DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

October 25, 2017

SIEMENS HEALTHCARE DIAGNOSTICS INC.
ALAN HALEY
REGULATORY CLINICAL AFFAIRS SPECIALIST
500 GBC Drive, M/S 514
NEWARK, DE. 19702

Re: k170293
Trade/Device Name: Emit II Plus Cocaine Metabolite Assay
Regulation Number: 21 CFR 862.3250
Regulation Name: Cocaine and cocaine metabolite test system
Regulatory Class: II
Product Code: DIO
Dated: October 16, 2017
Received: October 17, 2017

Dear Alan Haley:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
*See PRA Statement below.*

510(k) Number *(if known)*
K170293

Device Name
Emit® II Plus Cocaine Metabolite Assay

Indications for Use *(Describe)*
The Emit® II Plus Cocaine Metabolite Assay is a homogeneous enzyme immunoassay with a 150 ng/mL or 300 ng/mL cutoff. The assay is intended for use in the qualitative and semiquantitative analyses of benzoylecgonine (cocaine metabolite) in human urine. Emit® II Plus assays are designed for use with a number of chemistry analyzers.

The Emit® II Plus Cocaine Metabolite 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 (GC/MS) 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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

**CONTINUE ON A SEPARATE PAGE IF NEEDED.**

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# 510(k) Summary

This 510(k) Summary of Safety and Effectiveness is being submitted in accordance with the requirements of Safe Medical Device Act of 1990 and 21 CFR 807.92.

The assigned 510(k) number is **K170293**

## 1. Submitter


**Company** Siemens Healthcare Diagnostics Inc.

**Address** 500 GBC Drive, M/S 514 Newark, DE 19702

**Contact** Alan Haley

**Telephone** 302.631.9883

**Fax** 302.631.6299


## 2. Date of Preparation

October 24, 2017

## 3. Device Information

| | |
|---|---|
| Trade Name | Emit® II Plus Cocaine Metabolite Assay |
| Common Name | Cocaine Metabolite Assay |
| Classification Name | Enzyme Immunoassay, Cocaine and Cocaine Metabolites |
| Regulation | 21 CFR 862.3250 |
| Device Class | Class II |
| Product Code | DIO |

## 4. Indications for Use

The Emit® II Plus Cocaine Metabolite Assay is a homogeneous enzyme immunoassay with a 150 ng/mL or 300 ng/mL cutoff. The assay is intended for use in the qualitative and semiquantitative analyses of benzoylecgonine (cocaine metabolite) in human urine. Emit® II Plus assays are designed for use with a number of chemistry analyzers.

The Emit® II Plus Cocaine Metabolite 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 (GC/MS) 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.

## 5. Device Description

The Emit II Plus Cocaine Metabolite assay is a homogeneous enzyme immunoassay that qualitatively and semiquantitatively measures benzoylecgonine. The assay has cutoffs of 150 ng/mL and 300 ng/mL benzoylecgonine.

The assay is based on competition between drug in the specimen and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for antibody binding sites. Enzyme activity decreases upon binding to the antibody, so the drug concentration in the specimen can

be measured in terms of enzyme activity. Active enzyme converts nicotinamide adenine dinucleotide (NAD) to NADH, resulting in an absorbance change that is measured spectrophotometrically at 340 nm.

The Emit II Plus Cocaine Metabolite Assay consists of two ready-to-use reagents:

**Antibody/Substrate Reagent 1**
Sheep polyclonal antibodies to benzoylecgonine (2.2 µg/mL), bovine serum albumin, G6P (15 mM), NAD (12 mM), preservatives, and stabilizers

**Enzyme Reagent 2**
Benzoylecgonine labeled with bacterial G6PDH (0.46 U/mL), HEPES buffer, bovine serum albumin, preservatives, and stabilizers

## 6. Medical Device to Which Equivalence is Claimed

The Siemens Healthcare Diagnostics Inc. Emit® II Plus Cocaine Metabolite Assay has the same intended use and indications for use as the Emit II Plus Cocaine Metabolite Assay previously cleared under 510(k) K993988 (January 27, 2000). Siemens Healthcare Diagnostics provides instructions for using this assay on a number of chemistry analyzers.

The predicate and proposed device were considered side by side to examine the similarities and differences between the devices.

