JUN 1 - 2005

12.0 510(k) SUMMARY OF SAFETY AND EFFECTIVENESS

This summary of 510(k) safety and effectiveness is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

510(k) Number: k050784

1. Name of Submitter, Contact Person and Date Summary Prepared:

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Contact Person: Xie Qiyi, MD., MPH,
Director of Clinical and Regulatory Affairs
Date Prepared: 5/13/2005

2. Device Name and Classification

Trade/Proprietary Name:	Nichols Advantage® Aldosterone Assay
Common/Usual Name:	Aldosterone Immunoassay
Classification Name:	Radioimmunoassay System, Test, Aldosterone
Classification:	Class II Regulation Number: 862.1054 Product code: CJM, Clinical Chemistry

3. **Predicate Device:** DSL-8600 ACTIVE® Aldosterone Coated-Tube Radioimmunoassay Kit.

4. **Device Description:**

The Nichols Advantage® Aldosterone Assay is a competitive immunochemiluminometric in vitro diagnostic laboratory immunoassay (IVD device) that utilizes a biotinylated mouse monoclonal anti-aldosterone antibody as the capture reagent and an acridinium ester labeled aldosterone as a tracer reagent. This Aldosterone IVD device immunoassay is intended for use for the measurement of aldosterone in human serum, EDTA plasma, and extracted urine, as an extended diagnostic method utilized within the Nichols Advantage® Specialty System.

5. **Intended Use**

The Nichols Advantage Aldosterone Assay is intended for in vitro diagnostic laboratory use with the Nichols Advantage® Specialty System for quantitative measurement of aldosterone in human serum, EDTA plasma, and extracted urine. Aldosterone measurements are intended for use 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.

6. **Comparison to predicate device :**

The Nichols Advantage Aldosterone(Y) was compared to a commercially available Aldosterone radioimmunoassay (X) previously cleared by the FDA using the NCCLS EP9-A procedures for method comparison and bias analysis. (n=118) urine samples were assayed by both methods following each manufacturers' directions and without modifications. The range of values observed with the commercially available kit was 0.8 to 80.2 µg/24 Hr; with the Nichols Advantage Aldosterone the range was 0.4 to 66.7µg/24 Hr . Computing the Passing Bablok regression analysis of these data yielded an equation of Y = 1.23X – 1.19 (95% confidence intervals of the slope and intercept were 1.2 to 1.28, and –1.43 to –0.81 respectively). Pearson's correlation coefficient (r) of the paired data was 0.96 (95% confidence interval was 0.94 to 0.97). User laboratories should perform their own method comparison following their in-house procedures.

7. **Similarities:**

- Both assays use same specimen type [i.e., 24 hour human urine sampling]
- Both assays use human-derived aldosterone standards and controls.
- Both assays use a specific antibody to aldosterone, use competitive direct immunoassay methods to measure the hormone in urine.
- The sensitivity of both assays is sufficient to measure aldostrerone levels found in urine in the range of normal and abnormal values.
- Both assays are IVD laboratory-based medical device products.

8. **Differences:**

Feature	**DSL-8600 ACTIVE® Aldosterone Coated-Tube Radioimmunoassay Kit**	**Nichols Advantage® Aldosterone Assay**
Sample Volume	100 microliters	250 microliters
Sample preparation	Extracted Urine samples	Hydrolyzed Urine Samples
Analytical sensitivity	0.7 ng aldosterone/dL	1.2 ng aldosterone/dL
Analytical prinicpal	Radioimmunassay or RIA	Iimmunochemiluminometric Assay or ICL Assay
Incubation steps and temperature	Several steps, 18 hours at room temperature [~25C]	3 steps, 10 minutes each at 37C

9. **REPORTING RESULTS**

The recommended reportable range is 3 to 120 ng/dL. Values below 3 ng/dL should be reported as "less than 3 ng/dL" (< 3 ng/dL). The highest reportable value without dilution is the value of the highest point on the Master Curve (120

ng/dL). Samples reading above the Master Curve should be diluted and repeated, or reported as greater than the highest value on the Master Curve. The printout for the assay will show the location of the sample in the sample compartment, its identification number, and the time in which the assay was completed. In addition, the printout will show the RLU value for each replicate, the mean RLU, RLU %CV, %CV concentration, and the mean result in ng/dL. The mean result for all replicates should be reported.

10. EXPECTED VALUES (Urine)

Nichols Institute Diagnostics recommends that each laboratory establish its own range of expected values for the population they serve. To establish an expected reference range, 24 hours urine samples, n= 80 healthy, prescription medication free fasting adults (41 females and 39 males, age:18 to 78 years), were obtained. Non of the females were pregnant, taking birth control pills, or on estrogen treatment. After square root transformation of the data, the 95% confidence interval for normal 24-hour Urine Aldosterone results are as follows: 24-hour Urine Aldosterone Reference range: 0.7 to 23.0 µg/24 hours.

11. SPECIFIC PERFORMANCE CHARACTERISTICS

Feature	**DSL-8600 ACTIVE® Aldosterone Coated-Tube Radioimmunoassay Kit**	**Nichols Advantage® Aldosterone Assay**
Within-run (%CV)	3.3 to 7.4%	1.6 to 6.1%
Total Precision (%CV)	5.1 to 6.4%	10.2 to 15.3%
Recovery	92% to 138%	93% to 110%
Linearity	89% to 111%	85% to 116%

REPRODUCIBILITY FOR URINE

The within-run and total imprecision performance for the aldosterone assay was estimated using the NCCLS EP5-A method (Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline)[18]. The data represent one run per day over 20 days with 4 urine samples assayed in duplicate. The study was performed on a single system.

