SEP 2 4 2004

K041349

SUMMARY OF

SAFETY AND EFFECTIVENESS
FOR IBL ESTRADIOL LIA

Manufacturer: IBL Immuno Biological Laboratories
Flughafenstrasse 52A, D-22335
Hamburg Germany

Contact Information: Lehnus & Associates
Gary Lehnus
150 Cherry Lane Rd.
East Stroudsburg, PA 18301
Tel: (570) 620-0198

Device Name / Classification:
The device trade name is the IBL Estradiol LIA having FDA assigned name: Estradiol test system, 21 CFR, **862.1260**, categorized as Class I "exempt" medical devices for the Clinical Chemistry and Clinical Toxicology Panel, as Product Code **CHP.**

Device Description:
Luminescence immunoassay (LIA) based on the competition principle. An unknown amount of antigen present in the sample and a fixed amount of enzyme labeled antigen compete for the binding sites of the antibodies coated onto the wells. After incubation the wells are washed to stop the competition reaction. After addition of the luminescence substrate solution the intensity of the luminescence measured is inversely proportional to the amount of the antigen in the sample. Results of samples can be determined directly using the standard curve.

Device Intended Use:
Luminescence immunoassay for the *in vitro diagnostic* quantitative measurement of active free Estradiol, an estrogenic steroid, in saliva and serum. Measurements obtained by this device may be used in the diagnosis and treatment of various hormonal sexual disorders and can be used to evaluate ovarian function. This test is not intended for assessing placental function in complicated pregnancy.

Device Performance:
Normal Ranges in Saliva
To establish a normal range in saliva for this test, studies were performed to establish levels of estradiol in saliva throughout the menstrual cycles from 28 apparently healthy pre-menopausal women using no contraceptives. Three saliva samples were collected per day (morning, midday, and afternoon) and pooled and frozen prior to running the Estradiol LIA assay. Collection began at the last day of bleeding and continued daily until first day of bleeding. In addition, five postmenopausal women and 40 males were evaluated for the studies. One saliva sample was obtained for these 2 populations. The Normal Ranges in saliva obtained for the studies are as follows:

Normal ranges	**Estradiol (pg/mL)**		
♀	Premenopausal n=28 month profiles age 19 - 43	Follicular phase	0.6 – 10.4
		Mid-cycle Peak	4.5 - 21.2
		Luteal phase	0.5 - 10.8
	Postmenopausal n=5 age 42 - 62		< 3.2
♂	n = 40, age 20 - 63		< 3.4

Comparison of Serum and Saliva:

Comparison studies were performed using 50 saliva and 60 serum samples from adult healthy populations. The **saliva** samples were tested on the IBL Estradiol LIA and compared to a published procedure that used a modification in the handling of saliva for a typical RIA test. Results from measuring the saliva samples in both methods yielded a correlation of $r^2 = 0.97$ with a regression formula of Y=0.96*RIA + 0.55. The **serum** samples were tested against a commercially available RIA test kit. The comparison with serum yielded $r^2 = 0.95$ with a regression formula of Y= 1.00*RIA – 4.83.

Serum to Saliva Comparison:

A study was performed with the IBL Estradiol LIA to assess the levels of estradiol in serum versus those found in saliva. Saliva and serum pairs were collected at the same time between 10:00 AM and 4:00 PM. The paired samples were then run in the IBL Estradiol LIA test. The results of the comparison yielded the following regression formula – serum (pg/mL) = 43.491(saliva) - 4.680 with a $R^2 = 0.712$.

The overall performance of the IBL Estradiol LIA is shown following:

Analytical Specificity (Cross Reactivity)	**Substance**	**% Cross-reactivity**	Cross-reactivity of other substances tested : ≤ 0.01 %
	17β-Estradiol	100.0	
	Estrone	0.222	
	Estriol	0.138	
	Corticosterone	0.007	
	Dexamethasone	0.009	
	Cortisone	0.007	
	Progesterone	0.012	
	Testosterone	0.015	
	Prednisolone	0.005	
Analytical Sensitivity (Limit of Detection)	Saliva: 0.3 pg/ml	Mean signal (Zero-Standard) - 2SD	
	Serum: 7.3 pg/mL		
Functional Sensitivity	Saliva: 0.78 pg/ml	Mean Conc. <20% CV	
	Serum: 8.0 pg/mL		

