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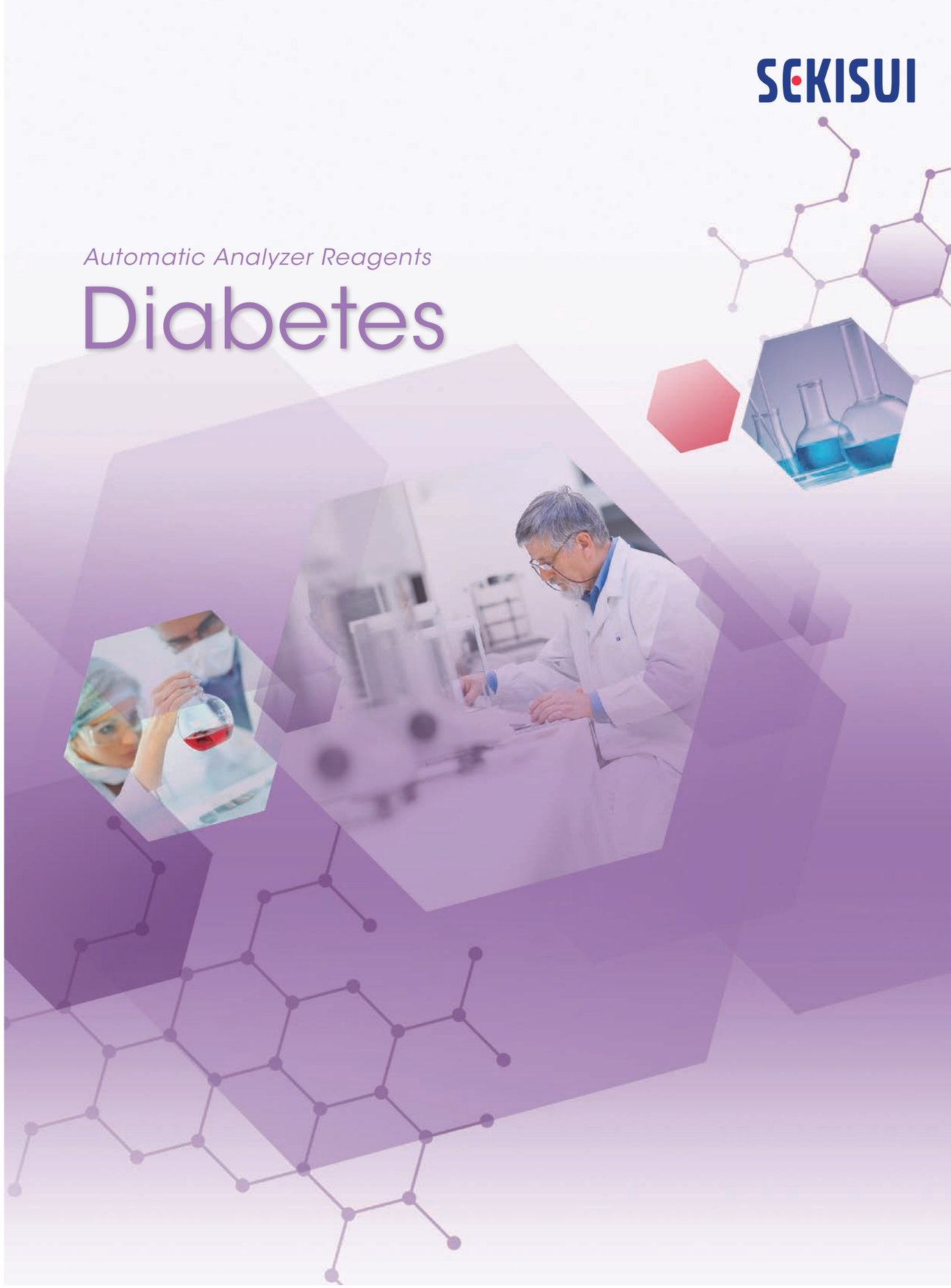
Automatic Analyzer Reagents

Diabetes



SEKISUI MEDICAL CO., LTD.

Sekisui Medical offers a wide range of diabetes related products, from the diagnosis stage to monitoring complications.
These products can be applied to various automated analyzers and will contribute to the efficiency of clinical laboratory tests.

