

Lab Updates

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February 2012

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UMassMemorial

Laboratories

Urine Drug Testing

Screening Immunoassays

The clinical toxicology laboratory of UMass Memorial Laboratories offers several screening and confirmatory tests for drugs of abuse, therapeutic and over the counter drugs in urine. Screening tests are typically immunoassay based and are usually the initial test performed. They are sensitive but not specific, detecting a drug class rather than identifying a particular drug. These tests are offered for many drugs, as individual drug/drug classes or as a panel for drugs of abuse, with the mnemonic DOA [Refer to Table I].

Table I.

Mnemonic	Drugs in Panel	Target	Cutoff concentration (ng/mL)
DOA4	Barbiturates	Secobarbital	200
	Cannabinoids	Carboxy-THC	50
	Cocaine metabolite	Benzoyllecgonine	300
	Opiates	Morphine	300
DOA5	Amphetamines	d-Methamphetamine	1000
	Cannabinoids	Carboxy-THC	50
	Cocaine metabolite	Benzoyllecgonine	300
	Opiates	Morphine	300
	Phencyclidine	Phencyclidine	25
DOA7	Amphetamines	d-Methamphetamine	1000
	Benzodiazepines	Oxazepam	200
	Barbiturates	Secobarbital	200
	Cannabinoids	Carboxy-THC	50
	Cocaine metabolite	Benzoyllecgonine	300
	Opiates	Morphine	300
	Phencyclidine	Phencyclidine	25
DOA9	Amphetamines	d-Methamphetamine	1000
	Benzodiazepines	Oxazepam	200
	Barbiturates	Secobarbital	200
	Cannabinoids	Carboxy-THC	50
	Cocaine metabolite	Benzoyllecgonine	300
	Opiates	Morphine	300
	Phencyclidine	Phencyclidine	25
	Methadone	Methadone	300
	Propoxyphene	Propoxyphene	300

Mnemonic	Drugs in Panel	Target	Cutoff concentration (ng/mL)	
DOA10	Amphetamines	d-Methamphetamine	1000	
	Benzodiazepines	Oxazepam	200	
	Barbiturates	Secobarbital	200	
	Cannabinoids	Carboxy-THC	50	
	Cocaine metabolite	Benzoyllecgonine	300	
	Opiates	Morphine	300	
	Phencyclidine	Phencyclidine	25	
	Methadone	Methadone	300	
	Propoxyphene	Propoxyphene	300	
	Alcohol	Alcohol/Ethanol	20 mg/dL	
	DOA12	Amphetamines	d-Methamphetamine	1000
		Benzodiazepines	Oxazepam	200
Barbiturates		Secobarbital	200	
Cannabinoids		Carboxy-THC	50	
Cocaine metabolite		Benzoyllecgonine	300	
Opiates		Morphine	300	
Phencyclidine		Phencyclidine	25	
Methadone		Methadone	300	
Propoxyphene		Propoxyphene	300	
Alcohol		Alcohol/Ethanol	20 mg/dL	
LSD		LSD	0.5	
LSM		Methaqualone	300	
UBUP	Buprenorphine	Buprenorphine	20	
UOXY	Oxycodone	Oxycodone	100	
UHERMTB	6-Acetylmorphine	6-Acetylmorphine	10	
MAHAQUR	Methaqualone	Methaqualone	300	
UMDMA	Ecstasy/MDMA	MDMA	500	
LSU5	LSD	LSD	0.5	

These drug tests are offered as qualitative screens, providing negative or presumptive positive results. The positive results are known as “presumptive” since the result indicates the likelihood or probability of the drug/drug class being present in the sample, as distinct from direct evidence or positive proof, which requires confirmation testing. The immunoassay testing is conducted utilizing EMIT® technology. The system can be utilized for routine or STAT samples.

Enzyme-multiplied immunoassay technique [EMIT] assays are based on competition between drug in the urine specimen and drug labeled



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with an enzyme, such as 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. The change in absorbance is directly related to the concentration of drug in the urine specimen. Endogenous serum G6PDH does not interfere because the coenzyme NAD functions only with the bacterial (*Leuconostoc mesenteroides*) enzyme employed in this assay.

