

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

A. 510(k) Number:

k051626

B. Purpose for Submission:

New device

C. Measurand:

Opiates

D. Type of Test:

Qualitative Immunoassay

E. Applicant:

Immunoanalysis Corporation

F. Proprietary and Established Names:

Immunoanalysis Opiates ELISA for Oral Fluids

G. Regulatory Information:

1. Regulation section:

21 CFR §862.3650, Opiate test system

2. Classification:

Class II

3. Product code:

DJG

4. Panel:

91, Toxicology

H. Intended Use:

1. Intended use(s):

See Indications for use

2. Indication(s) for use:

The Immunoanalysis Opiates ELISA test system utilizes an Enzyme Linked Immunoassay (ELISA) for the qualitative detection of Opiates in ORAL FLUID SAMPLES COLLECTED WITH THE QUANTISAL™ ORAL FLUID COLLECTION DEVICE ONLY using a cutoff of 40 ng/mL of Morphine. This in-vitro diagnostic device is intended for clinical and laboratory use only.

The Immunoanalysis Opiate ELISA Kit for oral fluids provides only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography/Mass Spectrometry (GC/MS) is the preferred confirmatory method. Clinical and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

3. Special conditions for use statement(s):

For Professional and In Vitro diagnostic use only.

4. Special instrument requirements:

Micro-plate reader capable of reading at 450 nm and 620 nm.

I. Device Description:

The device consists of a saliva collection device (collector) and an opiates ELISA kit. An oral fluid specimen is collected by placing the collection device, a cellulose pad affixed to a propylene stem, under the tongue until approximately one milliliter of saliva has saturated the pad. A blue indicator on the stem indicates when enough sample has been collected. The collector is transferred to a provided polypropylene tube containing preservative buffer (3 ml) and closed, ready for transport or storage. The ELISA assay consists of a 96-well micro-plate coated with high affinity purified rabbit polyclonal antibody, conjugated morphine, negative and positive controls, a cut-off calibrator, TMB substrate and stop reagent.

J. Substantial Equivalence Information:

1. Predicate device name(s):

DRI Opiates EIA Assay

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

k915180

3. Comparison with predicate:

| Similarities | | |
|-----------------|---|--------------------------------------|
| Item | Device | Predicate |
| Type of Product | Analytical Reagents | Analytical Reagents |
| Test System | Competitive enzyme linked immunosorbent assay (ELISA) | Competitive enzyme immunoassay (EIA) |

| Differences | | |
|-----------------------|--|-------------------|
| Item | Device | Predicate |
| Cutoff Concentrations | 40 ng/mL | 300 ng/mL |
| Sample Type | Oral Fluid | Urine |
| Measured Analytes | Morphine, Codeine, 6-Acetyl morphine and Hydrocodone | Morphine, Codeine |

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

None Referenced

L. Test Principle:

Enzyme-labeled drug and drug present in the sample compete for limited anti-morphine antibody binding sites. Binding of the enzyme-labeled drug inhibits its reaction with the substrate, thereby influencing the rate of absorbance change measured by the instrument. The rate of absorbance change is proportional to the concentration of drug in the sample. Concentrations of controls and unknowns are calculated from the standard curve. Results are read at 450 and 620 nm.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision was tested by spiking negative oral fluid samples with 0, 20, 30, 40, 60 and 80 ng/mL of Morphine; this corresponded to 0, 50%, 75%, 100%, 150% and 200% of the cutoff. One milliliter of the spiked fluids was pipetted onto the collection pad of the oral fluid collector and the pad then processed as per instructions.

