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

A. 510(k) Number:

k080381

B. Purpose for Submission:

New Device

C. Measurand:

Methamphetamine

D. Type of Test:

Qualitative Enzyme Immunoassay

E. Applicant:

Quest Diagnostics

F. Proprietary and Established Names:

Quest Diagnostics Methamphetamine Micro-Plate EIA

Quest Diagnostics Methamphetamine Micro-Plate EIA Calibrators

Quest Diagnostics Methamphetamine Micro-Plate EIA Controls

G. Regulatory Information:

1. Regulation section:

   21 CFR 862.3610 Methamphetamine Micro-Plate EIA
   21 CFR § 862.3200, Clinical toxicology calibrator
   21 CFR § 862.3280, Clinical toxicology control material

2. Classification:

   Class II (assay and calibrators)
   Class I, reserved (control)

3. Product code:

   LAF
   DLJ
   LAS

4. Panel:

   91 Toxicology

H. Intended Use:

1. Intended use(s):

   See indications for use section below.

2. Indication(s) for use:
   The Quest Diagnostics Methamphetamine Micro-Plate EIA is intended for the qualitative detection of Methamphetamine in oral fluid collected with the Orasure™ Oral Specimen Collection Device. It is a screen test with a cutoff of 40 ng/ml.

   The Quest Diagnostics Methamphetamine Micro-Plate EIA provides only a preliminary result. Clinical consideration and professional judgment must be applied to any drug of abuse test result, particularly in evaluating a preliminary positive result. To obtain confirmed analytical results a more specific alternate chemical method is needed. Gas chromatography/mass spectroscopy (GC/MS) is the recommended confirmatory method.

   The Quest Diagnostics Methamphetamine Micro-Plate EIA Calibrators are intended for medical purposes and for use only with the Quest Diagnostics Methamphetamine Micro-Plate EIA to establish points of reference that are used in the determination of values in the measurement of methamphetamine in oral fluid samples collected with OraSure™ Oral Specimen Collection Device.

   The Quest Diagnostics Methamphetamine Micro-Plate EIA Controls are intended for use as an assay quality control matrix to monitor the precision and accuracy of the laboratory testing procedures for methamphetamine in oral fluid samples collected with OraSure™ Oral Specimen Collection Device.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   A plate reader is required. All performance for this device was conducted on the Titertek Multiskan MCC/340 plate reader.

I. Device Description:

The Quest Diagnostics Methamphetamine Micro-Plate EIA kit contains EIA plates, conjugates, conjugate diluents, substrate, stop solution, wash solution, calibrators and controls. The EIA plates contain antiserum to methamphetamine immobilized on a polystyrene plate. The conjugate is composed of horseradish peroxides labeled with methamphetamine in buffer with protein stabilizers. The conjugate diluent is tris buffer containing BSA. The dual level calibrators' concentrations are 0 ng/mL and 40 ng/ml. The tri-level controls concentrations are 10 ng/mL, 20 ng/mL and 80 ng/ml MAP. Both calibrators and controls are included with the device. The OraSure collection device is not included with the device but can be purchased from Quest or OraSure.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   OraSure Methamphetamine Intercept Microplate EIA

2. Predicate K number(s):

   k993208

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Indications for use	Qualitative detection of methamphetamine in human saliva specimens collected with the OraSure oral fluid collection device	Same
Methodology	Microplate EIA	Same
Cutoff	40 ng/ml	Same

Differences		
Item	Device	Predicate
Controls/calibrators	5 levels in the same base as calibrator. Calibrator values: 0 and 40 ng/ml. Controls: 10, 20 and 80 ng/ml.	4 levels in the same base as calibrators (0,20, 40, and 80 ng/ml)

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

None referenced.

L. Test Principle:

The Quest Diagnostics Methamphetamine Micro-Plate EIA is a competitive immunoassay for the qualitative determination of Methamphetamine in oral fluid specimens. Methamphetamine in oral fluid and the methamphetamine in the enzyme conjugate compete for the limited binding sites of antibody fixed to a microtiter plate. If little or no methamphetamine is present in the specimen, more enzyme labeled methamphetamine will be bound by methamphetamine antibody. If a large or significant amount of methamphetamine is present in the specimen, less enzyme labeled methamphetamine will be bound to the plate, reducing overall activity and signal level. The absorbance produced is inversely proportional to the amount of methamphetamine in the specimen, calibrator or control.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision studies were performed on 5 negative patient samples by spiking with 0, 10, 20, 30, 40, 50, 60 and 70 ng/ml of methamphetamine; drug concentrations were confirmed by GC/MS. These concentrations correspond to 0, 25, 50, 75, 100, 125, 150 and 175% of the cutoff. Testing was performed in replicates of 4 for 10 days for 8 concentrations. The results are shown in the table below.

