

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

A. 510(k) Number:

k040923

B. Purpose for Submission:

New device

C. Analyte:

Progesterone

D. Type of Test:

Quantitative

E. Applicant:

IBL-Hamburg

F. Proprietary and Established Names:

IBL Progesterone LIA

G. Regulatory Information:

1. Regulation section:
21 CFR 862.1620
21 CFR 864.3250
2. Classification:
I (reserved per 21 CFR 862.9(a) for new intended use)
3. Product Code:
JLS
NNI
4. Panel:
75

H. Intended Use:

1. Intended use(s):
Luminescence immunoassay for the *in vitro diagnostic* quantitative measurement of active free progesterone (a female hormone) in saliva. Measurements obtained by this device may be used in the diagnosis and treatment of disorders of the ovaries and can be used as an aid for confirmation of ovulation.

The IBL SaliCap Set is used for the collection, handling, and storage of saliva used in the Progesterone LIA assay

2. Indication(s) for use:

Luminescence immunoassay for the *in vitro diagnostic* quantitative measurement of active free progesterone (a female hormone) in saliva. Measurements obtained by this device may be used in the diagnosis and treatment of disorders of the ovaries and can be used as an aid for confirmation of ovulation.

The IBL SaliCap Set is used for the collection, handling, and storage of saliva used in the Progesterone LIA assay.

3. Special condition for use statement(s):
None
4. Special instrument Requirements:
None

I. Device Description:

The IBL Progesterone LIA kit contains the following:

- Microtiter Plate coated with rabbit anti-mouse antibody
- Progesterone Antiserum (mouse anti-progesterone antibody)
- Standards A-G (0, 10, 25, 50, 100, 300, and 1000 pg/mL); progesterone in buffer with BSA and stabilizers
- Controls Level I and II
- Assay Buffer (Tris buffer with BSA and stabilizers)
- Enzyme Conjugate (alkaline phosphatase [calf] conjugate with stabilizers)
- Chemiluminescence Reagent AP (acridan based substrate)
- Wash Buffer (Tris buffer with Tween and stabilizer)
- Adhesive Foil

The IBL SaliCap Set consists of empty, non-sterile, plastic tubes available in quantities of 100, 500, and 1000.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Diagnostic Systems Laboratories DSL 3400 Progesterone RIA
2. Predicate K number(s):
K854649
3. Comparison with predicate:

Similarities		
Item	Device	Predicates
Analyte	progesterone	Same
Methodology	Immunoassay/competition principle	Same
Differences		
Item	Device	Predicate
Specimen	Saliva	Serum and plasma

Reading Indicator	Luminescent labeling	Radio labeling
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K. Standard/Guidance Document Referenced (if applicable):

None referenced

L. Test Principle:

The IBL Progesterone luminescence immunoassay (LIA) is 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.

M. Performance Characteristics (if/when applicable):1. Analytical performance:a. *Precision/Reproducibility:*

Saliva samples from six (6) individuals were run in replicates of ten (10) each within one assay run to determine within-run precision. The mean concentrations ranged from 11.54 to 822.10 pg/mL. The standard deviations (SDs) ranged from 0.69 to 5.92, resulting in %CVs ≤ 6.0 .

Between run reproducibility was determined by replicate measurements of ten (10) different saliva samples in ten (10) different test runs of three (3) different test lots. The mean concentrations ranged from 10.6 to 817.1 pg/mL. The SDs ranged from 1.99 to 42.6, resulting in %CVs between 3.4 and 18.8.

b. *Linearity/assay reportable range:*

A series of six (6) patient saliva samples were serially diluted two-fold with Standard A from the kit. All recoveries were within the acceptable range (80-120%) with the exception of one dilution in one sample in which the recovery was 78%. However, subsequent dilutions were within range. Linearity of the test was determined up to 1200 pg/mL.