CONTENTS

	Diagnosis	Pathological State /Follow-Up	Complication Monitoring
NORUDIA™ N HbA1c	☑	☑	
Pureauto™ S GLU-R	☑	☑	
NORUDIA™ Insulin		☑	
NORUDIA™ U-ALB			☑
NORUDIA™ Cystatin C			☑
NORUDIA™ L-FABP			☑

For measurement of Hemoglobin A1c (HbA1c) in whole blood

NORUDIA™ N HbA1c

1. Features

1. Specifically measures glycated dipeptides bound to the N-terminal of the hemoglobin β chain.
2. Applicability to a variety of autoanalyzers allows measurement of a large number of samples.
3. Does not stain reaction cells.
4. High reagent stability without calibration.
5. Is not influenced by modified hemoglobin and unstable hemoglobin A1c

2. Components

Reagent Kit	
HbA1c Reagent 1	30mL×2
HbA1c Reagent 2	10mL×2

Sold Separately	
HbA1c Calibrator	1mL × 2conc.× 3
HbA1c Control	1mL × 2conc.× 6
HbA1c Pretreatment	200mL×2
HbA1c blank Solution	5mL×1

3. Assay principle (enzymatic method)

Pretreatment

Red blood cells obtained by centrifugation of the whole blood are hemolyzed. Then hemoglobin is oxidized to methemoglobin.

First reaction (measurement of Hb)

Glycated dipeptides bound to the N-terminal of the hemoglobin β chain are cleaved by a protease. Then methemoglobin is converted to methemoglobin azide by the action of sodium azide, and the absorbance of methemoglobin azide is measured to determine the hemoglobin concentration.

HbA1c —(Protease)→ Glycated dipeptide

Second reaction (measurement of HbA1c)

Glycated dipeptides are reacted with fructosyl peptide oxidase (FPOX) to produce hydrogen peroxide, which develops color with a color coupler in the presence of peroxidase (POD). Then the absorbance of the colored reaction solution is measured to determine the concentration of HbA1c.

Glycated dipeptide + O_2 + H_2O —(FPOX)→ Glucosone + Dipeptide + H_2O_2

H_2O_2 + Color coupler —(POD)→ Color development

4. Reference data

Measurement range (Hitachi 917)
HbA1c (NGSP): 3.3%–16.6%　Hemoglobin concentration: 90–310 μmol/L

Measured values of the reference standard (JCCRM411-3 [JDS lot.5])

	Certified value and expanded uncertainty (NGSP, %)	Value obtained with Norudia™ N HbA1c (NGSP, %)
Level 1	5.10 ± 0.13	5.05
Level 2	5.77 ± 0.14	5.68
Level 3	7.39 ± 0.19	7.30
Level 4	9.60 ± 0.23	9.49
Level 5	11.98 ± 0.28	11.99

*Analyzer: Hitachi 7180 (HbA1c measurement option)

Calculation of HbA1c (%)

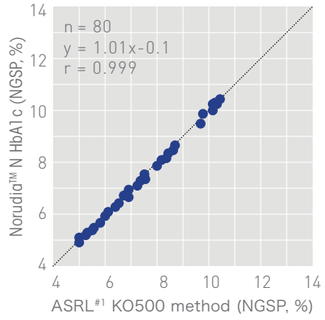
A formula using different parameters obtained by an autoanalyzer is required for conversion to HbA1c (NGSP, %).

Formula

$$91.5 \times \frac{\text{HbA1c}(\mu\text{mol/L})}{\text{Hb}(\mu\text{mol/L})} + 2.15$$

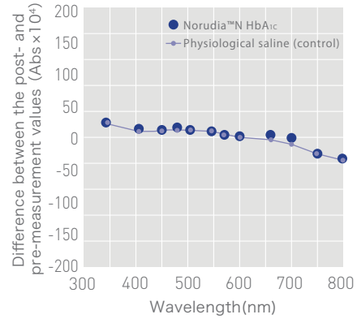
Reference: Wieland Hoelzel, Cas Weykamp, et al.: Clin. Chem, 50:166-174, 2004

Correlation to definitive method (KO500 method)



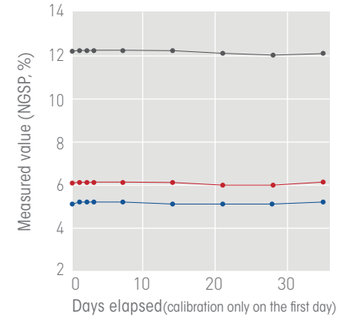
Asian Secondary Reference Laboratory (reference laboratory in Asia)
* Analyzer: Hitachi 7170S

