Lactate Dehydrogenase2

FOR USE WITH
ARCHITECT

en
LDH2
04T03
G93331R03
B4T030

Read Highlighted Changes: Revised March 2024.

REF 04T0320
REF 04T0330

Instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from these instructions.

For laboratory professional use only.

NAME

Lactate Dehydrogenase2 (also referred to as LDH2)

INTENDED USE

The Lactate Dehydrogenase2 assay is used for the quantitation of lactate dehydrogenase (LDH) in human serum or plasma on the ARCHITECT c Systems.

The Lactate Dehydrogenase2 assay is to be used as an aid in the diagnosis and treatment of liver diseases such as acute viral hepatitis, cirrhosis, and metastatic carcinoma of the liver, cardiac diseases such as myocardial infarction, and tumors of the lungs or kidneys.

SUMMARY AND EXPLANATION OF THE TEST

LDH is an enzyme found in the cells of many body tissues, including the heart, liver, kidneys, skeletal muscle, brain, red blood cells, and lungs. It is responsible for converting muscle lactic acid into pyruvic acid, an essential step in producing cellular energy. It is composed of four peptide chains of two subunits (M form and H form) which result in a possible five different isoenzymes which can be separated and quantitated by electrophoresis. Measurement of the total LDH activity in serum or plasma is non-specific and cannot differentiate the tissues of origin of the component isoenzymes.

LDH is used in the differential diagnosis of hemolytic anemia and as a tumor marker in some malignancies such as germ cell tumors.

LDH is elevated in hepatitis, glomerular nephritis, pulmonary embolism, muscle disease, and many leukemias and lymphomas.[1]

As LDH is a non-specific marker, it is used in combination with other markers in diagnosis and patient management.

PRINCIPLES OF THE PROCEDURE

The Lactate Dehydrogenase2 assay is an automated clinical chemistry assay.

Lactate dehydrogenase is a hydrogen transfer enzyme that catalyzes the oxidation of *L*-lactate to pyruvate with the mediation of NAD^+ as a hydrogen acceptor.[2] The rate of the absorbance increase at 340 nm is directly proportional to the LDH activity in the sample.

Methodology: This method uses the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) recommended[3-5] forward reaction - Lactate to Pyruvate.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Kit Contents

Lactate Dehydrogenase2 Reagent Kit 04T03

NOTE: Some kit sizes may not be available. Please contact your local distributor.

Volumes (mL) listed in the following table indicate the volume per cartridge.

REF	04T0320	04T0330
Tests per cartridge set	150	500
Number of cartridge sets per kit	4	4
Tests per kit	600	2000
R1	15.4 mL	44.2 mL
R2	10.7 mL	29.2 mL

R1 Active ingredient: *L*-(+)-lithium-lactate (19.200 g/L). Preservative: sodium azide.

R2 Active ingredient: NAD^+ (28.000 g/L). Preservative: ProClin 300.

Warnings and Precautions

- IVD
- For *In Vitro* Diagnostic Use
- Rx ONLY

Safety Precautions

CAUTION: This product requires the handling of human specimens. It is recommended that all human-sourced materials and all consumables contaminated with potentially infectious materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens. Biosafety Level 2 or other appropriate regional, national, and institutional biosafety practices should be used for materials that contain, are suspected of containing, or are contaminated with infectious agents.[6-9]

The following warnings and precautions apply to: R1	
Contains sodium azide.	
EUH032	Contact with acids liberates very toxic gas.
P501	Dispose of contents / container in accordance with local regulations.

Abbott

The following warnings and precautions apply to: R2	
	
WARNING	Contains hydroxylamine hydrochloride and methylisothiazolones.
H351	Suspected of causing cancer.
H317	May cause an allergic skin reaction.
H402*	Harmful to aquatic life.
H412	Harmful to aquatic life with long lasting effects.
Prevention	
P201	Obtain special instructions before use.
P202	Do not handle until all safety precautions have been read and understood.
P261	Avoid breathing mist / vapors / spray.
P272	Contaminated work clothing should not be allowed out of the workplace.
P273	Avoid release to the environment.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P308+P313	IF exposed or concerned: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

* Not applicable where regulation EC 1272/2008 (CLP) has been implemented.

Follow local chemical disposal regulations based on your location along with recommendations and content in the Safety Data Sheet to determine the safe disposal of this product.

For the most current hazard information, see the product Safety Data Sheet.

Safety Data Sheets are available at www.corelaboratory.abbott or contact your local representative.

