Siemens Healthcare Diagnostics Inc.
Julie Warren
Regulatory Affairs Professional
500 GBC Dr. P.O. Box 6101, Mailstop 514
Newark, DE 19714

Re: K221605
Trade/Device Name: Emit® II Plus Buprenorphine Assay
Regulation Number: 21 CFR 862.3650
Regulation Name: Opiate Test System
Regulatory Class: Class II
Product Code: DJG
Dated: March 16, 2023
Received: March 17, 2023

Dear Julie Warren:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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 Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR

803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Joseph A. Kotarek -S
Digitally signed by Joseph A. Kotarek -S
Date: 2023.07.25 10:40:32 -04'00'

Joseph Kotarek, Ph.D.
Branch Chief
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
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: 06/30/2023
*See PRA Statement below.*

510(k) Number *(if known)*
K221605

Device Name
Emit® II Plus Buprenorphine Assay

Indications for Use *(Describe)*
The Emit® II Plus Buprenorphine Assay is a homogeneous enzyme immunoassay with a 5 ng/mL cutoff. The assay is intended for use in laboratories for the qualitative and/or semiquantitative analyses of buprenorphine in human urine. Emit® II Plus assays are designed for use with a number of chemistry analyzers.

The semiquantitative mode is for the purpose of enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as Liquid Chromatography/Mass Spectrometry (LC/MS) or permitting laboratories to establish quality control procedures.

The Emit® II Plus Buprenorphine Assay provides only a preliminary analytical test result. A more specific alternative chemical method(s) must be used to obtain a confirmed analytical result. Gas Chromatography/Mass Spectrometry (GC/MS) or LC/MS are the preferred confirmatory methods. 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.

For Professional Use.

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

For in vitro diagnostic use.

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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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: K221605

## 1. Submitter

Siemens Healthcare Diagnostics Inc.
500 GBC Dr.
P.O. Box 6101
Newark, DE 19714

Primary Contact Person: Julie Warren
Date of Preparation: July 7, 2023

## 2. Device Information

| | |
|---|---|
| Trade Name | Emit® II Plus Buprenorphine Assay |
| Common Name | Buprenorphine Assay |
| Device | Enzyme Immunoassay, Opiates |
| Review Panel | Toxicology |
| Product Code | DJG |
| Submission Type | 510(k) |
| Regulation Number | 21 CFR § 862.3650 |
| Device Class | 2 |

## 3. Purpose of Submission

The purpose of this premarket notification is for the Emit® II Plus Buprenorphine Assay on the DxC 500 AU Clinical Chemistry Analyzer.

## 4. Predicate Device

Predicate Device Name: Emit® II Plus Buprenorphine Assay
510(k) Number: K150606

## 5. Device Description

### Emit® II Plus Buprenorphine Assay

The Emit® II Plus Buprenorphine Assay is a homogeneous enzyme immunoassay technique used for the analysis of specific compounds in human urine. The assay is based on competition between drug in the specimen and drug labeled with the recombinant glucose-6-phosphate dehydrogenase (rG6PDH) 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 in the presence of glucose-6-phosphate (G6P), resulting in an absorbance change that is measured spectrophotometrically. Endogenous serum G6PDH does not interfere because the coenzyme NAD functions only with the bacterial (Leuconostoc mesenteroides) enzyme employed in the assay.

The Emit® II Plus Buprenorphine Assay reagents are provided liquid, ready to use and may be used directly from the refrigerator. The product is sold in three (3) kit sizes: 28 mL, 115 mL, and 1000 mL. Reagents 1 and 2 are provided as a matched set. They should not be interchanged with components of kits with different lot numbers.

**Antibody/Substrate Reagent 1**

Mouse monoclonal antibodies to buprenorphine (0.53 µg/mL)*,NAD (6.9 mM), G6P (10.9 mM), bovine serum albumin, preservatives, and stabilizers.

*The antibody titer and enzyme conjugate activity may vary from lot to lot.

**Enzyme Reagent 2**

Norbuprenorphine labeled with bacterial rG6PDH (0.50 µg/mL), HEPES buffer, bovine serum albumin, preservatives, and stabilizers, where the antibody titer and enzyme conjugate activity may vary from lot to lot.

## 6. Intended Use/Indications for Use

**Emit® II Plus Buprenorphine Assay**

The Emit® II Plus Buprenorphine Assay is a homogeneous enzyme immunoassay with a 5 ng/mL cutoff. The assay is intended for use in laboratories for the qualitative and/or semiquantitative analyses of buprenorphine in human urine. Emit® II Plus assays are designed for use with a number of chemistry analyzers.

