materials Provided and Materials Required

Materials Provided

Celltac chemi D-dimer contains the following reagents used for D-dimer measurement in a single cartridge.

- DD hemolysis reagent
- DD latex reagent
- DD diluent

Materials Required (Not Provided with the Reagent)

- DD-CAL D-dimer Calibrator
- DD-QC D-dimer Control

Summary and Explanation

D-dimer is a global indicator of coagulation activation and fibrinolysis and, therefore, an indirect marker of thrombotic activity.

The process of D-dimer formation is as follows.
When blood clots by being damaged, thrombin is produced and soluble fibrin monomer is formed.
Soluble fibrin monomers polymerize into an insoluble fibrin network and stabilized by activated factor XIII (FXIIIa), creats covalent cross-links between the fibrin molecules. Plasmin, produced during fibrinolysis, degrades fibrin and stabilized fibrin degradation results in the generation of a mixture of fibrin degradation products, differing mostly in size and composition. All these molecules are classified under the name of D-dimer, irrespective of structure or size. The conventional half-life of D-dimer is around 6–8 h.

The major diagnostic application of D-dimer testing is in the exclusion of thromboembolic events, such as deep vein thrombosis (DVT) or pulmonary embolism (PE) and has been implemented into guidelines for diagnosis and management of DVT and PE. D-dimer testing is recommended for exclusion of DVT and PE in conjunction with a clinical pretest probability (PTP) assessment model in outpatients suspected of VTE.

A general increase in D-dimer concentration resulting in a reduced specificity for exclusion of VTE is observed for the marker D-dimer in patients with recent surgery, trauma or thrombolytic therapy, in patients with cancer, severe infections as well as in elderly patients and during pregnancy. Therefore, D-dimer testing should be used with these variables in mind.

Analyte or Marker

Cross-linked fibrin degradation products (D-dimer)

Target Treated Population

Testing population are non-pediatric general population patients undergoing evaluation for the associated conditions.

Specimen Collection and Preparation

- Whole blood or plasma samples with EDTA as anticoagulant or plasma samples with citrate as anticoagulant.
- For specimen collection and transportation, follow the instructions for use of the blood collection tube and general recommendations for blood sampling.
- Use the sample within the following period after drawing blood.

Whole blood:
- When storing in a refrigerator (2 to 8°C): 3 days
- When storing at room temperature (15 to 30 °C): 24 hours

Plasma:
- When storing in a refrigerator (2 to 8°C): 6 days
- When storing at room temperature (15 to 30°C): 3 days

Intended Users

Celltac chemi D-dimer is intended for professional use only. Qualified personnel (e.g., laboratory professionals) trained in hematology analysis techniques may use the device according to the Instructions for Use.

Symbols

The following symbols are used with the measurement kit. The descriptions of each symbol are given in the table below.

Symbol	Description
	Use by
LOT	Lot number
REF	Catalogue number
	Do not reuse
	Fragile
	Keep away from sunlight
	Temperature limits
	Contains sufficient for <n> tests
	Caution
	Operator's manual; operating instructions
#	Model number
	Manufacturer

Symbol	Description
UDI	Unique device identifier
IVD	In vitro diagnostic medical device
	Exclamation mark [1]
EC REP	Authorized representative in the European Community/ European Union
CE XXXX	The CE mark is a protected conformity mark of the European Union. The four digits after the CE mark indicate the identification number of the Notified Body involved in assessing the product's conformity as a medical device.

[1] The label is affixed in accordance with GHS requirements. For details, refer to "Hazards Identification" (p. 2).

Safety Information

⚠ **WARNING**	A warning alerts the user to the possible injury or death associated with the use or misuse of the instrument.
⚠ **CAUTION**	A caution alerts the user to possible injury or problems with the instrument associated with its use or misuse such as instrument malfunction, instrument failure, damage to the instrument, or damage to other property.

Pay attention to all safety information in this operator's manual.

⚠ WARNING

Always wear rubber gloves to protect yourself from infection when handling and measuring blood samples and test cartridge. The waste fluid may leak from the test cartridge after use.

⚠ CAUTION

- Do not swallow the reagent. If swallowed, rinse the mouth immediately. Do not force vomiting. See a physician.
- If the reagent contacts the eyes, mouth or skin, wash immediately with plenty of water and see a physician.

NOTE
- Do not use the product if it is past the expiration date on the package or if the product is stored under unspecified conditions.
- Store the product inside a polystyrene container and put it in a pharmaceutical refrigerator (2 to 8°C, 36 to 46°F) which allows temperature adjustment. Do not store the product in a domestic refrigerator. This may freeze the reagent.
- Do not freeze the product. Do not use it if it is frozen.
- The usage environment of the product is between 15 and 30°C (59 and 86°F).
- Be careful when handling the reagent because it contains a small amount of toxic sodium azide as a preservative.
- Before removing the outer film of the product, check that the film is not damaged. If the film is damaged, do not use the product.