Variation of blank cell values



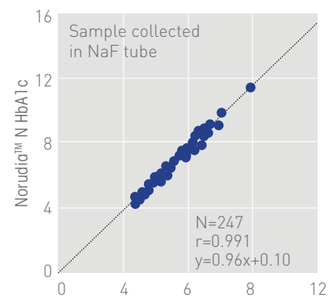
Value of the blank cell was determined by measuring the cell 25 times (comparison between pre- and post-measurement values). Similar variation between Norudia™ N HbA1c and physiological saline at all wavelengths, and there were no stains to the cell was seen with the reagents.
* Analyzer: Hitachi 7170S

On-board stability (stored in analyzer)



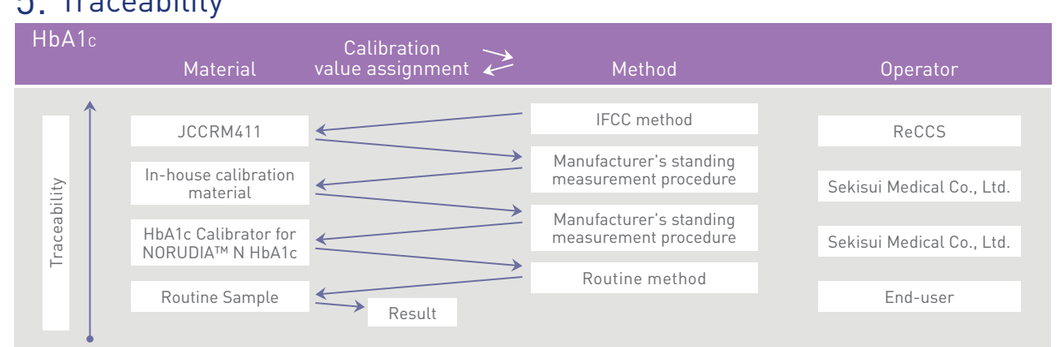
Calibration was performed at 2 points*.
* Calibration was performed at 3 points with some models.
* Analyzer: Hitachi 7180 (HbA1c measurement option)

Correlation to HPLC method



* Analyzer: BM9130

5. Traceability



For measurement of Glucose in blood serum, plasma, or urine

Pureauto™ S GLU-R

1. Features

1. Wide measurement range allows measurement of undiluted urine samples.
2. Rate assay method allows little influence of interfering substances.
3. High sensitivity and high reproducibility.

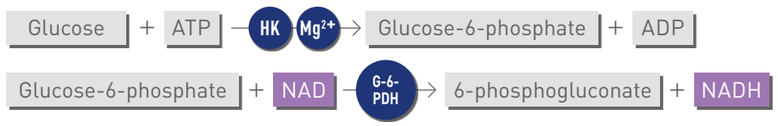
2. Components

Reagent Kit	
GLU-R Enzyme Solution 1	400mL×2
GLU-R Enzyme Solution2	200mL×2

Sold Separately	
Anaserum™ GLU Standard Solution	5mL×6

3. Assay principle (hexokinase method)

Glucose is phosphorylated by hexokinase (HK) to form glucose-6-phosphate in the presence of ATP. Glucose-6-phosphate is oxidized by glucose-6-phosphate dehydrogenase (G-6-PDH) to form 6-phosphogluconate. During this process, NAD is converted to NADH and the absorbance at 340 nm increases. The glucose concentration is determined by measuring the change of absorbance.



* ATP: Adenosine triphosphate
* ADP: Adenosine diphosphate
* NAD: Nicotinamide adenine dinucleotide (oxidized form)
* NADH: Nicotinamide adenine dinucleotide (reduced form)

4. Reference data (analyzer: Hitachi 717)

Measurement range (Hitachi 717): 3-8000 mg/dL
* urine parameter

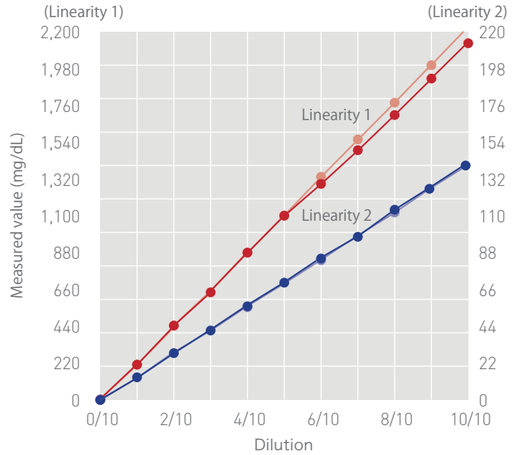
Reproducibility (mg/dL)