For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Reagent Handling

- Do not pool reagents within a kit or between kits.
- Do not use components from one lot with components from another lot.
- Do not reuse containers, caps or plugs due to the risk of contamination and the potential to compromise reagent performance.
- When either the R1 or R2 reagent cartridge becomes empty, replace both cartridges.
- Upon receipt, place reagent cartridges in an upright position for 4 hours before use to allow bubbles that may have formed to dissipate.
- If a reagent cartridge is dropped, place in an upright position for 6 hours before use to allow bubbles that may have formed to dissipate.
- Reagents are susceptible to the formation of foam and bubbles. Bubbles may interfere with the detection of the reagent level in the cartridge and cause insufficient reagent aspiration that may adversely affect results.

For a detailed discussion of reagent handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Reagent Storage

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened	2 to 8°C	Until expiration date	Store in upright position.
Onboard	System Temperature	30 days	
Opened	2 to 8°C	Until expiration date	Store in upright position.

Reagents may be stored on or off the ARCHITECT c System. If reagents are removed from the system, store at 2 to 8°C (with replacement caps) in their original boxes.

For information on unloading reagents, refer to the ARCHITECT System Operations Manual, Section 5.

Indications of Reagent Deterioration

Deterioration of the reagents may be indicated when a calibration error occurs or a control value is out of the specified range. Associated test results are invalid, and samples must be retested. Assay recalibration may be necessary.

For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

The Lactate Dehydrogenase2 assay file must be installed on the ARCHITECT c System prior to performing the assay.

Installation of all the required SmartWash updates on either the MULTIGENT Assay Disk Version 9.00 (or higher) or the Special Chemistry Assay Disk Version 7.00 (or higher) must be completed prior to performing the assay. See below for impacted assay:

				VERSION	
Assay Name	**Short Name**	**REF**	**Assay Number**	**Conventional Units / Alternate Units**	**SI Units / Alternate Units**
Lithium	Lith	8L25	2976	5	5

For detailed information on assay file installation and viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.

For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.

For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

Alternate Result Units

Conversion formula:

(Concentration in Default result unit) x (Conversion factor) = (Concentration in Alternate result unit)

Default Result Unit	Conversion Factor	Alternate Result Unit
U/L	0.01667	µkat/L

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

The specimen types listed below were verified for use with this assay.

Other specimen types and collection tube types have not been verified with this assay.

Specimen Types	Collection Tubes	Special Conditions
Serum	Serum Serum separator	The STD (1:3) Dilution or UNDILUTED Protocols may be used with serum samples.
Plasma	Lithium heparin Lithium heparin separator Sodium heparin	The STD (1:3) Dilution Protocol reduces pre-analytical variability as described in literature.[10-14] This pre-analytical phenomenon is due to platelets and other cellular aggregates present in a layer at the top of heparin plasma samples following centrifugation. For this reason, do not use the UNDILUTED Protocol for plasma samples. **NOTE:** Plasma from primary tubes handled according to the manufacturer's instructions may still contain cells, leading to elevated results. For optimal plasma performance, transfer the plasma from the primary tube to a secondary sample tube after centrifugation. To ensure accurate results, the plasma specimen tube should be filled with the prescribed minimum volume for an appropriate anticoagulant to specimen ratio.

- Liquid anticoagulants may have a dilution effect resulting in lower concentration values for individual specimens.

The instrument does not provide the capability to verify specimen types. It is the responsibility of the operator to verify that the correct specimen types are used in the assay.

Specimen Conditions

- Do not use:
  - heat-inactivated specimens
  - pooled specimens
  - hemolyzed specimens
  - specimens with obvious microbial contamination
  - specimens with fungal growth
- For accurate results, serum specimens should be free of fibrin, red blood cells, and other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- For accurate results, plasma specimens should be free of platelets and other particulate matter. Ensure centrifugation is adequate to remove platelets.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for collection tubes. Gravity separation is not sufficient for specimen preparation.
- Specimens should be free of bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

To ensure consistency in results, recentrifuge specimens prior to testing if

- they contain fibrin, red blood cells, or other particulate matter.

NOTE: If fibrin, red blood cells, or other particulate matter are observed, mix by low-speed vortex or by inverting 10 times prior to recentrifugation.

Prepare frozen specimens as follows:

- Frozen specimens must be completely thawed before mixing.
- Mix thawed specimens thoroughly by low-speed vortex or by inverting 10 times.
- Visually inspect the specimens. If layering or stratification is observed, mix until specimens are visibly homogeneous.
- If specimens are not mixed thoroughly, inconsistent results may be obtained.
- Recentrifuge specimens.

