

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

A. 510(k) Number:

k072409

B. Purpose for Submission:

Clearance of new device

C. Measurand:

Albumin
Creatinine

D. Type of Test:

Albumin – Quantitative immunochemical assay
Creatinine – Quantitative enzymatic assay

E. Applicant:

AXIS-SHIELD POC AS

F. Proprietary and Established Names:

Afinion™ ACR and Afinion™ ACR Control

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
<u>JIR</u>	<u>Class I subject to 862.9 (c)(5)</u>	<u>862.1645 - Urinary protein or albumin (nonquantitative) test system.</u>	<u>75</u>
<u>JFY</u>	<u>Class II</u>	<u>862.1225 Creatinine test system.</u>	<u>75</u>
<u>JJY</u>	<u>Class I reserved</u>	<u>862.1660 Quality control material (assayed and unassayed).</u>	<u>75</u>

H. Intended Use:

1. Intended use(s):

Afinion™ ACR is an in vitro diagnostic test for quantitative determination of albumin, creatinine and albumin/creatinine ratio (ACR) in human urine. The measurement of urine albumin, creatinine and albumin/creatinine ratio aids in the early diagnosis of nephropathy.

Afinion™ ACR Control is a assayed in vitro diagnostic quality control material used to confirm that the Afinion™ ACR and the Afinion™ AS100 Analyzer System is working properly and provides reliable results.

2. Indication(s) for use:

Afinion™ ACR is an in vitro diagnostic test for quantitative determination of albumin, creatinine and albumin/creatinine ratio (ACR) in human urine. The measure of urine albumin aids in the early diagnosis of nephropathy.

Afinion™ ACR Control is a assayed in vitro diagnostic quality control material used to confirm that the Afinion™ ACR and the Afinion™ AS100 Analyzer System is working properly and provides reliable results.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Afinion™ ACR is used with the Afinion™ AS100 Analyzer

I. Device Description:

The main components of the Afinion™ ACR Test Cartridge are the sampling device and the reaction container. The Test Cartridge has a handle, a barcode label with lot specific information and an area for sample ID.

Material provided: 15 Afinion™ ACR Test Cartridges packaged separately in foil pouches with a desiccant bag, 1 Package Insert

The Afinion™ ACR Control kit contains liquid preparations of albumin and creatinine in citrate buffer. The Afinion™ ACR Controls have been designed for use with the Afinion™ AS100 Analyzer and the Afinion™ ACR test.

Control kit contents: 1 Afinion™ ACR Control C I: Citrate buffer with albumin and creatinine (1x1.0 mL), 1 Afinion™ ACR Control C II: Citrate buffer with albumin and creatinine (1x1.0 mL), 1 Package Insert

J. Substantial Equivalence Information:

DCA 2000[®] Microalbumin/Creatinine Assay k963142

Predicate	Item	Similarities	Differences
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Analytes measured	Albumin, creatinine and ACR	N/A
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Intended use	In vitro diagnostic test for quantitative determination of albumin, creatinine and ACR	N/A
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Sample material	Human urine	N/A
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Type of test	Point of Care testing	N/A
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Assay principle for albumin	N/A	Afinion [™] ACR: Immunometric membrane flow-through principle where the color intensity of the membrane is measured by reflection. DCA [®] 2000 Microalbumin/Creatinine assay: A specific antibody binds with albumin in the presence of polyethylene glycol. The albumin antibody complexes are measured as absorbance.
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Assay principle for creatinine	N/A	Afinion [™] ACR: An enzymatic colorimetric test where the creatinine concentration is measured by transmission. DCA [®] 2000 Microalbumin/Creatinine assay: Benedict/Behre chemistry (non enzymatic) and the creatinine concentration is quantified by absorbance.
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Measuring range albumin	N/A	Afinion [™] ACR: Albumin 5.0-200.0 mg/L DCA [®] 2000 Microalbumin/Creatinine assay: 5.0-300.0 mg/L

