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

A. 510(k) Number:

k062929

B. Purpose for Submission:

New Device

C. Measurand:

Cocaine

D. Type of Test:

Qualitative

E. Applicant:

Quest Diagnostics Incorporated

F. Proprietary and Established Names:

Quest Diagnostics Urine Cocaine Metabolite EIA

G. Regulatory Information:

1. Regulation section:

   21 CFR 862.3250

2. Classification:

   II

3. Product code:

   DIO

4. Panel:

   91 (Toxicology)

H. Intended Use:

1. Intended use(s):

   See indications for use statement below.

2. Indication(s) for use:
   The Quest Diagnostics Urine Cocaine Metabolite EIA is intended for the qualitative detection of benzoylecgonine, the primary metabolite of cocaine, in human urine on automated clinical chemistry analyzers. It is a screen test with cutoffs of 300 ng/ml and 150 ng/ml of benzoylecgonine per ml of urine. This test is intended for laboratory use only. For in vitro diagnostic use.

   The Quest Diagnostics Urine Cocaine Metabolite 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 Urine Cocaine Metabolite EIA Calibrators are intended for medical purposes and for use only with the Quest Diagnostics Urine Cocaine Metabolite EIA to establish points of reference that are used in the determination of values in the measurement of benzoylecgonine in urine.
   The Quest Diagnostics Urine Cocaine Metabolite EIA Controls are intended for use as an assay quality control matrix to monitor the precision and accuracy of the laboratory testing procedures for benzoylecgonine.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   Olympus AU 5400 Analyzer

I. Device Description:

The Quest Diagnostics Urine Cocaine Metabolite EIA is a dual cutoff assay that consists of liquid reagents, buffer reagent, controls and calibrators. This assay contains sheep polyclonal antibodies in buffer. The tri-level controls and the four-level calibrators are included with the device.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Online DAT II Cocaine II

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

   k023281

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Qualitative detection of benzoylecgonine, the primary cocaine metabolite, in human urine specimens.	Qualitative and semi-quantitiative detection of benzoylecgonine, the primary cocaine metabolite, in human urine specimens.

Differences		
Item	Device	Predicate
Technology	Enzyme Immunoassay	Microparticle Immunoassay
Antibody	Polyclonal Sheep anti-Benzoylecgonine	Monoclonal anti-Benzoylecgonine
Controls	Tri-level included	Not included
Calibrators	4-level included	Non included

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

None referenced.

L. Test Principle:

The Quest Diagnostics Urine Cocaine Metabolite EIA is a competitive immunoassay for the qualitative determination of cocaine and cocaine metabolites in urine. Cocaine metabolites in urine and the cocaine metabolite Benzoylecgonine (BE) in the enzyme conjugate compete for the finite binding sites of antibody in solution. If little or no cocaine metabolite is present in the specimen, more enzyme labeled BE will be bound and inhibited by α-BE antibody. If a large or significant amount of cocaine metabolite is present in the specimen, less enzyme labeled BE will be bound and inhibited, allowing greater activity and a higher signal level. The absorbance produced is directly proportional to the amount of cocaine metabolite in the specimen, calibrator, or control.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*

      Precision was assessed for cocaine cutoffs (150 and 300 ng/mL) by conducting intra and inter-assay precision at the 0, -50% cutoff, the cutoff and +50 % or +60% the cutoff.

150 ng/ml cutoff summary of positive /negative results

Conc. (ng/ml)	Number	Results
0	200	200 Negative
75	200	200 Negative
150	200	133 Positive/67 Negative
300	200	200 Positive

300 ng/ml cutoff summary of positive /negative results

Conc. (ng/ml)	Number	Results
0	200	200 Negative
150	200	200 Negative
300	200	171 Positive/29 Negative
500	200	200 Positive

   b. *Linearity/assay reportable range:*

      The sponsor conducted a qualitative recovery study using spiked benzoylecgonine values that were confirmed by GC/MS as a reference. Ten negative urine samples were spiked and run in duplicate. For the 150 ng/ml cutoff, spiked specimens with values of 0, 75, 112, 188 and 225 ng/ml were run in duplicate (n=100, 20 per level) For the 300 ng/ml cutoff, spiked specimens with values of 0,150, 225,375 and 450 ng/ml were run in duplicate (n=100, 20 per level). The results for the 150 ng/ml showed that at concentrations of 0, 75 and 112, all 60 specimens were negative and for concentrations of 188 and 225 all 40 specimens were positive. The results for the 300 ng/ml showed that at concentrations of 0, 150 and 225, all 50 specimens were negative and for concentrations of 375 and 450 all 40 specimens were positive.

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

      This device has two levels of controls for each cocaine cutoff. The L1 control must be negative and the L2 control must be positive. The sponsor has placed in the insert the following "If control values do not fall within the established limits above, assay results are invalid". The supplied controls and calibrators are prepared gravimetrically and are available from a commercially available provider.