Recentrifugation of Specimens

- Transfer specimens to a centrifuge tube and centrifuge.
- Transfer clarified specimen to a sample cup or secondary tube for testing. For centrifuged specimens with a lipid layer, transfer only the clarified specimen and not the lipemic material.

Specimen Storage

Specimen Type	Temperature	Maximum Storage Time
Serum/Plasma	Room temperature (20 to 25°C)	3 days[15]
	2 to 8°C	3 days[15]
	-20°C	8 weeks[16]

Avoid multiple freeze/thaw cycles.[17]

It is the responsibility of the individual laboratory to determine specific specimen stability criteria for their laboratory per their laboratory workflow.

For additional information on sample handling and processing, refer to CLSI GP44-A4.[18] The storage information provided here is based on references.

Each laboratory may establish a range around -20°C from either the freezer manufacturer's specifications or your laboratory standard operating procedure(s) for specimen storage.

Stored specimens must be inspected for particulates. If present, mix with a low-speed vortex or by inversion and centrifuge the specimen to remove particulates prior to testing.

Specimen Shipping

Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.

Do not exceed the storage limitations listed above.

PROCEDURE

Materials Provided

04T03 Lactate Dehydrogenase2 Reagent Kit

Materials Required but not Provided

- Lactate Dehydrogenase2 assay file found on www.corelaboratory.abbott
- 04V1501 Consolidated Chemistry Calibrator, if using the Calibration method
- Controls containing lactate dehydrogenase
- Saline (0.85% to 0.90% NaCl) for specimen dilution

For information on materials required for operation of the instrument, refer to the ARCHITECT System Operations Manual, Section 1.

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

For a detailed description of how to run an assay, refer to the ARCHITECT System Operations Manual, Section 5.

- If using primary or aliquot tubes, refer to the ARCHITECT System Operations Manual, Section 5 to ensure sufficient specimen is present.
- Minimum sample cup volume is calculated by the system and printed on the Order List report. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.
- Minimum sample volume requirements:
  - Sample volume for single test: 35.0 µL (STD [1:3] Dilution Protocol); 3.2 µL (UNDILUTED Protocol).

    NOTE: This amount does not include the dead volume plus the additional over-aspiration volume. For total sample volume requirements, refer to the ARCHITECT System Operations Manual, Section 5.
- Refer to the Consolidated Chemistry Calibrator package insert REF 04V1501 and/or commercially available control material package insert for preparation and usage.
- For general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Sample Dilution Procedures

Samples with a lactate dehydrogenase value exceeding 4395 U/L (73.26 µkat/L) are flagged with the code "> 4395 U/L" ("> 73.26 µkat/L") if using the STD (1:3) Dilution Protocol and may be diluted with either the Automated Dilution Protocol or the Manual Dilution Procedure.

Samples with a lactate dehydrogenase value exceeding 2000 U/L (33.34 µkat/L) are flagged with the code "> 2000 U/L" ("> 33.34 µkat/L") if using the UNDILUTED Protocol and may be diluted with either the Automated Dilution Protocol or the Manual Dilution Procedure.

Automated Dilution Protocol

The system performs a 1:5 dilution of the sample and automatically calculates the concentration by multiplying the result by the dilution factor.

For details on configuring automated dilutions, refer to the ARCHITECT System Operations Manual, Section 2.

Manual Dilution Procedure

Dilute the sample with saline (0.85% to 0.90% NaCl).

The operator must enter the manual dilution factor in the Patient or Control order screen. The system will use this dilution factor to automatically calculate the concentration of the sample and report the result.

If the operator does not enter the manual dilution factor, the result must be manually multiplied by the appropriate manual dilution factor before reporting the result. If a diluted sample result is less than 24 U/L (0.39 µkat/L) when using the STD (1:3) Dilution Protocol, do not report the result. Rerun using an appropriate dilution.

NOTE: The default Low-Linearity value of the assay file corresponds to the limit of detection of 24 U/L (0.39 µkat/L) for the STD (1:3) dilution. To flag values using the lower limit of the analytical measuring interval of 30 U/L (0.48 µkat/L), the operator must edit the Low-Linearity value, adjusted by the standard dilution factor.

For detailed information on editing the result settings of assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.

For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration

For instructions on performing a calibration, refer to the ARCHITECT System Operations Manual, Section 6.