Predicate	Item	Similarities	Differences
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Measuring range creatinine	N/A	Afinion [™] ACR: 16.4-339.9 mg/dL DCA [®] 2000 Microalbumin/Creatinine assay: 15-500 mg/dL
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Measuring range ACR	N/A	Afinion [™] ACR: 1.0-1250.0 mg/g DCA [®] 2000: 1-2000 mg/g
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Sample volume	N/A	Afinion [™] ACR: 3.5 µL DCA [®] 2000 Microalbumin/Creatinine assay: 40 µL
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Test cartridges	Ready to use	N/A
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Control material	2 control levels	Afinion [™] ACR: ready to use DCA [®] 2000 Microalbumin/Creatinine assay: lyophilized
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Storage temperature for test cartridges and control material	2-8 °C	N/A
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Total precision (external study)	Afinion [™] ACR: albumin 3-8 %CV, creatinine 3-8 %CV. DCA [®] 2000 Microalbumin/Creatinine assay: albumin 2.7-6.6 %CV, creatinine 2.8-3.6 %CV	N/A
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Assay time	N/A	Afinion [™] ACR: 5 min 35 sec DCA [®] 2000 Microalbumin/Creatinine assay: 7 minutes
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Calibration	N/A	Afinion [™] ACR: Built in DCA [®] 2000 Microalbumin/Creatinine assay: Calibration card for test and controls

Predicate	Item	Similarities	Differences
K963142 - DCA 2000 [®] Microalbumin/Creatinine Assay	Kit size	Separately packed cartridges	Afinion™ ACR: 15 tests DCA [®] 2000 Microalbumin/Creatinine assay: 10 tests

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

STANDARDS
Title and Reference Number
Stability Testing of In Vitro Diagnostic Reagents (CEN-13640)
Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition (EP5-A2)

L. Test Principle:

Afinion™ ACR is a fully automated assay for determination of albumin, creatinine and ACR in human urine. Albumin is quantified using a solid phase immunochemical assay. In the Afinion™ ACR Test Cartridge the sample is automatically diluted and aspirated through a membrane coated with anti-albumin antibodies, which concentrates and immobilizes the albumin from the sample. A gold-antibody conjugate then binds to the immobilized albumin resulting in a red-brown colored membrane. Excess gold-antibody conjugate is removed in a washing step. The Afinion™ AS100 Analyzer measures the color intensity of the membrane, which is proportional to the amount of albumin in the sample.

Creatinine is quantified using an enzymatic colorimetric test that involves four enzymatic steps. The test requires incubation with two distinct enzyme solutions. A colored end product is measured in one of the cartridge wells.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

A 20 day study was performed with the Afinion™ ACR assay using the Afinion™ AS100 Analyzer to estimate the within-day, within-run, between-day and total precision according to Clinical and Laboratory Standards Institute (CLSI) guideline EP5-A2.

Within-day precision was run with 20 replicates in one day. For within-run, between day and total precision, the testing was performed over 20 operating days. Each sample was measured in duplicate in two daily runs with a minimum of two hours between the two runs. Three urine samples were

collected and stored frozen until use. No samples were spiked. The samples were analyzed in random order for each run.

Within day imprecision results (20 replicates in 1 day) for albumin, creatinine and ACR.

Sample	S 1		S 2		S 3	
	mean	CV %	mean	CV %	mean	CV %
Albumin, mg/L	176.7	3.9	55.7	4.6	13.0	3.5
Creatinine, mg/dL	52.7	3.2	163.7	3.8	351.4	3.3
ACR, mg/g	335.8	5.2	34.1	4.2	3.7	4.0

Within run imprecision results for albumin, creatinine and ACR, 20 days testing of 3 urine samples.

Sample	S 1		S 2		S 3	
	mean	CV %	mean	CV %	mean	CV %
Within run						
Albumin, mg/L	174.9	4.3	55.3	3.3	12.6	4.4
Creatinine, mg/dL	51.4	3.4	162.3	2.1	348.1	2.7
ACR, mg/g	340.6	5.3	34.1	3.7	3.6	5.0

Between day imprecision results for Albumin, Creatinine and ACR values after 20 days testing of 3 urine samples.

Sample	S 1		S 2		S 3	
	mean	CV %	mean	CV %	mean	CV %
Between day						
Albumin, mg/L	174.9	2.0	55.3	0.0	12.6	1.2
Creatinine, mg/dL	51.4	0.0	162.3	0.0	348.1	0.6
ACR, mg/g	340.6	2.8	34.1	0.7	3.6	0.0

Total imprecision of Albumin, Creatinine and ACR values after 20 days testing of 3 urine samples.

