Microalbumin (MA) - Urine
Beckman UniCel DxC Systems

Technical Procedure 3143

Principle

Intended Use

MA reagent, when used in conjunction with UniCel® DxC 800 System(s) and SYNCHRON® Systems MA Calibrator, is intended for the quantitative determination of albumin in human urine.

Clinical Significance

Measurement of albumin in urine aids in the diagnosis of kidney dysfunction, and is recommended by the American Diabetes Association to screen for microalbuminuria.(1)

Methodology

MA reagent is used to measure the albumin concentration by a turbidimetric method.(2,3) In the reaction, albumin combines with specific antibody to form insoluble antigen-antibody complexes.

The SYNCHRON® System(s) automatically proportions the appropriate sample and reagent volumes into the cuvette. The ratio used is one part sample to 24 parts reagent. The system monitors the change in absorbance at 380 nanometers. This change in absorbance is proportional to the concentration of albumin in the sample and is used by the System to calculate and express albumin concentration based upon a single-point, non-linear calibration curve.

Chemical Reaction Scheme

Specimen

Acceptable Sample Containers

Spot urine samples should be sent to the laboratory in a 13 X 75 Clear Cap Red Cork BD tube.

24 hour urine collections are received in 3000 ml plastic urine collection jugs.

Type of Specimen

Biological fluid samples should be collected in the same manner routinely used for any laboratory test.(4,5)

Urine is the only sample type recommended for MA. Urine samples should be collected without a preservative. The type of sample collection depends on how results are to be reported.(1,4) If the samples are turbid or contain particulate matter, clarify by centrifugation (4400 x g for 3 minutes).

Specimen Storage and Stability

It is recommended that random urine assays be performed within 2 hours of collection. Urine samples may be stored at 2°C to 8°C for up to 4 days (96 hours). **Frozen samples are not recommended**.

For timed specimens, the collection container is to be kept in the refrigerator or on ice during the collection period. No preservative is required. Upon receipt in the laboratory, the collection container must be stored refrigerated until testing is performed. **Testing must be performed within 4 days (96 hours) of start of collection**.(6,7)

Sample Volume

The optimum volume, when using a 0.5 mL sample cup, is 0.3 mL of sample. For optimum primary sample tube volumes and minimum volumes, refer to the Primary Tube Sample Template.

Unacceptable Specimens

Urine samples aspirated by the IRIS IQ are not acceptable for urine chemistry testing.

Urine collected in a BD UA Preservative Tube is not acceptable for urine chemistry testing.

Refer to the *Procedural Notes* section of this chemistry information sheet for information on unacceptable specimens.

Reagents

Contents

Each kit contains the following items: **Kit Reorder # 475100**

Two MA Reagent Cartridges (2 X 100 tests)

One lot-specific Parameter Card

Volumes per Test

Sample Volume	10 µL
ORDAC Sample Volume	3 µL
Total Reagent Volume	240 µL
Cartridge Volumes	
A	215 µL
B	25 µL
C	-----

Reactive Ingredients

Reagent Constituents

Reagent Buffer	33.0 mL
MA antibody specific for human albumin (goat)	7.2 mL

Also non-reactive chemicals necessary for optimal system performance.

CAUTION!

Sodium azide preservative may form explosive compounds in metal drain lines. See National Institute for Occupational Safety and Health Bulletin: Explosive Azide Hazards (8/16/76).

Materials Needed But Not Supplied With Reagent Kit

SYNCHRON® Systems MA Calibrator
At least two levels of control material Saline

Reagent Preparation

No preparation is required.

Date and initial cartridge and document in reagent log before loading each new cartridge.

Acceptable Reagent Performance

The acceptability of this reagent is determined by successful calibration and by ensuring that quality control results are within acceptance criteria, as defined in the Clinical Chemistry Quality Control Procedure #3000.T.

Reagent Storage and Stability

MA reagent, when stored unopened at 2°C to 8°C, will remain stable until the expiration date printed on the cartridge label. Once opened, the reagent is stable for 60 days unless the expiration date is exceeded.
DO NOT FREEZE.

Equipment

This test is performed on the Beckman UniCel DxC 800 systems; Beckman-Coulter, Brea, California. For technical assistance, call the Beckman-Coulter hotline: 1-800-854-3633.