Calibration can be performed using one of 2 methods:

- Calibration method, using the Consolidated Chemistry Calibrator REF 04V1501. For the Calibration method, use assay file LDH2.
- Calibration Factor method, using a fixed calibration factor value to calculate the result. For the Calibration Factor method, use assay file LDH2F.

Calibration is stable for approximately 15 days (360 hours) for the Calibration method and approximately 30 days (720 hours) for the Calibration Factor method but is required with each change in reagent lot. Verify calibration with at least 2 levels of controls according to the established quality control requirements for your laboratory. If control results fall outside acceptable ranges, recalibration may be necessary.

This assay may require recalibration after maintenance to critical parts or subsystems or after service procedures have been performed.

Quality Control Procedures

As appropriate, refer to your laboratory standard operating procedure(s) and/or quality assurance plan for additional quality control requirements and potential corrective actions.

- At least 2 levels of controls (low and high) are to be run every 24 hours.
- If more frequent control monitoring is required, follow the established quality control procedures for your laboratory.
- If quality control results do not meet the acceptance criteria defined by your laboratory, sample results may be suspect. Follow the established quality control procedures for your laboratory. Recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.
- Review quality control results and acceptance criteria following a change of reagent or calibrator lot.

Controls should be used according to the guidelines and recommendations of the control manufacturer. Concentration ranges provided in the control package insert should be used only for guidance.

For any control material in use, the laboratory should ensure that the matrix of the control material is suitable for use in the assay per the assay package insert.

Quality Control Guidance

Refer to “Basic QC Practices” by James O. Westgard, Ph.D. for guidance on laboratory quality control practices.[19]

RESULTS

Calculation

Calibration Method

The Lactate Dehydrogenase2 (LDH2) assay utilizes the Linear data reduction method to generate a calibration and results.

Calibration Factor Method

The Lactate Dehydrogenase2 (LDH2F) assay utilizes the Factor data reduction method to generate a calibration and results.

The calibration factor for the Lactate Dehydrogenase2 assay is 11270.

The Lactate Dehydrogenase2 assay is traceable to the IFCC reference method.[3-5]

For additional information, refer to the ARCHITECT System Operations Manual, Appendix C.

Flags

Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

Reportable Interval

Based on representative data for the limit of quantitation (LoQ) and the limit of detection (LoD), the ranges over which results can be reported are provided below according to the definitions from CLSI EP34, 1st ed.[20]

	U/L	µkat/L
Analytical Measuring Interval (AMI)[a]	30[d] - 4395	0.48[d] - 73.26
Extended Measuring Interval (EMI)[b]	4395 - 10 000	73.26 - 166.70
Reportable Interval[c]	6 - 10 000	0.10 - 166.70

[a] AMI: The AMI extends from the LoQ to the upper limit of quantitation (ULoQ) for the STD (1:3) dilution. This is determined by the range of values in U/L (µkat/L) that demonstrated acceptable performance for linearity, imprecision, and bias.

[b] EMI: The EMI extends from the ULoQ to the ULoQ × sample dilution when using the 1:5 dilution protocol.

[c] The reportable interval extends from the LoD to the upper limit of the EMI.

[d] Value determined based on the dilution factor and instrument rounding.

NOTE: The default Low-Linearity and High-Linearity values of the assay file correspond to the LoD of 24 U/L (0.39 µkat/L) and ULoQ of 4395 U/L (73.26 µkat/L) for the STD (1:3) dilution, respectively.

LIMITATIONS OF THE PROCEDURE

- Results should be used in conjunction with other data; e.g., symptoms, results of other tests, and clinical impressions.
- Hemolyzed specimens must not be used because erythrocytes contain approximately 150 times more LDH activity than serum.[2]
- Substances that demonstrated interference with the Lactate Dehydrogenase2 assay are listed in the SPECIFIC PERFORMANCE CHARACTERISTICS, Analytical Specificity, Interference section of this package insert.
- Potential interference has not been evaluated for substances other than those described in the SPECIFIC PERFORMANCE CHARACTERISTICS, Analytical Specificity, Interference section of this package insert.
- SmartWashes for assays impacted by Lactate Dehydrogenase2 must be configured to avoid interference due to reagent carryover. See the INSTRUMENT PROCEDURE section of this package insert for the required assay file updates.

EXPECTED VALUES

It is recommended that each laboratory determine its own reference range based upon its particular locale and population characteristics.

Reference Range[21]

Age	Range (U/L)	Range* (µkat/L)
Adult	125 - 220	2.08 - 3.67

* Alternate result units were calculated by Abbott.

SPECIFIC PERFORMANCE CHARACTERISTICS

Representative performance data are provided in this section. Results obtained in individual laboratories may vary.