The semiquantitative mode is for the purpose of enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as Liquid Chromatography/Mass Spectrometry (LC/MS) or permitting laboratories to establish quality control procedures.

The Emit® II Plus Buprenorphine Assay provides only a preliminary analytical test result. A more specific alternative chemical method(s) must be used to obtain a confirmed analytical result. Gas Chromatography/Mass Spectrometry (GC/MS) or LC/MS are the preferred confirmatory methods. 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.

For Professional Use.

**Caution:** Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

For *in vitro* diagnostic use.

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

The similarities and differences between the proposed device Emit II Plus Buprenorphine Assay on Beckman Coulter DxC AU 500 Clinical Chemistry Analyzer and the predicate device, Emit II Plus Buprenorphine Assay, were compared side by side.

| Feature | Predicate Device:<br>Emit II Plus Buprenorphine Assay | Proposed Device:<br>Emit II Plus Buprenorphine Assay |
|---|---|---|
| Intended Use | A homogeneous enzyme immunoassay with a 5 ng/mL cutoff. The assay is intended for use in laboratories for the qualitative and/or | Same |

| Feature | Predicate Device:<br>Emit II Plus Buprenorphine Assay | Proposed Device:<br>Emit II Plus Buprenorphine Assay |
|---|---|---|
| | semiquantitative analyses of buprenorphine in human urine. Preliminary analytical test result. | |
| Analyte | Buprenorphine | Same |
| Cutoff Level | 5 ng/mL | Same |
| Measurement | Qualitative, semi-quantitative | Same |
| Methodology | EMIT® technology: Homogeneous enzyme immunoassay | Same |
| Detection | Absorbance change measured Spectrophotometrically at 340nm | Same |
| Instrument | Analyzers must be capable of maintaining a constant reaction temperature, pipette specimens/reagents, mix thoroughly, measure enzyme rates precisely and time the reaction accurately. | Beckman Coulter DxC 500 AU Analyzer |
| Sample Type | Human Urine | Same |
| Reagent form and storage | Liquid – ready to use, on-board storage | Same |
| Calibrator | 0, 2.5, 5, 15, and 25 ng/mL | Same |
| Control Levels | Positive: 7 ng/mL<br>Negative: 3 ng/mL | Same |

## 8. Performance Data

The following performance studies were conducted to demonstrate substantial equivalence of the Emit II Plus Buprenorphine Assay on the DXC 500 AU Clinical Chemistry Analyzer to the Emit II Plus Buprenorphine Assay previously cleared under premarket notification 510(k), K150606.

### 8.1 Method Comparison

The method comparison study was evaluated in accordance with CLSI EP09c 3rd Edition Measurement Procedure Comparison and Bias Estimation Using Patient Samples Evaluation of Precision Performance of Quantitative Measurement Methods and CLSI EP 12-A2 User Protocol for Evaluation of Qualitative Test Performance to determine accuracy and verification of the 5 ng/mL cutoff.

One hundred twenty (120) native urine individual patient samples were collected from external suppliers. The samples were received frozen, and thawed before testing. The samples were distributed across the assay range, 21% of which were within -50% of the cutoff and 19% of which were within +50% of the cutoff.

Each specimen was tested on the DxC 500 AU and on LC/MS/MS The results were analyzed using a 2x2 box plot to assess qualitative agreement relative to the 5 ng/mL cutoff value.

**Table 1. Method Comparison - Qualitative Analysis**

| | | LC/MS/MS | |
|---|---|---|---|
| | | Neg | Pos |
| Emit II Plus Buprenorphine on DxC 500 AU | Neg | 48 | 0 |
| | Pos | 9 | 63 |

Result: 92.5% Agreement

**Table 2. Method Comparison – Discordant Results**

| Sample ID | DxC 500 AU (ng/mL) | Buprenorphine (ng/mL) | Norbuprenorphine (ng/mL) | Buprenorphine+ Norbuprenorphine (ng/mL) | DxC 500 AU Pos/Neg | LC/MS/MS Pos/Neg |
|---|---|---|---|---|---|---|
| BUP35 | 6.1 | 0.0 | 4.2 | 4.2 | Pos | Neg |
| BUP45 | 6.0 | 0.0 | 4.6 | 4.6 | Pos | Neg |
| BUP51 | 6.1 | 0.0 | 4.3 | 4.3 | Pos | Neg |
| BUP60 | 5.6 | 0.0 | 3.8 | 3.8 | Pos | Neg |
| BUP62 | 6.1 | 0.0 | 3.9 | 3.9 | Pos | Neg |
| BUP87 | 5.5 | 0.0 | 4.3 | 4.3 | Pos | Neg |
| BUP95 | 5.6 | 0.0 | 4.5 | 4.5 | Pos | Neg |
| BUP101 | 6.3 | 0.0 | 4.8 | 4.8 | Pos | Neg |
| BUP109 | 5.0 | 0.0 | 4.3 | 4.3 | Pos | Neg |