Hazards Identification

Signal Word

Warning

Hazard Statement

- H317 May cause an allergic skin reaction.

Precautionary Statement Prevention

- P261 Avoid breathing dust/fume/gas/mist/vapours/spray.
- P272 Contaminated work clothing should not beallowed out of the workplace.
- P280 Wear protective gloves/protective clothing/eye protection/face protection.

Precautionary Statement Response

- P302 + P352 IF ON SKIN: Wash with plenty of water.
- P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.
- P362 + P364 Take off contaminated clothing and wash it before reuse.

Precautionary Statement Disposal

- P501 Dispose of contents/container in accordance with local and national regulations.

Supplemental Hazard Information (EU)

- EUH032 Contact with acids liberates very toxic gas
- EUH071 Corrosive to the respiratory tract

Ethylene glycol monophenyl ether	0.50%
2-methylisothiazol-3(2H)-one	≥0.0015%
Sodium azide	<0.1%

Measurement

NOTE: Refer to the analyzer operator's manual for details on measurement.

Measurement Principle

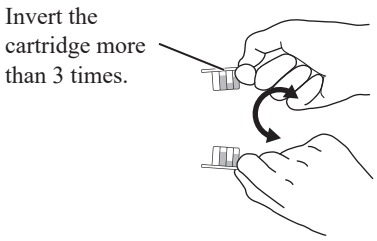
Celltac chemi D-dimer (DD-421W) uses the Latex agglutination immunoturbidimetric assay method to measure cross-linked fibrin degradation products (D-dimer) in the blood.

DD hemolysis reagent and DD diluent are added to a whole blood or plasma sample. After hemolysis, DD latex reagent is added. The D-dimer antigen in the sample reacts with D-dimer antibody in the DD latex reagent, and it agglutinates.

The change in optical absorbance of the agglutinated clumps at a fixed time is measured and this provides the concentration of D-dimer in the sample.

Procedure

1. Prepare the analyzer. Refer to the analyzer operator's manual.
2. Take a test cartridge out of the refrigerator. Wipe off condensation with a dry cloth.
3. Set the test cartridge into the analyzer. Gently invert the test several times. If the agitation is not enough, the result may be inaccurate.



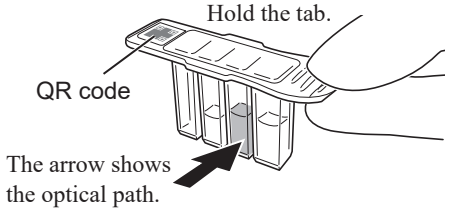
   The analyzer starts reading the QR code on the cartridge, which includes the calibration curve information of the reagent. If an error message appears, refer to the analyzer operator's manual.

4. Measure a sample of whole blood or plasma.

   When using a whole blood sample, gently invert and mix the sample before use because the red blood cell components settle easily and become unhomogenous.

   NOTE
   - No dirt or damage on the test cartridge
   - No leakage from the test cartridge
   - Before setting the test cartridge, check that the reagent is at the bottom of the wells and that there are no bubbles at the bottom of the wells. If the reagent is at the top of the wells or there are bubbles at the bottom of the wells, gently shake the cartridge to make the reagent go down. Otherwise the test result may be inaccurate.

   - Do not use a test cartridge which fell on the floor because the light path surface may be dirty.
   - Do not scratch the test cartridge.
   - Do not touch the QR code and optical path side of the cartridge.



   - In rare cases, depending on the measured sample, the following may occur and cause incorrect measurement.
     - The reagent reacts to an unwanted component in the sample.
     - An interference reaction occurs during measurement.
     - If the measurement value is too high or too low for the patient's condition or if the measurement result is suspicious, remeasure the sample or measure the sample by another measurement method.

- The measurement results are shown in D-dimer units (DDU). When converting the measurement value of this reagent to fibrinogen equivalent units FEU, the measurement device converts it as follows: [µg/mL (DDU)] × 0.58 = [µg /mL (FEU)][1]

  [1] Dempfle, CE. et al.:The Fibrin Assay Comparison Trial (FACT) Evaluation of 23 Quantitative D-dimer Assays as Basis for the Development of D-dimer Calibrators. Thromb Haemost, 85:671-678, 2001.

Calibration

Perform calibration in the following cases.

- Calibration is required as a result of regular quality control.
- Calibration is required as a result of quality control performed after maintenance.
- Other cases where calibration is required.

Reagents Used

Use the D-dimer Calibrator in combination with an DD-421W Celltac chemi D-dimer.

Frequency of Performing Calibration

Determine according to inspections performed by each laboratory.

Procedure

Refer to the analyzer operator's manual.

Quality Control

"Measurement of a control is recommended for statistical quality control of the measurement accuracy of the analyzer.

