DRI® Oxycodone Assay for Beckman Coulter* SYNCHRON* and UniCel* Systems

Thermo SCIENTIFIC

IVD **For In Vitro Diagnostic Use**

Rx Only

REF 10012653

Intended Use

The DRI® Oxycodone Assay for SYNCHRON Systems is intended for the qualitative and semi-quantitative determination of oxycodone and its metabolite, oxymorphone, in human urine at a cutoff of 300 ng/mL. The assay provides a simple and rapid analytical screening procedure to detect oxycodone and oxymorphone in human urine.

This assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. 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 preliminary results are used.

Summary and Explanation of the Test

Oxycodone is a semi-synthetic opioid prescribed for pain management in patients with moderate to severe pain. It is similar to codeine and morphine in its analgesic properties but it is more potent than morphine and has higher dependence potential. The drug oxycodone is supplied as OxyContin® (Oxycodone HCl) or in combination with aspirin (Percodan®) or acetaminophen (Percocet®).[1] Drug abusers crush the pills into powder and snort them for faster effect which may result in a potentially fatal outcome. According to Drug Abuse Warning Network (DAWN), there has been a dramatic increase in oxycodone related deaths.[2,3] Oxymorphone, noroxycodone and noroxymorphone are the only known metabolites of oxycodone.[2] The metabolite, oxymorphone, is a potent narcotic analgesic, while the other two metabolites are relatively inactive. From 33-61% of a single dose of oxycodone is excreted in urine within 24 hours as unconjugated oxycodone (13-19%), conjugated oxycodone (7-29%), and conjugated oxymorphone (13-14%).[4]

The DRI Oxycodone Assay for SYNCHRON Systems is supplied as a liquid ready-to-use homogeneous enzyme immunoassay. The assay uses specific antibodies that can detect oxycodone and oxymorphone without any significant cross-reactivity to other opiate compounds. The assay is based on competition between a drug labeled with glucose-6-phosphate dehydrogenase (G6PDH), and free drug from the urine sample for a fixed amount of specific antibody binding sites. In the absence of free drug from the sample, the specific antibody binds the drug labeled with G6PDH and causes a decrease in enzyme activity. This phenomenon creates a direct relationship between the drug concentration in urine and enzyme activity. The enzyme activity is determined spectrophotometrically at 340 nm by measuring the conversion of nicotinamide adenine dinucleotide (NAD) to NADH.

Reagents

Antibody/Substrate Reagent: Contains mouse monoclonal anti-oxycodone derivative antibody, glucose-6-phosphate (G6P), and nicotinamide adenine dinucleotide (NAD) in Tris buffer with sodium azide as a preservative.

Enzyme Conjugate Reagent: Contains oxycodone derivative labeled with glucose-6-phosphate
dehydrogenase (G6PDH) in Tris buffer with sodium azide as a preservative.

Additional Materials Required (sold separately):

Catalog No.: A44121 DRI Negative Calibrator, 10 mL
A53734 DRI Oxycodone Calibrator 100, 10 mL
A53738 DRI Oxycodone Calibrator 300, 10 mL
A53733 DRI Oxycodone Calibrator 500, 10 mL
A53736 DRI Oxycodone Calibrator 1000, 10 mL
A53731 DRI Oxycodone Control Kit 300, 2 x 10 mL

⚠ Precautions and Warnings

DANGER: DRI Oxycodone Assay for SYNCHRON Systems contains ≤0.2% bovine serum albumin (BSA) and ≤0.5% drug-specific antibody.
H317 - May cause allergic skin reaction.
H334 - May cause allergy or asthma symptoms or breathing difficulties if inhaled.

Avoid breathing mist or vapor. Contaminated work clothing should not be allowed out of the workplace. Wear protective gloves/eye protection/face protection. In case of inadequate ventilation wear respiratory protection. If on skin: Wash with plenty of soap and water. IF INHALED: If breathing is difficult, remove victim to fresh air and keep at rest in a position comfortable for breathing. If skin irritation or rash occurs: Get medical advice/attention. If experiencing respiratory symptoms: Call a POISON CENTER or doctor/physician. Wash contaminated clothing before reuse. Dispose of contents/container to location in accordance with local/regional/national/international regulations.

1. This test is for in-vitro diagnostic use only. The reagents are harmful if swallowed.
2. Reagents used in the assay components contain sodium azide, which may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of such reagents, always flush with a large volume of water to prevent azide build-up.
3. Do not use the reagents beyond their expiration dates.

Reagent Preparation and Storage

The reagents are ready-to-use. No additional reagent preparation is required. The reagents should be stored refrigerated (2-8°C). All assay components, opened or unopened, are stable until the expiration date indicated on their respective labels. Do not use the reagents beyond their expiration dates.

Specimen Collection and Handling

Collect urine specimens in plastic or glass containers. Testing of fresh urine specimens is suggested.

The Mandatory Guidelines for Federal Workplace Drug Testing Programs; Final Guidelines recommend that specimens that do not receive an initial test within 7 days of arrival in the laboratory should be placed into secure refrigeration units.