	Sample1	Sample2	Sample3
n	20	20	20
Mean	93.7	240.2	139.7
S.D.	0.49	1.01	0.80
C.V. (%)	0.52	0.42	0.57
Max.	94	242	142
Min.	93	238	139
Range	1	4	3

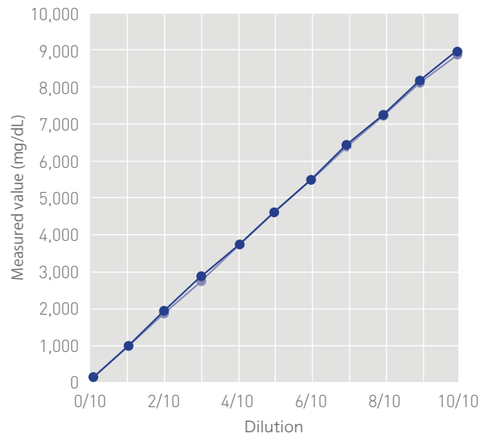
Interference (mg/dL)

	Concentration	Measured value	
		Base serum	Serum containing the substance
Free bilirubin	20 mg/dL	127	129
Conjugated bilirubin	20 mg/dL	127	130
Hemoglobin	500 mg/dL	128	128
Chyle	3000 formazin turbidity units	128	129
Ascorbic acid	50 mg/dL	129	130
Rheumatoid factor	500 IU/mL	137	136

Linearity (serum parameter)



Linearity (urine parameter)



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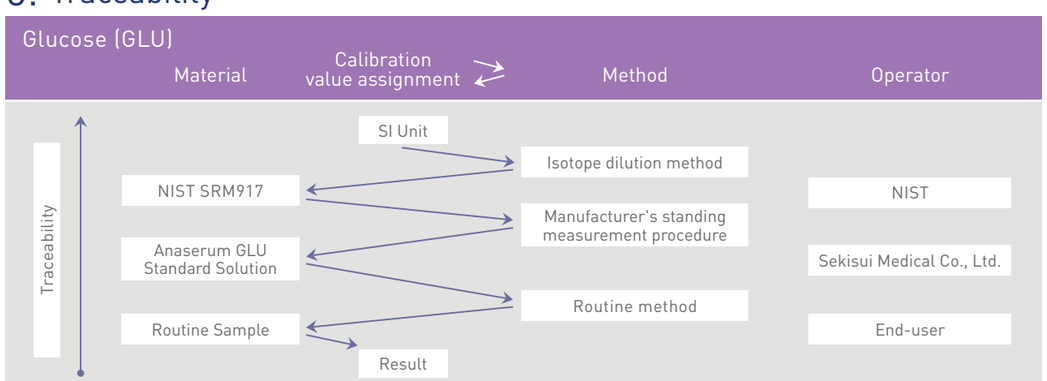


WARNINGS*: This product may show falsely elevated blood glucose levels in patients receiving pralidoxime iodide. Obtain information about the influence of pralidoxime iodide on measured blood glucose values in such patients from the marketer of this product before use. (Since this product may show blood glucose levels higher than the actual values in such patients, if a hypoglycemic agent like insulin is administered in response to a falsely elevated blood glucose level, serious hypoglycemia with symptoms such as coma may occur.)

For measurement of Insulin in blood serum or plasma

NORUDIA™ Insulin

1. Features

1. An excellent marker to identify the cause, pathologic state, and monitor treatment of patients diagnosed with diabetes and impaired glucose tolerance.
2. Simultaneous measurement of blood glucose and insulin can be obatined from a single blood test.(NaF tube)
3. Excellent on-board stability.

2. Components

Reagent Kit	
Insulin Buffer Solution 1	15mL×2
Insulin Latex Reagent 2	5mL×2

Sold Separately	
Insulin Calibrator	1mL × 6conc.
Insulin Control	1mL × 2conc.×3

3. Assay principle (latex agglutination turbidimetry)

Insulin in samples causes agglutination of latex particles coated with mouse anti-human insulin monoclonal antibody via an antigen-antibody reaction. The change of absorbance due to this agglutination process is measured to determine the insulin level.