Refer to the UniCel DxC 800 systems *Reference Manual* for detailed instructions.

Calibration

Calibrator Required

SYNCHRON® Systems MA Calibrator **Reorder #475089**

Calibrator Preparation

No preparation is required.

Calibrator Storage and Stability

SYNCHRON® Systems MA Calibrator is stable until the expiration date printed on the calibrator bottle if capped and stored in the original container at 2°C to 8°C.

CAUTION

Because this product is of human origin, it should be handled as though capable of transmitting infectious diseases. Each serum or plasma donor unit used in the preparation of this material was tested by United States Food and Drug Administration (FDA) approved methods and found to be negative for antibodies to HIV and HCV and nonreactive for HbsAg. Because no test method can offer complete assurance that HIV, hepatitis B virus, and hepatitis C virus or other infectious agents are absent, this material should be handled as though capable of transmitting infectious diseases. This product may also contain other human source material for which there is no approved test. The FDA recommends such samples to be handled as specified in Centers for Disease Control's Biosafety Level 2 guidelines.(6)

Calibration Information

The system must have a lot-specific parameter card and a valid calibration adjustment in memory before controls or patient samples can be run.

Under typical operating conditions the MA reagent cartridge must be calibrated every 30 days and also with certain parts replacements or maintenance procedures, as defined in the UniCel DxC 800 Systems *Instructions for Use* (IFU) manual. This assay has within-lot calibration available. Refer to the UniCel DxC 800 System Instructions For Use (IFU) manual for information on this feature.

For detailed calibration instructions, refer to the UniCel DxC 800 System *Instructions For Use* (IFU) manual.

The system will automatically perform checks on the calibration and produce data at the end of calibration. In the event of a failed calibration, the data will print out with error codes and the system will alert the operator of the failure. The explanation of these error codes can be found in the UniCel DxC 800 System *Instructions For Use* (IFU) manual.

Traceability

The measurand (MA) in this calibrator is traceable to the IFCC reference preparation for plasma proteins. BCR-470* (1,2) Traceability process is based on prEN ISO 17511.

The assigned values were established using representative samples from this lot of calibrator and are specific to the assay methodologies of the SYNCHRON LX and the UniCel DxC reagents. Values assigned by other methodologies may be different.

*BCR is a registered trademark of EC-JRC-IRMM

Quality Control

At least two levels of control material should be analyzed each shift. In addition, these controls should be run with each new calibration, with each new reagent cartridge, and after specific maintenance or troubleshooting procedures as detailed in the UniCel DxC 800 System *Instructions For Use* manual. More frequent use of controls or the use of additional controls is left to the discretion of the user based on workload and workflow.

The following controls should be used in accordance with the package instructions for use inserts. Quality control results should be evaluated and handled with respect to the Clinical Chemistry Quality Control Procedure #3000.T. Controls are compiled statistically in the LIS and reagent lot changes are documented on DxC Reagent Log sheets.

Quality Control Material

Control	Storage	Catalog No.
MAS UriChemTrak 1	2°C to 8°C*	UR11001
MAS UriChemTrak 2	2°C to 8°C*	UR22002

*Unopened vials are stable until the expiration date on the label. Once opened, vials of control are stable for 30 days when stored tightly capped at 2°C to 8°C. **Do not freeze**. Bacterial contamination produces an increase in turbidity and/or a characteristic odor. Discard vial if evidence of microbial contamination is observed.

Testing Procedure

1. If necessary, load the reagent onto the system. A lot-specific parameter card must be loaded one time for each lot.
2. After reagent load is completed, calibration may be required.
3. Program samples and controls for analysis.
4. After loading samples and controls onto the system, follow the protocols for system operation. For detailed testing procedures, refer to the UniCel DxC 800 System *Instructions For Use* (IFU) manual.

Calculations

UniCel DxC Systems perform all calculations internally to produce the final reported result. The system will calculate the final result for sample dilutions made by the operator when the dilution factor is entered into the system during sample programming.

If the dilution was programmed in the DataLink, the final calculated result from a dilution will not be calculated by the UniCel DxC system but by the DataLink.