Quest Diagnostics Methamphetamine Micro-Plate EIA Intra-Assay %CV Results

Sample	**SP 1**	**SP 2**	**SP 3**	**SP 4**	**SP 5**	**SP 6**	**SP 7**	**SP 8**
MAP (ng/ml)	**0**	**10**	**20**	**30**	**40**	**50**	**60**	**70**
Mean OD	2.498	0.946	0.694	0.576	0.490	0.442	0.399	0.375
Positive	0	0	0	15	40	40	40	40
Negative	40	40	40	25	0	0	0	0
Total	40	40	40	40	40	40	40	40
Agreement	100%	100%	100%	65.5%	NA	100%	100%	100%

b. *Linearity/assay reportable range:*

Not applicable. This assay is intended for qualitative use.

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

All calibrator and control stock solutions are prepared from commercially available solutions. The methamphetamine concentrations of the stock solution were determined by GC/MS. From the stock solution, a secondary stock solution was prepared gravimetrically. The positive control was prepared from the secondary stock. The cutoff calibrator, negative control and low negative control were prepared by serial dilutions of the positive controls. All of the components were confirmed by GC/MS.

Claimed shelf-life of the Quest Diagnostics Methamphetamine Micro-Plate EIA calibrator and controls is 110 days for when stored at 2-8 C. The Quest Diagnostics Methamphetamine Micro-Plate EIA reagents are stable at room temperature (21-25 C) for 30 days. Real-time studies are ongoing.

The stability of methamphetamine in the OraSure collection device was determined by taking a pool of negative oral fluid samples spiked at ten different concentrations. The samples were run at day one with the EIA device and leftover samples were stored at room temperature (21-25 ˚C) for 28 days. Those stored samples were tested again with the EIA device for direct comparison with day one results. The result support the sponsor's claim that saliva specimens collected with the OraSure collection devices remain stable for at least 28 days when stored at 21 -25 ˚C.

Shipment stability was assessed by spiking eight negative neat saliva samples (in pairs) with various concentrations of methamphetamine. One set was shipped within the US and returned. The shipped collection devices testing results were compared to that of the non-shipped collection device. The results showed that shipping did not after the performance of the Quest Diagnostics Methamphetamine Micro-Plate EIA device and that the results were identical for both the shipped and non-shipped devices.

d. *Detection limit:*

See the precision/reproducibility section above for performance around the stated cutoff concentration.

e. *Analytical specificity:*

Cross reactivity of structurally similar compounds was determined by spiking concentrations of different drugs into negative oral fluid. Fourteen members of the amphetamine family, and structurally similar compounds, (see table

below) were tested for cross reactivity to the Quest Diagnostics Methamphetamine Micro-Plate EIA using d-Methamphetamine as the 100% reference. A negative pool was spiked with 4,000 ng/ml of each compound; three substances (MDMA, PMA and PMMA) tested positive at that level were tested with further dilutions until a negative result was produced. The Quest Diagnostics EIA produced the following cross-reactivity results methamphetamine.

Quest Diagnostics Methamphetamine Micro-Plate EIA Cross reactivity data

Compound	Test Conc. (ng/ml)	Cross Reactivity
Phentermine	4000	<1.0%
Phenylpropanolamine	4000	<1.0%
Ephedrine	4000	<1.0%
Pseudoephedrine	4000	<1.0%
S-Amphetamine	4000	< 1.0%
MDMA	35	117.3%
MDA	4000	< 1.0%
R-Methamphetamine	4000	<1.0%
R-Amphetamine	4000	<1.0%
Ranitidine	4000	<1.0%
Mephentermine	4000	<1.0%
Fenfluramine	4000	<1.0%
PMA	2500	1.7 %
PMMA	20	217.5%

MDMA- PMA dose response curve was used to determine its MAP equivalent concentration. Based on this data (shown below), the cross-reactivity of MDMA with the Quest Diagnostics EIA was determined to be 117.3%.

MDMA ODs

Tested Conc. ng/ml	P/N Result
0	N
15	N
20	N
25	N
30	N
35	P
40	P

PMMA-the MAP dose response curve was used to determine MAP equivalent concentration for the PMMA. Based on this data (shown below), the cross-reactivity of PMMA with the Quest Diagnostics EIA is 217.5%

PMMA ODs

Tested Conc. ng/ml	P/N Result
0	N
15	N
20	P
25	P
40	P

PMA- the MAP dose response curve was used to determine MAP equivalent concentration for the PMA. Based on this data, the cross-reactivity of PMA with the Quest Diagnostics EIA is 1.7%

PMA ODs

Tested Conc. ng/ml	P/N Result
0	N
1500	N
2000	N
2500	P
3000	P
3500	P
4000	P

Interference of various potentially cross-reacting or interfering commonly used substances was evaluated with the Quest Diagnostics Methamphetamine Micro-Plate EIA device. A positive (60 ng/ml) and a negative base (20 ng/ml) was created by spiking a negative pool collected with the OraSure device with methamphetamine. Ten ug/ml of each of the test compounds listed in the package insert were spiked into the negative and positive base pools and none of the 64 tested compounds exhibited any negative or positive interference with the assay.