The specificity of these tests for the drug of interest varies by vendor. It may also vary by specific lots as vendors change antibodies and other components within the reagent kits. The following are therefore, general guidelines. Each test has a target drug [see Table I], the antigen, which is present as a calibrator at a specific concentration. This is known as the cutoff concentration [see Table I] and is the concentration of analyte below which all measured values are considered negative. For example, in the DOA panel the opiate test targets morphine with a cutoff concentration of 300 ng/mL. Since morphine is the target analyte, the test will produce a presumptive positive response for drugs with similar chemical structures to morphine such as codeine and heroin. The test demonstrates less affinity/cross reactivity for drugs with dissimilar structures even though they may be classed as opiates/opioids. Therefore, the opiate assay in this panel WILL NOT detect opioids such as oxycodone or oxymorphone until the urine concentrations are significant [10,500 and 37,000 ng/mL, respectively]. This assay should also not be utilized for the detection of methadone, meperidine, levorphanol, hydromorphone, fentanyl, buprenorphine, propoxyphene and tramadol. Table II shows the percent cross reactivity of several common opioids with the opiate assay currently in use. Since the target drug is morphine, it demonstrates 100% cross reactivity. Drugs with low cross reactivity are less likely to be detected by this assay.

Table II.

Compound	% cross reactivity at 300 ng/mL*
Morphine	100
6-Acetylmorphine	107
Codeine	200
Hydrocodone	46
Hydromorphone	21
Morphine 3-glucuronide	88
Oxycodone	3
Oxymorphone	<1
Fentanyl	<1
Methadone	<1
Meperidine	1.5
Naloxone	<1
Tramadol	<1

*Package insert 0140-4, 2008 05.

Another component, available in DOA panels 7 and higher, the benzodiazepine test, targets oxazepam, a common metabolite of several benzodiazepines, with a cutoff of 200 ng/mL. This drug class is highly metabolized and as Table III illustrates, this test demonstrates low cross reactivity with drugs which do not metabolize through oxazepam, such as lorazepam.

Table III

Compound	% cross reactivity at 200 ng/mL*
Oxazepam	100
Alprazolam	190
7-Aminoclonazepam	8
Clonazepam	40
Desmethyldiazepam	200
Diazepam	210
Lorazepam	20
Temazepam	160
Triazolam	160

*Package insert 0372-4 2007 10.

Confirmation

Confirmation testing is available, either in house or through a referral laboratory. If a physician wishes to confirm all presumptive positives from the DOA testing, adding “R” such as DOA7R, will automatically reflex presumptive positive results for confirmation.

Comprehensive urine drug screen-UTOX

The clinical toxicology laboratory also offers a test known as the comprehensive urine drug screen, with the mnemonic, UTOX. This test is available on a routine and STAT basis. It is a gas



chromatographic mass spectrometric assay, therefore, permitting identification of the drug. This test is designed for emergency toxicological testing where rapid drug identification is necessary in potential overdose and poisonings. The advantage of the UTOX is that it has the capability of detecting many drugs such as over the counter, prescription drugs [antidepressants, antipsychotics] in addition to drugs of abuse such as phencyclidine. Typical compounds include cotinine, caffeine, lidocaine, diphenhydramine, amitriptyline, trazodone, cyclobenzaprine, ketamine, metoclopramide, and citalopram. However, this test is not sufficiently sensitive to detect low concentrations of drug which may be present during routine therapy i.e. to monitor compliance with a medication. This is especially true of drugs administered in low doses such as adderall® [amphetamine].

For additional information contact:

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Therapeutic Drug Monitoring (TDM): Optimal Specimen Collection Times in Relation to Drug Dosing

Therapeutic Drug Monitoring (TDM) is performed to determine the presence and quantification of specific drugs in order to achieve desired therapy, while minimizing toxicity. TDM is not necessary for every medication, but is important when association between plasma concentrations and therapeutic effect exists. An optimal concentration (therapeutic range) exists for certain drugs in which most patients achieve the desired therapeutic response. Toxic side effects may occur when concentrations exceed the upper limit of this range. Quantitative measurements of therapeutic drugs should be used to adjust dosage regimens, monitor patient compliance, and assess toxicity.

The recommendations presented in the chart below are intended to inform and guide health care staff in providing the laboratory with an optimal specimen at the appropriate time for clinically relevant, cost effective TDM services.

If you have questions, comments or suggestions, please contact:

