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

A. 510(k) Number:

k183048

B. Purpose for Submission:

New device

C. Measurand:

Not applicable.

D. Type of Test:

Collection, preservation, and transport of oral fluid specimens with drugs of abuse testing for tetrahydrocannabinol (THC), benzoylecgonine, cocaine, morphine, codeine, oxycodone, hydrocodone, 6-acetylmorphine, phencyclidine, amphetamine, methamphetamine, buprenorphine, methadone, benzodiazepines and tramadol.

E. Applicant:

Immunalysis Corporation

F. Proprietary and Established Names:

Quantisal II Oral Fluid Collection Device

G. Regulatory Information:

Regulation	Classification	Product Code	Panel
21 CFR 862.1675, Blood specimen collection device	Class II	PJD, Oral Fluid Drugs of Abuse and Alcohol Test Specimen Collection Device	Clinical Chemistry (75)

H. Intended Use:

1. Intended use:
   See Indications for use.

2. Indications for use:
   The Quantisal II Oral Fluid Collection Device is intended for the collection, preservation and transport of oral fluid specimens for tetrahydrocannabinol (THC), benzoylecgonine, cocaine, morphine, codeine, oxycodone, hydrocodone, 6-acetylmorphine, phencyclidine, amphetamine, methamphetamine, buprenorphine, methadone, benzodiazepines and tramadol. This device is for prescription use only.

3. Special conditions for use statements:
   For prescription use only.

4. Special instrument requirements:
   Not applicable.

I. Device Description:

The Quantisal II Oral Fluid Collection Device is intended for the collection, preservation and transport of oral fluid. An oral fluid specimen is collected by placing two cellulose pads affixed to a polypropylene stem collector under the tongue of an individual until a defined volume of saliva has saturated the cellulose pads. When sufficient volume is collected a blue color is shown in a window on the stem. The collector is then separated into two pads A and B, then transferred into two separate polypropylene tubes, both containing a volume of preservative buffer. The tubes are stoppered with caps. The design with two pads and two tubes allows for one aliquot to be used for screening and confirmation testing, and the other aliquot to be stored in reserve in cases where re-testing by the confirmation method is required. The Quantisal II Oral Fluid Collection System collects 1 mL of neat oral fluid and is diluted with 3 mL of preservative buffer.

J. Substantial Equivalence Information:

1. Predicate device name:
   Saliva Sampler

2. Predicate 510(k) number:
   k942435

3. Comparison with predicate:

Similarities and differences		
Item	Subject device, Quantisal II Oral Fluid Collection Device k183045	Predicate device, Saliva Sampler k942435
Intended use	Intended for the collection, preservation and transport of oral fluid specimens for drug testing.	Same
Collection type / Specimen collection site	Two absorbent pads for under tongue collection.	One absorbent pad for under tongue collection.
Collection volume	1 mL with built-in sample volume adequacy window.	Same
Collection tube	Tube for 1 to 4 dilution with preservation fluid.	Tube for 1 to 2 dilution with preservation fluid.

K. Standard/Guidance Document Referenced:

None referenced.

L. Test Principle:

Not applicable.

M. Performance Characteristics:

1. Analytical performance:

a. Precision/Reproducibility:

Not applicable.

b. Linearity/assay reportable range:

Not applicable.

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

Sample Volume
A sample volume study was conducted to verify the consistency of oral fluid volume collected by the Quantisal II Oral Fluid Collection Device. In the study, oral fluid samples were collected from a total of 125 subjects (including 75 drug users) following the instructions for use. Prior to collection, each stem (A and B) was

weighed. After the volume adequacy indicator turned blue on both A and B collector stems, each stem was weighed again. The volume was calculated from the weight change and using the specific gravity for saliva based on scientific literature references. The study found the mean ± standard deviation volume collected was 0.997 ± 0.05 mL (range 0.860 – 1.103) and 1.001 ± 0.05 (range 0.902 – 1.093) mL for collectors A and B, respectively.

Sample Collection Time

A sample collection time study was conducted to verify the collection time range for Quantisal II Oral Fluid Collection Device. The product labeling states that the collection time may take from 2 to 10 minutes, and if the indicator has not turned blue within 15 minutes, the pad should be removed from the mouth and discarded. In the study, oral fluid samples were collected from a total of 125 subjects (including 75 drug users) following the instructions for use. The timer started when the collector was placed into subject's mouth, and stopped when the volume adequacy indicator turned blue on both A and B collector stems. The sponsor reported that 99.2% (124 of 125) subjects were able to provide sufficient oral fluid within the recommended 10 minute collection. The mean time required for collection was 3 minutes and 54 seconds. The maximum time required for collection was reported as 11 minutes.