Intra-assay precision was assessed with sixteen replicates of each concentration analyzed in one run. The results are in the chart below:

| Morphine Conc. (ng/ml) | Mean O.D. | S.D | CV % |
|------------------------|-----------|-------|------|
| 0 | 2.521 | 0.048 | 1.92 |
| 20 (50% c/o) | 1.405 | 0.071 | 5.05 |
| 30 (75% c/o) | 1.253 | 0.048 | 3.85 |
| 40 (100% c/o) | 1.095 | 0.050 | 4.57 |
| 60 (150% c/o) | 0.946 | 0.051 | 5.37 |
| 80 (200% c/o) | 0.739 | 0.046 | 6.25 |

Inter-assay precision was assessed by eight replicates of each concentration run in ten different assay runs over 7 days. Results are expressed as B/BO% where B = absorbance of sample and BO = absorbance of the zero calibrator. The results are in the chart below:

| | Morphine concentration (ng/mL) | | | | |
|---------|--------------------------------|-----------------|------------------|------------------|------------------|
| | 20 (50% c/o) | 30 (75% c/o) | 40 (100% c/o) | 60 (150% c/o) | 80 (200% c/o) |
| Mean | 56.99 % | 49.934 % | 42.699 % | 37.239 % | 28.648 % |
| Std Dev | 1.006 | 0.869 | 0.679 | 1.270 | 0.625 |
| % CV | 1.76 | 1.74 | 1.59 | 3.41 | 2.18 |

Reproducibility of the oral fluid collection device was assessed by collecting oral fluid from 50 subjects with a pre-weighed collector and tube as per the package instructions. After the volume indicator turned blue, the collector and tube were weighed and the net weight of the saliva was determined and converted to volume (mLs). The results are in the chart below:

| Avg. Vol. mL) | Std. Dev. | C.V. | Mean +3 SD (mL) | Mean -3 SD (mL) |
|------------------|--------------|-------|--------------------|--------------------|
| 0.993 | 0.029 | 2.88% | 1.079 | 0.907 |

These results support the sponsors' claim that the device collects 1 mL \pm 10% saliva.

b. Linearity/assay reportable range:

Not applicable. This is a qualitative assay.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

All calibrator and control stock solutions are prepared from commercially available DEA exempt solution. The concentration of morphine in each solution is confirmed by GC/MS.

Stability Studies:

Claimed shelf-life of the oral fluid collection device and the ELISA kit and components is 24 months and 12 months respectively. Real-time studies are ongoing.

Stability of morphine in the collection device was determined by spiking a pool of negative oral fluid with morphine at a concentration around the cutoff and another pool at a concentration two-fold higher (2x). Samples were stored at 4°C and at room temperature. The specimens kept at room temperature were assayed in duplicate by GC-MS after 7 days, 14 days and 30 days; samples kept at 4°C were assayed in duplicate by GC-MS after 14 days and 30 days. The same process was performed for the testing of 6-Acetyl morphine. The sponsors' acceptance criterion was recovery of \pm 20% of the initial value. The results are in the chart below:

| Stability at Room Temperature | | | | | | | | |
|--------------------------------------|------------------------|-----------------|---------------------------|-----------------|---------------------------------|-----------------|------------------------------------|-----------------|
| Day | Morphine spike (ng/mL) | % initial value | 2x Morphine spike (ng/mL) | % initial value | 6-acetyl morphine spike (ng/mL) | % initial value | 2x 6-acetyl morphine spike (ng/mL) | % initial value |
| 0 | 26.37 | 100 | 58.58 | 100 | 2.727 | 100 | 5.798 | 100 |
| 7 | 26.76 | 101.48 | 59.65 | 101.8 | 2.562 | 93.95 | 5.734 | 98.90 |
| 14 | 25.23 | 95.68 | 55.64 | 94.99 | 2.823 | 103.52 | 5.81 | 100.21 |
| 21 | 26.76 | 101.49 | 56.27 | 96.05 | 2.377 | 87.17 | 5.983 | 103.19 |
| 30 | 27.66 | 104.92 | 58.39 | 99.67 | 2.035 | 74.62 | 4.75 | 81.92 |
| Stability at 4°C | | | | | | | | |
| 0 | 26.37 | | 58.58 | | 2.727 | 100 | 5.798 | 100 |
| 14 | 26.47 | 100.41 | 54.07 | 92.30 | 2.83 | 1003.78 | 5.879 | 101.40 |
| 30 | 27.95 | 106.01 | 62.15 | 106.09 | 2.317 | 84.97 | 4.825 | 83.22 |

A shipping study showed that morphine spiked oral fluid acceptable recovery was $\pm 15\%$ after transport.

d. Detection limit:

See the Precision/Reproducibility section above for performance around the stated cutoff concentration.

e. Analytical specificity:

The cross reactivity was established by spiking various concentrations of different drugs into synthetic oral fluid.

