

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

A. 510(k) Number:

K032188

B. Analyte:

Aldosterone

C. Type of Test:

Quantitative

D. Applicant:

Nichols Institute Diagnostics, Inc.

E. Proprietary and Established Names:

Nichols Advantage Chemiluminescent Aldosterone Immunoassay

F. Regulatory Information:

1. Regulation section:
862.1045 ; 862.1150; 862.1660
2. Classification:
Class II; Class II; Class I
3. Product Code:
CJM ; JIS; JJX
4. Panel:
Clinical Chemistry

G. Intended Use:

1. Intended use(s):
The Nichols Advantage[®] Aldosterone assay is intended for use with the Nichols Advantage[®] Specialty System to quantitatively measure aldosterone in human serum and EDTA plasma.
2. Indication(s) for use:
Aldosterone measurements are used in the diagnosis and treatment of primary aldosteronism (a disorder caused by excessive secretion of aldosterone by the adrenal gland), hypertension caused by primary aldosteronism, selective hypoaldosteronism, edematous states, and other conditions of electrolyte imbalance.
3. Special condition for use statement(s):
None
4. Special instrument Requirements:
Nichols Advantage[®] Specialty System

H. Device Description:

The Nichols Advantage[®] Aldosterone assay contains sufficient reagents for 100 tests, is a competitive binding assay for aldosterone in serum or EDTA-plasma, and utilizes the Nichols Advantage[®] Specialty System, under FDA PMN device clearance (K961142) .

I. Substantial Equivalence Information:

1. Predicate device name(s):
Diagnostic Product Corp. Coat-A-Count® Aldosterone
2. Predicate K number(s):
K831178
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
specimen	serum or plasma	serum or plasma
Differences		
Item	Device	Predicate
Binding Technology	Magnetic particles - avidin coated	<u>Antibody coated tubes</u>

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

NCCLS EP5-A method (Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline)

K. Test Principle:

This Nichols Advantage® Chemiluminescent Aldosterone Immunoassay [i.e., Nichols Advantage® Aldosterone or **NAA**] is an in vitro diagnostic (IVD) chemiluminescence immunoassay designed for professional use with Nichols Advantage® Specialty System [NASS] for quantitatively assaying aldosterone in human serum and EDTA plasma. The NAA is based upon competitive binding between aldosterone in the patient sample and acridinium ester labeled aldosterone (labeled aldosterone for chemiluminescence) for a specific mouse monoclonal antibody to human aldosterone.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. *Precision/Reproducibility:*

The within-run and total imprecision performance for the assay was estimated using the NCCLS EP5-A method (Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline). The data represent one run per day over 21 days with each serum pool or assay control run in duplicate. The study was performed on a single system.

Pool or Control	Mean (ng/dL)	Within-Run		Total Imprecision	
		SD	%CV	SD	%CV
Pool 1	4.3	0.6	14.0%	0.8	18.6%
Pool 2	8.2	0.4	5.4%	0.7	8.5%
Pool 3	19.7	0.8	4.1%	1.0	5.2%
Pool 4	71.7	2.1	2.9%	3.5	4.9%
Control 1	6.3	0.5	7.9%	1.0	16.0%
Control 2	23.1	1.0	4.3%	1.2	5.2%
Control 3	76.5	3.6	4.7%	5.8	7.6%

b. Linearity/assay reportable range:

Samples with varying concentrations were manually diluted with Sample Diluent before placing onto the system. The observed and corrected results are presented. The results demonstrate linearity across the range of the assay.

Sample	Dilution	Observed (ng/dL)	Expected (ng/dL)	% Recovery
A	Undiluted	18.1		
	1:2	8.4	9.1	92%
	1:4	5.2	4.5	116%
	1:8	2.5	2.3	110%
B	Undiluted	22.2		
	1:2	11.8	11.1	106%
	1:4	5.2	5.6	93%
	1:8	2.8	2.8	100%
C	Undiluted	113.2		
	1:2	52.5	56.6	93%
	1:4	26.2	28.3	93%
	1:8	14.9	14.2	105%
D	Undiluted	53.8		
	1:2	27.7	26.9	103%
	1:4	12.8	13.5	91%
	1:8	6.5	6.7	97%

c. Traceability (controls, calibrators, or method):

Both the calibrators and controls contain aldosterone spiked into a liquid matrix containing processed human serum and $\leq 0.095\%$ sodium azide. The lyophilized calibrators and controls are assigned their concentrations against non-lyophilized materials.

d. Detection limit:

The analytical sensitivity (Limit Of Detection, LOD) was determined by reading the -2SD response from n=20 replicate measurements of the zero standard from the stored master curve from several runs and instruments. The sensitivity for this assay was estimated to be ≤ 1.2 ng/dL.

e. Analytical specificity:

The antisera for the assay is specific for aldosterone, and demonstrates low crossreactivity to other steroidal compounds in patient samples. Crossreactivity in the chart below were calculated on a weight-per-weight basis at approximately 50% binding intercept or less.