One hundred twenty (120) samples were tested. Relative to the 5 ng/mL cutoff, forty-eight (48) samples were negative by Emit II Plus Buprenorphine Assay and LC/MS/MS, and sixty-three (63) were positive. Nine (9) discordant samples were observed as positive by Emit II Plus Buprenorphine and negative by LC/MS/MS.

### 8.2 Recovery

The recovery was evaluated in accordance with the following testing protocol.
Nine (9) urine samples were prepared by spiking buprenorphine into negative urine pools. The following levels were tested: 2.0, 3.0, 4.0, 5.0, 8.0, 12.0, 18.0, 22.0, and 25.0 ng/mL.

Experimental design was (1) reagent lot, one (1) calibrator lot, one (1) instrument, one (1) calibration with two (2) replicate measurements each. Samples were assayed in five (5) replicates. Samples were additionally analyzed by LC/MS/MS to determine the reference value. The nominal value was determined gravimetrically based on the stock concentration.

**Table 3. Recovery of Emit II Plus Buprenorphine - Semi-Quantitative Analysis**

| Sample ID | Nominal Value (ng/mL) | DxC 500 AU Value (ng/mL) | % Recovery vs Nominal | LC/MS/MS (ng/mL) | % Recovery vs LC/MS/MS |
|---|---|---|---|---|---|
| BUP1 | 2.0 | 1.9 | 95 | 2.2 | 86 |
| BUP2 | 3.0 | 2.9 | 97 | 3.2 | 91 |
| BUP3 | 4.0 | 4.1 | 103 | 4.4 | 93 |
| BUP4 | 5.0 | 4.9 | 98 | 5.1 | 96 |
| BUP5 | 8.0 | 7.6 | 95 | 8.8 | 86 |
| BUP6 | 12.0 | 11.6 | 97 | 13.1 | 89 |
| BUP7 | 18.0 | 18.1 | 101 | 18.1 | 100 |
| BUP8 | 22.0 | 22.9 | 104 | 22.9 | 100 |
| BUP9 | 25.0 | 24.7 | 99 | 25.6 | 96 |

### 8.3 Precision

**Repeatability and Within-Lab Precision**

The precision was evaluated in accordance with CLSI EP05-A3 *Evaluation of Precision Performance of Quantitative Measurement Methods*.

Eleven (11) urine samples were prepared by spiking buprenorphine into negative urine pools, aliquoted and frozen prior to the start of testing. The following levels were tested: 0, 1.25, 2.5, 3.0, 3.75, 5.0, 6.25, 7.0, 7.5, 8.75, and 10.0 ng/mL.

Experimental design was a 20x2x2 design using (1) reagent lot, one (1) calibrator lot, one (1) instrument, one (1) calibration, twenty (20) test days and two (2) runs per test

day with two (2) replicate measurements each. Each day, two runs were performed, with a minimum of two (2) hours in between.

**Table 4. Precision of Emit II Plus Buprenorphine Qualitative Analysis**

| Sample Concentration (ng/mL) | % of the Cutoff | # of Results | Results (Pos/Neg) | Mean (mA/min) |
|---|---|---|---|---|
| 0.0 | -100% | 80 | 80 Negative | 280 |
| 1.25 | -75% | 80 | 80 Negative | 297 |
| 2.5 | -50% | 80 | 80 Negative | 316 |
| 3.0 | -40% | 80 | 80 Negative | 323 |
| 3.75 | -25% | 80 | 80 Negative | 333 |
| 5.0 | 0% | 80 | 21 Negative<br>59 Positive | 363 |
| 6.25 | +25% | 80 | 80 Positive | 380 |
| 7.0 | +40% | 80 | 80 Positive | 392 |
| 7.5 | +50% | 80 | 80 Positive | 402 |
| 8.75 | +75% | 80 | 80 Positive | 427 |
| 10.0 | +100% | 80 | 80 Positive | 444 |