Also, it is recommended to use the D-dimer control (DD-QC) to measure the control.

Frequency of Performing Quality Control

Determine according to the procedures established by each laboratory.

Control Used

Use the D-dimer control in combination with an DD-421W Celltac chemi D-dimer.

Procedure

Refer to the analyzer operator's manual.

Variable Factors

Variable factors that should be considered when setting appropriate upper and lower limits for quality control include the following.

- Calibrator lots
- Control lots, etc.
- Reagent lots
- Analyzer used for the control measurements
- Measurement frequency

Technical Information

Metrological Traceability of Values Assigned to the Calibrator

D-dimer Calibrator consists of high molecular weight fraction of human cross-linked fibrin degradation products obtained by plasmin fibrinolysis.

Since there is no recognized certified reference material or reference measurement procedure for D-dimer defined in ISO 17511, the traceability of the calibration will be established to a working calibrator prepared.

Values of D-dimer in the reference material are determined using UV spectrophotometry, and the D-dimer value using Celltac chemi D-dimer is calculated according to traceability of the calibration for this system.

Quality Control, Analytical Performance Characteristics

Sensitivity Test

Variation in optical absorbance is over 0.12 when the standard sample containing about 8.0 µg/mL of D-dimer concentration is used as the sample.

Accuracy Test

Test result is 100 ±20% of the known concentration when a control sample of a known concentration is used as the sample.

Repeatability Test

C.V. (coefficient of variation) of test result is within 10% when a control sample of a known concentration is assayed 5 times.

Measurement Range (Measuring Interval)

Plasma: 0.5 to 25 µg/mL

Whole blood (for HCT 40%): 0.5 to 40 µg/mL

Expected Values

- The expected value in the normal population (healthy individuals) was confirmed by clinical performance study using Celltac chemi D-dimer, obtained the following values:

  <0.80 µg/mL (N=575, 95th Percentile)

- Reference guidance: CLSI EP28-A3C

- Expected value in healthy individuals may vary depending on the method, reagent equipment, laboratory operating conditions and population characteristics. It is therefore inappropriate to uniformly apply sample data from a specific country or region, and it is recommended for each laboratory to establish corresponding expected values.
- The Diagnostic Sensitivity, Diagnostic Specificity, and Negative Predictive Value of Celltac chemi D-dimer based on the correlation between similar D-dimer test devices and Celltac chemi D-dimer, and with reference to the Scientific peer-reviewed literature using similar D-dimer test devices. As a result, the cutoff value for excluding venous thromboembolism of Celltac chemi D-dimer was therefore established at 1.0 µg/mL, and the sensitivity, specificity and NPV of Celltac chemi D-dimer using this cutoff value were determined as having clinical performance equivalent to 97.7 to 100%, 28.9 to 97.8%, and 100%, respectively.

Composition

Test cartridge composition:

- DD hemolysis reagent: Colorless to pale yellow or brown liquid
- DD latex reagent: Milky white suspension liquid
- DD diluent: Colorless to pale yellow liquid

Sterilization Method

Celltac chemi D-dimer is not intended to be sterilized or kept in a sterile environment.

Interfering Substances or Limitations

Interfering Substances

The following interfering substances have been confirmed to have no effect on test results below the listed concentrations.

Endogenous substance	Max. concentration
Rheumatoid factor	448 IU/mL
Bilirubin C (conjugated type)	19.2 mg/dL
Bilirubin F (free type)	19.8 mg/dL
Chyle	1388 FTU

Exogenous substance	Max. concentration
Tetracycline	5 mg/dL
Ampicillin	10 mg/dL
Cefotaxime	58 mg/dL
Erythromycin	26 mg/dL
Levofloxacin	4 mg/dL
Azilsartan	23 µg/mL
Atenolol	1 mg/dL
Nifedipine	1.12 mg/dL
Captopril	0.3 mg/dL
Warfarin	9.3 mg/dL
Rivaroxaban	0.3 mg/dL

Exogenous substance	Max. concentration
Acetaminophen	3 mg/dL
Acetylsalicylic Acid	25 mg/dL
Ethinylestradiol	1 ng/mL
Norethisterone	49 ng/mL
Ethanol	600 mg/dL

Cross-reactivity

The following substances at the following up to concentration will not affect the significant cross-reactivity.

Cross-reactant	Max. concentration	Percent Cross-reactivity
Fibrinogen	5070 µg/mL	0.010%
Fragment D	20 µg/mL	None Detected
Fragment E	33 µg/mL	None Detected

Percent cross-reactivity = apparent D-dimer concentration divided by the concentration of the cross-reactant multiplied by 100.

Reference guidance: CLSI EP07-ED3

Analytical Performance Characteristics

Values shown in this section are representative performance data of the Celltac chemi D-dimer and may differ from values acquired in individual facilities.