Precision	**Saliva (pg/mL)**				**Serum (pg/mL)**			
	Mean	**SD**	**CV (%)**	**N**	**Mean**	**SD**	**CV (%)**	**N**
Intra-Assay	3.5	0.3	7.9	10	37.5	3	7.4	10
	11.8	0.5	7.3	10	167	8	4.8	10
	33.0	1.2	3.7	10	334	10	3.1	10
Inter-Assay	2.4	0.3	13.9	10	34.1	3.2	9.3	10
	9.4	0.9	9.1	10	159.2	11.9	7.5	10
	38.5	2.2	5.9	10	329	14.1	4.3	10

Linearity	**Saliva**			**Serum**		
	Dilution	Meas. (pg/mL)	Rec. (%)	Dilution	Calculated (x10) (pg/mL)	Rec. (%)
	-	8.0		-	312	
	1:2	3.9	98	1:2	134	86
	1:4	2.2	111	1:4	65	83
	1:8	1.1	106	1:8	34	88
	-	15.5		1:16	18	94
	1:2	7.9	102	-	178	
	1:4	4.1	106	1:2	72	81
	1:8	1.6	80	1:4	38	85
	-	49.6		1:8	19	86

	1:2	24.4	98	1:16	13	117		
	1:4	11.3	91	-	38			
	1:8	7.1	114	1:2	19	100		
	1:16	3.4	111	1:4	8	87		
	1:32	1.4	90	1:8	5	98		
Recovery	Conc. (pg/mL)	Added pg/mL	Meas. pg/mL	Rec. %	Conc. (pg/mL)	Added pg/mL	Calculated (x10) pg/mL	Rec. %
	Saliva 1 (14.6)	0.9	15.2	98	Serum 1 (52)	9	58	96
		2	15.9	95		20	67	93
		4	18.8	101		40	81	89
		8	24.5	109		80	110	83
		16	28.7	94		160	188	89
		32	56.9	122		320	313	84
	Saliva 2 (5.5)	0.9	5.9	92	Serum 2 (221)	9	207	90
		2	6.2	83		20	229	95
		4	9.1	95		40	230	88
		8	14.4	106		80	257	85
		16	21.8	101		160	335	88
		32	47.9	128		320	434	80
	Saliva 3 (2.4)	0.9	3.8	113	Serum 3 (364)	9	375	101
		2	5.2	116		20	387	101
		4	6.7	105		40	394	97
		8	11.1	106		80	427	96
		16	20.3	110		160	469	90
		32	41.2	120		320	636	93
Comparison to Published Procedure	Saliva	IBL-Assay = 0.96 x RIA + 0.55 R^2 = 0.97; n = 50			Range = 0 – 51 pg/mL RIA 0 – 55 pg/mL LIA			
Comparison to Commercial RIA	Serum	IBL-Assay = 1.00 x RIA – 4.83 R^2 = 0.95; n = 60			Range = 22 – 448 pg/mL RIA 2 – 444 pg/mL LIA			
Serum to Saliva Comparison IBL LIA	Serum (pg/mL) = 43.491(saliva) - 4.680				R^2 = 0.712			

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

SEP 2 4 2004

IBL Hamburg
c/o Mr. Gary Lehnus
Lehnus & Associates Consulting
150 Cherry Lane Rd.
East Stroudsburg, PA 18301

Re: k041349
Trade/Device Name: IBL Estradiol LIA Test
Regulation Number: 21 CFR 862.1260
Regulation Name: Estradiol test system
Regulatory Class: Class I
Product Code: CHP
Dated: September 3, 2004
Received: September 7, 2004

Dear Mr. Lehnus:

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 (301) 594-3084. 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/dsma/dsmamain.html.

Sincerely yours,

Jean M. Cooper MS, D.V.M.

Jean M. Cooper, MS, D.V.M.
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 (if known): K041349

Device Name: IBL Estradiol LIA Test

Indications For Use:

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Prescription Use X **AND/OR** **Over-The-Counter Use** _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

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

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K041349