Endogenous substances were tested for interference with the Quest Diagnostics Methamphetamine Micro-Plate EIA. Pools of the OraSure saliva specimens that tested negative to the device were divided and one was spiked with 80 ng/ml of methamphetamine. Human Serum Albumin (HSA), bilirubin, ascorbic acid and hemoglobin was tested at varying concentrations and run in duplicate with the Quest Diagnostics Methamphetamine Micro-Plate EIA. The results did not show any negative or positive interference with the assay for bilirubin up to 50 mg/ml, ascorbic acid up to 10,000 mg/;L, hemoglobin up to 1000 mg/L and HAS up to 5000, mg/L.

Commonly encountered consumable substances (along with blood and distilled water) was evaluated with the Quest Diagnostics Methamphetamine Micro-Plate EIA device. The sponsor reported no interference (positive or negative) from the substances shown below with the device.

Consumable Substance Interference

Substance	**Test Conc.**	**Pos./Neg.**	
		Neg. Pool with 0 ng/ml MAP	Neg. Pool with 80 ng/ml MAP
Sucrose	3.3% w/v	N	P
Cranberry Juice	33% v/v	N	P
Baking Soda	3.3% w/v	N	P
Orange Juice	33% v/v	N	P
Cola	33% v/v	N	P
Cough Syrup	33% v/v	N	P
Antiseptic Mouth Wash	33% v/v	N	P
Toothpaste	5% w/v	N	P
Dental Adhesive A	4 mg/ml	N	P
Dental Adhesive B	4 mg/ml	N	P

Matrix	DI Water 0 ng/ml	DI Water 80 ng/ml
100% Sample (Unaltered Sample Pool) - control	N	P
50% Sample 50% Water (v/v)	N	P
25% Sample 75% Water (v/v)	N	P
10% Sample 90% Water (v/v)	N	P

Matrix	Blood from 4 different patients 0 ng/ml	Blood from 4 different patients 80 ng/ml
1% Blood #1 99% Unaltered Sample Pool (v/v)	N	P
1% Blood #2 99% Unaltered Sample Pool (v/v)	N	P
1% Blood #3 99% Unaltered Sample Pool (v/v)	N	P
1% Blood #4 99% Unaltered Sample Pool (v/v)	N	P

f. Assay cut-off:

The sponsor conducted a cutoff study in which the cutoff calibrator was tested in triplicate by GC/MS to verify their chosen cutoff of 40 ng/ml. Five aliquots of pooled negative patient specimens were spiked with 0, 20, 30, 50 and 60 ng/ml methamphetamine. The concentrations were confirmed by GC/MS and were run in replicates of 20 with the Quest Diagnostics Methamphetamine Micro-Plate EIA. The results shown below support the sponsor chosen cutoff of 40 ng/mL.

Cutoff Challenge Results

Concentration (ng/ml)	**Number**	**Results**	**% Agreement**
0	24	24 Negative	100
20	24	24 Negative	100
30	24	7 Negative	29
50	24	24 Positive	100
60	24	24 Positive	100

2. Comparison studies:

a. Method comparison with predicate device:

One-hundred patient samples were collected in accordance with the OraSure collection device test insert by trained professionals from Quest diagnostics. Specimens were stored at 2-8 ˚C prior to testing. Specimen results from the Quest Diagnostics Methamphetamine Micro-Plate EIA device was compared to GC/MS reference method (with 40 ng/ml as the cutoff).

Quest EIA v. GC/MS

A total of 100 samples were tested	**Methamphetamine Conc. by GC/MS (ng/mL)**					
	Range	**0 to -50% C/O**	**-50% C/O to C/O**	**C/O to +50%C/O**	**> 50% C/O**	**Overall Agreement**
	Conc. (ng/ml)	**<20**	**20-39**	**40.0-60**	**>60**	
Quest EIA (Screen)	**Positive**	4[1]	6[2]	11	34	81.8%
	Negative	41	3	1[3]	0	97.8%
Agreement:		91.1%	33.3%	91.7%	100%	89.0%

[1]All four specimens were tested by GC/MS and contain MDMA, a compound know to produce positive results with the Quest EIA at 35 ng/ml (cross-reactivity of 117.3%). Three (3) specimens contained more than 35 ng/ml MDMA (38, 100, 480 ng/ml respectively). One specimen contained 31 ng/ml MDMA and 16 ng/ml Methamphetamine. The combined reactivities produced a positive result with the Quest EIA, as would be expected given the cross-reactivity rate for MDMA.

[2]Among these six false positive specimens by EIA, all had Methamphetamine concentrations in the range of -50% to Cutoff (31, 31, 25, 23, 33, 35 ng/ml respectively). Two specimens also had significant amounts MDMA (32 & 135 ng/ml respectively).

[3]This sample contained 45 ng/ml of MAP.

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):

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.