**Table 5. Precision of Emit II Plus Buprenorphine Semi-Quantitative Analysis**

| | | | | | Repeatability | | Within-Lab Precision | |
|---|---|---|---|---|---|---|---|---|
| Sample Concentration (ng/mL) | % of the Cutoff | # of Results | Results (Pos/Neg) | Mean (ng/mL) | SD | %CV | SD | %CV |
| 0.0 | -100% | 80 | 80 Negative | 0.1 | 0.06 | - | 0.11 | - |
| 1.25 | -75% | 80 | 80 Negative | 1.2 | 0.08 | 6.6 | 0.08 | 6.6 |
| 2.5 | -50% | 80 | 80 Negative | 2.3 | 0.09 | 3.7 | 0.11 | 4.6 |
| 3.0 | -40% | 80 | 80 Negative | 2.7 | 0.07 | 2.8 | 0.15 | 5.7 |
| 3.75 | -25% | 80 | 80 Negative | 3.3 | 0.08 | 2.5 | 0.15 | 4.4 |
| 5.0 | 0% | 80 | 24 Negative<br>56 Positive | 5.1 | 0.08 | 1.6 | 0.18 | 3.5 |
| 6.25 | +25% | 80 | 80 Positive | 6.1 | 0.08 | 1.3 | 0.21 | 3.4 |
| 7.0 | +40% | 80 | 80 Positive | 6.8 | 0.11 | 1.7 | 0.24 | 3.5 |
| 7.5 | +50% | 80 | 80 Positive | 7.3 | 0.08 | 1.1 | 0.21 | 2.9 |
| 8.75 | +75% | 80 | 80 Positive | 8.8 | 0.10 | 1.1 | 0.24 | 2.8 |
| 10.0 | +100% | 80 | 80 Positive | 9.7 | 0.10 | 1.1 | 0.37 | 3.8 |

**Reproducibility Precision**

The reproducibility was evaluated in accordance with the following protocol.

Three (3) urine samples were tested: Emit II Plus Specialty Drug Control Negative (3 ng/mL) Emit II Plus Specialty Drug Cal/Ctrl (Cutoff Calibrator), and the Emit II Plus Specialty Drug Control Positive (7 ng/mL).

Experimental design was a 3x5x5 design; 3 (Sites/Instruments) × 5 (days) × 5 (replicates per day) for a total seventy-five (75) replicates per reagent lot. To capture lot-to-lot variability, three (3) Emit II Plus Buprenorphine reagent lots were processed in parallel in this study design. Testing was completed by three (3) operators. Each testing day, one (1) run was performed on three (3) instruments.

**Table 6. Total Reproducibility Precision of Emit II Plus Buprenorphine Assay**

| Sample | N | Mean (ng/mL) | SD | %CV |
|---|---|---|---|---|
| Negative Control | 225 | 3.1 | 0.17 | 5.3 |
| Cutoff Calibrator | 225 | 5.0 | 0.18 | 3.7 |
| Positive Control | 225 | 7.1 | 0.21 | 3.0 |

**Table 7. Reproducibility Precision of Emit II Plus Buprenorphine Assay**

| | | | Repeatability | | Between Day | | Between Lot | | Between Instrument/Site | |
|---|---|---|---|---|---|---|---|---|---|---|
| Sample | N | Mean (ng/mL) | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| Negative Control | 225 | 3.1 | 0.11 | 3.6 | 0.06 | 1.8 | 0.03 | 0.8 | 0.11 | 3.4 |
| Cutoff Calibrator | 225 | 5.0 | 0.11 | 2.2 | 0.07 | 1.4 | 0.00 | 0.0 | 0.13 | 2.6 |
| Positive Control | 225 | 7.1 | 0.12 | 1.7 | 0.08 | 1.2 | 0.05 | 0.7 | 0.15 | 2.1 |

### 8.4 Limit of Detection

The limits of detection, Limit of Blank (LoB) and Limit of Detection (LoD) were evaluated in accordance with CLSI EP17-A2: *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures.*

Blank samples were drug-free negative urine, and the low samples were drug-free urine spiked with buprenorphine.

Experimental design was (2) reagent lots, one (1) calibrator lot, one (1) instrument, one (1) calibration, three (3) testing days, four (4) blank samples with minimum of sixty (60) replicate measurements (across all blank samples, days, instrument) and four (4) samples, each containing a low level of measurand (LoD) with minimum of sixty (60) replicate measurements (across all low-level samples, days, instrument).

