

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

A. 510(k) Number:

K033713

B. Analyte:

benzoylecgonine

C. Type of Test:

Qualitative and/or semi-quantitative immunoassay

D. Applicant:

Dade Behring Inc.

E. Proprietary and Established Names:

Dimension Urine Cocaine Metabolite Screen (COC) Flex

F. Regulatory Information:

1. Regulation section:
21 CFR §862.3250, Cocaine and Cocaine Metabolite Test System
2. Classification:
Class II
3. Product Code:
DIO
4. Panel:
Toxicology (91)

G. Intended Use:

1. Intended use(s):
The COC Flex reagent cartridge is used on the Dimension clinical chemistry system. It provides reagents for the qualitative and semi-quantitative determination of benzoylecgonine in human urine at a cutoff of 150 or 300 ng/mL.
Reviewer Note: Only data that supports the cutoff claim of 150 ng/mL is presented in this review since data that supports the 300 ng/mL claim has been presented in an earlier submission (K031512). Expansion of the indications for use at a 150 ng/mL cutoff is designed to comply with new criteria proposed by the Substance Abuse and Mental Health Services Administration (SAMSHA).
2. Indication(s) for use:
The COC Flex Assay is a homogeneous enzyme immunoassay for measurement of benzoylecgonine in human urine to aid in the diagnosis and treatment of cocaine use or overdose. The COC Flex Assay is intended for use

with automated analyzers, and has a cutoff concentration of 150 or 300 ng/mL. The device is for in vitro diagnostic use. It is intended for prescription use only.

3. Special condition for use statement(s):

The COC Flex Assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used to obtain a confirmed analytical result. Gas chromatography/Mass spectrometry is the preferred confirmatory method. Other chemical confirmation methods are available. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

The Cocaine Metabolite Assay must only be used by suitably qualified laboratory personnel under appropriate laboratory conditions.

Semi-quantitative results may be helpful in estimating the concentrations of drug(s) in samples. This can aid users when they are preparing dilutions of the samples for further analysis. The assay is not designated for use in point-of-care settings. The assay was not evaluated in point-of-care settings.

4. Special instrument Requirements:

The device is for use on the Dimension Clinical Chemistry analyzer family.

H. Device Description:

The product is a single-use *in vitro* diagnostic device in a plastic eight-well cartridge format. It contains three wet reagents which contain the key components of the immunoassay; polyclonal antibody against the drug, substrate, and enzyme-labeled benzoylecgonine (conjugate).

I. Substantial Equivalence Information:

1. Predicate device name(s):

Syva's Emit II Plus Cocaine Metabolite Assay for the 30-R Biochemical System

2. Predicate K number(s):

K031512

3. Comparison with predicate:

Indications for use, sample type, operating principle, technology type, and reagent composition are similar to the predicate device. The predicate cutoff value was 300 ng/mL; this product requests a cutoff of 150 ng/mL.

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

NCCLS EP5-A

K. Test Principle:

The test is an enzyme immunoassay for use on Dimension® automated clinical chemistry analyzers. Enzyme-labeled benzoylecgonine and benzoylecgonine present

in the sample compete for limited benzoylecgonine-specific sheep antibody binding sites in the presence of substrates. The concentration of the drug in the sample determines the amount of conjugate that binds to the antibody. Unbound conjugate catalyzes the oxidation of G6PDH with the simultaneous reduction of NAD⁺ to NADH more rapidly than the bound conjugate. The rate of increase in sample absorbance at 340 nm is related to the concentration of the cocaine metabolite in the sample by a mathematical function.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

All performance characteristics were established on Dimension® RxL and Xpand clinical chemistry systems in a Dade-Behring laboratory unless otherwise noted. The sponsor claims this assay has been validated on the Xpand (as well as the XL, ARx, AR, and RxL Max) system.

a. Precision/Reproducibility:

Precision was determined by assaying Detectabuse™ GC/MS controls (Biochemical Diagnostics Inc.) and Syva Emit® Cutoff Controls in duplicate for 20 days, 2 runs per day. According to the sponsor, calculations were according to NCCLS EP5-A.

Precision of Candidate Device

Concentration (ng/ml)	Mean (ng/mL)	Within-run precision		Total precision	
		standard deviation	%CV	standard deviation	%CV
Detectabuse™ Control Level 1 (113 ng/mL)	109	5.2	4.8	8.8	8.1
Syva Emit® Cutoff Control (150 ng/mL)	153	6.6	4.3	10.0	6.5
Detectabuse™ Control Level 2 (188 ng/mL)	204	10.8	5.3	12.3	6.0

Reproducibility: Semi-quantitative Analysis

Reproducibility was determined by spiking negative human urine with known concentrations of benzoylecgonine throughout the range of 45 ng/ml to 900 ng/mL. The analyzer was calibrated in the semi-quantitative mode using a 150 ng/mL cutoff. The averaged recoveries of these replicate determinations ranged from 87-106%.

Semi-quantitation of positive results enables the laboratory to determine an appropriate dilution of the specimen for confirmation by GC/MS. The semi-quantitative mode also

permits the laboratory to establish quality control procedures and assess control performance.

Analytical Recovery of Semi-quantitative Results

Nominal Benzoylecgonine Concentration (ng/mL)	Mean Concentration with COC Flex (ng/mL)	Replicates	Coefficient of Variation	Recovery (%)
45	47	20	8.5	105
60	54	20	6.9	89
75	59	20	8.2	79
135	131	20	5.2	97
165	156	10	2.9	95
225	223	5	5.4	99
600	630	5	10.0	105
750	733	5	6.4	98
900	958	5	10.6	106

Analytical Recovery of Qualitative Analysis

Recovery was determined by spiking negative human urine with known concentrations of benzoylecgonine throughout the range 0 ng/mL to 3000 ng/mL. The analyzer was calibrated in the semi-quantitative mode using a 150 ng/mL cutoff.