Drug Recovery

A drug recovery study was conducted to verify adequate analytical recovery of 15 drugs from oral fluid collected by the Quantisal II Oral Fluid Collection Device. The samples under test for each drug (THC, benzoylecgonine, cocaine, morphine, codeine, oxycodone, hydrocodone, 6-acetylmorphine, phencyclidine, amphetamine, methamphetamine, buprenorphine, methadone, nordiazepam, and tramadol) were prepared by spiking the drug into negative oral fluid at ±25% and +50% from the concentrations listed in the table below. The sample concentrations were assayed by LC/MS/MS or GC/MS prior to introduction into the collector. For each sample, three Quantisal II Oral Fluid Collection Devices were sequentially dipped and removed after the volume adequacy indicator turned blue. The collectors (pad A and B) were then placed into the collection tubes, sealed with the cap, and stored overnight at room temperature. The next day the liquids in the tubes were assayed by LC/MS/MS or GC/MS in replicates of three per pad for each collection device for a total of 18 replicates at each concentration.

Analyte	**Concentration (ng/mL)**
THC	4
Benzoylecgonine	15
Cocaine	15
Morphine	30
Codeine	30
Oxycodone	30
Hydrocodone	30
6-acetylmorphine	4

Analyte	Concentration (ng/mL)
Phencyclidine	10
Amphetamine	50
Methamphetamine	50
Buprenorphine	3
Methadone	20
Nordiazepam	5
Tramadol	50

The recovery results are summarized in the following table:

Analyte	Mean	Min.	Max.
THC	87%	80%	96%
Benzoylecgonine	98%	89%	108%
Cocaine	98%	92%	108%
Morphine	95%	86%	109%
Codeine	97%	84%	107%
Oxycodone	97%	86%	105%
Hydrocodone	98%	90%	108%
6-acetylmorphine	98%	88%	103%
Phencyclidine	95%	86%	106%
Amphetamine	99%	93%	104%
Methamphetamine	100%	94%	107%
Buprenorphine	96%	80%	107%
Methadone	95%	82%	105%
Nordiazepam	98%	88%	104%
Tramadol	98%	83%	107%

Oral Fluid Sample Stability

Sample stability studies were conducted to verify the stability of 15 drugs in human oral fluid under the claimed storage stability conditions in the product labeling when diluted with preservative buffer and stored in the Quantisal II Oral Fluid Collection Device polypropylene tube. The product labeling identifies that certain drugs in oral fluid specimens collected with pad A of the Quantisal II Oral Fluid Collector are stable for 10 days if stored refrigerated (2-8°C; 36-46°F) and stable for 5 or 10 days (depending on the drug type) if stored at room temperature (8-25°C; 46-77°F). For pad B specimens, certain drugs in oral fluid are stable for 1 month if stored refrigerated. The product labeling also identifies that samples should be stored diluted for a minimum of 4 hours at room temperature prior to testing to allow sufficient time for any drug(s) present to be extracted from the pad into the preservation buffer. The transportation claims were also supported by the specimen stability studies.

Pad A refrigerated storage

To verify the claimed refrigerated storage conditions, a study was conducted by

testing samples stored for 5 and 10 days using three collection devices at each condition and time point. Samples were drug-free oral fluid spiked with the drug (THC, benzoylecgonine, cocaine, morphine, codeine, oxycodone, hydrocodone, 6-acetylmorphine, phencyclidine, amphetamine, methamphetamine, buprenorphine, methadone, nordiazepam, or tramadol) at +50% above the concentrations listed in table under Drug Recovery. The samples were each applied into the collection device per the required volume and then diluted with buffer. At each time point, an aliquot was taken from the storage tube and assayed in replicates of 3 by LC/MS/MS or GC/MS. The analyte recovery results after storage for 10 days support the claimed refrigerated storage conditions and are given in the following table.