Insulin + Latex particles coated with mouse anti-human insulin monoclonal antibody

↓

Agglutination via an antigen-antibody reaction

4. Reference data (analyzer: Hitachi 7180)

Measurement range (Hitachi 7180): 1–150 μU/mL

Reproducibility

(μU/mL)

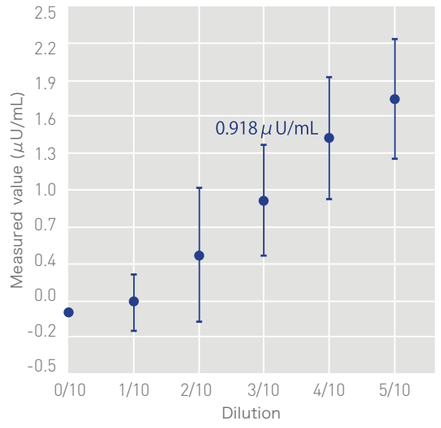
	Sample1	Sample2	Sample3
n	10	10	10
Mean	6.8	20.4	120.0
S.D.	0.07	0.09	1.42
C.V. (%)	0.99	0.47	1.18
Max.	6.9	20.5	122.2
Min.	6.7	20.2	118.0
Range	0.2	0.3	4.2

Interference

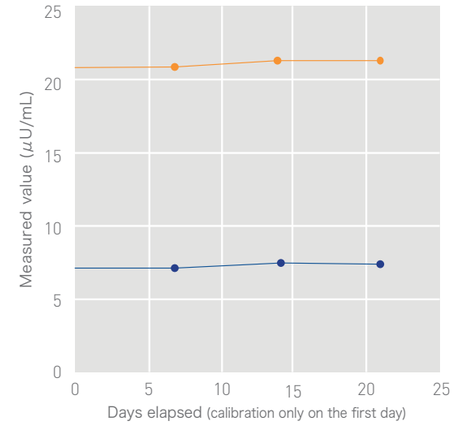
(μU/mL)

	Concentration	Measured value	
		Base serum	Serum containing the substance
Free bilirubin	20 mg/dL	12.7	12.9
Conjugated bilirubin	20 mg/dL	12.7	12.7
Chyle	2000 formazin turbidity units	12.6	13.3
Intralipos	5%	12.2	12.0
Rheumatoid factor	500 IU/mL	16.8	18.6
Gastrin	10 μg/mL	14.2	14.2
Glucagon	10 μg/mL	14.2	13.9
Secretin	10 μg/mL	14.2	13.4
Proinsulin	12.2 ng/mL	0.0	0.0
C-peptide	3.9 ng/mL	0.0	0.0

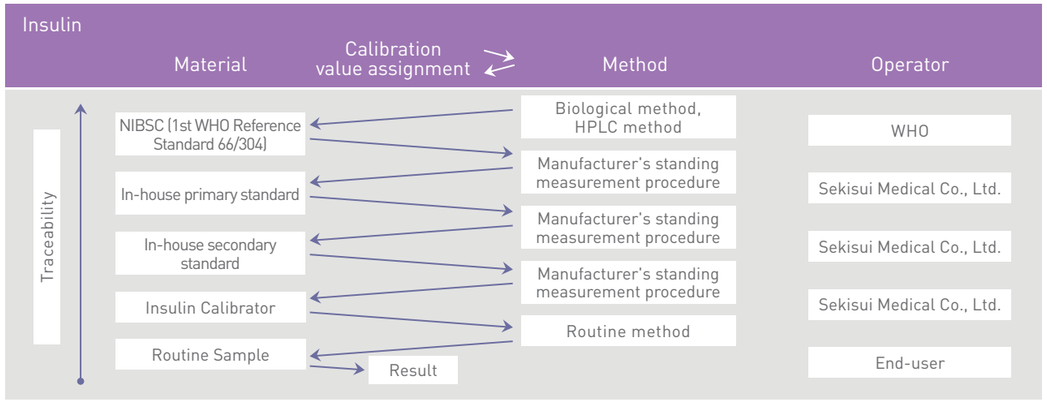
Detection limit (±2.6S.D.)



On-board stability (stored in analyzer)



5. Traceability



For measurement of urinary microalbumin concentration

NORUDIA™ U-ALB

1. Features

1. No hook effect in the high concentration range due to use of the competitive method.
2. Highly sensitive measurement of urinary microalbumin.