**Table 8. Limit of Detection Summary**

| Sample | Limit of Detection Lot 1 (ng/mL) | Limit of Detection Lot 2 (ng/mL) | Limit of Detection Final (ng/mL) | Claimed Limit of Detection (ng/mL) |
|---|---|---|---|---|
| **LoD Sample** | 0.7 | 0.8 | 0.8 | ≤ 1.0 |

### 8.5 Specificity and Cross-reactivity

The specificity was evaluated in accordance with CLSI EP07-ED3 *Interference Testing Clinical Chemistry*.

The experimental design was one (1) reagent lot, one (1) calibrator lot, one (1) instrument, one (1) sample pool for each compound tested. The samples were assayed in five (5) replicates.

**Table 9. Specificity - Buprenorphine Metabolites**

| Compound | Concentration Tested (ng/mL) | Mean (ng/mL) | Cutoff (ng/mL) | % Cross-reactivity |
|---|---|---|---|---|
| Buprenorphine | 5 ng/mL | 4.9 | 5.0 | 98% |
| Norbuprenorphine | 5 ng/mL | 5.3 | 5.0 | 106% |
| Buprenorphine Glucuronide | 1,000 ng/mL | 1.4 | 5.0 | 0.10% |
| Norbuprenorphine Glucuronide | 1,000 ng/mL | 1.4 | 5.0 | 0.10% |

**Table 10. Cross-reactivity - Structurally Related Compounds**

| Description | Concentration @ Testing | Mean Rate (mA/min) | Cutoff Rate (mA/min) | Response vs. Cutoff (Pos/Neg) | Mean (ng/mL) | %Cross-reactivity to 5 ng/mL Cutoff |
|---|---|---|---|---|---|---|
| 6-Acetylcodeine | 100,000 ng/mL | 131 | 167 | Neg | -0.6 | <0.1% |
| 6-Acetylmorphine | 100,000 ng/mL | 137 | 167 | Neg | 0.4 | <0.1% |
| Codeine | 100,000 ng/mL | 135 | 167 | Neg | 0.1 | <0.1% |
| Dextromethorphan | 100,000 ng/mL | 137 | 167 | Neg | 0.3 | <0.1% |
| Dihydrocodeine | 100,000 ng/mL | 136 | 167 | Neg | 0.3 | <0.1% |
| Ethyl Morphine | 100,000 ng/mL | 136 | 167 | Neg | 0.3 | <0.1% |
| Heroin | 100,000 ng/mL | 133 | 167 | Neg | 0.0 | <0.1% |
| Hydrocodone | 100,000 ng/mL | 136 | 167 | Neg | 0.2 | <0.1% |

| Description | Concentration @ Testing | Mean Rate (mA/min) | Cutoff Rate (mA/min) | Response vs. Cutoff (Pos/Neg) | Mean (ng/mL) | %Cross-reactivity to 5 ng/mL Cutoff |
|---|---|---|---|---|---|---|
| Hydromorphone | 100,000 ng/mL | 137 | 167 | Neg | 0.4 | <0.1% |
| Levorphanol | 100,000 ng/mL | 141 | 167 | Neg | 1.0 | <0.1% |
| Morphine | 100,000 ng/mL | 135 | 167 | Neg | 0.1 | <0.1% |
| Morphine 3-glucuronide | 100,000 ng/mL | 137 | 167 | Neg | 0.4 | <0.1% |
| Morphine 6-glucuronide | 100,000 ng/mL | 136 | 167 | Neg | 0.3 | <0.1% |
| Nalorphine | 100,000 ng/mL | 136 | 167 | Neg | 0.3 | <0.1% |
| Naloxone | 100,000 ng/mL | 138 | 167 | Neg | 0.6 | <0.1% |
| Naltrexone | 100,000 ng/mL | 137 | 167 | Neg | 0.4 | <0.1% |
| Norcodeine | 100,000 ng/mL | 135 | 167 | Neg | 0.1 | <0.1% |
| Normorphine | 100,000 ng/mL | 136 | 167 | Neg | 0.2 | <0.1% |
| Noroxycodone | 100,000 ng/mL | 135 | 167 | Neg | 0.2 | <0.1% |
| Noroxymorphone | 100,000 ng/mL | 136 | 167 | Neg | 0.2 | <0.1% |
| Oxycodone | 100,000 ng/mL | 136 | 167 | Neg | 0.3 | <0.1% |
| Oxymorphone | 100,000 ng/mL | 137 | 167 | Neg | 0.4 | <0.1% |