Unless otherwise specified, the study results provided in this package insert were generated using the Calibration method.

Precision

Within-Laboratory Precision

A study was performed based on guidance from CLSI EP05-A3.[22]

STD (1:3) Dilution Protocol

Testing was conducted using 3 lots of the Lactate Dehydrogenase2 reagents, 3 lots of the Consolidated Chemistry Calibrator, 1 lot of commercially available controls, and 3 instruments. Two controls and 4 serum panels were tested in a minimum of 2 replicates, twice per day on 20 days on 3 reagent lot/calibrator lot/instrument combinations, where a unique reagent lot and a unique calibrator lot are paired with 1 instrument. The performance from a representative combination is shown in the following table.

			Within-Run (Repeatability)		Within-Laboratory[a]	
Sample	n	Mean (U/L)	SD	%CV	SD (Range[b])	%CV (Range[b])
Control Level 1	80	133	2.9	2.2	4.1 (3.1-5.1)	3.1 (2.4-3.6)
Control Level 2	80	381	4.7	1.2	5.6 (4.5-12.4)	1.5 (1.2-3.0)
Panel A	80	32	3.7	11.6	3.9 (2.8-3.9)	12.4 (7.3-12.4)
Panel B	80	154	3.4	2.2	5.2 (3.7-5.7)	3.4 (2.3-3.4)
Panel C	80	1749	14.0	0.8	15.3 (15.3-53.1)	0.9 (0.9-2.7)
Panel D	80	3629	30.4	0.8	41.1 (41.1-119.1)	1.1 (1.1-3.0)

[a] Includes within-run, between-run, and between-day variability.

[b] Minimum and maximum SD or %CV across the 3 reagent lot/calibrator lot/instrument combinations.

			Within-Run (Repeatability)		Within-Laboratory[a]	
Sample	n	Mean (µkat/L)	SD	%CV	SD (Range[b])	%CV (Range[b])
Control Level 1	80	2.22	0.048	2.2	0.068 (0.053-0.085)	3.1 (2.4-3.6)
Control Level 2	80	6.35	0.079	1.2	0.095 (0.075-0.207)	1.5 (1.2-3.0)
Panel A	80	0.53	0.062	11.7	0.067 (0.046-0.067)	12.6 (7.3-12.6)
Panel B	80	2.57	0.056	2.2	0.086 (0.063-0.095)	3.3 (2.3-3.3)
Panel C	80	29.16	0.233	0.8	0.255 (0.255-0.887)	0.9 (0.9-2.7)
Panel D	80	60.50	0.507	0.8	0.686 (0.686-1.986)	1.1 (1.1-3.0)

[a] Includes within-run, between-run, and between-day variability.

[b] Minimum and maximum SD or %CV across the 3 reagent lot/calibrator lot/instrument combinations.

UNDILUTED Protocol

Testing was conducted using 3 lots of the Lactate Dehydrogenase2 reagents, 3 lots of the Consolidated Chemistry Calibrator, 1 lot of commercially available controls, and 3 instruments. Two controls and 3 serum panels were tested in a minimum of 2 replicates, twice per day on 20 days on 3 reagent lot/calibrator lot/instrument combinations, where a unique reagent lot and a unique calibrator lot are paired with 1 instrument. The performance from a representative combination is shown in the following table.

			Within-Run (Repeatability)		Within-Laboratory[a]	
Sample	n	Mean (U/L)	SD	%CV	SD (Range[b])	%CV (Range[b])
Control Level 1	80	137	1.7	1.3	3.9 (1.8-3.9)	2.8 (1.3-2.8)
Control Level 2	80	389	3.3	0.8	8.9 (4.1-11.7)	2.3 (1.1-3.0)
Panel A	80	10	1.3	13.2	1.5 (0.8-1.5)	15.1 (9.0-15.1)
Panel B	80	163	1.6	1.0	4.2 (1.9-4.2)	2.6 (1.2-2.7)
Panel C	80	1853	11.9	0.6	44.5 (27.7-51.0)	2.4 (1.5-2.8)

[a] Includes within-run, between-run, and between-day variability.

[b] Minimum and maximum SD or %CV across the 3 reagent lot/calibrator lot/instrument combinations.