24-hour timed urine specimens are calculated from the following equation:

$$\text{Microalbumin } \frac{\text{mg}}{\text{dL}} \text{ X } \frac{\text{dL}}{\text{100mL}} \text{ X Total volume collected (mL) = mg/24hr}$$

Calculations are only performed on 24 hour collections (±15 minutes) and reported as mg/24 hrs. Do not round off total collection time.

Urine albumin:creatinine ratio (random collection):

$$\frac{\text{urine albumin, mg/dL}}{\text{urine creatinine, mg/dL}} \text{ X } \frac{\text{1000 mg}}{\text{g}} = \text{mg/g creatinine}$$

Reporting Results

Equivalency between the SYNCHRON LX and UniCel DxC 800 Systems has been established. Chemistry results between these systems are in agreement and data from representative systems may be shown.

Reference Intervals

The following reference intervals were taken from literature and a study performed on SYNCHRON Systems.(1)

Reference Intervals

Intervals	Sample Type	Conventional Units	S.I Units
SYNCHRON LX	Random Urine	< 1.9 mg/dL	< 19.0 mg/L

American Diabetes Association Definition of Microalbuminuria

Category	24-Hour Collection	Timed Collection	Spot Collection
Normal	< 30 mg/24 hrs	< 20 µg/min	< 30 µg/mg creatinine
Microalbuminuria	30 - 300 mg/24 hrs	20 - 200 µg/min	30 - 300 µg/mg creatinine
Clinical albuminuria	>300 mg/24 hrs	> 200 µg/min	> 300 µg/mg creatinine

Refer to References (8,9,10) for guidelines on establishing laboratory-specific reference intervals.

Procedural Notes

Limitations

An effort should be made to keep pipetted samples free from gross debris. It is recommended that highly turbid specimens be centrifuged before analysis.

Urine samples contaminated with blood are not recommended.

If serum protein carryover is suspected, a saline cup should be assayed prior to analysis of microalbumin samples.

Interferences

The following substances were tested for interference with this methodology:

Interferences[a]

Substance	Source	Level Tested	Observed Effect
Ascorbic Acid	NA[a]	500 mg/dL	NSI[b]
Calcium	NA	130 mg/dL	NSI
Citrate	NA	50 mg/dL	NSI
Creatinine	NA	160 mg/dL	NSI
Glucose	NA	200 mg/dL	NSI
Magnesium	NA	400 mg/dL	NSI
Oxalate	NA	30 mg/dL	NSI
Urea	NA	140 mg/dL	NSI

[a] NA = Not applicable.

[b] NSI = No Significant Interference (within ±0.25 mg/dL or 10.8%).

Refer to References (11,12,13) for other interferences caused by drugs, disease and preanalytical variables.

Performance Characteristics

Analytical Measurement Range (AMR)

The SYNCHRON® System(s) method for the determination of MA provides the following AMR:

Analytical Measurement Range (AMR)

Sample Type	Conventional Units	S.I. Units
Urine	0.2 - 30 mg/dL	2 - 300 mg/L
Urine (ORDAC)	24 - 97 mg/dL	240 - 970 mg/L

Clinical Reportable Range (CRR)

Clinical Reportable Range (CRR)

Sample Type	Conventional Units	S.I. Units
Urine	0.2 - diluted result mg/dL	2 - diluted result mg/L

Samples with concentrations below the AMR and CRR (0.2 mg/dL) are reported as "**< 0.2 mg/dL**".
Samples with concentrations greater than the AMR are diluted with saline and reanalyzed.

If the dilution was programmed in Remisol, the final calculated result from a dilution will not be calculated by the UniCel DxC system but by Remisol.

Sensitivity

Sensitivity is defined as the lowest measurable concentration which can be distinguished from zero with 95% confidence. Sensitivity for MA determination is 0.2 mg/dL (2.0 mg/L).

Equivalency

Equivalency was assessed by Deming regression analysis of patient samples to accepted clinical methods.

As determined by Beckman.

Urine (in the range of 0.4 to 26.1 mg/dL):

Y (SYNCHRON LX Systems)	= 0.968X - 0.06
N	= 111
MEAN (SYNCHRON LX Systems)	= 3.97
MEAN (Nephelometric Immunochemistry Analyzer)	= 4.16
CORRELATION COEFFICIENT (r)	= 0.993

Refer to References (14) for guidelines on performing equivalency testing.