**Table 11. Cross-reactivity - Structurally Un-Related Compounds**

| Compound | Conc. Tested (µg/mL) | -40% Control Mean Semi-Quant (ng/mL) | -40% Control Response vs. Cutoff (Pos/Neg) | +40% Control Mean Semi-Quant (ng/mL) | +40% Control Response vs. Cutoff (Pos/Neg) |
|---|---|---|---|---|---|
| 10,11-Dihydrocarbamazepine | 85.0 | 2.8 | Neg | 6.9 | Pos |
| Acetaminophen | 1000.0 | 2.5 | Neg | 7.0 | Pos |
| Acetylsalicylic Acid | 1500.0 | 2.5 | Neg | 7.0 | Pos |
| Amitriptyline | 100.0 | 3.1 | Neg | 7.5 | Pos |
| Amoxicillin | 500.0 | 2.5 | Neg | 6.9 | Pos |
| AZT (Zidovudine) | 2000.0 | 2.5 | Neg | 6.8 | Pos |
| Brompheniramine | 75.0 | 2.7 | Neg | 6.9 | Pos |
| Caffeine | 1000.0 | 2.7 | Neg | 7.0 | Pos |
| Captopril | 500.0 | 2.6 | Neg | 6.9 | Pos |

| Compound | Conc. Tested (µg/mL) | -40% Control Mean Semi-Quant (ng/mL) | -40% Control Response vs. Cutoff (Pos/Neg) | +40% Control Mean Semi-Quant (ng/mL) | +40% Control Response vs. Cutoff (Pos/Neg) |
|---|---|---|---|---|---|
| Chlordiazepoxide | 100.0 | 2.6 | Neg | 7.1 | Pos |
| Chlorpromazine | 10.0 | 2.9 | Neg | 7.2 | Pos |
| Cimetidine | 1000.0 | 2.9 | Neg | 7.4 | Pos |
| Clomipramine | 2.5 | 2.8 | Neg | 7.3 | Pos |
| Clonidine | 1000.0 | 2.9 | Neg | 7.2 | Pos |
| Cyclobenzaprine | 125.0 | 3.1 | Neg | 7.6 | Pos |
| d-Amphetamine | 700.0 | 2.9 | Neg | 7.3 | Pos |
| Desipramine | 800.0 | 3.3 | Neg | 8.0 | Pos |
| Diazepam | 100.0 | 3.1 | Neg | 7.4 | Pos |
| Digoxin | 0.01 | 2.9 | Neg | 6.9 | Pos |
| Diphenhydramine | 1000.0 | 4.6 | Neg | 8.8 | Pos |
| d-Methamphetamine | 500.0 | 2.9 | Neg | 7.2 | Pos |
| Doxepin | 100.0 | 3.0 | Neg | 7.6 | Pos |
| EDDP (2-Ethylidene-1.5dimethyl-3.3-duogenylidine) | 1000.0 | 3.6 | Neg | 8.3 | Pos |
| EMDP | 100.0 | 2.7 | Neg | 7.0 | Pos |
| Enalapril | 500.0 | 2.7 | Neg | 7.3 | Pos |
| Fluoxetine | 500.0 | 3.0 | Neg | 7.8 | Pos |
| Glutethimide | 500.0 | 2.8 | Neg | 7.4 | Pos |
| Haloperidol | 100.0 | 2.7 | Neg | 7.4 | Pos |
| Hydroxyzine (dihydrochloride) | 500.0 | 3.3 | Neg | 8.0 | Pos |
| Ibuprofen | 1000.0 | 2.9 | Neg | 7.4 | Pos |
| Imipramine | 200.0 | 3.2 | Neg | 7.6 | Pos |
| Ketamine | 100.0 | 2.6 | Neg | 7.0 | Pos |
| Ketorolac Tromethamine | 400.0 | 2.3 | Neg | 6.7 | Pos |
| LAAM (L-a-Acetylmethadol) | 25.0 | 2.7 | Neg | 7.4 | Pos |
| L-Cotinine | 100.0 | 2.6 | Neg | 7.0 | Pos |