## 7. Comparison of Technological Characteristics with the Predicate Device

| Attribute | Emit II Plus Cocaine Metabolite Assay (K993988) | Emit II Plus Cocaine Metabolite Assay (Proposed) |
|---|---|---|
| Intended Use | The Emit® II Plus Cocaine Metabolite Assay is a homogeneous enzyme immunoassay with a 150 ng/mL (SAMHSA initial test cutoff level) or 300 ng/mL cutoff. The assay is intended for use in the qualitative and semiquantitative analyses of benzoylecgonine (cocaine metabolite) in human urine. Emit® II Plus assays are designed for use with a number of chemistry analyzers.<br><br>The Emit® II Plus Cocaine Metabolite 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 (GC/MS) is the | The Emit® II Plus Cocaine Metabolite Assay is a homogeneous enzyme immunoassay with a 150 ng/mL or 300 ng/mL cutoff. The assay is intended for use in the qualitative and semiquantitative analyses of benzoylecgonine (cocaine metabolite) in human urine. Emit® II Plus assays are designed for use with a number of chemistry analyzers.<br><br>The Emit® II Plus Cocaine Metabolite 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 (GC/MS) is the preferred confirmatory method. |

| Attribute | Emit II Plus Cocaine Metabolite Assay (K993988) | Emit II Plus Cocaine Metabolite Assay (Proposed) |
|---|---|---|
| | 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. | 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. |
| Measurand | Benzoylecgonine | Same |
| Type of Test | Qualitative and semi-quantitative homogeneous enzyme immunoassay | Same |
| Antibody | Sheep polyclonal | Same |
| Reagent Form | Liquid, ready to use | Same |
| Reagent Composition | **Antibody/Substrate Reagent 1** Sheep polyclonal antibodies to benzoylecgonine (2.2 µg/mL), bovine serum albumin, G6P (15 mM), NAD (12 mM), preservatives, and stabilizers<br><br>**Enzyme Reagent 2** Benzoylecgonine labeled with bacterial G6PDH (0.46 U/mL), HEPES buffer, bovine serum albumin, preservatives, and stabilizers | Same |
| Cutoffs/Controls | 150 ng/mL (±25%)<br>300ng/mL (±25%) | Same |
| Sample Matrix | Human Urine | Same |

## 8. Performance Data

The following tests were conducted to assess the critical performance parameters of the Emit® II Plus Cocaine Metabolite assay on the Beckman Coulter DxC 700 AU Clinical Chemistry Analyzer.

### *8.1 Method Comparison*

The benzoylecgonine values of native patient urine samples were measured using the Emit® II Plus Cocaine Metabolite assay on the Beckman Coulter DxC 700 AU Clinical Chemistry Analyzer (proposed) and were compared to the values measured using GC/MS.

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**Table 8.1(a) Method Comparison Results for the 150 ng/mL Cutoff (n = 102)**

| | | GC/MS | | | |
|---|---|---|---|---|---|
| | | Negative (<75 ng/mL) | Negative (75 – 149 ng/mL) | Positive (150 – 225 ng/mL) | Positive (> 225 ng/mL) |
| *Qualitative* | | | | | |
| DxC 700 AU | Positive | 2 | 7 | 10 | 51 |
| | Negative | 28 | 4 | 0 | 0 |
| *Semi-Quantitative* | | | | | |
| DxC 700 AU | Positive | 2 | 7 | 10 | 51 |
| | Negative | 28 | 4 | 0 | 0 |

Result: 91% agreement

**Table 8.1(b) Summary of Discordant Results, 150 ng/mL cutoff, Qualitative**

| Emit II Plus Cocaine Metabolite Assay (pos/neg) | GC/MS (ng/mL) | Major Drug Present by GC/MS |
|---|---|---|
| Positive | 124 | Benzoylecgonine |
| Positive | 34 | Benzoylecgonine |
| Positive | 73 | Benzoylecgonine |
| Positive | 83 | Benzoylecgonine |
| Positive | 102 | Benzoylecgonine |
| Positive | 80 | Benzoylecgonine |
| Positive | 105 | Benzoylecgonine |
| Positive | 101 | Benzoylecgonine |
| Positive | 75 | Benzoylecgonine |

**Table 8.1(c) Summary of Discordant Results, 150 ng/mL cutoff, Semi-Quantitative**

| Emit II Plus Cocaine Metabolite Assay (pos/neg) | GC/MS (ng/mL) | Major Drug Present by GC/MS |
|---|---|---|
| Positive | 124 | Benzoylecgonine |
| Positive | 34 | Benzoylecgonine |
| Positive | 73 | Benzoylecgonine |
| Positive | 83 | Benzoylecgonine |
| Positive | 102 | Benzoylecgonine |
| Positive | 80 | Benzoylecgonine |
| Positive | 105 | Benzoylecgonine |
| Positive | 101 | Benzoylecgonine |
| Positive | 75 | Benzoylecgonine |

