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

A. 510(k) Number:
k043175

B. Purpose for Submission:
Expanded Indications to "For the in vitro quantitative determination of cortisol in human serum, plasma, urine and **saliva**"
Serum and plasma cleared under k000270 and urine cleared under k021218.

C. Measurand:
CORTISOL

D. Type of Test:
Quantitative / electrochemiluminescence

E. Applicant:
ROCHE DIAGNOSTICS CORP.

F. Proprietary and Established Names:
ELECSYS CORTISOL TEST SYSTEM, ADDITION OF SALIVA SAMPLE TYPE

G. Regulatory Information:
1. Regulation section:
   21CFR Sec.-862.1205-Cortisol (hydrocortisone and hydroxycorticosterone) test system.
2. Classification:
   2
3. Product code:
   NHG - ENZYME IMMUNOASSAY, CORTISOL, SALIVARY
4. Panel:
   Chemistry (75)

H. Intended Use:
1. Intended use(s):
   For the in vitro quantitative determination of cortisol in human serum, plasma, urine and saliva.

2. Indication(s) for use:
   The Elecsys Cortisol Test System is for the in vitro quantitative determination of cortisol in human serum, plasma, urine and saliva. The determination of cortisol is used for the recognition and treatment of functional disorders of the adrenal gland. The electrochemilumensecence immunoassay "ECLIA" is intended for use on the Roche Elecsys 1010/2010 and MODULAR ANALYTICS E170 (Elecsys

module) immunoassay analyzers.

3. Special conditions for use statement(s):
   Not Applicable

4. Special instrument requirements:
   The electrochemilumensecence immunoassay "ECLIA" is intended for use on the Roche Elecsys 1010/2010 and MODULAR ANALYTICS E170 (Elecsys module) immunoassay analyzers. Systems cleared under k961491. No changes have been made to the instrument or software for the use of the new sample type.

I. Device Description:

The Elecsys Cortisol Assay is a two step sandwich immunoassay with streptavidin microparticles and electrochemiluminescence detection. Results are determined using a calibration curve that is generated specifically on each instrument by a 2-point calibration and a master curve provided with the reagent bar code. The Elecsys Cortisol Assay is intended for use on the Elecsys Immunoassay Family of Analyzers. The Salivette device is required for the collection of saliva for testing. The Elecsys Cortisol CalSet is the calibration material for the assay. The recommended control material is the Elecsys PreciControl Universal.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   SALIMETRICS, HIGH SENSITIVITY CORTISOL ENZYME IMMUNOASSAY

2. Predicate 510(k) number(s):
   k011323

3. Comparison with predicate:

Similarities
Both systems are intended for the measurement of cortisol in saliva for the treatment of functional disorders of the adrenal gland. Both are immunoassays employing competitive technology as the test principle. Both devices specify use of the Sarstedt Salivettes for sample collection.

Differences
The Elecsys Cortisol immunoassay is a fully automated system for the measurement of cortisol in human serum, plasma and urine while the predicate device incorporates manual steps and is only for measurement of cortisol in saliva. The Elecsys Cortisol is traceable to the Enzymun Test Cortisol which in turn is standardized via ID-MS. The Elecsys Cortisol has a measuring range of 0.036 to 63 ug/dL with an analytical sensitivity of < 0018 ug/dL. The predicate device has a measuring range of 0.007 to 1.80 ug/dL with an analytical sensitivity of <0.007 ug/dL The Elecsys Cortisol has within run precision with CVs ranging from 1.5% to 6.1% on sample concentrations of 0.170 ug/dL to 0.718 ug/dL. The predicate has intra-assay precision with CVs ranging from 4.25% to 5.73% on sample concentrations of 0.115 ug/dL to 1.591ug/dL.

K. Standard/Guidance Document Referenced (if applicable):
None referenced

L. Test Principle:
The Elecsys Cortisol Assay is a two step sandwich immunoassay with streptavidin microparticles and electrochemiluminescence detection. Results are determined using a calibration curve that is generated specifically on each instrument by a 2-point calibration and a master curve provided with the reagent bar code. The Elecsys Cortisol Assay is intended for use on the Elecsys Immunoassay Family of Analyzers. The Salivette device is required for the collection of saliva for testing. The Elecsys Cortisol CalSet is the calibration material for the assay. The recommended control material is the Elecsys PreciControl Universal.

M. Performance Characteristics (if/when applicable):
1. Analytical performance:
   a. *Precision/Reproducibility:*
   Inter-Assay precision of Elecsys® Cortisol for saliva application was evaluated on the Elecsys 2010 Immunoassay Analyzer by measuring 5 saliva samples in 10 runs.

	Sample 1 (nmol/L)	Sample 2 (nmol/L)	Sample 3 (nmol/L)	Sample 4 (nmol/L)	Sample 5 (nmol/L)
Mean	0.93	7.72	16.95	34.57	42.47
SD	0.345	0.557	1.05	1.69	1.76
CV	37.1 *	7.2	6.2	4.9	4.1

   * Concentration of sample 1 lies below functional sensitivity claim of < 2.0 nmol/L (< 0.07 µg/dL)

   The intra-assay precision for the saliva application was determined by 21- fold determination of saliva samples with the Elecsys Cortisol Test System on the Elecsys® 2010 Immunoassay Analyzer.