Cross-reactivity with similar compounds:

| Compound | Concentration tested ng/mL | Percent (%) Cross-reactivity |
|------------------------|----------------------------|------------------------------|
| Morphine | 40 | 100 |
| Codeine | 30 | 313 |
| 6-Acetyl Morphine | 20 | 70 |
| | 40 | 61 |
| Hydrocodone | 40 | 163 |
| Hydromorphone | 40 | 40 |
| Dihydrocodeine | 40 | 210 |
| Diacetylmorphine | 100 | 30 |
| Oxycodone | 250 | 4 |
| Oxymorphone | 250 | 2 |
| Normorphine | 1000 | 0.64 |
| Nalorphine | 5000 | 0.33 |
| Morphine-3-Glucoronide | 10000 | 1.1 |

Fifty-eight unrelated compounds were spiked at the equivalent to 10,000 ng/mL in synthetic oral fluid. None of the spiked oral fluid had an immunoassay response greater than the 50% control of the assay (Morphine 20 ng/mL). A complete list can be found in the package insert.

A variety of consumable substances (including 145 mg/mL sugar, 25 mg/mL toothpaste, 25% v/v cranberry juice, orange juice, carbonated cola and mouthwash, 25 mg/mL baking soda, 10% v/v cough syrup, and distilled water) were evaluated for interference. Dextromethorphan present in cough syrup at 100,000 ng/mL will cause false positive results. The other compounds tested did not affect results at these concentrations.

f. Assay cut-off:

Performance around the assay cut-off of 40 ng/mL is demonstrated in the intra-assay precision section above.

The Substance Abuse and Mental Health Services Administration (SAMHSA) has recommended 40 ng/mL as a cutoff level for Morphine oral fluid tests.

2. Comparison studies:

a. Method comparison with predicate device:

One hundred and sixty-five specimens were collected from volunteers who admitted drug use. Each volunteer provided a urine and oral fluid sample which were collected at the same time. Urine samples were tested by the predicate assay using a cutoff of 300 ng/mL. Oral fluid samples were tested in duplicates using a screening cutoff was 40 ng/mL: all samples were tested by GC/MS at an independent facility. Results are tabulated below:

| | | Predicate Urine Assay | |
|---------------------------------|-----|--------------------------|-----|
| | | Pos | Neg |
| Morphine Oral Fluid Assay | Pos | 55 | 12 |
| | Neg | 21 | 77 |

Positive agreement: 82.1 %
Negative agreement: 78.6 %
Overall agreement: 80.0 %

| | | GC/MS | |
|------------------------------|-----|-------|-----|
| | | Pos | Neg |
| Morphine Oral Fluid Assay | Pos | 51 | 16 |
| | Neg | 2 | 96 |

Positive agreement: 76 %
Negative agreement: 97.96 %
Overall agreement: 89.1 %

Of the 16 ELISA positive screening results that did not confirm by GC/MS, 9 of the samples had either Morphine, Codeine or Hydrocodone concentrations below the confirmation cutoff of 40 ng/mL. The GC/MS of the other 7 samples did not have the presence of Codeine, Morphine, 6-Acetyl Morphine, Hydrocodone, Hydromorphone and Oxycodone.

Agreement between Opiate Oral Fluid Assay and GC/MS (Cutoff 40 ng/mL)

| | Opiates (morphine/Codeine/Hydrocodone) Concentration by GC/MS (ng/mL) | | | | | |
|----------------------------|--|----------|--------------|------------|----------------|----------|
| | | Negative | <-25% C/O | -25 to C/O | C/O to +25% | >25% C/O |
| | Conc. | 0 | <30 | 30-40 | 40-50 | >50 |
| Opiate Oral Fluid Assay | Pos | 7 | 10 | 2 | 1 | 47 |
| | Neg | 92 | 4 | 2 | 0 | 0 |

b. Matrix comparison:

Not applicable; this device is intended for use with oral fluid only.

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):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Not applicable

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.