**Table 8.1(d) Method Comparison Results for the 300 ng/mL Cutoff (n = 95)**

| | | GC/MS | | | |
|---|---|---|---|---|---|
| | | Negative (<150 ng/ml) | Negative (150 – 299 ng/mL) | Positive (300 – 450 ng/mL) | Positive (> 450 ng/mL) |
| *Qualitative* | | | | | |
| DxC 700 AU | Positive | 1 | 10 | 18 | 25 |
| | Negative | 40 | 1 | 0 | 0 |
| *Semi-Quantitative* | | | | | |
| DxC 700 AU | Positive | 1 | 10 | 18 | 25 |
| | Negative | 40 | 1 | 0 | 0 |

Result: 88% agreement

**Table 8.1(e) Summary of Discordant Results, 300 ng/mL cutoff, Qualitative**

| Emit II Plus Cocaine Metabolite Assay (pos/neg) | GC/MS (ng/mL) | Major Drug Present by GC/MS |
|---|---|---|
| Positive | 217 | Benzoylecgonine |
| Positive | 240 | Benzoylecgonine |
| Positive | 173 | Benzoylecgonine |
| Positive | 207 | Benzoylecgonine |
| Positive | 233 | Benzoylecgonine |
| Positive | 143 | Benzoylecgonine |
| Positive | 217 | Benzoylecgonine |
| Positive | 173 | Benzoylecgonine |
| Positive | 232 | Benzoylecgonine |
| Positive | 157 | Benzoylecgonine |
| Positive | 234 | Benzoylecgonine |

**Table 8.1(f) Summary of Discordant Results, 300 ng/mL cutoff, Semi-Quantitative**

| Emit II Plus Cocaine Metabolite Assay (pos/neg) | GC/MS (ng/mL) | Major Drug Present by GC/MS |
|---|---|---|
| Positive | 217 | Benzoylecgonine |
| Positive | 240 | Benzoylecgonine |
| Positive | 173 | Benzoylecgonine |
| Positive | 207 | Benzoylecgonine |
| Positive | 233 | Benzoylecgonine |
| Positive | 143 | Benzoylecgonine |
| Positive | 217 | Benzoylecgonine |
| Positive | 173 | Benzoylecgonine |
| Positive | 232 | Benzoylecgonine |
| Positive | 157 | Benzoylecgonine |
| Positive | 234 | Benzoylecgonine |

### *8.2 Repeatability and Within-Lab Precision*

A precision study was performed for 20 days, 2 runs per day, 2 replicates per run per day (N=80). Nine sample levels were tested for each cutoff : equal to the cutoff, ± 25% of the cutoff, ± 50% of the cutoff, ± 75% of the cutoff, and ±100% of the cutoff. Data were analyzed using a nested, two factor (days and runs nested within days) ANOVA model. Testing was performed on a Beckman Coulter DxC 700 AU Clinical Chemistry Analyzer.

**Table 8.2(a) Precision, Qualitative, 150 ng/mL Cutoff**

| Benzoylecgonine Concentration (ng/mL) | % of cutoff | # of determinations | Repeatability Result | Within-Lab Result |
|---|---|---|---|---|
| 0 | -100% | 80 | 80 Negative | 80 Negative |
| 38 | -75% | 80 | 80 Negative | 80 Negative |
| 75 | -50% | 80 | 80 Negative | 80 Negative |
| 113 | -25% | 80 | 80 Negative | 80 Negative |
| 150 | Cutoff | 80 | 9 Negative<br>71 Positive | 9 Negative<br>71 Positive |
| 188 | +25% | 80 | 80 Positive | 80 Positive |
| 225 | +50% | 80 | 80 Positive | 80 Positive |
| 263 | +75% | 80 | 80 Positive | 80 Positive |
| 300 | 100% | 80 | 80 Positive | 80 Positive |

**Table 8.2(b) Precision, Semi-Quantitative, 150 ng/mL Cutoff**

| Benzoylecgonine Concentration (ng/mL) | % of cutoff | # of determinations | Repeatability Result | Within-Lab Result |
|---|---|---|---|---|
| 0 | -100% | 80 | 80 Negative | 80 Negative |
| 38 | -75% | 80 | 80 Negative | 80 Negative |
| 75 | -50% | 80 | 80 Negative | 80 Negative |
| 113 | -25% | 80 | 80 Negative | 80 Negative |
| 150 | Cutoff | 80 | 9 Negative<br>71 Positive | 9 Negative<br>71 Positive |
| 188 | +25% | 80 | 80 Positive | 80 Positive |
| 225 | +50% | 80 | 80 Positive | 80 Positive |
| 263 | +75% | 80 | 80 Positive | 80 Positive |
| 300 | 100% | 80 | 80 Positive | 80 Positive |