			Within-Run (Repeatability)		Within-Laboratory[a]	
Sample	n	Mean (µkat/L)	SD	%CV	SD (Range[b])	%CV (Range[b])
Control Level 1	80	2.29	0.029	1.3	0.064 (0.029-0.064)	2.8 (1.3-2.8)
Control Level 2	80	6.49	0.053	0.8	0.147 (0.068-0.194)	2.3 (1.1-3.0)
Panel A	80	0.17	0.021	12.8	0.025 (0.013-0.025)	14.9 (8.3-14.9)
Panel B	80	2.71	0.026	1.0	0.069 (0.032-0.071)	2.6 (1.2-2.7)
Panel C	80	30.89	0.198	0.6	0.742 (0.462-0.850)	2.4 (1.5-2.8)

[a] Includes within-run, between-run, and between-day variability.

[b] Minimum and maximum SD or %CV across the 3 reagent lot/calibrator lot/instrument combinations.

Reproducibility

A study was performed based on guidance from CLSI EP05-A3.[22]

STD (1:3) Dilution Protocol

Testing was conducted using 1 lot of the Lactate Dehydrogenase2 reagents, 1 lot of the Consolidated Chemistry Calibrator, 1 lot of commercially available controls, and 3 instruments. Each instrument was operated by a different technician, and each technician prepared an individual sample set. Two controls and 1 serum panel were tested in a minimum of 3 replicates at 2 separate times per day on 5 different days.

					Within-Laboratory[a]			
		Mean	Repeatability				Reproducibility[b]	
Sample	n	(U/L)	SD	%CV	SD	%CV	SD	%CV
Control Level 1	90	129	3.1	2.4	3.4	2.7	3.4	2.7
Control Level 2	90	373	4.9	1.3	5.3	1.4	5.7	1.5
Panel A	90	288	3.8	1.3	5.0	1.7	5.0	1.7

[a] Includes repeatability (within-run), between-run, and between-day variability.

[b] Includes repeatability (within-run), between-run, between-day, and between-instrument variability.

					Within-Laboratory[a]			
		Mean	Repeatability				Reproducibility[b]	
Sample	n	(µkat/L)	SD	%CV	SD	%CV	SD	%CV
Control Level 1	90	2.15	0.050	2.3	0.057	2.6	0.057	2.6
Control Level 2	90	6.22	0.081	1.3	0.088	1.4	0.095	1.5
Panel A	90	4.79	0.064	1.3	0.082	1.7	0.082	1.7

[a] Includes repeatability (within-run), between-run, and between-day variability.

[b] Includes repeatability (within-run), between-run, between-day, and between-instrument variability.

UNDILUTED Protocol

Testing was conducted using 1 lot of the Lactate Dehydrogenase2 reagents, 1 lot of the Consolidated Chemistry Calibrator, 1 lot of commercially available controls, and 3 instruments. Each instrument was operated by a different technician, and each technician prepared an individual sample set. Two controls and 1 serum panel were tested in a minimum of 3 replicates at 2 separate times per day on 5 different days.

					Within-Laboratory[a]			
		Mean	Repeatability				Reproducibility[b]	
Sample	n	(U/L)	SD	%CV	SD	%CV	SD	%CV
Control Level 1	90	131	1.3	1.0	1.6	1.2	1.9	1.5
Control Level 2	90	377	2.4	0.6	2.5	0.7	3.0	0.8
Panel A	90	299	1.9	0.6	4.4	1.5	4.6	1.5

[a] Includes repeatability (within-run), between-run, and between-day variability.

[b] Includes repeatability (within-run), between-run, between-day, and between-instrument variability.

					Within-Laboratory[a]			
		Mean	Repeatability				Reproducibility[b]	
Sample	n	(µkat/L)	SD	%CV	SD	%CV	SD	%CV
Control Level 1	90	2.19	0.021	0.9	0.026	1.2	0.033	1.5
Control Level 2	90	6.28	0.040	0.6	0.041	0.7	0.049	0.8
Panel A	90	4.98	0.032	0.6	0.074	1.5	0.076	1.5

[a] Includes repeatability (within-run), between-run, and between-day variability.

[b] Includes repeatability (within-run), between-run, between-day, and between-instrument variability.

Accuracy

A study was performed to estimate the bias of the Lactate Dehydrogenase2 assay relative to material standardized to the IFCC reference method.[3-5]

STD (1:3) Dilution Protocol

Calibration Method

Testing was conducted using 3 lots of the Lactate Dehydrogenase2 reagents, 2 lots of the Consolidated Chemistry Calibrator, and 3 instruments. The bias ranged from -2.0% to 2.2% across all instruments, calibrator, and reagent lots.

