

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

**A. 510(k) Number:**

k062094

**B. Purpose for Submission:**

New device

**C. Measurand:**

Phencyclidine (PCP)

**D. Type of Test:**

Qualitative and semi-quantitative enzyme immunoassay

**E. Applicant:**

Ortho-Clinical Diagnostics, Inc.

**F. Proprietary and Established Names:**

VITROS Chemistry Products PCP Reagent

VITROS Chemistry Products Calibrator 26

VITROS Chemistry Products FS Calibrator 1

VITROS Chemistry Products DAT Performance Verifiers I, II, III, IV and V

**G. Regulatory Information:**

1. Regulation section:

Unclassified, PCP test system

21 CFR 862.3200, Clinical Toxicology Calibrator

21 CFR 862.3180, Clinical Toxicology Control

2. Classification:

Reagent is unclassified, 510(k) required

II (calibrator)

I, reserved (control)

3. Product code:

LCM, DLJ and DIF

4. Panel:

Toxicology (91)

**H. Intended Use:**

1. Intended use(s):

See Indications for use.

2. Indication(s) for use:

**VITROS Chemistry Products PCP Reagent:** For *in vitro* diagnostic use only. VITROS Chemistry Products PCP Reagent is used on VITROS 5,1 FS Chemistry Systems for the semi-quantitative or qualitative determination of phencyclidine (PCP) in human urine using a cutoff of 25 ng/mL. Measurements obtained with the VITROS PCP method are used in the diagnosis and treatment of phencyclidine use or overdose.

The VITROS Chemistry Products PCP assay is intended for use by professional laboratory personnel. It provides only a preliminary test result. A more specific alternative chemical method must be used to confirm a result with this assay. Gas Chromatography/Mass Spectrometry(GC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug-of-abuse test result, particularly when evaluating a preliminary positive result.

**VITROS Chemistry Products Calibrator Kit 26:** For *in vitro* diagnostic use only. VITROS Chemistry Products Calibrator Kit 26 is used to calibrate VITROS 5,1 FS Chemistry Systems for the qualitative or semi-quantitative measurement of drugs of abuse.

**VITROS Chemistry Products FS Calibrator 1:** For *in vitro* diagnostic use only. VITROS Chemistry Products FS Calibrator 1 is used in conjunction with VITROS Chemistry Products Calibrator Kits to calibrate VITROS 5,1 FS Chemistry Systems

**VITROS Chemistry Products DAT Performance Verifiers I, II, III, IV & V:** For *in vitro* diagnostic use only. VITROS Chemistry Products DAT Performance Verifiers are assayed controls used to monitor performance of urine drugs of abuse screening assays on VITROS 5,1 FS Chemistry Systems.

3. Special conditions for use statement(s):

For use by professional laboratory personnel. For *in vitro* diagnostic use only.

4. Special instrument requirements:

Ortho-Clinical Diagnostics VITROS 5,1 FS Chemistry System

**I. Device Description:**

The VITROS Chemistry Products PCP Reagent is a dual chambered reagent pack containing two ready-to-use liquid reagents. The reactive ingredients in Reagent 1 include sheep polyclonal antibodies reactive to phencyclidine, Glucose 6-phosphate and Nicotinamide adenine nucleotide (NAD). The other ingredients in Reagent 1 include organic salt, proteins, inorganic polymer, protease inhibitor, surfactant and preservative. The reactive ingredients in Reagent 2 include phencyclidine labeled with glucose-6-phosphate dehydrogenase. The other ingredients in Reagent 2 include buffers, organic salt, inorganic salt, proteins, protease inhibitors, biological material, surfactant and preservatives.

VITROS Chemistry Products Calibrator Kit 26 is prepared from human urine to which drugs of abuse, metabolites of drugs of abuse, organic salts, surfactants and preservative have been added.

VITROS Chemistry Products FS Calibrator 1 is prepared from sodium chloride and processed water. These products are used to calibrate VITROS 5,1 FS Chemistry Systems for the qualitative and semi-quantitative measurement of phencyclidine (PCP).

VITROS DAT Performance Verifiers I, II, III, IV & V are prepared from a human urine pool to which analytes, surfactant and preservative have been added. These are assayed controls used to monitor performance of the VITROS PCP Reagent on VITROS 5,1 FS Chemistry Systems.