| Compound | Conc. Tested (µg/mL) | -40% Control Mean Semi-Quant (ng/mL) | -40% Control Response vs. Cutoff (Pos/Neg) | +40% Control Mean Semi-Quant (ng/mL) | +40% Control Response vs. Cutoff (Pos/Neg) |
|---|---|---|---|---|---|
| Levofloxacin | 100.0 | 2.8 | Neg | 7.1 | Pos |
| Levothyroxine (L-Thyroxine) | 50.0 | 2.6 | Neg | 7.1 | Pos |
| Lidocaine | 1000.0 | 2.7 | Neg | 7.1 | Pos |
| Lormetazepam | 1.0 | 2.5 | Neg | 7.0 | Pos |
| LSD | 10.0 | 2.5 | Neg | 7.1 | Pos |
| MDMA (Ecstasy) | 1000.0 | 2.6 | Neg | 7.3 | Pos |
| Meperidine | 800.0 | 2.9 | Neg | 7.5 | Pos |
| Methadone | 500.0 | 3.3 | Neg | 7.9 | Pos |
| Methaqualone | 600.0 | 3.0 | Neg | 7.6 | Pos |
| NAPA (N-Acetylprocainamide) | 400.0 | 2.6 | Neg | 6.8 | Pos |
| Naproxen | 1000.0 | 2.4 | Neg | 6.6 | Pos |
| Nicotinic Acid | 500.0 | 2.5 | Neg | 7.2 | Pos |
| Nifedipine | 500.0 | 2.5 | Neg | 6.4 | Pos |
| Nordiazepam | 100.0 | 2.7 | Neg | 7.2 | Pos |
| Nortriptyline | 250.0 | 2.6 | Neg | 7.4 | Pos |
| Oxazepam | 300.0 | 2.4 | Neg | 6.6 | Pos |
| Perphenazine | 150.0 | 2.9 | Neg | 7.6 | Pos |
| Phencyclidine | 900.0 | 4.6 | Neg | 8.9 | Pos |
| Phenobarbital | 500.0 | 2.5 | Neg | 7.1 | Pos |
| Phenelzine (sulfate) | 100.0 | 2.6 | Neg | 6.0 | Pos |
| Phenytoin | 1000.0 | 2.4 | Neg | 6.0 | Pos |
| Procainamide (HCl) | 1000.0 | 2.6 | Neg | 7.0 | Pos |
| Procyclidine (HCl) | 800.0 | 3.2 | Neg | 8.0 | Pos |
| Promethazine (HCl) | 100.0 | 3.7 | Neg | 8.1 | Pos |
| Propoxyphene | 1000.0 | 3.5 | Neg | 8.0 | Pos |
| Protriptyline (HCl) | 200.0 | 3.3 | Neg | 7.9 | Pos |
| Pseudoephedrine | 1000.0 | 2.7 | Neg | 7.0 | Pos |

| Compound | Conc. Tested (µg/mL) | -40% Control Mean Semi-Quant (ng/mL) | -40% Control Response vs. Cutoff (Pos/Neg) | +40% Control Mean Semi-Quant (ng/mL) | +40% Control Response vs. Cutoff (Pos/Neg) |
|---|---|---|---|---|---|
| Quinacrine (HCl) | 900.0 | 4.8 | Neg | 9.0 | Pos |
| Ranitidine | 1000.0 | 2.6 | Neg | 7.1 | Pos |
| Ritalin | 1000.0 | 2.7 | Neg | 7.5 | Pos |
| Salicylic Acid | 500.0 | 2.5 | Neg | 7.1 | Pos |
| Scopolamine | 500.0 | 2.5 | Neg | 6.9 | Pos |
| Secobarbital | 1000.0 | 2.7 | Neg | 7.5 | Pos |
| Tapentadol | 100.0 | 2.4 | Neg | 7.0 | Pos |
| THC (11-nor-Δ9-THC-9-COOH) | 100.0 | 2.4 | Neg | 6.7 | Pos |
| Thioridazine | 100.0 | 4.1 | Neg | 8.6 | Pos |
| Tramadol | 1000.0 | 3.0 | Neg | 7.8 | Pos |
| Trazodone | 5.0 | 2.4 | Neg | 6.8 | Pos |
| Trimethoprim | 1000.0 | 2.5 | Neg | 7.1 | Pos |
| Triprolidine (zymine) | 50.0 | 2.6 | Neg | 7.2 | Pos |
| Tyramine | 100.0 | 2.5 | Neg | 6.9 | Pos |
| Verapamil | 500.0 | 2.8 | Neg | 7.6 | Pos |
| Zolpidem | 100.0 | 2.7 | Neg | 7.1 | Pos |

### 8.6 Interference

Interference was evaluated in accordance with CLSI EP07-ED3 *Interference Testing Clinical Chemistry*.