Calibration Factor Method

Testing was conducted using 3 lots of the Lactate Dehydrogenase2 reagents and 3 instruments. The bias ranged from -3.2% to 0.6% across all instruments and reagent lots.

UNDILUTED Protocol

Calibration Method

Testing was conducted using 3 lots of the Lactate Dehydrogenase2 reagents, 2 lots of the Consolidated Chemistry Calibrator, and 3 instruments. The bias ranged from 0.6% to 2.5% across all instruments, calibrator, and reagent lots.

Calibration Factor Method

Testing was conducted using 3 lots of the Lactate Dehydrogenase2 reagents and 3 instruments. The bias ranged from -0.5% to 1.8% across all instruments and reagent lots.

Lower Limits of Measurement

A study was performed based on guidance from CLSI EP17-A2.[23] Testing was conducted using 3 lots of the Lactate Dehydrogenase2 reagents on each of 2 instruments over a minimum of 3 days. The limit of blank (LoB), limit of detection (LoD), and limit of quantitation (LoQ) values are summarized below. These representative data support the lower limit of the analytical measuring interval.

STD (1:3) Dilution Protocol

	U/L	µkat/L
LoB[a]	17[d]	0.28
LoD[b]	24[e]	0.39[e]
LoQ[c]	30[e]	0.48[e]

UNDILUTED Protocol

	U/L	µkat/L
LoB[a]	3	0.05
LoD[b]	6	0.10
LoQ[c]	10	0.17

[a] The LoB represents the 95th percentile from n ≥ 60 replicates of zero-analyte samples.

[b] The LoD represents the lowest concentration at which the analyte can be detected with 95% probability based on n ≥ 60 replicates of low-analyte level samples.

[c] The LoQ is defined as the lowest concentration at which a maximum allowable precision of 20 %CV was met and was determined from n ≥ 60 replicates of low-analyte level samples.

[d] The LoB presented in the table was generated using the Calibration Factor method.

[e] Value determined based on the dilution factor and instrument rounding.

Linearity

A study was performed based on guidance from CLSI EP06-A.[24]

This assay is linear across the analytical measuring interval of 30 to 4395 U/L (0.48 to 73.26 µkat/L) when using the STD (1:3) Dilution Protocol.

This assay is linear across the analytical measuring interval of 10 to 2000 U/L (0.17 to 33.34 µkat/L) when using the UNDILUTED Protocol.

STD (1:3) Dilution Protocol

The STD (1:3) Dilution Protocol High-Linearity value of 1465 U/L (24.42 µkat/L) was derived by dividing the ULoQ of 4395 U/L (73.26 µkat/L) by the dilution factor (1:3).

The STD (1:3) Dilution Protocol Low-Linearity value of 8 U/L (0.13 µkat/L) was derived by dividing the LoD of 24 U/L (0.39 µkat/L) by the dilution factor (1:3).

UNDILUTED Protocol

To utilize the full reportable interval of 6 to 10 000 U/L (0.10 to 166.70 µkat/L), edit the Low-Linearity value to 6 U/L and High-Linearity value to 2000 U/L.

For detailed information on editing the result settings of assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.

Analytical Specificity

Interference

Potentially Interfering Endogenous Substances

A study was performed based on guidance from CLSI EP07, 3rd ed.[25] Each substance was tested at 2 levels of the analyte (approximately 170 U/L and 250 U/L).

No significant interference (interference within ± 9%) was observed at the following concentrations.

STD (1:3) Dilution Protocol

No Significant Interference (Interference within ± 9%)		
	Interferent Level	
Potentially Interfering Substance	Default Units	Alternate Units
Bilirubin (conjugated)	60 mg/dL	712 µmol/L
Bilirubin (unconjugated)	60 mg/dL	1026 µmol/L
Triglycerides	1500 mg/dL	17 mmol/L
Total Protein	15 g/dL	150 g/L

UNDILUTED Protocol

No Significant Interference (Interference within ± 9%)		
	Interferent Level	
Potentially Interfering Substance	Default Units	Alternate Units
Bilirubin (conjugated)	60 mg/dL	712 µmol/L
Bilirubin (unconjugated)	50 mg/dL	855 µmol/L
Triglycerides	1500 mg/dL	17 mmol/L
Total Protein	13 g/dL	130 g/L

Interference beyond ± 9% (based on 95% Confidence Interval [CI]) was observed at the concentrations shown below for the following substances.