Cross-reactant	Highest Amt. Tested ($\mu\text{g/dL}$)	Apparent Amt. Detected (ng/dL)	% Crossreactivity
Aldosterone			100%
Pregnenolone	11,600	<1.5	none detected
Progesterone	50,000	25.6	<0.0001%
11-Deoxycorticosterone	50,000	18.9	<0.0001%
Corticosterone	50,000	31.4	<0.0001%
18-Hydroxycorticosterone	5.0	20.9	0.42%
17-Hydroxyprogesterone	50,000	20.1	<0.0001%

11-Deoxycortisol	50,000	28.5	<0.0001%
Cortisol	50,000	26.1	<0.0001%
Testosterone	100,000	25.1	<0.0001%
Androsterone	100,000	11.4	<0.0001%
DHEA	48,000	11.6	<0.0001%
Androstendione	47,800	50.8	0.0001%
Estradiol	287,000	<1.5	none detected
Estrone	8,000	6.1	<0.0001%
Estriol	8,400	<1.5	none detected
Cortisone	25,000	20.7	<0.0001%
Dexamethasone	50,000	7.1	<0.0001%
Prednisone	32,600	26.3	<0.0001%
Prednisolone	50,000	27.3	<0.0001%
Spironolactone	50,000	22	<0.0001%

f. Assay cut-off:
N/A

2. Comparison studies:

a. Method comparison with predicate device:

Nichols Advantage® Aldosterone or **NAA** assay (Y) was compared to a current marketed predicate assay kit, the **DPC Coat-A-Count Aldosterone RIA** device (X), previously cleared by the FDA (K831178, 5/27/83). One hundred three (103) clinical undiagnosed remnant serum samples were assayed in duplicate by both methods following each manufacturers' directions. The aldosterone assay range observed with **RIA** method "X" was 2.7 to 125 ng/dL; range for **NAA** method "Y" was 2.7 to 120 ng/dL. The Passing-Bablok regression analysis of these data yielded an equation of $Y = 1.04X + 0.1$ (95% confidence intervals for slope and intercept were 0.98 to 1.10, and -1.0 to +1.1, respectively). Deming regression analysis of these data yielded an equation of $Y = 1.09X - 0.6$ (95% confidence intervals for slope and intercept were 1.03 to 1.15, and -3.2 to +2.1 respectively). Pearson's correlation coefficient (r) of the paired data was 0.96 (95% confidence interval was 0.94 to 0.97), showing that essentially equivalent results were provided by both cleared predicate, the **DPC Coat-a-Count® Aldosterone RIA** device and the **NAA** immunoassay device.

b. Matrix comparison:
N/A

3. Clinical studies:

a. Clinical sensitivity:
N/A

b. Clinical specificity:
N/A

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

4. Clinical cut-off:
N/A

5. Expected values/Reference range:

To establish an expected reference range, AM (8-10 AM) and PM (4-6 PM) serum samples were obtained. For AM, serum from n=171 healthy, prescription medication free fasting adults (102 females and 69 males, age: 18 to 79 years) were obtained in the upright/sitting posture and supine posture. The upright/sitting

blood sample was obtained while the fasting volunteer was ambulatory for at least 15 minutes prior to sitting down to have their blood drawn. Individuals who underwent further supine blood sampling laid down immediately after their upright sample was drawn. The supine blood sample was obtained after the volunteer was laying down for at least 30 minutes.

All individuals had normal blood pressures (systolic ≤ 139 mm Hg; diastolic ≤ 89 mm Hg), normal serum electrolytes, normal fasting glucose, BUN, and creatinine levels, and none were hyperlipidemic. None of the individuals were on restricted diets. Pregnancy and breast feeding mothers, individuals who were taking prescription medications, and anyone who were taking medications for weight loss were excluded. The supine cohort (n=62) was a subset of the larger AM population. The PM cohort (n=44) was a different subset of the AM population. Aldosterone levels were not age dependent. The 95% confidence intervals observed from these studies are as follows.

Time and Posture	Serum: 95% Confidence Intervals:
8-10 AM Upright/Sitting	3-34 ng/dL
8-10 AM Supine	2-19 ng/dL
4-6 PM Upright/Sitting	2-23 ng/dL

To establish a suggested reference range using EDTA plasma samples, n=51 adults (27 females, 24 males) ages 22-59 years of the above cohort was evaluated.

Time and Posture	EDTA: 95% Confidence Intervals:
8-10 AM Upright/Sitting	3-22 ng/dL
8-10 AM Supine	2-14 ng/dL

M. Conclusion:

Based on Third Party Review Report, the Nichols Advantage Chemiluminescent Adosterone Immunoassay is substantially equivalent (SE) to device regulated under:

Aldosterone test system; 21 CFR §862.1045; CJM; Class II

Calibrator; 21 CFR §862.1150; JIS; Class II

Quality Control Material (Assayed and Unassayed); 21 CFR §862.1660; JJX Class I