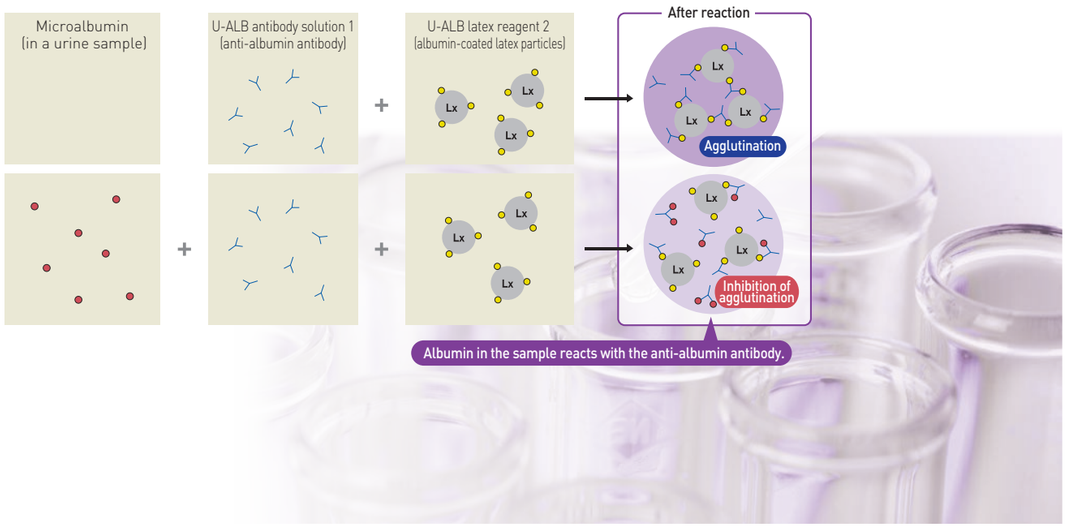
2. Components

Reagent Kit	
U-ALB Antibody Solution 1	10mL×1
U-ALB Latex Reagent 2	10mL×1

Sold Separately		
U-ALB Calibrator	Level A	2mL × 5conc.
	Level B	2mL × 6conc.
U-ALB Control		2mL × 2conc.× 3

3. Assay principle (latex agglutination turbidimetry [competitive method])

When a certain amount of mouse anti-human albumin monoclonal antibody (albumin antibody) is added to a sample, the albumin antibody binds to albumin in the sample until it has reacted with all of the available albumin. Then human albumin-coated latex particles are added, which react with the residual albumin antibody, leading to agglutination.
The concentration of albumin in the sample can be determined by measuring the change of absorbance due to this agglutination process.



4. Reference data (analyzer: Hitachi 917)

Measurement range (Hitachi 917): 5–500 µg/mL

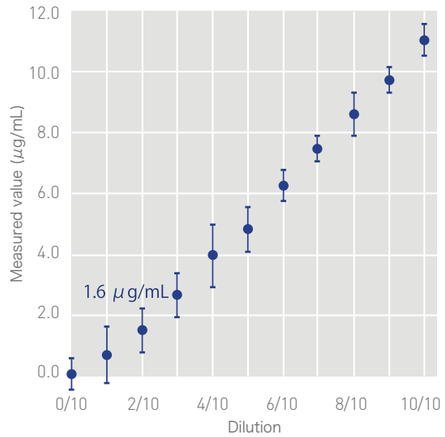
Reproducibility (µg/mL)

	Sample1	Sample2	Sample3
n	10	10	10
Mean	10.91	29.25	98.92
S.D.	0.21	0.36	1.70
C.V. (%)	1.9	1.2	1.7
Max.	11.2	29.6	102.3
Min.	10.5	28.5	96.4
Range	0.7	1.1	5.9

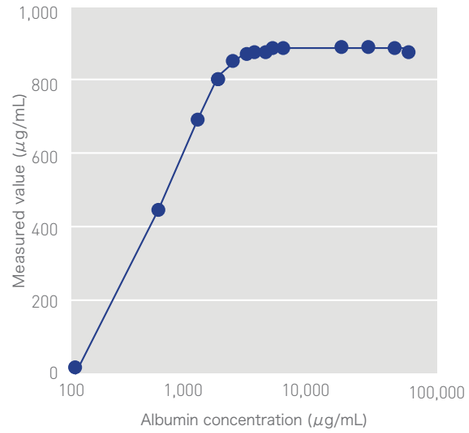
Interferene (µg/mL)

	Concentration	Measured value	
		Base sample	Sample containing the substance
Free bilirubin	10 mg/dL	38.0	35.6
Conjugated bilirubin	10 mg/dL	38.0	36.9
Chyle	2000 formazin turbidity units	37.4	38.5
Ascorbic acid	500 mg/dL	82.2	78.5
Hemoglobin	500 mg/dL	82.5	85.1
Glucose	4000 mg/dL	82.6	82.1
Urea	400 mg/dL	80.1	80.8
Chloroform	1.0 mL/dL	83.8	83.9
Formalin	1.0 mL/dL	83.3	82.7
NaCl	2000 mg/dL	43.5	44.4
KCl	1000 mg/dL	43.1	43.7