Sample	S 1		S 2		S 3	
	mean	CV %	mean	CV %	mean	CV %
Total						
Albumin, mg/L	174.9	5.0	55.3	4.8	12.6	5.5
Creatinine, mg/dL	51.4	3.8	162.3	2.8	348.1	3.0
ACR, mg/g	340.6	6.0	34.1	4.6	3.6	6.0

b. *Linearity/assay reportable range:*

Afinion™ ACR reportable range is supported by linearity and detection limit below:

	Albumin	Creatinine	ACR
Reportable range	5.0-200.0 mg/L	16.4-339.9 mg/dL	1.0-1250.0 mg/g

If the patient's albumin or creatinine value is outside the reportable range, no ACR test result will be reported

Procedure:

Two dilution series, one for albumin, AL1-AL10 and one for creatinine, CL1-CL10, were prepared by inter-mixing the high and low concentration of albumin and creatinine in urine samples as described in the table below:

Sample name	Sample Low (μL) = V_1	Sample High (μL) = V_2
AL1 or CL1	0	300
AL2 or CL2	60	240
AL3 or CL3	90	210
AL4 or CL4	120	180
AL5 or CL5	150	150
AL6 or CL6	180	120
AL7 or CL7	210	90
AL8 or CL8	240	60
AL9 or CL9	270	30
AL10 or CL110	300	0

The following linear regression results were obtained:

Analyte	r^2	slope	y-intercept
Albumin	1.00	1.01 ± 0.02	$-4.1 \pm 1.9 \text{ mg/L}$
Creatinine	1.00	0.99 ± 0.01	$0.5 \pm 2.1 \text{ mg/dL}$

Theoretical and measured albumin values.

Sample	Theoretical albumin (mg/L)	Measured Mean albumin (mg/L)	CV %	% Recovery
AL1	201.8	201.8	5.3	N/A
AL2	162.2	159.0	3.9	98
AL3	142.5	148.4	3.0	104
AL4	122.7	124.3	4.0	101

Sample	Theoretical albumin (mg/L)	Measured Mean albumin (mg/L)	CV %	% Recovery
AL5	102.9	106.8	4.7	104
AL6	83.1	89.7	4.6	108
AL7	63.3	67.3	4.6	106
AL8	43.6	48.3	2.7	111
AL9	23.8	27.5	4.4	116
AL10	4.0	4.0	4.3	N/A

Theoretical and measured creatinine values

Sample	Measured Mean creatinine (mg/dL)	Theoretical creatinine (mg/dL)	CV %	% Recovery
CL1	343.7	343.7	2.2	N/A
CL2	275.3	277.2	2.0	99
CL3	250.8*	244.0	2.0	103
CL4	217.4	210.7	3.8	103
CL5	174.2	177.5	4.4	98
CL6	145.8	144.3	1.5	101
CL7	109.5	111.0	3.5	99
CL8	77.4	77.8	1.8	99
CL9	44.4	44.5	4.1	100
CL10	11.3	11.3	8.2	N/A

The albumin and creatinine assays show acceptable linearity over the measuring ranges.

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

Test specific calibration data are established for each lot of test cartridges and then stored in the barcode label. When the Test Cartridge enters the Analyzer, the integrated camera reads the barcode. The calibration data for the actual lot are transferred to the instrument and used for calculating results. Calibration by the operator is thus not required.

The albumin standards are traceable to ERM®-DA 470 and the creatinine standards are traceable to SRM 914a. Controls and calibrators are prepared gravimetrically. Values are assigned using analysis of multiple replicates on multiple analyzers and multiple lots.

Afinion™ ACR Control C I and C II were used when performing the external precision study for Afinion™ ACR Control. The controls C I and C II represent two different levels of albumin and creatinine according to table below and contains liquid preparations of albumin and creatinine in citrate buffer.

Target values for Afinion™ ACR Control C I and C II are assigned within the following ranges.

Specification	Target value Albumin (mg/L)	Target value Creatinine (mg/dL)	Target value ACR (mg/g)
Afinion™ ACR Control C I	9-15	79.2-101.8	8.8-18.9
Afinion™ ACR Control C II	65-95	203.6-248.8	26.1-46.7

Stability studies are conducted to determine the stability of Afinion™ ACR Control at the following conditions:

1. Real time storage at 5 ± 3 °C.
2. Open bottle at recommended storage at 5 ± 3 °C.
3. Continuous open bottle at room temperature.
4. Controlled room temperature storage..
5. Transport simulation (Warehouse/Shipping, W/S) of kits stressed at 37 ± 2 °C for 3 days followed by storage at 5 ± 3 °C.
6. Transport simulation (Freeze/Thaw, F/T) of kits stressed for 3 freeze/thaw cycles followed by storage at 5 ± 3 °C.

Study protocols and acceptance criteria were described and found to be acceptable.

d. Detection limit:

The applicant determined the Limits of Detection (LoD) and the Limits of Quantitation (LoQ) for Albumin and Creatinine in the ACR assay according to CLSI protocol EP17-A.