Samples within a pH range of 3 to 11 are suitable for testing with this assay.

An effort should be made to keep pipetted samples free of gross debris. Centrifuge highly turbid specimens before analysis. Adulteration of the urine sample may cause erroneous results. If adulteration is suspected, obtain another sample and forward both specimens to the laboratory for testing.

Handle all urine specimens as if they were potentially infectious.

Assay Procedure

Before performing the assay, refer to the instrument specific application sheet available from Thermo Fisher Scientific at http://www.thermo.com/BCI_Applications.

Quality Control and Calibration

Good laboratory practice suggests the use of control specimens to ensure proper assay performance. Use controls near the cutoff calibrator to validate the calibration. Control results must fall within established ranges, as determined by laboratory procedures and guidelines. If results fall outside of established ranges, assay results are invalid. All quality control requirements should be performed in conformance with local, state and/or federal regulations or accreditation requirements. Each laboratory should establish its own control frequency.

Qualitative analysis

For qualitative analysis of samples, use the Oxycodone 300 calibrator as a cutoff level.

Semi-quantitative analysis

For semiquantitative analysis, use all calibrators.

Results and Expected Values

Qualitative

The 300 calibrator can be used as a cutoff reference for distinguishing "positive" from "negative" samples. A sample that exhibits a change in absorbance (ΔA) value equal to or greater than the value obtained with the cutoff calibrator is considered positive. A sample that exhibits a change in absorbance (ΔA) value lower than the value obtained with the cutoff calibrator is considered negative.

Semi-quantitative

A rough estimate of drug concentration in the samples can be obtained by running a standard curve with all calibrators and quantitating samples off the standard curve. Sample results above the high
calibrator should be diluted with negative urine and retested.

Limitations

1. A positive result from this assay indicates only the presence of oxycodone or oxymorphone and does not necessarily correlate with the extent of physiological and psychological effects.
2. Care should be taken when reporting concentration results since there are many factors, e.g., fluid intake and other biologic factors, that may influence a urine test result.
3. It is possible that substances other than those investigated in the specificity study may interfere with the test and cause false results.

Specific Performance Characteristics

Typical performance data results obtained on the UniCel DxC analyzer are shown below. The results obtained in your laboratory may differ from these data. For additional analyzer specific performance data, refer to the analyzer specific application sheet.

Precision

The DRI Oxycodone Controls (225 and 375 ng/mL) and cutoff calibrator (300 ng/mL) were tested in qualitative (mA/min) and semi-quantitative (ng/mL) mode using a modified NCCLS protocol. Results presented below were generated by testing all samples in replicates of 6, twice per day for 10 days on the UniCel DxC.

Qualitative (mA/min)

Calibrator/Control	300 ng/mL Cutoff				
n=120	Mean	Within-run Precision		Total Precision	
		SD	%CV	SD	%CV
225 ng/mL	410.3	2.1	0.5	4.5	1.1
300 ng/mL	440.2	2.1	0.5	5.2	1.2
375 ng/mL	471.2	2.1	0.4	5.0	1.1

Semi-quantitative (ng/mL)

Calibrator/Control	300 ng/mL Cutoff				
n=120	Mean	Within-run Precision		Total Precision	
		SD	%CV	SD	%CV
225 ng/mL	227.2	4.3	1.9	7.6	3.4
300 ng/mL	293.2	5.1	1.7	9.9	3.4
375 ng/mL	377.9	7.8	2.1	14.3	3.8

Cutoff Characterization

Oxycodone samples around the cutoff were prepared by the addition of oxycodone stock solution to negative urine. The samples were targeted at the following control concentrations, 225 ng/mL and 375 ng/mL (± 25% of the 300 ng/mL cutoff). The samples were assayed in replicates of 21. Cutoff characterization was deemed acceptable if the observed oxycodone concentration for 95% of the 21 replicates was appropriately greater or lesser than the cutoff calibrator concentration. For all 21 replicates, the 225 ng/mL samples assayed correctly, as less than their respective cutoff calibrators 100 % of the time. The 375 ng/mL samples assayed as greater than their respective cutoff calibrators 100 % of the time.

Accuracy

One hundred and forty-nine samples were analyzed by the DRI Oxycodone Assay for SYNCHRON Systems on the UniCel DxC in both the qualitative and semi-quantitative modes. The results were compared to the DRI Oxycodone Assay on the Hitachi 717 and to GC/MS.

Qualitative: The overall concordance between the DRI Oxycodone Assay for SYNCHRON Systems and the DRI Oxycodone Assay for the Hitachi 717 was 98.7%. The overall concordance between the DRI Oxycodone Assay for SYNCHRON Systems and GC/MS was 95.3%. The samples noted as discrepant were less than 12 mA/min from the cut-off.

		DRI Oxycodone Hitachi 717 -	DRI Oxycodone Hitachi 717 +
DRI Oxycodone for SYNCHRON Systems on UniCel DxC	-	80	1
	+	1	67

		GC/MS -	GC/MS +
DRI Oxycodone for SYNCHRON Systems on UniCel DxC	-	78	3
	+	4	64

Semi-quantitative: The overall concordance between the DRI Oxycodone Assay for SYNCHRON Systems and the DRI Oxycodone Assay for the Hitachi 717 was 94.0%. The 9 discrepant samples which were positive in the DRI Oxycodone Assay for SYNCHRON Systems were confirmed to be positive by GC/MS. The overall concordance between the DRI Oxycodone Assay for SYNCHRON Systems and GC/MS was 97.3%.