UNDILUTED Protocol

Interference beyond ± 9% (based on 95% Confidence Interval [CI])					
Potentially Interfering Substance	Interferent Level		Analyte Level		% Interference (95% CI)
	Default Units	Alternate Units	Default Units	Alternate Units	
Bilirubin (unconjugated)	60 mg/dL	1026 µmol/L	170 U/L	2.83 µkat/L	10% (9%, 10%)
Total Protein	15 g/dL[a]	150 g/L	170 U/L	2.83 µkat/L	-9% (-10%, -8%)

[a] The total protein interferent level presented in the table was generated using the Calibration Factor method.

Potentially Interfering Exogenous Substances

A study was performed based on guidance from CLSI EP07, 3rd ed.[25] Each substance was tested at 2 levels of the analyte (approximately 170 U/L and 250 U/L).

No significant interference (interference within ± 9%) was observed at the following concentrations.

STD (1:3) Dilution and UNDILUTED Protocols

No Significant Interference (Interference within ± 9%)		
	Interferent Level	
Potentially Interfering Substance	Default Units	Alternate Units
Acetaminophen	160 mg/L	1059 µmol/L
Acetylcysteine	150 mg/L	920 µmol/L
Acetylsalicylic acid	30 mg/L	167 µmol/L
Amikacin	15 mg/dL	257 µmol/L
Ampicillin-Na	80 mg/L	215 µmol/L
Ascorbic acid	60 mg/L	341 µmol/L
Biotin	4250 ng/mL	17 µmol/L
Ca-dobesilate	60 mg/L	143 µmol/L
Cefotaxime	53 mg/dL	1166 µmol/L
Cefoxitin	6600 mg/L	15 mmol/L
Cyclosporine	2 mg/L	1.7 µmol/L
Desacetylcefotaxime	6 mg/dL	145 µmol/L
Dipyrone	2 mg/dL	60 µmol/L
Doxycycline	20 mg/L	45 µmol/L

No Significant Interference (Interference within ± 9%)		
	Interferent Level	
Potentially Interfering Substance	Default Units	Alternate Units
Ibuprofen	220 mg/L	1067 µmol/L
Ketoprofen	12 mg/dL	472 µmol/L
Levodopa	8 mg/L	41 µmol/L
Methotrexate	140 mg/dL	3080 µmol/L
4-Methylaminoantipyrine	3.3 mg/dL	152 µmol/L
Methyldopa	25 mg/L	118 µmol/L
Metronidazole	130 mg/L	759 µmol/L
Phenobarbital	70 mg/dL	3017 µmol/L
Phenylbutazone	330 mg/L	1069 µmol/L
Rifampicin	50 mg/L	61 µmol/L
Sodium heparin	4 U/mL	N/A
Suramin	50 mg/dL	386 µmol/L
Theophylline (1,3-dimethylxanthine)	60 mg/L	333 µmol/L

N/A = Not Applicable

Interferences from medication or endogenous substances may affect results.[26]

Method Comparison

A study was performed based on guidance from CLSI EP09-A3[27] using the Passing-Bablok regression method.

Lactate Dehydrogenase2 vs Lactate Dehydrogenase on the ARCHITECT c System						
	n	Units	Correlation Coefficient	Intercept	Slope	Concentration Range
Serum, STD (1:3) Dilution Protocol	116	U/L (µkat/L)	1.00	2.86 (0.05)	0.99	38-1681 (0.63-28.03)
Serum, UNDILUTED Protocol	121	U/L (µkat/L)	1.00	-1.79 (-0.03)	1.02	20-1869 (0.33-31.15)

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Key to Symbols

ISO 15223 Symbols	
	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
REF	List Number
SN	Serial number

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Other Symbols	
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
DISTRIBUTED IN THE USA BY	Distributed in the USA by
FOR USE WITH	Identifies products to be used together
INFORMATION FOR USA ONLY	Information needed for United States of America only
PRODUCT OF IRELAND	Product of Ireland
R1	Reagent 1
R2	Reagent 2
Rx ONLY	For use by or on the order of a physician only (applicable to USA classification only).

Note for number formatting:

- A space is used as thousands separator (example: 10 000 specimens).
- A period is used to separate the integer part from the fractional part of a number written in decimal form (example: 3.12%).

The ARCHITECT c System family of instruments consists of c4000, c8000, and c16000 instruments.

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For customers in the European Union: if, in the course of using this device, you have reason to believe that a serious incident has occurred, report it to the manufacturer and to your national authority.

A summary of safety and performance (SSP) for this device is available at https://ec.europa.eu/tools/eudamed. This is the SSP location after the launch of European Database on Medical Devices. Search for the device using the UDI-DI provided on the outer packaging of the device.

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