

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k113072

B. Purpose for Submission:

New device

C. Measurand:

Albumin (microalbumin) in urine

D. Type of Test:

Quantitative, immunoturbidimetric

E. Applicant:

Roche Diagnostics

F. Proprietary and Established Names:

Tina-quant Albumin Gen.2

G. Regulatory Information:

1. Regulation section:

21 CFR 866.5040, Albumin immunological test system

2. Classification:

Class II

3. Product code:

DCF

4. Panel:

Immunology (82)

H. Intended Use:

1. Intended use(s):

Refer to indications for use below.

2. Indication(s) for use:

The Tina-quant Albumin Gen. 2 assay is an immunoturbidimetric assay intended for the quantitative determination of albumin in urine on Roche/Hitachi cobas c systems. Measurement of albumin aids in the diagnosis of kidney and intestinal diseases

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Roche/Hitachi Cobas c311 analyzer

I. Device Description:

The Tina-quant Albumin Gen. 2 assay consists of three reagents:

R1 TRIS buffer: 50 mmol/L, pH 8.0; PEG: 4.2 %; EDTA: 2.0 mmol/L; preservative

R2 Polyclonal anti-human albumin antibodies (sheep); TRIS buffer: 100 mmol/L, pH7.2; preservative

R3 Reagent for antigen excess check. Albumin in diluted serum (human); NaCl: 150 mmol/L; phosphate buffer: 50 mmol/L, pH 7.0; preservative

The calibrator is C.f.a.s. PUC (cleared under k050026) and the recommended control materials are Precinorm / Precipath PUC (cleared under k050026) and Precinorm / Precipath Protein (cleared under k981401). The calibrator and controls are sold separately.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Roche Tina-quant albumin gen 2 (Roche/Hitachi Cobas c501 analyzer only)

2. Predicate 510(k) number(s):

k101203

3. Comparison with predicate:

Similarities (to urine)		
Item	Device	Predicate
Indications for Use	Same	Quantitative measurement of albumin in urine. Measurement of albumin aids in the diagnosis of kidney and intestinal diseases.
Assay Type	Same	Immunturbidimetric
Detection Limit	Same	Limit of Blank (LoB) 2 mg/L Limit of Detection (LoD) 3 mg/L Limit of Quantitation (LoQ) 12 mg/L
Calibrator	Same	C.f.a.s. (Calibrator for Automated Systems) PUC (Proteins in Urine/CSF)
Calibration Frequency	Same	Calibrate after reagent lot change and as required following quality control procedures
Reagent Stability	Same	On-board in use: 12 weeks at 2-8° C
Analytical Specificity	Icterus: No conjugated bilirubin interference was observed up to 50 mg/dL bilirubin. Hemolysis: No hemolysis interference was observed to 400 mg/dL hemoglobin	Icterus: No conjugated bilirubin interference was observed up to an I index of 52. The I Index Value corresponds to approximately 1 mg/dL bilirubin. Hemolysis: No hemolysis interference was observed up to an H index of 487. The H Index Value corresponds approximately to 1 mg/dL hemoglobin
Precision performance	Same	Repeatability: CVs < 2% Between Day: CVs < 3% Total: CVs < 3%

Differences		
Item	Device	Predicate
Sample Types	Urine Only	Serum, plasma, urine, and CSF
Analyzer	Roche Hitachi Cobas c311	Roche Hitachi Cobas c501
Measuring Range	12 – 200 mg/L	12 – 400 mg/L

K. Standard/Guidance Document Referenced (if applicable):

- CLSI EP5-A2, Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline - 2nd edition
- CLSI EP6, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach
- CLSI EP17-A, Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

L. Test Principle:

The Roche Tina-quant Albumin Gen 2 assay is an immunoturbidimetric assay for the quantitative in vitro determination of albumin in human urine on the Roche/Hitachi cobas c 311 analyzer. The test principle is a particle enhanced immunoturbidimetric assay. Human albumin (the antigen) agglutinates with latex particles coated with anti-albumin antibodies. The precipitate is determined turbidimetrically following agglutination.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

This data was collected as follows:

Specimen description: urine controls and human urine
Number of analyzers: one
Number of days/ reps: two reps/run, two runs/day over 21 days
Lots of reagent used: one
Number of calibrations: one
Operators: one

Repeatability

Sample type	Urine Control	Urine Control	Human Urine	Human Urine	Human Urine
n	84	84	84	84	84
Mean (mg/L)	36.9	124.8	15.6	47.4	172.8
SD	0.260	1.592	0.241	0.500	3.056
CV%	0.70	1.28	1.54	1.05	1.77

Intermediate Precision (Between Day)

Sample type	Urine Control	Urine Control	Human Urine	Human Urine	Human Urine
n	84	84	84	84	84
Mean (mg/L)	36.9	124.8	15.6	47.4	172.8
SD	0.567	2.183	0.227	0.624	3.170
CV%	1.54	1.75	1.46	1.32	1.83

Intermediate Precision (Total)

Sample type	Urine Control	Urine Control	Human Urine	Human Urine	Human Urine
n	84	84	84	84	84
Mean (mg/L)	36.9	124.8	15.6	47.4	172.8
SD	0.731	2.779	0.362	0.897	4.580
CV%	1.98	2.23	2.32	1.89	2.65

b. Linearity/assay reportable range:

To determine the linearity of the Tina-quant Albumin Gen.2 **cobas c 311** urine assay, two dilution series were prepared using high analyte level native human urine samples. The diluent used was NaCl. Albumin levels were measured and the recovered value was compared to the theoretical value. Pure samples (0% and 100%) were run n=6, with mean measured value reported. Diluted samples were run n=3 with mean measured values reported.