The LoD is 0.5 mg/L for Albumin and 1.9 mg/dL for Creatinine
 The LoQ is 2.5 mg/L for Albumin and 5.0 mg/dL for Creatinine

e. *Analytical specificity:*

No cross-reaction was found when the albumin monoclonal antibodies were tested on human hemoglobin, IgG, IgA, beta-2 microglobulin, myoglobin and bovine serum albumin. (Note: See below. Interference from blood was observed with this device)

Interference

No significant interference was observed for both albumin and creatinine up to the following concentrations in urine:

Acetoacetate	0.84 mg/mL	7.8 mmol/L
Acetone	800 mg/L	13.8 mmol/L
Ascorbic acid	3000 mg/L	16.7 mmol/L
Bilirubin	3.5 mg/dL	0.06 mmol/L
Creatine	0.52 mg/mL	4.0 mmol/L
Glucose	45 mg/mL	250 mmol/L
beta-hydroxybutyric acid	5.9 mg/mL	46.8 mmol/L
IgG	20 mg/L	
Beta-2 microglobulin	20 mg/L	
Myoglobin	20 mg/L	
Urea	30 mg/mL	500 mmol/L

Over the counter and prescription drugs:

Acetaminophen	0.2 mg/mL	1.5 mmol/L
Acetaminophen-glucuronide	10.5 mg/mL	30.0 mmol/L
Glyburide	14.8 µg/mL	30 µmol/L
Ibuprofen	2.0 mg/mL	10 mmol/L
Metformin	4.0 mg/mL	24 mmol/L

Blood interference

Interference from blood may falsely elevate assay results when urine stick results are greater than or equal to 25 erythrocytes/uL.

No “Hook effect” was observed at albumin concentrations up to 5000 mg/L.

f. *Assay cut-off:*
Not Applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

External study

A method comparison study, comprising 169 urine samples was performed at four physicians' office laboratories. Analyte concentrations were evenly distributed with albumin ranging from 5.0 to 200.0 mg/dL and for creatinine from 17.0 and 339.4. Urine samples were collected from the donors and analyzed with Afinion™ ACR and another point-of-care method at the four study sites. The operators were either nurses or medical assistants.

The correlation data (Passing-Bablok analysis) are summarized below from the method comparison study - Afinion™ ACR (y) vs. another point-of care method (x) at four sites. (Linear regression analysis data, N= number of samples, r=correlation coefficient).

Analyte	N	Regression line	r
Albumin	169	$Y=1.10x + 1.4$	0.99
Creatinine	169	$Y=0.93x + 2.3$	0.99
ACR	169	$Y=1.16x + 1.0$	0.99

Internal study performed at Axis shield PoC

Similarly another method comparison study comprised of 95 urine samples, with concentrations evenly distributed for albumin ranging from 5.0 to 199.6 mg/dL and creatinine from 17.4 and 332.2. were analyzed with Afinion™ ACR and another point-of-care method. The correlation data (Passing-Bablok analysis) are summarized here.

Analyte	N	Regression line	r
Albumin	91	$Y=0.92x + 2.1$	0.99
Creatinin e	95	$Y=1.00x - 3.2$	0.99
ACR	91	$Y=1.01x + 0.7$	0.99

b. *Matrix comparison:*

Not Applicable

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):
Not Applicable
- 4. Clinical cut-off:
Not Applicable

5. Expected values/Reference range:

Reportable range of the Afinion™ ACR assay for Albumin: 5.0-200 mg/L.

Albumin values and medical decision points:

- * Normal: < 20 mg/L
- * Microalbuminuria: 20-200 mg/L
- * Clinical albuminuria: > 200 mg/L

Ref: Janssen, W. M. T et al. Clin Chem Lab Med; 38 (11): 1107-1110; 2000.
Torffvit, O. Diabetolognytt; No 1-2; 2002.

Reportable range of the Afinion™ ACR assay for Creatinine is 16.4-339.9 mg/dL

The normal range for urine creatinine: 34-147 mg/dL

Ref: Foss OP. Fysiologi Patofysiologi Klinisk Kjem. Noen momenter for fysiokjemikere, 2nd ed. Ulleval sykehus, Oslo, 1981; 99/

Reportable range of the Afinion™ ACR assay for Albumin Creatinine Ratio (ACR): 1.0-1250 mg/g.

ACR values and medical decision points:

- * Normal: < 30 mg/g
- * Microalbuminuria: 30-300 mg/g
- * Clinical albuminuria: > 300 mg/g

Ref: American Diabetes Association. Diabetes care, Vol. 25, Suppl.1, January 2002.

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.