Urine testing samples were prepared by spiking exogenous materials (metabolites and structurally related compounds) into urine samples at ± 40% positive and negative control levels (3 ng/mL and 7 ng/mL respectively).

The experimental design was one (1) reagent lot, one (1) calibrator lot, one (1) instrument, one (1) sample pool for each compound tested. The samples were assayed in five (5) replicates.

**Table 12. Interference – Endogenous and Exogenous Substances**

| Interferent Sample | Interference concentration | -40% Control Response vs. Qual Cutoff (Pos/Neg) | -40% Control Sample Mean (ng/mL) | +40% Control Response vs. Qual Cutoff (Pos/Neg) | +40% Control Sample Mean (ng/mL) |
|---|---|---|---|---|---|
| Acetone | 1.0 g/dL | Neg | 2.6 | Pos | 6.3 |
| Ascorbic Acid | 1.5 g/dL | Neg | 2.9 | Pos | 6.3 |
| Bilirubin (Conjugated) | 2.0 mg/dL | Neg | 2.2 | Pos | 6.2 |
| Bilirubin (Unconjugated) | 2.0 mg/dL | Neg | 2.4 | Pos | 5.9 |
| Creatinine | 0.5 g/dL | Neg | 2.7 | Pos | 6.3 |
| Ethanol | 1.0 g/dL | Neg | 2.5 | Pos | 6.4 |
| IgG | 0.5 g/dL | Neg | 2.5 | Pos | 7.1 |
| Glucose | 2.0 g/dL | Neg | 2.5 | Pos | 6.1 |
| Hemoglobin | 115 mg/dL | Neg | 3.0 | Pos | 6.7 |
| Human Serum Albumin | 0.5 g/dL | Neg | 2.9 | Pos | 6.7 |
| Oxalic Acid | 0.1 g/dL | Neg | 2.5 | Pos | 6.5 |
| Riboflavin | 7.5 mg/dL | Neg | 2.5 | Pos | 6.4 |
| Sodium Chloride | 6.0 g/dL | Neg | 2.5 | Pos | 6.6 |
| Urea | 6.0 g/dL | Neg | 2.4 | Pos | 6.2 |
| Sodium Azide | 1% w/v | Neg | 2.5 | Pos | 6.4 |
| Sodium Fluoride | 1% w/v | Neg | 2.5 | Pos | 6.1 |
| Galactose | 1.0 g/dL | Neg | 2.5 | Pos | 5.8 |

**Table 13. Interference – pH and Specific Gravity**

| Interferent Sample | -40% Control Response vs. Qual Cutoff (Pos/Neg) | -40% Control Mean (ng/mL) | +40% Control Response vs. Qual Cutoff (Pos/Neg) | +40% Control Mean (ng/mL) |
|---|---|---|---|---|
| pH 3 | Neg | 2.9 | Pos | 7.2 |
| pH 4 | Neg | 2.9 | Pos | 7.5 |
| pH 5 | Neg | 3.0 | Pos | 7.3 |
| pH 6 | Neg | 3.0 | Pos | 7.3 |
| pH 7 | Neg | 2.6 | Pos | 7.0 |
| pH 8 | Neg | 2.4 | Pos | 6.9 |
| pH 9 | Neg | 2.6 | Pos | 6.2 |
| pH 10 | Neg | 2.6 | Pos | 6.0 |
| pH 11 | Neg | 2.5 | Pos | 6.2 |
| sG 1.002 | Neg | 2.7 | Pos | 6.4 |
| sG 1.005 | Neg | 2.9 | Pos | 6.8 |
| sG 1.010 | Neg | 2.9 | Pos | 7.0 |
| sG 1.015 | Neg | 2.9 | Pos | 7.2 |
| sG 1.020 | Neg | 2.9 | Pos | 7.2 |
| sG1.025 | Neg | 3.0 | Pos | 7.2 |
| sG 1.030 | Neg | 2.6 | Pos | 7.0 |
| sG 1.035 | Neg | 2.5 | Pos | 6.9 |

## 9. Conclusion

Based on a comparison of the technological characteristic similarities and differences, the Emit® II Plus Buprenorphine Assay (K150606) and the Emit® II Plus Buprenorphine Assay have equivalent intended use and technology attributes. Performance studies were completed to demonstrate the performance of the proposed device to the predicate device were substantially equivalent. Through the accuracy comparison of both methods to the reference LC/MS/MS as well as performance studies of precision, recovery, and specificity, the substantial equivalence is supported.