**Table 8.2(c) Precision, Qualitative, 300 ng/mL Cutoff**

| Benzoylecgonine Concentration (ng/mL) | % of cutoff | # of determinations | Repeatability Result | Within-Lab Result |
|---|---|---|---|---|
| 0 | -100% | 80 | 80 Negative | 80 Negative |
| 75 | -75% | 80 | 80 Negative | 80 Negative |
| 150 | -50% | 80 | 80 Negative | 80 Negative |
| 225 | -25% | 80 | 80 Negative | 80 Negative |
| 300 | Cutoff | 80 | 54 Negative<br>26 Positive | 54 Negative<br>26 Positive |
| 375 | +25% | 80 | 80 Positive | 80 Positive |
| 450 | +50% | 80 | 80 Negative | 80 Negative |
| 525 | +75% | 80 | 80 Positive | 80 Positive |
| 600 | +100% | 80 | 80 Positive | 80 Positive |

**Table 8.2(d) Precision, Semi-Quantitative, 300 ng/mL Cutoff**

| Benzoylecgonine Concentration (ng/mL) | % of cutoff | # of determinations | Repeatability Result | Within-Lab Result |
|---|---|---|---|---|
| 0 | -100% | 80 | 80 Negative | 80 Negative |
| 75 | -75% | 80 | 80 Negative | 80 Negative |
| 150 | -50% | 80 | 80 Negative | 80 Negative |
| 225 | -25% | 80 | 80 Negative | 80 Negative |
| 300 | Cutoff | 80 | 54 Negative<br>26 Positive | 54 Negative<br>26 Positive |
| 375 | +25% | 80 | 80 Positive | 80 Positive |
| 450 | +50% | 80 | 80 Negative | 80 Negative |
| 525 | +75% | 80 | 80 Positive | 80 Positive |
| 600 | +100% | 80 | 80 Positive | 80 Positive |

### *8.3 Recovery/Linearity*

Samples were prepared by spiking two aliquots of negative urine pool with known concentrations of benzoylecgonine and sequentially mixing them to create samples across the analytical range. Five replicates were tested at each level. Testing was performed on a Beckman Coulter DxC 700 AU Clinical Chemistry Analyzer.

**Table 8.3(a) Recovery/Linearity, Semiquantitative**

| Nominal Benzoylecgonine (ng/mL) | Mean Measured Benzoylecgonine (ng/mL) | % Recovery |
|---|---|---|
| 50 | 53 | 6.1% |
| 100 | 103 | 3.1% |
| 150 | 150 | 0.2% |
| 225 | 235 | 4.3% |
| 300 | 298 | -0.7% |
| 375 | 380 | 1.4% |
| 500 | 543 | 8.6% |
| 750 | 792 | 5.6% |
| 900 | 906 | 0.6% |
| 1000 | 1029 | 2.9% |

### *8.4 Specificity - Structurally Related Compounds*

The Emit® II Plus Cocaine Metabolite Assay detects benzoylecgonine, the major metabolite of cocaine, in human urine. Tables 8.4(a) and 8.4(b) list the cross-reactivity for structurally related compounds. Data presented are representative of typical performance of this assay.

**Table 8.4(a) Structurally Related Compounds, 150 ng/mL cutoff**

| Compound | Concentration Tested (ng/mL) | % Cross-Reactivity |
|---|---|---|
| Ecgonine* | 5,000 | 3% |
| Cocaine* | 29,000 | 0.5% |
| Norcocaine | 100,000 | <0.01% |
| Cocaethylene | 100,000 | <0.01% |
| Ecgonine Methyl Ester | 100,000 | <0.01% |

**Table 8.4(b) Structurally Related Compounds, 300 ng/mL cutoff**

| Compound | Concentration Tested (ng/mL) | % Cross-Reactivity |
|---|---|---|
| Ecgonine* | 15,000 | 2% |
| Cocaine* | 61,000 | 0.5% |
| Norcocaine | 100,000 | <0.01% |
| Cocaethylene | 100,000 | <0.01% |
| Ecgonine Methyl Ester | 100,000 | <0.01% |

*Ecgonine and cocaine tested at the concentrations above produced a result approximately equivalent to the cutoff.

## 9. Conclusion

The information presented in this premarket notification demonstrates that the Emit® II Plus Cocaine Metabolite Assay is substantially equivalent to the legally marketed predicate device identified above.