The sponsor conducted a stability study by comparing the performance of reagent lots stores at 2-8 C for 3 months with that of freshly prepared reagents. The result supported the sponsors three month stability claim.

d. *Detection limit:*
This is a qualitative device. See "Precision" section above and "Assay Cut-off" section below for a summary of device performance around the cutoff.

e. *Analytical specificity:*
Commonly used substances
Eighty-one commonly used compounds were tested for interference with 2 pools of specimens per cutoff level: one with -50% (75 or 150 ng/ml) of the cutoff, which was the highest concentration to consistently render negative results and the other with +50% (300 or 600 ng/ml) of the cutoff, which was the lowest concentration to consistently render positive results. All 81 tested compounds exhibited no positive or negative interferences with the device.

Endogenous substances
Endogenous substances were also tested for interference on the Quest Diagnostics Urine Cocaine Metabolite EIA. Bilirubin concentrations of up to 50 mg/L, Ascorbic Acid concentrations of up to 10,000 mg/L, Hemoglobin concentrations of up to 1000 mg/L and Creatine concentrations of up to 5000 mg/L were found not to interfere with the device.

Cross-reactivity
A study with cocaine metabolites were tested for cross-reactivity with the Quest Diagnostics Urine Cocaine Metabolite EIA with BE as the 100% reference. The results are presented in the table below.

Compound	Spiked Conc. (ng/ml)	BE Equivalent (ng/ml)	% Cross Reactivity
Cocaethylene	600	187	31.2
Ecgonine methyl ester hydrochloride	19,800	108	0.5
Cocaine	1200	192	16
Ecgonine hydrochloride	9,600	151	1.6
Hydroxybenzoylecgonine	150	118	78.7
Benzoylecgonine	150	150	100

pH
Drug free urine samples were adjusted to pH values from 2 to 12. The samples were spiked with benzoylecgonine to give final concentrations of 75 ng/ml, 150 ng/ml, 300 ng/ml and 450 ng/ml. The spiked, pH-adjusted urine was tested with the Quest Diagnostics Urine Cocaine Metabolite EIA test. The results demonstrate that varying ranges of pH did not interfere with the performance of the test.

f. Assay cut-off:

Studies demonstrating assay performance around the cutoff (150 ng/ml and 300 ng/ml of benzoylecgonine) are described in the precision section above. An additional study to challenge the sponsor's chosen cutoff was also conducted.

Cutoff challenge samples were prepared by spiking commercially available BE stock into a negative urine pool. Five levels were tested for each cutoff method. Each level was tested 20 times. Four lots of cutoff calibrators were tested in duplicate by GC/MS to confirm analyte concentration. The results are presented below:

150 ng/ml Cutoff

Concentration (ng/ml)	Number	Results
0	20	20 Negative
75	20	20 Negative
113	20	20 Negative
188	20	20 Positive
225	20	20 Positive

300 ng/ml Cutoff

Concentration (ng/ml)	Number	Results
0	20	20 Negative
150	20	20 Negative
225	20	20 Negative
375	20	20 Positive
450	20	20 Positive

2. Comparison studies:

a. Method comparison with predicate device:

The sponsor conducted a method comparison to both the Roche Diagnostic DAT II Cocaine II device and to GC/MS. The method comparison evaluation was conducted using 153 and 165 specimens for the 150 ng/ml and 300 ng/ml cutoff respectively. The results yielded the following tables:

Patient Specimen Percent Agreement: Quest EIA vs. GC/MS BE Result Cutoff 150 ng/ml

GC/MS BE (ng/ml)	Range	Negative < 75	Near Cutoff Negative 75-149	Near Cutoff Positive 150-225	High Positive > 225	Agreement with GC/MS
Quest EIA	Positive	0	2	15	59	97.4%
	Negative	57	16	4	0	94.8%

Patient Specimen Percent Agreement: Quest EIA vs. GC/MS BE Result Cutoff 300 ng/ml

GC/MS BE (ng/ml)	Range	Negative < 150	Near Cutoff Negative 150-299	Near Cutoff Positive 300-450	High Positive > 450	Agreement with GC/MS
Quest EIA	Positive	0	12	19	49	85.0%
	Negative	58	22	2	0	97.6%

Patient Specimen Screen Agreement Results: Quest EIA (New Device) vs. Roche (Predicate)

		Roche Method (Predicate)					
		150 ng/ml Cutoff			300 ng/ml Cutoff		
		Negative	Positive	Agreement with Roche	Negative	Positive	Agreement with Roche
Quest EIA	Positive	5	71	93.4%	9	71	88.8%
	Negative	74	3	96.1%	81	1	98.8%

b. Matrix comparison:

Not applicable. This assay is intended for use with urine 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.