A series of five (5) saliva samples were used to evaluate recovery in the LIA test. Purified progesterone was weighed and added at the following concentrations and the samples retested: 0, 10, 25, 50, 100, 300, and 1000 pg/mL. The initial concentrations of the saliva samples ranged between 27.1 and 199.5 pg/mL. All recoveries were within the acceptable range (80-120%) with the exception of one sample with a recovery of 121.4%.

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

Purified progesterone stock

d. *Detection limit:*

The zero Standard A was dispensed in 20 replicates and assayed to assess the lowest level detectable in the assay. The mean minus 2SD was calculated, and using a four-parameter curve fit calculation, the analytical sensitivity was found to be 2.6 pg/mL.

e. *Analytical specificity:*

The cross-reactivity of the progesterone antiserum was measured against various compounds. The percent cross-reactivity is expressed as the ratios of progesterone concentration to the concentration of the reacting compound at 50% binding of the zero standard. The percent cross-reactivities were as follows:

17 α -Hydroxyprogesterone	1.84
6 α -Methyl-17 α -Hydroxyprogesterone	1.41
Pregnenolone	0.41
Deoxycorticosterone	0.28
Androsterone Sulfate	0.25
Androstenedion	0.20
Androsterone	0.20
DHEA-S	0.11
Corticosterone	0.06

Cross-reactivities of other substances tested were $\leq 0.1\%$.

The influence of blood, thimerosal, and sodium azide on the assay was also evaluated. Low and high progesterone level female saliva samples were enriched with different concentrations of whole blood to see the effect on measured progesterone values. The results found that bleeding does not affect results until visible (e.g., $>0.25\%$ blood contamination in saliva samples).

Increasing concentrations of thimerosal were added to saliva samples with known concentrations of progesterone to assess the affect of adding the preservative to saliva might have on the results. Thimerosal in very high concentrations (e.g., $>0.25\%$ to stabilize samples) may interfere with the measurement and give false low results.

Increasing concentrations of sodium azide were added to saliva samples with known concentrations of progesterone. The results found that high concentrations (up to 1.0%) do not influence test results. Recoveries ranging between 90 to 98% were observed.

f. *Assay cut-off:*

See "Detection limit."

2. Comparison studies:
 - a. *Method comparison with predicate device:*
See “Other clinical supportive data.”
 - 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):*
The IBL Progesterone LIA was compared to a published RIA procedure. The progesterone content from saliva samples collected from apparently healthy female individuals was assessed by both methods. All samples were stored frozen at -20 °C then thawed and assayed. The regression analysis on a total of ninety-seven (97) samples was as follows: $y = 0.89x + 25.5$, $r^2 = 0.94$. The range of samples on the subject device was 2–945 pg/mL. The range of samples on the RIA procedure was 0-916 pg/mL.
4. Clinical cut-off:
Not applicable
5. Expected values/Reference range:
A study was conducted to determine the normal range. Saliva samples were collected from apparently healthy females known to be premenopausal and using no contraceptives. Three saliva samples were collected per day (AM, midday, and PM), pooled, and frozen prior to running the assay. Collection began at the last day of bleeding and continued daily until the first day of bleeding. A total of 27 women were evaluated for the study. The range for premenopausal women age 15-43 was found to be 28-82 pg/mL (follicular phase) and 127-446 pg/mL (luteal phase). Note that salivary progesterone levels of 32.2-94.3 for the follicular phase and 106.3-311.0 for the luteal phase were reported from literature. Four women in this study exhibited atypical progesterone profiles.

Saliva samples were collected from six women (one from each woman) known to be postmenopausal and assayed in the Progesterone LIA test. The range for postmenopausal women age 42-62 was found to be 18-51 pg/mL.

Saliva samples were collected from forty-nine healthy male volunteers (one from each male) and assayed in the Progesterone LIA test. The range for males age 20-63 was found to be <59 pg/mL. Note that salivary progesterone levels of 9-32 pg/mL in males were reported from literature.

N. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.