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Characteristics of Commonly Monitored Drugs							
Drug Class	Drug	Average Half-Life (Hrs)	Protein Binding %	Therapeutic Range	Toxic Range	Optimal Specimen Collection	Comments
Anti Convulsants	Carbamazepine (Tegretol)	15-24	75	4-12 mcg/mL	>15 mcg/mL	Pre-dose, consistent time of day after steady state.	Co-administration with Erythromycin, phenytoin, Valproic acid reduces the blood concentration. Consider monitoring the active metabolite epoxide in patients receiving concurrent valproic acid and lamotrigine and in patients exhibiting toxicity with low parent drug concentrations. Half-life is variable due to autoinduction which is usually complete 3-5 weeks after initiation.
	Ethosuximide (Zarontin)	30-60	0	40-100 mcg/mL	>200 mcg/mL	Pre-dose, consistent time of day after steady state.	Carbamazepine, Phenobarbital, Phenytoin and primidone reduces the blood concentration.
	Phenobarbital (Luminal)	70-100	40-60	15-40 mcg/mL	>60 mcg/mL	Pre-dose, consistent time of day after steady state.	Valproic acid and Salicylates increase serum levels.
	Phenytoin (Dilantin)	6-60 (Adult) 7-29 (Child)	90	10-20 mcg/mL	>40 mcg/mL	Pre-Dose (Oral Dosing) 1-4 hr post I.V. Loading dose.	Highly bound to albumin and its binding can be affected by the concentration of albumin as well as presence of other acidic drugs that bind to albumin such as valproic acid, salicylates, phenylbutazone, and sulfonyleureas.
	Primidone (Mysoline)	3-8	19	5-12 mcg/mL	>24 mcg/mL	Pre-dose, consistent time of day after steady state.	Measure the metabolite of Primidone, Phenobarbital concurrently with the parent drug.

Characteristics of Commonly Monitored Drugs (continued)

Drug Class	Drug	Average Half-Life (Hrs)	Protein Binding %	Therapeutic Range	Toxic Range	Optimal Specimen Collection	Comments
	Valproic Acid (Depakene)	9-18 (Adult) 7-13 (Child)	90	50-100 mcg/mL	>200 mcg/mL	Pre-dose, consistent time of day after steady state.	An unusual feature of this drug is that once plasma concentration reaches approximately 75 mcg/mL, the free fraction increases rapidly if the dose is increased. Free portion of the drug rapidly metabolizes, therefore total plasma concentrations increases slightly with increasing dose.
Cardioactive Drugs	Digoxin (Lanoxin)	36-48	23	0.8-2.0 ng/mL	>2.5 ng/mL	8-12 hr post-dose	Drug Concentrations be determined after the patient reaches steady state and at least 8 hours after the last dose. The serum concentration of digoxin does not correlate with the pharmacological activity until the post distribution period (at least 8-12 hours after the last dose). Levels of 0.5-1.0 mcg/mL suggested for CHF and levels above 1.0 for CHF have no additional benefit.
	Lidocaine (Xylocaine)	1.5-2	60-80	1.5-5 mcg/ml	>6 mcg/ml	>30 min post I.V. dose (5-10 hr after start of drug administration.)	Routine monitoring is not recommended. It is recommended when propanolol is co-administered or toxicity is suspected. Dose adjustment and drug level monitoring recommended for hepatic impairment. Consider alternative therapy in severe hepatic dysfunction.
	Procainamide (Pronestyl)	2.5-4.7	15-20	4-10 mcg/ml	>10 mcg/ml	For oral therapy 1 hr prior to next dose after Steady State. For IV infusion, draw 6-12 hours after infusion has started.	NAPA exhibits genetic polymorphism. Patients who are slow acetylators are at risk of developing Lupus like symptoms while on procainamide therapy. Hemolysis may occur in patients with G6PD deficiency.
	NAPA	6 to 8	15-20	15-25 mcg/ml	>30 mcg/mL (Proc + NAPA)	Metabolite of Procainamide	
	Quinidine (Duraquin)	6 to 8	80-88	2-5 mcg/ml	>6 mcg/mL	1 hr prior to next dose after Steady State	Causes increased Digoxin levels (up to 2 fold)

Characteristics of Commonly Monitored Drugs (continued)