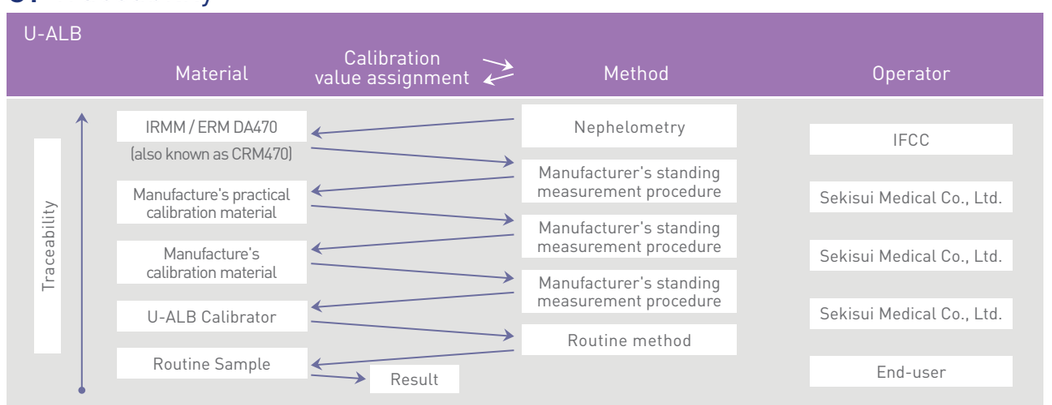
Detection limit (±2.6S.D.)



Prozone



5. Traceability



For measurement of Cystatin C in blood serum or plasma

NORUDIA™ Cystatin C

1. Features

1. Highly specific method using monoclonal antibody.
2. Highly specificity with little effect from RF and other substances.
3. Wide measurement range (0.1–10 mg/L).
4. Excellent on-board stability.
5. Complies with IFCC certified reference material(ERM-DA471)

2. Components

Reagent Kit	
Cystatin C Buffer Solution 1	12mL×2
Cystatin C Latex Reagent 2	12mL×2

Sold Separately	
Cystatin C Calibrator N	2mL × 5conc.
Cystatin C Control N	2mL × 2conc.× 3

3. Assay principle (latex agglutination turbidimetry)

Cystatin C in samples causes agglutination of latex particles coated with mouse anti-human cystatin C monoclonal antibody via an antigen-antibody reaction. The change of absorbance due to this agglutination process is measured to determine the cystatin C level.

Cystatin C + Latex particles coated with mouse anti-human cystatin C monoclonal antibody

↓

Agglutination via an antigen-antibody reaction

4. Reference data (analyzer: Hitachi 7180)

Measurement range (Hitachi 7180): 0.1–10 mg/L

Reproducibility

(mg/L)

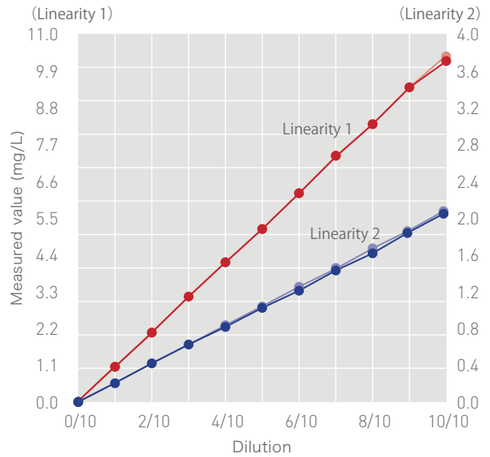
	Sample 1	Sample 2	Sample 3
n	20	20	20
Mean	0.469	1.945	6.142
S.D.	0.01	0.03	0.10
C.V. (%)	1.68	1.65	1.70
Max.	0.48	1.99	6.33
Min.	0.46	1.88	5.96
Range	0.02	0.11	0.37

Interferene

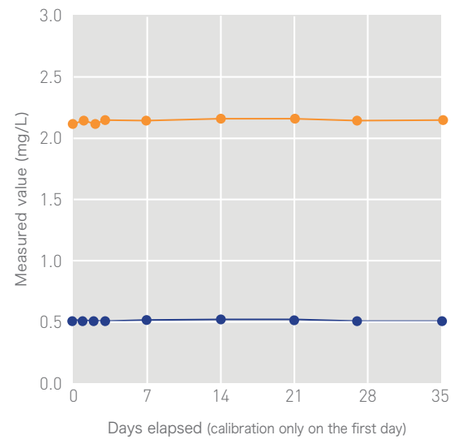
(mg/L)