As determined at UCDMC

Urine (in the range of 0.2 to 37.4 mg/dL):

Y (UniCel DxC800-4118)	= 0.959X + 0.08
N	= 25
MEAN (UniCel DxC800-4118)	= 3.34
MEAN (SYNCHRON LX20-2194)	= 3.40
CORRELATION COEFFICIENT (r)	= 0.9999

Urine (in the range of 0.2 to 37.4 mg/dL):

Y (UniCel DxC800-4427)	= 0.942X + 0.14
N	= 25
MEAN (UniCel DxC800-4427	= 3.35
MEAN (SYNCHRON LX20-2194)	= 3.40
CORRELATION COEFFICIENT (r)	= 0.9998

Urine (in the range of 0.2 to 37.4 mg/dL):

Y (UniCel DxC800-4449)	= 0.948X + 0.13
N	= 25
MEAN (UniCel DxC800-4449)	= 3.35
MEAN (SYNCHRON LX20-2194)	= 3.40
CORRELATION COEFFICIENT (r)	= 0.9998

Urine (in the range of 0.2 to 35.9 mg/dL):

Y (UniCel DxC800-4427)	= 0.9983X + 0.07
N	= 25
MEAN (UniCel DxC800-4427)	= 3.35
MEAN (UniCel DxC800-4118)	= 3.34
CORRELATION COEFFICIENT (r)	= 0.9999

Urine (in the range of 0.2 to 35.9 mg/dL):

Y (UniCel DxC800-4449)	= 0.988X + 0.05
N	= 25
MEAN (UniCel DxC800-4449)	= 3.35
MEAN (UniCel DxC800-4118)	= 3.34
CORRELATION COEFFICIENT (r)	= 0.9999

Urine (in the range of 0.2 to 35.3 mg/dL):

Y (UniCel DxC800-4449)	= 1.005X - 0.02
N	= 25
MEAN (UniCel DxC800-4449)	= 3.35
MEAN (UniCel DxC800-4427)	= 3.35
CORRELATION COEFFICIENT (r)	= 1.000

Precision

A properly operating UniCel DxC System(s) should exhibit precision values less than or equal to the following: As determined by Beckman

Precision Values

Type of Precision	Sample Type	1 SD		Changeover Value[a]		%CV
		mg/dL	mg/L	mg/dL	mg/L	
Within-run	Urine	0.125	1.25	2.3	23	5.4
	Urine (ORDAC)	NA[b]	NA	NA	NA	5.4
Total	Urine	0.187	1.87	2.3	23	8.0
	Urine (ORDAC)	NA	NA	NA	NA	8.0

[a] When the mean of the test precision data is less than or equal to the changeover value, compare the test SD to the SD guideline given above to determine the acceptability of the precision testing. When the mean of the test precision data is greater than the changeover value, compare the test % CV to the guideline given above to determine acceptability. Changeover value = (SD guideline/CV guideline) x 100.

[b] NA = Not aplicable

Refer to References (15) for guidelines on performing precision testing.

Precision established at UCDMC

Type of Precision	Sample Type	n	Mean (mg/dL)	1 SD	%CV
DxC800-4118 Within-run	MAS UriChemTrak 1	20	2.21	0.02	1.0
	MAS UriChemTrak 2	20	10.72	0.11	1.0
DxC800-4427 Within-run	MAS UriChemTrak 1	20	2.20	0.03	1.5
	MAS UriChemTrak 2	20	11.77	0.12	1.0
DxC800-4449 Within-run	MAS UriChemTrak 1	20	2.20	0.02	1.0
	MAS UriChemTrak 2	20	11.52	0.10	0.8

Type of Imprecision	Sample Type	n	Mean (mg/dL)	SD	%CV
DxC800-4118 Day to Day	MAS UriChemTrak 1	268	2.2	0.07	3.2
	MAS UriChemTrak 2	293	11.2	0.27	2.4
DxC800-4427 Day to Day	MAS UriChemTrak 1	372	2.2	0.11	5.0
	MAS UriChemTrak 2	386	11.3	0.32	2.8
DxC800-4449 Day to Day	MAS UriChemTrak 1	363	2.2	0.09	4.1
	MAS UriChemTrak 2	361	11.5	0.28	2.4