Analyte	**Mean**	**Min.**	**Max.**
THC	100%	98%	103%
Benzoylecgonine	110%	104%	109%
Cocaine	95%	90%	95%
Morphine	98%	95%	102%
Codeine	98%	93%	100%
Oxycodone	98%	96%	100%
Hydrocodone	100%	98%	102%
6-acetylmorphine	100%	97%	102%
Phencyclidine	107%	100%	107%
Amphetamine	99%	96%	100%
Methamphetamine	97%	93%	100%
Buprenorphine	102%	98%	107%
Methadone	97%	97%	100%
Nordiazepam	100%	97%	103%
Tramadol	103%	100%	104%

Pad A room temperature storage

To verify the claimed room temperature storage conditions, a study was conducted by testing samples stored for 5 and 10 days at room temperature using three collection devices at each condition and time point. Samples were drug-free oral fluid spiked with the drug (THC, benzoylecgonine, cocaine, morphine, codeine, oxycodone, hydrocodone, 6-acetylmorphine, phencyclidine, amphetamine, methamphetamine, buprenorphine, methadone, nordiazepam, or tramadol) at a +50% above the concentrations listed in table under Drug Recovery. The samples were each applied into the collection device per the required volume and then diluted with buffer. At each time point an aliquot was taken from the storage tube and assayed in replicates of 3 by LC/MS/MS or GC/MS. The analyte recovery results after storage at room temperature for 5 days (for cocaine) and 10 days (for the other 14 drugs) support the claimed room temperature storage conditions and are given in the following table.

Analyte	**Mean**	**Min.**	**Max.**
THC	98%	98%	100%
Benzoylecgonine	105%	100%	109%
Cocaine *	95%	95%	100%

Analyte	Mean	Min.	Max.
Morphine	100%	95%	102%
Codeine	98%	93%	100%
Oxycodone	96%	93%	100%
Hydrocodone	100%	96%	102%
6-acetylmorphine	100%	97%	103%
Phencyclidine	100%	100%	107%
Amphetamine	97%	95%	100%
Methamphetamine	99%	93%	101%
Buprenorphine	102%	98%	107%
Methadone	97%	97%	100%
Nordiazepam	100%	99%	103%
Tramadol	101%	97%	105%

* 5 days at room temperature for cocaine. The sponsor identified that cocaine is unstable in samples stored greater than 5 days at room temperature and converts to benzoylecgonine. Benzoylecgonine is the metabolite of cocaine and is found only in samples from subjects who have taken cocaine.

Pad B refrigerated storage

To verify the claimed long term refrigerated storage conditions for pad B, a study was conducted by testing samples stored for 1 month using three collection devices at each condition and time point. Samples were drug-free oral fluid spiked with the drug (THC, benzoylecgonine, cocaine, morphine, codeine, oxycodone, hydrocodone, 6-acetylmorphine, phencyclidine, amphetamine, methamphetamine, buprenorphine, methadone, nordiazepam, or tramadol) at +50% above the concentrations listed under Drug Recovery. The samples were each applied into the collection device per the required volume and then diluted with buffer. At each time point an aliquot was taken from the storage tube and assayed in replicates of 3 by LC/MS/MS or GC/MS. The analyte recovery results support the claimed one month storage stability at refrigerated conditions for specimen B and are given in the following table.

Analyte	Mean	Min.	Max.
THC	92%	91%	93%
Benzoylecgonine	101%	100%	102%
Cocaine	97%	96%	98%
Morphine	97%	93%	101%
Codeine	110%	109%	110%
Oxycodone	97%	96%	97%
Hydrocodone	103%	99%	107%
6-acetylmorphine	107%	102%	111%
PCP	98%	97%	98%
Amphetamine	95%	92%	96%
Methamphetamine	102%	101%	103%
Buprenorphine	99%	98%	100%
Methadone	96%	94%	97%

Analyte	Mean	Min.	Max.
Benzodiazepines	94%	92%	95%
Tramadol	101%	99%	105%

Clinical Specimens Testing

Quantisal II Oral Fluid Collection Device versus expectoration
A study was conducted to verify that drug concentrations in oral fluid samples collected by Quantisal II Oral Fluid Collection Device are analytically comparable to the neat oral fluid samples collected by expectoration. The samples used in the study were collected from self-reported drug user patients at a clinical research facility. For each patient, a single neat oral fluid sample was collected by expectoration into a borosilicate glass vial. An aliquot of each sample was subsequently processed through the Quantisal II Oral Fluid Collection Device by dipping the collection pad into the oral fluid until the volume adequacy indicator turned blue. The expectoration samples and Quantisal II samples were assayed by LC-MS/MS or GC-MS. The assay results from expectoration samples and for Quantisal II (pad A) were compared by linear regression. The results are given in the following table.