Analytical Recovery of Qualitative Results

Nominal Benzoylecgonine Concentration (ng/mL)	Replicates	Qualitative Result Relative to the 150 ng/mL Cutoff (positive or negative)
0	20	20 negative
75	20	20 negative
112.5	20	20 negative
187.5	10	10 positive
225	5	5 positive
600	5	5 positive
750	5	5 positive
900	5	5 positive
3000	5	5 positive

b. Traceability (controls, calibrators, or method):

The calibrators used by the Dimension clinical chemistry system and referenced in the package insert are distributed as Syva® Emit™ Calibrator, Levels 0-5 and were cleared by the FDA in K993755 (12/21/1999). They are not supplied in the kit.

c. Detection limit:

The sponsor claims that the sensitivity of the assay is 35 ng/mL. This value was 2 standard deviations above 0 ng/mL using the Emit Level 0 Calibrator assayed 20 times.

d. Analytical specificity

A variety of over-the-counter and prescription drugs were tested for interference by spiking into negative urine (n=46). The drugs and levels in the samples tested are listed in the package insert. No unusual interference was observed from these tests at either the 150 ng/mL or the 300 ng/mL cutoff. Samples with a high initial background are flagged as problem samples by the software. High initial backgrounds could be due to interferants and drugs other than the drug measured

Cross-reactivity was established by spiking various concentrations of similarly structured drug compounds into a negative urine sample. By analyzing various concentration of each compound the sponsor determined the concentration of the drug that produced a response approximately equivalent to the cutoff concentration of the assay. Results of those studies appear in the table(s) below:

Cross Reactivity of Candidate Device

Compound	Response equivalent to 150 ng/mL cutoff (ng/mL)	Response equivalent to 300 ng/mL cutoff (ng/mL)
Cocaine	37	64
Ecgonine	5	28

Endogenous compounds (n=13) at a given concentration, listed in the package insert, added to urine at +/- 25% of either the 150 or 300 ng/mL cutoff did not yield a false response. The sponsor did not evaluate the effects of pH or specific gravity on the assay. There is the possibility that other substances and/or factors not listed above may interfere with the test and cause false results, e.g., technical or procedural errors.

e. Assay cut-off:

The sponsor-identified cutoff concentration(s) of the assay are 150 ng/mL or 300 ng/mL. The SAMHSA guidelines currently recommend a cutoff level of 300 ng/mL; the proposed expansion of use for this product complies with new proposed SAMSHA guidelines.

Characterization of how the device performs analytically around the claimed cutoff concentration appears in method comparison studies below. Of 125 tested samples, 22 were within +/- 25% (113 to 188 ng/mL) of the proposed 150 ng/mL cutoff.

2. Comparison studies:

a. Method comparison with predicate device:

At the manufacturer's site 125 urine samples (120 native samples and 5 diluted samples) were evaluated with the COC Flex® cartridge on a Dimension® clinical chemistry system and with the Emit II Plus polyclonal Cocaine Metabolite Assay on the Syva®-30R system. Sample concentrations ranged from 0 to greater than 1000 ng/mL and included 11 samples within +25% and 11 samples within -25% of the two cutoff concentrations. Of the samples tested, five (5) were dilutions of high concentration urine samples diluted into confirmed negative urine; these samples were prepared to evaluate the range between 700 and 900 ng/mL and above 1000 ng/mL. Sample selection criterion was not described by the sponsor.

**Candidate Device Results vs. Predicate Device Results:
Semi-Quantitative**

	Positive by Predicate Device	Negative by Predicate Device
Positive by COC Flex	69	2*
Negative by COC Flex	2*	52

* All discrepant were within +/- 25% of the cutoff by both methods

% Agreement among positives is 97%

% Agreement among negatives is 96%

**Candidate Device Results vs. Predicate Device Results:
Qualitative**

	Positive by Predicate Device	Negative by Predicate Device
Positive by COC Flex	71	2
Negative by COC Flex	0	52

% Agreement among positives is 100%

% Agreement among negatives is 96%

b. Method Comparison with Reference Method

The samples described above were also tested by GC/MS.

**Candidate Device Results vs. Reference Method:
Semi-Quantitative**

	Positive by GC/MS	Negative by GC/MS
Positive by COC Flex	66	5*
Negative by COC Flex	3*	51

* All discrepant were within +/- 25% of the cutoff by both methods

% Agreement among positives is 96%

% Agreement among negatives is 91%

**Candidate Device Results vs. Reference Method:
Qualitative**

	Positive by GC/MS	Negative by GC/MS
Positive by COC Flex	68	5
Negative by COC Flex	1	51

% Agreement among positives is 99%

% Agreement among negatives is 91%

c. Matrix comparison:

Not applicable. The assay is intended for urine samples only.

3. Clinical studies:

a. Clinical sensitivity:

Not applicable. Clinical studies are not typically submitted for this device type.

b. Clinical specificity:

Not applicable. Clinical studies are not typically submitted for this device type.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

Not applicable.

M. Conclusion:

I recommend that the COC Flex reagent cartridge be found substantially equivalent to the predicate device and recommend that the indications for use include a 150 ng/mL cutoff value.