The product labeling for the Calibrator Kit 26 and Performance Verifiers contains warnings regarding the presence of human source materials and recommends the use of Universal Precautions when handling these products.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):  
Syva EMIT II Plus Phencyclidine assay  
Bio-Rad Liquicheck Urine Toxicology Controls
2. Predicate 510(k) number(s):  
k993983  
k022707
3. Comparison with predicate:

| Similarities |  |           |
|--------------|--|-----------|
| Item         | Device   | Predicate |
| Intended Use | For use in the qualitative and semi-quantitative analysis of phencyclidine in human urine. | Same      |

| <b>Similarities</b> |                                |           |
|---------------------|--------------------------------|-----------|
| Item                | Device                         | Predicate |
| Reagent             | Liquid, ready to use           | Same      |
| Principle           | Homogeneous enzyme immunoassay | Same      |
| Matrix              | Urine                          | Same      |
| Antibody            | Sheep polyclonal               | Same      |

| <b>Differences</b> |                                 |   |
|--------------------|---------------------------------|---|
| Item               | Device                          | Predicate   |
| Instrumentation    | VITROS 5,1 FS Chemistry Systems | Multiple automated clinical chemistry analyzers             |
| Calibrators        | Six levels                      | Qualitative: three levels<br>Semi-quantitative: five levels |
| Controls           | Three levels                    | Two levels  |

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

- CSLI EP9-A2: Method Comparison and Bias Estimation Using Patient Samples
- CLSI EP5-A: Evaluation of Precision Performance of Clinical Chemistry Devices
- CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures, A Statistical Approach
- CLSI EP7-P: Interference Testing in Clinical Chemistry
- CLSI EP17-A: Protocols for Demonstration, Verification and Evaluation of Limits of Detection and Quantitation
- CLSI EP12-A: User Protocols for Evaluation of Qualitative Test Performance

**L. Test Principle:**

The VITROS PCP assay is a homogenous immunoassay based on the competition between phencyclidine in the treated urine sample and phencyclidine labeled with the enzyme glucose-6-phosphate dehydrogenase (G6P-DH) for antibody binding sites. Enzyme activity decreases upon binding to the antibody, therefore the concentration of phencyclidine in the urine sample is directly proportional to measured enzyme activity. Active enzyme converts oxidized nicotinamide adenine dinucleotide (NAD<sup>+</sup>) to NADH, resulting in an absorbance change that is measured spectrophotometrically.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:
  - a. *Precision/Reproducibility:*

Precision was evaluated with quality control materials on the VITROS 5,1 FS Chemistry System following CLSI EP5-A. The samples were run in duplicate, twice a day for twenty-two days using two reagent lots and four instruments. The results are presented in the table below.

| <b>Semi-quantitative</b> |               |               |                |                  |          |
|--------------------------|---------------|---------------|----------------|------------------|----------|
| Mean Conc. ng/mL         | Within-Day SD | Within-Lab SD | Within-Lab %CV | No. Observations | No. Days |
| 18.3                     | 0.79          | 1.55          | 8.5            | 86               | 22       |
| 30.8                     | 1.02          | 1.66          | 5.4            | 86               | 22       |
| 63.3                     | 1.44          | 2.89          | 4.6            | 86               | 22       |

Qualitative imprecision was assessed using drug-spiked human urine pools with concentrations targeted at approximately  $\pm 25\%$  of the 25 ng/mL cutoff concentration. The concentrations of the targeted test fluids were confirmed by GC/MS. The sponsor performed one to two runs per day with two replicates per run for 22 days using a single lot of reagent on one analyzer. The results are presented below:

| <b>Qualitative</b> |                                |                        |                  |                        |                       |
|--------------------|--------------------------------|------------------------|------------------|------------------------|-----------------------|
| Cutoff ng/mL       | Test Fluid Concentration ng/mL | Test Fluid % of Cutoff | No. Observations | No. of Correct Results | Confidence Level      |
| 25                 | 18.3                           | -25% of the cutoff     | 86               | 86                     | >95% negative reading |
| 25                 | 30.8                           | +25% of the cutoff     | 86               | 86                     | >95% positive reading |

*b. Linearity/assay reportable range:*

The sponsor followed CLSI EP6-A in determining the linear range of their device. Two urine pools were prepared with phencyclidine concentrations at the low (0 ng/mL) and high (80 ng/mL) end of the calibration range. The two pools were mixed to give 13 admixtures of intermediate concentrations. Linearity was evaluated using three assay reagent lots and comparing the measured results against the expected results from 13 pooled samples. The concentration of these samples ranged from 0.5 to 81.8 ng/mL as determined by a reference method. A linear regression was performed and the results demonstrated a linear fit with an R-square value of 0.9972, a slope of 0.9998, and an intercept

of 0.0078. The range of the assay is 6.0 – 72.0 ng/mL.

