

# Cross-reacts with all major metabolites

## CEDIA Buprenorphine II Assay

### Qualitative / Semi-Quantitative Detection of Buprenorphine and its Metabolites

Buprenorphine is a long-acting (24-72 hours) opioid that is used for the treatment of pain and narcotic addiction (Suboxone®, Subutex®)<sup>1</sup>. It is classified as a Schedule III drug by the United Nations Convention of Psychotropic Substances of 1971, which requires all countries to place it under control.<sup>2</sup> By comparison, methadone is classified in different countries as either Schedule I or II, which places more restrictions on its control, distribution and use.

Buprenorphine is considered a more practical, and in some cases effective alternative to methadone in the treatment of opioid addiction, as it can be prescribed on an outpatient basis rather than in methadone clinics. In addition, because buprenorphine only partially activates the opioid receptors, it produces a milder effect than other opiates such as heroin or methadone.<sup>2</sup>

Since the Thermo Scientific™ CEDIA® Buprenorphine II Assay does not cross-react with morphine even at 100,000 ng/mL, the assay is suitable for testing the urine samples from patients on Slow Releasing Oral Morphine (SROM) (tradename Substilo®). The assay can accurately differentiate buprenorphine treatment samples from SROM treatment samples.<sup>3, 4</sup>

***The CEDIA Buprenorphine II Assay is the only assay currently available on the market which cross-reacts with all three major metabolites: buprenorphine-glucuronide, norbuprenorphine, norbuprenorphine-glucuronide. With this cross-reactivity and an LC-MS/MS concordance of 99%, the set cutoff of 10 ng/mL is considered comparable to a 5 ng/mL cutoff established for other on-market assays.<sup>5</sup>***



### Benefits of Using the Thermo Scientific™ CEDIA Buprenorphine II Assay

- Specifically detects Buprenorphine
- Cross-reacts with all major metabolites: buprenorphine-glucuronide, norbuprenorphine and norbuprenorphine-glucuronide
- No significant cross-reactivity to other opioids
- Applications available on a wide range of clinical analyzers
- Qualitative and semi-quantitative detection

## Specificity

The cross-reactivity of Buprenorphine and its metabolites was evaluated by adding known amounts of each analyte to drug-free urine. As indicated by the results in the table below, Buprenorphine, Norbuprenorphine and Norbuprenorphine-glucuronide exhibited  $\geq 100\%$  cross-reactivity. Buprenorphine-glucuronide demonstrated less cross-reactivity.

Buprenorphine and its metabolites	Tested Concentration (ng/mL)	Cross-reactivity (%)
Buprenorphine	10	100%
Norbuprenorphine	8	125%
Buprenorphine- $\beta$ -D-glucuronide	13	76.9%
Norbuprenorphine- $\beta$ -D-glucuronide	10	100%

## Accuracy

The parent compound, Buprenorphine, is rapidly metabolized and as such, the majority of detected analytes in the urine are its three major metabolites: norbuprenorphine, buprenorphine-glucuronide, and norbuprenorphine-glucuronide.<sup>5,6</sup>

The CEDIA Buprenorphine II assay was designed to detect buprenorphine and these three major metabolites. When compared with LC-MS/MS, the CEDIA Buprenorphine II Assay has an overall agreement of 63.4% when only Buprenorphine is included in the analysis and the metabolites are excluded. On the other hand, when the CEDIA Buprenorphine II assay is compared with LC-MS/MS for Buprenorphine and its three metabolites, the overall agreement is 100%.<sup>4</sup>

## Precision

Samples were prepared by spiking buprenorphine into drug-free urine at the cutoff (10 ng/mL) and 25%, 50%, 75% & 100% above and below the cutoff for an n=80 at each level. Results presented below were generated by testing all samples in the qualitative and semi-quantitative mode with replicates of 2, twice per day for 20 days (n=80 samples/level).<sup>4</sup>

Levels Tested (n=80 for each level)	Qualitative	Semi-quantitative
Below the cutoff (-25%, -50%, -75%, -100%)	All negative	All below cutoff
Above the cutoff (25%, 50%, 75%, 100%)	All positive	All above the cutoff
At the cutoff (10 ng/mL)	27 negative / 53 positive	35 negative / 45 positive

## Ordering

Part Number	Description	Size
<b>Reagents</b>		
10020849	CEDIA Buprenorphine II Assay	3 x 17 mL
10020850	CEDIA Buprenorphine II Assay	65 mL
<b>Calibrators</b>		
10021390	CEDIA Negative Calibrator II	1 x 7.5 mL
10020799	CEDIA Buprenorphine II Calibrator 10 ng/mL	1 x 5 mL
10020800	CEDIA Buprenorphine II Calibrator 20 ng/mL	1 x 5 mL
10020801	CEDIA Buprenorphine II Calibrator 50 ng/mL	1 x 5 mL
10020802	CEDIA Buprenorphine II Calibrator 100 ng/mL	1 x 5 mL
<b>Controls</b>		
10020804	CEDIA Buprenorphine II Low (7.5 ng/mL) and High (12.5 ng/mL) Controls	2 x 5 mL each