		DRI Oxycodone Hitachi 717 -	DRI Oxycodone Hitachi 717 +
DRI Oxycodone for SYNCHRON Systems on UniCel DxC	-	78	0
	+	9†	62

		GC/MS -	GC/MS +
DRI Oxycodone for SYNCHRON Systems on UniCel DxC	-	78	0
	+	4‡	67

† Oxycodone concentrations measured 301-332 ng/mL.
‡ Oxycodone concentrations measured 270-299 ng/mL.

Specificity

The cross-reactivity of oxycodone metabolites, oxymorphone, noroxymorphone and noroxycodone, was evaluated by adding known amounts of each metabolite to oxycodone free urine. As indicated by the results in the table below, oxymorphone exhibits 106% cross reactivity with oxycodone; noroxymorphone and noroxycodone show no evidence of significant cross-reactivity.

Compound	Concentration Tested (ng/mL)	Recovery (ng/mL)	% Cross-reactivity
Oxycodone	300	300	100
Oxymorphone	300	318.2	106
Noroxymorphone	500,000	385	0.1
Noroxycodone	50,000	120	0.2

The potential cross-reactivity posed by drugs commonly coadministered with oxycodone was evaluated by adding each substance to oxycodone free urine at the concentration indicated. A drug was considered to cross-react if the observed oxycodone concentration exceeded 300 ng/mL. As shown in the tables below, all of the pharmacologic compounds evaluated, including a number of the opiate compounds, exhibited no cross-reactivity at the concentrations listed.

Structurally related opiate compounds that tested negative at 300 ng/mL cutoff

Compound	Concentrations (µg/mL)
6-Acetyl Morphine	50
Codeine	500
Dihydrocodeine	100
Heroin	300
Hydrocodone	75
Hydromorphone	30
Levorphanol	200
Morphine	350
Morphine-3-glucuronide	900
Naloxone	200
Naltrexone	500
Norcodeine	1000
Normorphine	1000

Structurally unrelated compounds that tested negative at 300 ng/mL cutoff

Compound	Concentrations (µg/mL)
Acetaminophen	1000
Acetylsalicylic acid	1000
Amitriptyline	500
Amoxicillin	500
Amphetamine	2000
Benzoylecgonine	2000
Caffeine	1000
Carbamazepine	1000
Chlorpromazine	2000
Clomipramine	1000
Cimetidine	1000
Desipramine	1000
Dextromethorphan	200
Doxepine	200
Ephedrine	2000
Fentanyl	200
Fluoxetine	1000
Fluphenazine	500
Ibuprofen	1000
Imipramine	1000
Maprotiline	1000
Meperidine	1000
Methadone	1000
Metroniazole	2000
Nalbuphine	1000
Nortriptyline	500
Oxazepam	500
Phencyclidine	1000
Phenobarbital	1000
Ranitidine	3000
Secobarbital	1000
Talwin	500
Thebaine	20
Thioridazine	1000
Tramadol	500

Interference
The potential interference of pH and endogenous physiologic substances on recovery of oxycodone using the DRI Oxycodone Assay for SYNCHRON Systems was assessed by spiking known amounts of potentially interfering substances into the low (225 ng/mL) and high (375 ng/mL) controls for the 300 ng/mL cutoff. No interference was observed by the addition of the compounds up to the concentrations listed below.

Compound	Concentrations (mg/dL)
Acetone	1000
Ascorbic Acid	1500
Creatinine	500
Ethanol	1000
Galactose	10
Glucose	3000
Hemoglobin	300
Human Serum Albumin	500
Oxalic Acid	100
Riboflavin	7.5
Sodium chloride	1000
Urea	2000
	Range
pH	3-11

Sensitivity
The sensitivity of the assay using the negative calibrator is 6.1 ng/mL.

References

1. Anderson D.T., Fritz K.L., and Muto J.J. OxyContin®: The concept of a "Ghost Pill" and the Postmortem Tissue Distribution of Oxycodone in 36 Cases. J. Anal. Toxicol. 2002, **26:** 448-459.
2. Clinical & Forensic Toxicology News, Oxycodone: Recognition and Pharmacogenomics. By Jannetto P.J. and Gock S.B. March 2003.
3. Cone E.J., etal, Oxycone Involvement in Drug Abuse Deaths: A DAWN-Based Classification Scheme applied to an Oxycodone Postmortem Database Containing over 1000 Cases. J. Anal. Toxicol. 2003, **27:** 57-67.
4. Oxycodone. In: Baselt R.C. and Cravey R.H. Disposition of toxic druds and chemicals in man, 4th ed. Chemical Toxicology Institute, Foster City, California: 1995: 572-574.

Glossary:
http://www.thermofisher.com/symbols-glossary

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