Analyte	Slope	Intercept	R^2	N
THC	0.939	0.9	0.992	60
Benzoylecgonine	0.901	1.5	0.988	60
Cocaine	0.908	2.1	0.990	60
Morphine	0.914	3.1	0.992	60
Codeine	0.919	0.6	0.992	60
Oxycodone	0.978	0.4	0.993	60
Hydrocodone	0.918	2.0	0.992	60
6-acetylmorphine	0.900	5.6	0.992	60
Phencyclidine	1.005	0.6	0.998	60
Amphetamine	0.958	2.1	0.992	60
Methamphetamine	0.930	3.9	0.982	60
Buprenorphine	0.910	2.9	0.999	60
Methadone	0.962	0.4	0.994	60
Nordiazepam	0.971	0.2	0.986	60
Tramadol	0.985	4.7	0.991	60

The sponsor also provided a study demonstrating that the borosilicate glass vials used to collect expectoration samples were analytically fit for purpose because of high analyte recovery properties of the vial material. In the study, samples were prepared in the subject vial by spiking drug free expectorated oral fluid with the drug analytes (THC, benzoylecgonine, cocaine, morphine, codeine, oxycodone, hydrocodone, 6-acetylmorphine, phencyclidine, amphetamine, methamphetamine, buprenorphine, methadone, nordiazepam, or tramadol) at +50% above the concentrations listed in table under Drug Recovery. The initial concentration of each sample was assayed by LC-MS/MS or GC-MS. For each sample, three aliquots were subsequently taken from the vial and dispensed into three vials. The vialed samples were stored at 25°C

for 48 hours and then tested in replicates of three for each vial using the same analytical method. The recovery for all test samples in the subject vial was within 100 ±10%.

Pad A versus pad B

A second study was conducted to demonstrate that both collection pads on the Quantisal II Oral Fluid Collection Device are equivalent when used under real world conditions. In the study, samples were collected from self-reported drug user patients at a clinical research facility using the Quantisal II Oral Fluid Collection Device. At least 40 unaltered drug negative oral fluid samples and 40 unaltered oral fluid samples containing analyte from each drug class were collected. The samples were assayed by LC-MS/MS or GC-MS. The assay results from samples for pad A and pad B were compared by linear regression. The results are given in the following table.

Analyte	**Slope**	**Intercept**	**R^2**
THC	1.047	-3.4	0.995
Benzoylecgonine	0.990	0.2	0.999
Cocaine	0.976	3.2	0.994
Morphine	1.039	5.2	0.998
Codeine	1.008	0.5	0.999
Oxycodone	0.989	0.8	0.999
Hydrocodone	1.018	0.3	0.999
6-acetylmorphine	1.015	4.5	0.997
Phencyclidine	1.033	-6.2	0.996
Amphetamine	0.989	7.6	0.999
Methamphetamine	0.982	48.1	0.997
Buprenorphine	1.006	11.2	0.998
Methadone	1.024	-8.9	0.997
Nordiazepam	1.024	-0.2	0.997
Tramadol	0.947	51.1	0.997

In the study, the patient samples included 40 drug negative oral fluid samples that were collected using the Quantisal II Oral Fluid Collection Device and also collected by expectoration into a borosilicate glass vial. A comparison of the expectoration samples and Quantisal II samples was conducted by assaying for drugs using LC-MS/MS or GC-MS. To remove bias, the sequence of collection between expectoration and the Quantisal II Oral Fluid Collection Device was randomized. The assay results across all drugs were negative for both the expectoration samples and samples collected by the Quantisal II Oral Fluid Collection Device.

Biocompatibility

The Quantisal II Oral Fluid Collection Device has short term contact (up to 15 minutes) with the patient's mouth during oral fluid collection. The materials comprising the Quantisal II Oral Fluid Collection Device are the same as those of the Quantisal I Oral Fluid Collection Device (cleared under k942435 with tradename Saliva Sampler), and therefore no new biocompatibility testing was performed.

d. Detection limit:

Not applicable.

e. Analytical specificity:

Not applicable.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Not applicable.

b. Matrix comparison:

Not applicable.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable.

c. Other clinical supportive data:

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 Parts 801 and 809, as applicable.

O. Conclusion:

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