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

The assigned values for the calibrators and controls are traceable to the Cerilliant PCP standard catalogue P-047 and are verified by GC/MS.

Real time and accelerated stability studies were conducted; protocols and acceptance criteria were described and found to be acceptable. These studies support the manufacturer’s stability claims for the following products:

| Reagent  | Storage                              | Stability*  |
|----------|--------------------------------------|-------------|
| Unopened | 2-8°C                                | 12 months   |
| Opened   | On board analyzer, system turned off | ≤14 days    |
| Opened   | On board analyzer, system turned on  | ≤30 minutes |

| Calibrator | Storage | Stability* |
|------------|---------|------------|
| Unopened   | ≤18°C   | 8 months   |
| Opened     | 2-8°C   | 4 weeks    |

| Controls | Storage | Stability* |
|----------|---------|------------|
| Unopened | 2-8°C   | 6 months   |
| Opened   | 2-8°C   | 4 weeks.   |

\*Note: Real time studies are ongoing.

d. *Detection limit:*

The detection limit was determined according to protocol recommendations in CLSI EP-17 on three different lots of reagent and one instrument platform. The claimed lower limit for VITROS PCP is 4.7 ng/mL.

e. *Analytical specificity:*

The sponsor conducted interference studies following CLSI EP7-A2. The substances listed in the table below were determined not to interfere in the PCP concentration tested at 25 ng/mL, up to the concentrations shown:

| Compound | Concentration Tested |            |
|----------|----------------------|------------|
|          | Conventional         | SI         |
| ammonia  | 570 mg/dL            | 334 µmol/L |

| Compound            | Concentration Tested |                   |
|---------------------|----------------------|-------------------|
|                     | Conventional         | SI                |
| ascorbic Acid       | 500 mg/dL            | 28.4 mmol/L       |
| Bilirubin           | 26 mg/dL             | 444.6 $\mu$ mol/L |
| Calcium             | 30 mg/dL             | 7.5 mmol/L        |
| ciprofloxacin       | 10 mg/dL             | 300.3 $\mu$ mol/L |
| citric acid         | 100 mg/dL            | 5.2 mmol/L        |
| Cloxacillin         | 10 mg/dL             | 229.4 $\mu$ mol/L |
| creatinine          | 300 mg/dL            | 26.5 mmol/L       |
| ethacrylnic acid    | 10 mg/dL             | 329.9 $\mu$ mol/L |
| Ethanol             | 780 mg/dL            | 169.3 mmol/L      |
| Glucose             | 4000 mg/dL           | 222 mmol/L        |
| Hemoglobin          | 500 mg/dL            | 5 g/L             |
| Human IgG           | 200 mg/dL            | 2 g/L             |
| Human serum albumin | 200 mg/dL            | 2 g/L             |
| Indomethacin        | 10 mg/dL             | 280 $\mu$ mol/L   |
| Iron                | 0.1 mg/dL            | 18 $\mu$ mol/L    |
| KCl                 | 1118 mg/dL           | 150 mmol/L        |

| Compound          | Concentration Tested |                 |
|-------------------|----------------------|-----------------|
|                   | Conventional         | SI              |
|                   |                      |                 |
| Magnesium         | 60 mg/dL             | 24.7 mmol/L     |
| Methoxyphenamine  | 10 mg/dL             | 558 $\mu$ mol/L |
| Metronidazole     | 10 mg/dL             | 584 $\mu$ mol/L |
| NaCl              | 1500 mg/dL           | 1027 mmol/L     |
| Nylidrin HCl      | 10 mg/dL             | 334 $\mu$ mol/L |
| Oxalic acid       | 300 mg/dL            | 24 mmol/L       |
| pH = 4            |                      |                 |
| pH = 9            |                      |                 |
| Phenylbutazone    | 10 mg/dL             | 324 $\mu$ mol/L |
| Phosphate         | 1420 mg/dL           | 100 mmol/L      |
| Propanolol        | 10 mg/dL             | 386 $\mu$ mol/L |
| Pyruvate          | 100 mg/dL            | 11 mmol/L       |
| Ranitidine HCl    | 10 mg/dL             | 285 $\mu$ mol/L |
| Riboflavin        | 2 mg/dL              | 53 $\mu$ mol/L  |
| Tolmetin/tolectin | 10 mg/dL             | 389 $\mu$ mol/L |
| Trihexylphenidyl  | 10 mg/dL             | 296 $\mu$ mol/L |
| Trimethobenzamide | 10 mg/dL             | 257 $\mu$ mol/L |
| Tyramine          | 10 mg/dL             | 576 $\mu$ mol/L |
| Urea              | 3000 mg/dL           | 500 mmol/L      |
| Uric acid         | 120 mg/dL            | 7 mmol/L        |