Data were calculated per EP6-A guidelines. The linearity data were analyzed with regards to linear, quadratic, and cubic polynomials. A linearity check was performed with a first order (linear) regression and then with higher order models (quadratic and cubic).

Linear regression produces the following:

Slope: 0.97 (95% CI 0.96 to 0.98)

Intercept: 0.90 (95% CI -0.31 to 2.10)

Correlation Coefficient: 0.998

The claimed measuring range for the assay is 12 – 200 mg/L.

The extended measuring range using automated rerun with dilution was validated by performing an experiment comparing the instrument auto-rerun result with a simple manual dilution. Two **cobas c 311** analyzers were used. Three samples were manually diluted in triplicate per analyzer and the recoveries were compared to the instrument auto-rerun results. All auto-rerun results were within $\pm 4\%$ of the manual dilution results.

A known high-dose hook effect occurs with this assay. Due to the antigen excess check reagent R3, no unflagged high-dose hook effect should occur up to an albumin concentration of 40,000 mg/L in urine samples. The sponsor verified the correct flagging with 2 serially spiked samples up to 41,000 mg/L analyzed on the cobas c311 analyzer.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

The C.f.a.s. PUC calibrator, Precinorm PUC/Precipath PUC and Precinorm Protein/Precipath Protein controls are traceable to the reference preparation IRMM (Institute for Reference Materials and Measurements) BCR470/CRM470 (RPPHS - Reference Preparation for Proteins in Human Serum).

d. *Detection limit:*

The analytical limits at low levels are as follows:

Limit of Blank 2 mg/L
Limit of Detection 3 mg/L
Limit of Quantitation 12 mg/L

e. *Analytical specificity:*

The effects of endogenous interference on the quantitation of albumin by the Tina-quant Albumin Gen.2 **cobas c 311** urine assay were determined on the **cobas c 311** analyzer. Pooled human urine samples were spiked with varying levels of interferents. The resulting sample series (ten dilution steps per sample) were tested in triplicate and the median values used to calculate recovery, by comparing the measured albumin concentration to the expected albumin concentration (which is the albumin concentration when no interferent was added). All recoveries were within $\pm 10\%$.

The following compounds were tested at the concentrations listed:

Conjugated bilirubin	69 mg/dL
Hemoglobin	788 mg/dL

Acetone	60 mmol/L
Ammonium chloride	6.4 g/L
Calcium	40 mmol/L
Creatinine	20 g/L
γ -globulin	500 mg/L
Glucose	35.0 g/L
Urea	800 mmol/L
Uric acid	1.2 g/L
Urobilinogen	200 mg/L

No interference was found at therapeutic concentrations of the following drugs in urine.

Acetaminophen
 N-Acetyl cysteine
 Salicylic Acid
 Ascorbic Acid
 Calcium dobesilate
 Na₂-Cefoxitin
 Gentamycin Sulfate
 Ibuprofen
 Levodopa
 Methyldopa
 Ofloxacin
 Phenyloxyethane
 Doxycycline

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

The Tina-quant Albumin Gen.2 was compared to the predicate device. All samples were tested in duplicate by the new device and the predicate device. There were no retests or discards. Linear regression using Passing-Bablok produced the following:

$$n = 69$$

$$y = 1.04x - 0.42$$

$$\text{Pearson's } r = 0.972$$

Sample concentration range: 13.0 – 189.6 mg/L

b. *Matrix comparison:*

Not applicable. This device is only being cleared for urine on the c311 at this time.

3. Clinical studies:

a. *Clinical Sensitivity:*

Not applicable.

b. *Clinical specificity:*

Not applicable.

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

2nd morning urine:¹

Adults: < 20 mg albumin/g creatinine or
< 2.26 g (34.35 μ mol) albumin/mol creatinine

Children (3-5 years):² < 20 mg/L (0.304 μ mol/L, 2 mg/dL) albumin
< 37 mg albumin/g creatinine

24-hour urine:³ < 20 mg/L (0.304 μ mol/L, 2 mg/dL)
< 30 mg/24 h (0.456 μ mol/24 h)

1. Hofmann W, Guder WG. A diagnostic program for quantitative analysis of proteinuria. J Clin Chem Clin Biochem 1989;27:589-600.
2. Hubbuch A. Results of a multicenter study of provisional reference ranges for albumin in urine of children and adults. Roche publication.
3. Hasslacher CH. Aid Endokrin Stoffw 1989;10:60-63.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.