Comparative performance

Data for a SYNCHRON LX System evaluated using the NCCLS Approved Guideline EP5-A appears in the table below.(14)

NCCLS EP5-A Precision Estimate Method

Type of Imprecision	Sample Type	No. Systems	No. Data Points[a]	Test Mean Value (mg/dL)	EP5-A Calculated Point Estimates	
					SD	%CV
Within-run	Urine Control 1	1	80	1.0	0.09	8.7
	Urine Control 2	1	80	3.0	0.11	3.7
	Urine Control 3	1	80	39.3	0.62	1.6
Total	Urine Control 1	1	80	1.0	0.12	12.2
	Urine Control 2	1	80	3.0	0.15	5.1
	Urine Control 3	1	80	39.3	0.72	1.8

[a] The point estimate is based on the data from one system, run for twenty days, two runs per day, two observations per run on an instrument operated and maintained according to the manufacturer's instructions.

NOTICE

These degrees of precision and equivalency were obtained in typical testing procedures on a SYNCHRON LX® System and are not intended to represent the performance specifications for this reagent.

Additional Information

For more detailed information on UniCel DxC Systems, refer to the *Instructions for Use* and *Reference* manual.

References

1. American Diabetes Association, "Diabetic Nephropathy", Diabetes Care, 20 [Suppl 1]: 524 7 (1997).
2. Boyden, A., Button, E., Germerog, D., "Precipitin Testing With Special Reference to the Measurement of Turbidity", J. Immunol., 57:211 (1947).
3. Hellsing, K., "The Effects of Different Polymers for Enhancement of the Antigen-Antibody Reaction as Measured with Nephelometry", Protides of the Biological Fluids, 23:579 (1973).
4. Tietz, N. W., "Specimen Collection and Processing; Sources of Biological Variation", Textbook of Clinical Chemistry, 5th Edition, W. B. Saunders, Philadelphia, PA (2005).
5. National Committee for Clinical Laboratory Standards, Routine Urinalysis and Collection, Transportation and Preservation of Urine Specimens Tentative Guideline, NCCLS publication GP16-T, Villanova, PA (1992).
6. CDC-NIH, Biosafety in Microbiological and Biomedical Laboratories, 5th Edition, (Washington, D.C.: U.S. Government Printing Office, 2009). (CDC 21-1112).
7. van Berkel, E.A.T., Schel, O., Boer, A.K., “Influence of the Storage Temperature on Urine Analysis in Timed Samples”, Ned Tijdschr Klin Chem Labgeneesk, 35:173-174 (2010).
8. Tietz, N. W., ed., Fundamentals of Clinical Chemistry, 6th Edition, W. B. Saunders, Philadelphia, PA (2007).
9. National Committee for Clinical Laboratory Standards, How to Define, Determine, and Utilize Reference Intervals in the Clinical Laboratory Approved Guideline, NCCLS publication C28-A, Villanova, PA (1995).
10. Henry, J. B., Clinical Diagnosis and Management by Laboratory Methods, 22nd Edition, W. B. Saunders Company, Philadelphia, PA (2006).
11. Young, D. S., Effects of Drugs on Clinical Laboratory Tests, 3rd Edition, AACC Press, Washington, D.C. (1990).
12. Friedman, R. B., Young, D. S., Effects of Disease on Clinical Laboratory Tests, 2nd Edition, AACC Press, Washington, D.C. (1989).
13. Young, D. S., Effects of Preanalytical Variables on Clinical Laboratory Tests, AACC Press, Washington, D.C. (1993).
14. National Committee for Clinical Laboratory Standards, Method Comparison and Bias Estimation Using Patient Samples, Approved Guideline, NCCLS publication EP9-A, Villanova, PA (1995).
15. National Committee for Clinical Laboratory Standards, Evaluation of Precision Performance of Clinical Chemistry Devices, Approved Guideline, Vol. 19, No. 2, NCCLS publication EP5-A, Villanova, PA (1999).
16. MA, SYNCHRON® System(s) Chemistry Information Sheet A18520 AH, (4/2013), Instruction for use sheet, https://www.beckmancoulter.com/wsrportal/techdocs?docname=/cis/A18520/AH/EN_MA.pdf

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			11/27/2000	G. Kost
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			09/15/2009	G. Kost
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