Analytical Sensitivity

To determine Limit of Detection (LoD), Limit of Blank (LoB), and Limit of Quantification (LoQ) of the Celltac chemi D-dimer.

Reference guidance: CLSI EP17-A2

LOB	LOD	LOQ
0.09 µg/mL	0.16 µg/mL	0.40 µg/mL

Precision

One lot of Celltac chemi D-dimer was used to evaluate precision. Two levels of control sample and one level of pooled plasma were repeated twice in the morning and evening for 20 days.

Reference guidance: CLSI EP05-A3

Sample	Mean (µg/mL)	n	Repeatability		Within-laboratory precision	
			SD	%CV	SD	%CV
Control Lv.1	1.152	80	0.045	3.9%	0.052	4.5%
Control Lv.2	14.294	80	0.225	1.6%	0.317	2.2%
Pooled plasma	2.024	80	0.043	2.1%	0.046	2.2%

Linearity

Samples were measured in quadruplicate to confirm linearity across the measuring range.

Reference guidance: CLSI EP06-ED2

This kit measuring interval obtained was below:

Linearity Measuring Interval
0.50 to 29.67 µg/mL

Correlation

To determine the correlation between the Celltac chemi D-dimer and another commercially available assay correlation coefficient and slope are calculated by Peason's method and Passing bablok fit. (y: Celltac chemi D-dimer, EDTA treated human whole blood sample, x: Another commercially system, citrated plasma samples,)

System (Analyzer)	n	Correlation coefficient	Slope
Other company A	120	0.983	0.9928
Other company B	114	0.998	1.0830

Reference guidance: CLSI EP09-A3

- CLSI. *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition.* CLSI document EP17-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.
- CLSI. *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition.* CLSI document EP05-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.
- CLSI. *Evaluation of Linearity of Quantitative Measurement Procedures, Second Edition.* CLSI document EP06-ED2 Wayne, PA: Clinical and Laboratory Standards Institute; 2020.
- CLSI. *Interference Testing in Clinical Chemistry, Third Edition*. CLSI document EP07-ED3 Wayne, PA :Clinical and Laboratory Standards Institute; 2018.
- CLSI. *Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Third Edition*. CLSI document EP09-A3. Wayne, PA:Clinical and Laboratory Standards Institute; 2013.
- CLSI. *Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory, Third Edition*. CLSI document EP28-A3C. Wayne, PA:Clinical and Laboratory Standards Institute; 2010.

Mathematical Approach upon which the Calculation of the Analytical Result is Made

Calibration information is determined at the factory for each reagent lot. The calibration information is recorded in the QR code, and the analyzer reads the information before measurement and calculates the D-dimer value.

Environmental Conditions

Storage and Transport Environment

Temperature: 2 to 8°C (36 to 46°F)

Usage Environment

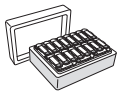
Temperature: 15 to 30°C (59 to 86°F)

Expiration Date

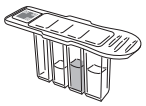
The expiration date is shown on the package.

Lifetime: 18 months

Package and Catalog Number



DD-421W



Test cartridge

Model	Qty	Catalog Number
DD-421W	25 test cartridges	DD-421W

Disposal

⚠ WARNING

Dispose of the test cartridge according to your local laws and your facility's guidelines (including incineration, melt treatment, sterilization, disinfection and request for waste disposal) for disposing of infectious medical waste. Otherwise, it may affect the environment. If there is a possibility that the product may have been contaminated with infection, it may cause infection.

When disposing of the test cartridges, such as when the expiration date is past, follow the instructions on the SDS of the Celltac chemi D-dimer.

Revision History

Edition	Date	Details	Code Number
1st Edition	13 Feb 2026	Initial issue	0614-908216

NOTE: Changes made in the most recent edition are indicated by a bar in the left margin of each page.

Note for users in the territory of the EEA and Switzerland:
Any serious incident that has occurred in relation to the device must be reported to the European Representative designated by the manufacturer and the Competent Authority of the Member State of the EEA and Switzerland in which the user and/or patient is established.

Manufacturer
NIHON KOHDEN CORPORATION
1-31-4 Nishiochiai, Shinjuku-ku,
Tokyo 161-8560, Japan
Phone +81 3-5996-8041
https://www.nihonkohden.com/

EC REP European Representative
NIHON KOHDEN EUROPE GmbH
Raiffeisenstrasse 10, 61191 Rosbach, Germany
Phone +49 6003-827-0 Fax +49 6003-827-599

UK Responsible Person
NIHON KOHDEN UK LTD.
Unit 3, Heyworth Business Park,
Old Portsmouth Road, Peasmarsh,
Guildford, Surrey, GU3 1AF, UK
Phone +44 14-8333-1328

1st Edition: 13 Feb 2026

IVD CE 0123