## References

1. US Department of Justice, Drug Enforcement Administration, Buprenorphine, [https://www.deadiversion.usdoj.gov/drug\\_chem\\_info/buprenorphine.pdf](https://www.deadiversion.usdoj.gov/drug_chem_info/buprenorphine.pdf) (accessed December 19, 2016).
2. The European Monitoring Centre for Drugs and Drug Addiction, Annual Report 2005, pg 35.
3. Beck, T, Haasen, C, Verthein, U, Walcher, S, Schuler, C, Backmund, J, Ruckes C, and Reimer, J. Maintenance treatment of opioid dependence with slow-release oral morphine: a randomized cross-over, non-inferiority study versus methadone. *Addiction* 2013, 109, 617-626.
4. CEDIA Buprenorphine II Assay package insert.
5. Pitterl, F, Saxl, B, Anne, L, and Pavlic, M. Comparison of CEDIA Buprenorphine II Assay vs on Market CEDIA Buprenorphine Assay in Human Urine. The International Association of Forensic Toxicologists (TIAFT), 2016, Brisbane, Australia.
6. Kacinko, SL, Jones, HE, Johnson, RE, Choo, RE, Concheiro-Guissan, J, and Huestis, MA. Urinary Excretion of Buprenorphine, Norbuprenorphine, Buprenorphine-Glucuronide, and Norbuprenorphine-Glucuronide in Pregnant Women Receiving Buprenorphine Maintenance Treatment. *Clin Chem*. 2009 June; 55(6): 1177-1187.
7. McMillin, GA, Davis, R, Carlisle, H, Clark, C, Marlin, SJ, and Moody DE. Patterns of Free (Unconjugated) Buprenorphine, Norbuprenorphine, and Their Glucuronides in Urine Using Liquid Chromatography – Tandem Mass Spectrometry. *Journal of Analytical Toxicology* 2012;36:81-87.

---

### Diagnostics

#### USA

46500 Kato Road  
Fremont, CA 94538 USA  
Tel. 800-232-3342 / + 1 510-979-5000  
[sales.diagnostics.fmt@thermofisher.com](mailto:sales.diagnostics.fmt@thermofisher.com)

#### Asia Pacific

Fax: +65 6896 2147  
[cdd.asia.info2@thermofisher.com](mailto:cdd.asia.info2@thermofisher.com)

#### Australia

Tel. + 61 1800 333 110  
[auiinfo@thermofisher.com](mailto:auiinfo@thermofisher.com)

#### Belgium Netherlands & Luxembourg

Tel. + 31 76 579 5555  
[info.belux.cdd@thermofisher.com](mailto:info.belux.cdd@thermofisher.com)

#### Canada

Tel. 905-286-4290  
[CDD.Canada@thermofisher.com](mailto:CDD.Canada@thermofisher.com)

#### China

Tel. + 86 800 810 5118  
[sales.china@thermofisher.com](mailto:sales.china@thermofisher.com)

#### France

Tel. + 33 (0) 1 40 86 65 00  
[cdx.fr.info@thermofisher.com](mailto:cdx.fr.info@thermofisher.com)

#### Germany

Tel. + 49 (0) 851 886 890  
[cdx.de.info@thermofisher.com](mailto:cdx.de.info@thermofisher.com)

#### Hong Kong

Tel. + 852 28854613  
[sales.hk@thermofisher.com](mailto:sales.hk@thermofisher.com)

#### Japan

Tel. + 81 (0)120-147-075  
[JPYOK-CDD.QC@thermofisher.com](mailto:JPYOK-CDD.QC@thermofisher.com)

#### New Zealand

Tel. + 61 0800933 966  
[nzinfo@thermofisher.co.nz](mailto:nzinfo@thermofisher.co.nz)

#### Nordic

Tel. + 46 8 594 691 30  
[info.nordic.cdd@thermofisher.com](mailto:info.nordic.cdd@thermofisher.com)

#### Russia

Tel. + 7 495 739 76 41  
[info.btd.moscow@thermofisher.com](mailto:info.btd.moscow@thermofisher.com)

#### Spain, Portugal & Italy

Tel. + 34 93589 8338  
[cdx.es.info@thermofisher.com](mailto:cdx.es.info@thermofisher.com)

#### Switzerland & Austria

Tel. + 41 26 663 86 70  
[cdx.ch.info@thermofisher.com](mailto:cdx.ch.info@thermofisher.com)

#### United Kingdom & Ireland

Tel. + 44 1442 868 940  
[cdx.UK.info@thermofisher.com](mailto:cdx.UK.info@thermofisher.com)

#### For Countries Not Listed

[distributor.cdd@thermofisher.com](mailto:distributor.cdd@thermofisher.com)

Find out more at [thermofisher.com/diagnostics](http://thermofisher.com/diagnostics)