Drug Class	Drug	Average Half-Life (Hrs)	Protein Binding %	Therapeutic Range	Toxic Range	Optimal Specimen Collection	Comments
Antibiotics	Amikacin (Amikin)	2-3	1-11	See Comments	Peak >35 mcg/ml Trough >10 mcg/mL	Traditional Dosing: Peak: 30 min after 30 minute infusion of the 3rd dose (1 hr after the start of infusion). Trough: 1 Hr before 3rd dose. Extended Interval dosing: Peak: No need to monitor. Trough: 1 Hr before dose.	Traditional dosing: Target Peaks: 15 mcg/ml for synergy against gram positive organisms. 20-40 mcg/ml for gram negative infections Target Trough: < 8 mcg/ml Extended interval dosing: 8 Hr Level after first dose: divide by 2 and plot on Hartford Nomogram If in range as above, monitor trough levels a minimum of twice weekly Target Trough: < 2 mcg/ml
	Gentamicin (Garamycin)	2-3	0-30	See Comments	Peak >20 mcg/ml Trough >2.5 mcg/mL	Traditional Dosing: Peak: 30 min after 30 minute infusion of the 3rd dose (1 hr after the start of infusion). Trough: 1 Hr before 3rd dose. Extended Interval dosing: Peak: No need to monitor. Trough: 1 Hr before dose.	Traditional dosing: Target Peaks: 3-4 mcg/ml for synergy against gram positive organisms. 6-10 mcg/ml for gram negative infections Target Trough: < 1 mcg/ml for synergy and < 2 mcg/ml for gram negative infections Extended interval dosing: 8 Hr Level after first dose: plot on Hartford Nomogram If in range as above, monitor trough levels a minimum of twice weekly Target Trough: < 0.5 mcg/ml
	Tobramycin (Nebcin)	2-3	0-30	See Comments	Peak >20 mcg/ml Trough >2.5 mcg/mL	Traditional Dosing: Peak: 30 min after 30 minute infusion of the 3rd dose (1 hr after the start of infusion). Trough: 1 Hr before 3rd dose. Extended Interval dosing: Peak: No need to monitor. Trough: 1 Hr before dose.	Traditional dosing: Target Peaks: 3-4 mcg/ml for synergy against gram positive organisms. 6-10 mcg/ml for gram negative infections Target Trough: < 1 mcg/ml for synergy and < 2 mcg/ml for gram negative infections Extended interval dosing: 8 Hr Level after first dose: plot on Hartford Nomogram If in range as above, monitor trough levels a minimum of twice weekly Target Trough: < 0.5 mcg/ml

Characteristics of Commonly Monitored Drugs (continued)

Drug Class	Drug	Average Half-Life (Hrs)	Protein Binding %	Therapeutic Range	Toxic Range	Optimal Specimen Collection	Comments
	Tobramycin (Nebcin)	2-3	0-30	See Comments	Peak >20 mcg/ml Trough >2.5 mcg/mL	Traditional Dosing: Peak: 30 min after 30 minute infusion of the 3rd dose (1 hr after the start of infusion). Trough: 1 Hr before 3rd dose. Extended Interval dosing: Peak: No need to monitor. Trough: 1 Hr before dose.	Traditional dosing: Target Peaks: 3-4 mcg/ml for synergy against gram positive organisms. 6-10 mcg/ml for gram negative infections Target Trough: < 1 mcg/ml for synergy and < 2 mcg/ml for gram negative infections Extended interval dosing: 8 Hr Level after first dose: plot on Hartford Nomogram If in range as above, monitor trough levels a minimum of twice weekly Target Trough: < 0.5 mcg/ml
	Vancomycin (Vancocin)	4-6	10-55	See Comments	Peak >80 mcg/ml Trough >25 mcg/mL	Peak: Not Recommended. In rare cases (eg; meningitis) contact ID physician on call Trough: Immediately Prior to 3rd dose	Target troughs 15-20 mcg/ml - Pneumonia, Meningitis, Osteomyelitis, Bacteremia, and Endocarditis caused by S. aureus (i.e. MRSA) 10-15 mcg/ml - Skin/soft tissue infections, uncomplicated bacteremias (without S. aureus or endovascular source), other indications
Psychotropics	Lithium (Eskalith)	8-24	0	0.6-1.2 mmol/l	>2 mmol/l	12 Hr Post dose after steady state with careful attention to timing.	Lithium undergoes extended distribution phase. Therefore, specimens for monitoring should not be collected prior to the noted time. Specimens collected before distribution is complete yield inappropriate information which can not be used to establish dosing regimen.
	Amitriptyline (Elavil)	9-46	>90	95-250 ng/ml	>500 ng/ml	Predose after steady state; 10-12 hr after single daily dose, 4-6 hr after divided dose.	Range includes amitriptyline and its metabolite nortriptyline.
	Nortriptyline (Aventyl)	18-56	>90	50-150 ng/ml	>500 ng/ml	Predose after steady state; 10-12 hr after single daily dose, 4-6 hr after divided dose.	Metabolite of amitriptyline and may be given separately.
	Imipramine (Tofranil)	6-28	80-90	150-300 ng/ml	>400 ng/ml	Predose after steady state; 10-12 hr after single daily dose, 4-6 hr after divided dose.	Range includes imipramine and its metabolite desipramine.
	Desipramine (Norpramin)	12-28	>90	100-300 ng/ml	>400 ng/ml	Predose after steady state; 10-12 hr after single daily dose, 4-6 hr after divided dose.	Metabolite of imipramine and may be given separately.



Laboratories

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New Billing Company UMass Memorial Laboratories

Beginning on January 14, 2012, UMass Memorial Laboratories outsourced its billing functions to Laboratory Billing Solutions (LBS). There is no change other than your contact for billing questions will be an LBS representative. The contact numbers for LBS are as follows:

Laboratory Billing Customer Service:
1-855-242-4521
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Please contact your Account Manager with any questions or concerns.