The sponsor determined that a high specific gravity does not interfere with the assay by evaluating the primary causes of high specific gravity: high concentrations of NaCl, protein and glucose in urine.

The specificity of VITROS PCP assay for phencyclidine and structurally similar compounds was determined by generating a dose response curve for each of the compounds and determining the approximate quantity of each compound that is equivalent in assay reactivity to the PCP 25 ng/mL cutoff.

| Compound                                      | Quantity equivalent to 25 ng/mL | Approx. % Cross-reactivity |
|---|---------------------------------|----------------------------|
| 1-[1-(2-thienyl)-cyclohexyl] piperidine (TCP) | 24                              | 104                        |
| Phencyclidine                                 | 25                              | 100                        |
| 1-(1-phenylcyclohexyl) morpholine (PCM)       | 30                              | 83                         |
| 1-(1-phenylcyclohexyl) morpholine (PCPy)      | 30                              | 83                         |
| 1-(1-phenylcyclohexyl) pyrrolidine (TCPy)     | 42                              | 60                         |
| N,N diethyl-1-phenylcyclohexylamine (PCDE)    | 95                              | 26                         |
| Mesoridazine                                  | 18000                           | 0.1                        |

*f. Assay cut-off:*

The identified cutoff (25 ng/mL PCP) is recommended by the Substance Abuse and Mental Health Services Administration.

2. Comparison studies:

*a. Method comparison with predicate device:*

One hundred and thirty eight unaltered human urine samples were assayed on the device and the results were compared to the predicate and GC/MS. The results are presented in the tables below:

Comparison of VITROS PCP to Predicate device

| Cutoff   |          | <50%        | -50% to cutoff | Cutoff to +50% | >+50%       | % Agreement | % Agreement | % Agreement |
|----------|----------|-------------|----------------|----------------|-------------|-------------|-------------|-------------|
|          |          | <12.5 ng/mL | 12.5-25 ng/mL  | 25-37.5 ng/mL  | >37.5 ng/mL | Negative    | Positive    | Overall     |
| 25 ng/mL | VITROS + | 0           | 0              | 10             | 62          | 100         | 98.6        | 99.3        |
|          | VITROS - | 54          | 11             | 1*             | 0           |             |             |             |

\*Summary of Discordant Results

| Cutoff   | VITROS PCP | Predicate |
|----------|------------|-----------|
| 25 ng/mL | 24.5       | 25.2      |

Comparison of VITROS PCP to GC/MS

| Cutoff   |          | <50%<br><12.5 ng/mL | -50% to cutoff<br>12.5-25 ng/mL | Cutoff to +50%<br>25-37.5 ng/mL | >+50%<br>>37.5 ng/mL | % Agreement<br>Negative | % Agreement<br>Positive | % Agreement<br>Overall |
|----------|----------|---------------------|---------------------------------|---------------------------------|----------------------|-------------------------|-------------------------|------------------------|
| 25 ng/mL | VITROS + | 0                   | 5*                              | 12                              | 55                   | 92.8                    | 97.1                    | 94.9                   |
|          | VITROS - | 56                  | 8                               | 2*                              | 0                    |                         |                         |                        |

\*Summary of Discordant Results

| Cutoff   | VITROS PCP | GC/MS | Major Drug Present |
|----------|------------|-------|--------------------|
| 25 ng/mL | 24.5       | 25    | PCP                |
|          | 24.5       | 36.6  |                    |
|          | 29         | 23    |                    |
|          | 29.4       | 23    |                    |
|          | 29.9       | 23    |                    |
|          | 36.3       | 22    |                    |
|          | 40.5       | 24    |                    |

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.