	Sample 1 (nmol/L)	Sample 2 (nmol/L)	Sample 3 (nmol/L)	Sample 4 (nmol/L)	Sample 5 (nmol/L)
Mean	4.88	11.49	15.13	15.94	19.81
SD	0.29	0.309	0.611	0.24	0.552
CV	6.1	2.7	4.0	1.5	2.8

b. *Linearity/assay reportable range:*

The measurement range 1.00-1750 nmol/L or 0.036-63 µg/dL (defined by the lower detection limit and the maximum of the master curve). Values below the detection limit are reported as < 1.00 nmol/L (< 0.036 µg/dL). Values above the measuring range are reported as > 1750 nmol/L (> 63 µg/dL) (or up to 17,500 nmol/L or 630 µg/dL for 10-fold diluted samples). The measurement range is supported by linearity data from k000270 clearance.

The saliva linearity data supports a linear range of 5.4 to 121.4 nmol/L.

% high saliva Sample 1	Measured (nmol/L)	Expected (nmol/L)	% Recovery (meas. vs.exp.)
0	5.83	5.83	100.0
10	8.76	8.65	101.3
20	11.63	11.47	101.4
30	14.08	14.28	98.5
40	17.02	17.10	99.5
50	19.52	19.92	98.0
60	22.40	22.74	98.5
70	24.96	25.56	97.7
80	27.65	28.38	97.4
90	30.78	31.20	98.7
100	34.02	34.02	100.0
Sample 2			
0	6.09	6.09	100.0
10	11.18	11.73	95.3
20	16.57	17.37	95.4
30	22.42	23.01	97.4
40	28.46	28.65	99.3
50	33.99	34.29	99.1
60	38.62	39.93	96.7
70	44.65	45.57	98.0
80	50.70	51.21	99.0
90	56.27	56.85	99.0
100	62.49	62.49	100.0
Sample 3			
0	5.40	5.40	100.0
10	17.31	17.00	101.8
20	27.84	28.60	97.3
30	40.69	40.20	101.2
40	52.01	51.80	100.4

50	64.76	63.40	102.1
60	75.50	75.00	100.7
70	87.60	86.60	101.1
80	97.93	98.20	99.7
90	109.30	109.80	99.5
100	121.40	121.40	100.0

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The Elecsys Cortisol is standardized against the Enzymun- Test Cortisol. The Enzymun- Test Cortisol was standardized via ID-MS. Elecsys Cortisol shows recovery results from 89%-111% in the IRMM IFFC-451 Panel (ID/GC/MS).

See k000270 - Elecsys Cortisol Immunoassay Test System which included reagents, Elecsys Cortisol CalSet (calibrator) and PreciControl Universal (controls) for information about stability.

Controls should be measured at least once every 24 hours when the assay is in use, once per reagent kit, and after every calibration.

d. *Detection limit:*
Analytical sensitivity (lower detection limit)
< 0.500 nmol/L (< 0.018 µg/dL)
The detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying two standard deviations above that of the lowest standard (master calibrator, standard 1 + 2 SD, within-run precision, n = 21).

Functional sensitivity
< 2.0 nmol/L (< 0.07 µg/dL)
The functional sensitivity is the lowest analyte concentration that can be reproducibly measured with a between-run coefficient of variation of 20%. It was determined by using low concentration saliva samples.

e. *Analytical specificity:*
The saliva application of the Elecsys Cortisol performs in the same manner of the already cleared Elecsys Cortisol serum, plasma and urine applications. Cross-reactivity and interfering substance testing is applicable to the saliva application therefore no repeated testing was performed.

f. *Assay cut-off:*
Not Applicable

2. Comparison studies:
a. *Method comparison with predicate device:*
The predicate device is the Salimetrics Cortisol assay. The Salimetrics High Sensitivity Salivary Cortisol Enzyme Immunoassay kit is a competitive

immunoassay intended for the measurement of salivary cortisol which is the desired sample type for addition to the Elecsys Cortisol immunoassay.

Samples were obtained in the morning and afternoon from individuals employed by Roche to provide normal samples. Fifteen samples were then spiked with cortisol in order to prove technical equivalency at higher cortisol levels. Native and spiked saliva samples were tested in the study.

Samples were collected at Roche Diagnostics GmbH. Testing was internally performed at Roche Diagnostics GmbH, Germany. There is no potential for user influenced differences in the executing and reading of the tests due to the fully automatic operation of the Elecsys systems. Testing was conducted between June 2004 through August 2004. Samples were collected prospectively. A sample identification number is associated with the human sample for de-identification.

The samples were stored at -20 degrees prior to being tested. The centrifuged saliva sample is stable for 5 days at 2-8 degrees C and 3 months at -20 degrees C. Freeze only once.

A total of 326 saliva samples having Cortisol values ranging from 1.29-50.44 nmol/L were tested. Each sample was tested in singleton.

The results were calculated using the Passing/Bablok and Least Squares regression analyses.

	Passing/Bablok	Least Squares
N	326	326
Range	1.29 – 50.44	1.29 – 50.44
Slope	1.12	0.90
Y intercept	0.53	1.71
r	0.531	0.942
SEE	1.74	1.96

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):
      See expected values

4. Clinical cut-off:
   Not Applicable

5. Expected values/Reference range:
   The following values were determined in saliva samples from 154 healthy individuals (5th-95th percentile) using Elecsys Cortisol.
   Morning hours 8-10 AM: 1.90 - 19.1 nmol/L
   Afternoon hours 2:30 - 3:30 PM: 2.05 - 11.9 nmol/L

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.