	Concentration	Measured value	
		Base serum	Serum containing the substance
Free bilirubin	20 mg/dL	1.22	1.20
Conjugated bilirubin	20 mg/dL	1.20	1.22
Hemoglobin	500 mg/dL	1.20	1.20
Chyle	3000 formazin turbidity units	1.20	1.22
Ascorbic acid	50 mg/dL	1.20	1.21
Rheumatoid factor	500 IU/mL	1.33	1.34

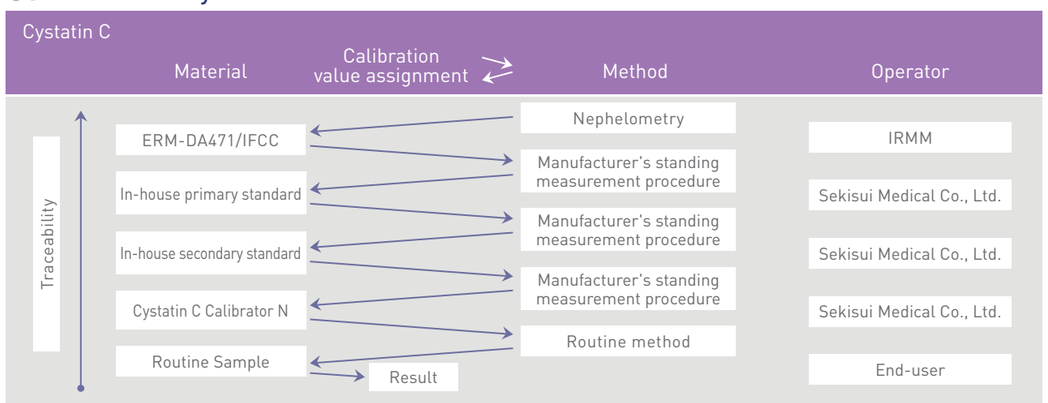
Linearity



On-board stability (stored in analyzer)



5. Traceability



For measurement of Liver – type Fatty Acid Binding Protein (L-FABP) in urine

NORUDIA™ L-FABP

1. Significance

1. Urinary L-FABP increases when the proximal tubules of the kidneys are under stress (due to ischemia or oxidative substances) and its excretion in the urine increases. Therefore, it is a new biomarker reflecting the severity of stress on the tubules before progression of tissue damage.
2. The urinary L-FABP level is considered to reflect the severity of renal tubular dysfunction, and is considered useful for evaluation of peritubular microcirculatory disturbance (ischemia), staging of diabetic nephropathy, evaluation of the response to treatment, assessment of the risk of severe acute kidney injury (AKI), and prediction of contrast nephropathy.

2. Components

Reagent Kit	
L-FABP Buffer Solution 1	18mL×1
L-FABP Latex Reagent 2	7mL×1

Sold Separately	
L-FABP Calibrator	1mL × 5conc.
L-FABP Control	1mL × 2conc.× 3

3. Assay principle (latex agglutination turbidimetry)

L-FABP in samples causes agglutination of latex beads coated with mouse anti-human L-FABP monoclonal antibody via an antigen-antibody reaction. The change of absorbance due to this agglutination process is measured to determine the L-FABP level.

L-FABP + Latex beads coated with mouse anti-human L-FABP monoclonal antibody

↓

Agglutination via an antigen-antibody reaction

4. Reference Data (analyzer: Hitachi 7180)

Measurement range (Hitachi 7180): 1.5 – 200 ng/mL

Reproducibility (ng/mL)

	Sample 1	Sample 2	Sample 3
n	10	10	10
Mean	10.2	50.3	101.9
S.D.	0.28	0.50	1.47
C.V. (%)	2.75	0.99	1.44
Max.	10.5	51.3	104.0
Min.	9.7	49.7	98.9
Range	0.8	1.6	5.1

Interference (ng/mL)

	Concentration	Measured value	
		Base sample	Sample containing the substance
Free bilirubin	20 mg/dL	10.2	10.1
		38.7	40.0
Conjugated bilirubin	20 mg/dL	10.0	9.6
		38.2	40.5
Hemoglobin	500 mg/dL	7.3	7.5
		39.4	40.4
Chyle	2000 formazin turbidity units	8.0	7.5
		40.1	38.9
Glucose	4000 mg/dL	6.7	6.3
		37.3	37.4
Ascorbic acid*	300 mg/dL	8.1	7.2
	100 mg/dL	47.8	53.2

In some samples, measured values may be affected by ascorbic acid at concentrations of about 100 mg/dL or more.

Detection limit (±2.6S.D.)

Correlation

6. Traceability