Urine Sample	Mean	Within-Run		Total Imprecision	
	(ng/dL)	SD	%CV	SD	%CV
Sample A	8.6	0.53	6.1	1.32	15.3
Sample B	17.6	0.4	2.3	1.95	11.1
Sample C	37.4	0.61	1.6	3.84	10.3
Sample D	61.2	1.32	2.2	6.21	10.2

PARALLELISM FOR URINE

Urine samples were extracted following the normal protocol. The reconstituted extracts were serially diluted with Nichols Advantage Aldosterone Urine Sample Diluent and assayed in duplicate.

Sample	Dilution	Observed (ng/dL)	Expected (ng/dL)	% Recovery
1	Neat	67.4		
	1:2	34.3	33.7	102%
	1:4	17.9	16.9	106%
	1:8	7.2	8.4	85%
2	Neat	82.2		
	1:2	41.3	41.1	100%
	1:4	20.5	20.5	100%
	1:8	9.4	10.3	92%
3	Neat	92.3		
	1:2	49.1	46.1	106%
	1:4	24.9	23.1	108%
	1:8	13.3	11.5	116%
4	Neat	86.2		
	1:2	46.4	43.1	108%
	1:4	23.7	21.6	110%
	1:8	11.4	10.8	106%
5	Neat	74.7		
	1:2	40.8	37.3	109%
	1:4	20.0	18.7	107%
	1:8	9.0	9.3	96%

RECOVERY FOR URINE

A high and low urine sample was extracted and assayed in duplicate. The reconstituted extracts from the high and low urine samples were mixed in 2 to 1, 1 to 1, and 1 to 2 ratios and assayed in duplicate.

Sample	Observed (ng/dL)	Expected (ng/dL)	% Recovery
Sample A	53.5		
1:1	30.7	32.9	93%
1:2	28.0	26.0	108%
2:1	36.9	39.6	93%
Sample B	12.5		
Sample C	49.9		
1:1	33.1	31.1	107%
1:2	27.4	24.8	110%
2:1	37.2	37.3	100%
Sample D	12.5		
Sample I	62.4		
1:1	39.7	40.7	97%
1:2	35.8	33.5	107%
2:1	44.3	47.8	93%
Sample J	19.3		99%

SPECIFICITY FOR URINE

Crossreactant	Highest Amt. Tested (µg/dL)	Apparent Amt. Detected (ng/dL)	% Crossreactivity
17-Hydroxy Corticosterone (Cortisol)	5000	23.9	Undetectable
	2500	24.2	Undetectable
	1250	27.5	Undetectable
Cortisone	45.00	26.0	Undetectable
	22.50	25.3	Undetectable
	11.25	25.4	Undetectable
17-Ketosteroids (DHEA)	9000	21.7	Undetectable
	4500	27.0	Undetectable
	2250	27.0	Undetectable
Estradiol	9.00	26.6	Undetectable
	4.50	27.4	Undetectable
	2.25	28.9	0.85%
Estriol	59.00	26.3	Undetectable
	29.50	27.8	Undetectable
	14.75	28.3	Undetectable
Aldosterone	2.9	37.5	102%
	1.5	43.9	98%

URINE EXTRACTION EFFICIENCY

Extraction efficiency is determined by spiking known quantities of Aldosterone into urine and measuring the recovery of the spiked Aldosterone. Different amounts of a pure Aldosterone stock solution are spiked into a normal urine sample. Each sample is then hydrolyzed, extracted and tested in n=8 replicates per level.

Sample	Spiked Dose	µg/24 Hr	Corrected Dose (Spiked -	% Recovery
Endogenous	0.0	7.0		
A	46.1	53.7	46.8	101%
B	31.9	39.7	32.7	103%
C	16.6	23.2	16.2	98%

12. METHOD COMPARISON

For urine samples

The Nichols Advantage Aldosterone(Y) was compared to a commercially available Aldosterone radioimmunoassay (X) previously cleared by the FDA using the NCCLS EP9-A procedures for method comparison and bias analysis. (n=118) urine samples were assayed by both methods following each manufacturers' directions and without modifications. The range of values observed with the commercially available kit was 0.8 to 80.2 µg/24 Hr; with the Nichols Advantage Aldosterone the range was 0.4 to 66.7µg/24 Hr . Computing the Passing Bablok regression analysis of these data yielded

an equation of Y = 1.23X – 1.19 (95% confidence intervals of the slope and intercept were 1.2 to 1.28, and –1.43 to –0.81 respectively). Pearson's correlation coefficient (r) of the paired data was 0.96 (95% confidence interval was 0.94 to 0.97). User laboratories should perform their own method comparison following their in-house procedures.

13. Conclusions:

These data, which were provided to FDA, demonstrates safety and effectiveness of the Nichols Advantage Aldosterone for its intended in vitro diagnostic use. Furthermore, based on performance characteristics, the Nichols Advantage Aldosterone assay is substantially equivalent to the predicated method in urine application.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 1 - 2005

Nichols Institute Diagnostics
c/o Alfredo J. Quattrone, Ph.D., D.A.B.T.
California Department of Health Services
Food and Drug Branch
P.O. Box 997 413
FDB Mailstop 7602
Sacramento, CA 95899

Re: k050784
Trade/Device Name: Nichols Advantage® Aldosterone Assay
Regulation Number: 21 CFR 862.1045
Regulation Name: Aldosterone test system
Regulatory Class: Class II
Product Code: CJM
Dated: May 19, 2005
Received: May 26, 2005

Dear Dr. Quattrone:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Carol C. Benson

Carol C. Benson, M.A.
Acting Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (k050784):

Device Name: Nichols Advantage® Aldosterone Assay

Indications For Use:

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Prescription Use √ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (~~ODE~~ OND)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) k050784