

Urine Toxicology Screening on Labor and Delivery *Clinical Guidelines*

Urine should be collected from all patients admitted to labor and delivery who have ANY of the following risk factors:

- History of Drug Abuse^{1,4,5}
- Poor Prenatal Care (prenatal care starting after 16 weeks gestation or less than 4 prenatal visits)^{1,4,5}
- History of child abuse, neglect or court ordered placement of children outside of the home^{2,4}
- History of Domestic Violence^{4,5}
- History of hepatitis, HIV, syphilis or prostitution^{3,4,5}
- Unexplained Placental Abruption^{1,4,5}

Confirmation Testing (samples are retained for 4 days, during which confirmation testing can be ordered)

- Recommended for initially positive screens for:
 - Opiates (require confirmation testing to distinguish between different drugs within this class)
 - Benzodiazepines (same as for opiates)
 - Amphetamines (most prone to false positives)
- Should be considered if patient is denying use of drugs and you want to have definitive result, particularly if the result will be used to alter patient care or newborn management

For assistance interpreting results please refer to “Toxicology Testing at UNCH” below, or contact pathology (Dr. Catherine Hammett-Stabler @ 966-3724)

References

1. Horn P, Mendelsohn J, Bowers M, Chappen M, Schrieer J, Spalding S, Weyher J, Berkelhamer J. Clinical and Laboratory Observations: Effectiveness of a targeted screening program in identifying infants with positive urine toxicology screening results in a regular neonatal nursery. *The Journal of Pediatrics* 1993; 123: 137-9.
2. MacMahon, James. Perinatal Substance Abuse: The Impact of Reporting Infants to Child Protective Services. *Pediatrics*. 1997
3. Bauer C, Langer J, Shankaran S, Bada H, Lester B, Wright L, Krausse-Steinrauf H, Semeriglio V, Finnegan L, Maza P, Verter J. Acute Neonatal Effects of Cocaine Exposure during Pregnancy. *Archives of Pediatric Adolescent Medicine*. 2005. 159: 824-834.
4. University of Iowa Hospitals and Clinics Protocol
5. UNC Newborn Critical Care Center Newborn Drug Screen Protocol

Toxicology Testing at UNCH

Several toxicology tests are available through the Core Laboratory, UNCH: serum Alcohol Panel (including ethylene glycol), Urine Toxicology Screen, and specific drug confirmation tests. This site will guide you through the tests performed in-house and through our reference laboratories.

The **ALCOHOL PANEL** http://labs.unchealthcare.org/labstestinfo/a_tests/alcohols.htm includes identification and quantification of ethanol, methanol, isopropanol (and acetone), and ethylene glycol. The test is performed on serum using an in-house developed gas chromatography-based method. This method is specific for the listed agents. It is available stat or routine, 24-7.

The **URINE TOXICOLOGY SCREEN** http://labs.unchealthcare.org/labstestinfo/u_tests/urine_tox.htm is appropriate for the Emergency Department, and all other locations, for drugs of abuse testing. The panel is available stat or routine, 24-7. Non-emergency testing of urine for drugs of abuse is performed either to determine compliance with drug rehabilitation programs, or to detect drug abuse in asymptomatic patients. The **Urine Toxicology Screen** includes **amphetamines, barbiturates, benzodiazepines, cocaine metabolite, opiates (opioids), cannabinoids, and methadone**. Each of these is an independent test and may be ordered separately or in any combination. Fifty milliliters of urine should be collected in a clean urine cup and sent to the Core Laboratory for analysis.

The Core Laboratory uses immunoassays manufactured by Ortho Clinical Diagnostics on the Vitros 5600 for testing. These are considered screening assays and yield only qualitative, class-specific information. Specific drugs within a class are not identified using these methods. These assays vary in their ability to detect parent compounds and metabolites. Slight variations may be seen due to changes in reagent lots.

Screening results are reported as “≥” (presumptive positive) or “<” (less than) according to the cutoff values listed in the **table** below. Presumptive positive results only indicate the presence of the drug or metabolite in urine and do not indicate or measure intoxication or efficacy of elimination. Negative results reflect concentrations that fall below the cutoff and do not necessarily exclude the presence of the drug or metabolite. Results are to be used for clinical evaluation only. **CONFIRMATION TESTING** must be requested to be performed.

CONFIRMATION TESTING requires additional testing using a more sensitive and specific method. Gas chromatography/mass spectrometry (GC/MS) and liquid chromatography tandem mass spectrometry (LC-MS/MS) are the two most popular techniques used to perform these types of tests. The techniques are able to provide positive identification of compounds present as well as the concentration of the identified compound. The Core Laboratory currently performs the following confirmation tests (tests will be added in the future based on referral testing volumes):

BUPRENORPHINE http://labs.unhealthcare.org/labstestinfo/b_tests/buprenorphine.htm The Core Laboratory uses an in-house developed method using LC-MS/MS to identify and quantify buprenorphine and norbuprenorphine. The test is performed twice a week and is not available stat. Urine concentrations are dependent upon physiology and do not correlate with dose or serum concentrations. These results should not be used for therapeutic drug monitoring purposes.

OPIATES http://labs.unhealthcare.org/labstestinfo/o_tests/opiates_conf.htm The Core Laboratory uses an in-house developed method using LC-MS/MS to identify and quantify morphine, codeine, 6-acetylmorphine (heroin metabolite), oxycodone, oxymorphone, hydrocodone, and hydromorphone. The test is performed twice a week and is not available stat.

Confirmation testing for

amphetamines http://labs.unhealthcare.org/labstestinfo/a_tests/amphetamine_conf.htm,

barbiturates,

benzodiazepines http://labs.unhealthcare.org/labstestinfo/b_tests/benzodia_conf.htm,

cocaine http://labs.unhealthcare.org/labstestinfo/c_tests/cocaine_conf.htm,

cannabinoids (THC, marijuana) http://labs.unhealthcare.org/labstestinfo/c_tests/cannab_conf.htm,

methadone http://labs.unhealthcare.org/labstestinfo/m_tests/methadone_conf.htm,

fentanyl http://labs.unhealthcare.org/labstestinfo/f_tests/fentanyl.htm

and other drugs is available through Referral Testing (966-2362). Requests for confirmation should be ordered as an “add-on” within 3 days of the sample collection. Those linked are for urine but other sample types may be available. Contact Referral Testing for information regarding collection, costs, and turn-around times.

October 18, 2011

DRUG CLASS OR DRUG	CUTOFF Concentration (ng/mL)		DURATION OF POSITIVE RESULT *	COMMENTS
	Screen	Confirmation		
AMPHETAMINES d- amphetamine d-methamphetamine MDA (methylenedioxy-amphetamine), MDMA (methylenedioxy-methamphetamine) or Ecstasy	500	25-200**	2 hours after use, up to 3 days	<ul style="list-style-type: none"> • Target analyte: d-amphetamine • Methamphetamine is metabolized to amphetamine. • Benzphetamine metabolizes to amphetamine and methamphetamine. • Selegiline metabolizes to L-amphetamine and L-methamphetamine. • Prescription amphetamines do not metabolize to methamphetamine. • Assays detect legal and illicit amphetamines and methamphetamines. • Window of detection depends upon urinary pH.

BARBITURATES Barbital Butabarbital(butisol) Butalbital (fiorinal) Pentobarbital (nembutal) Phenobarbital Secobarbital (seconal) Thiopental (pentothal)	200	100**	1 to 21 days after use depending on specific agent (short- vs long-acting).	<ul style="list-style-type: none"> • Target analyte: secobarbital
BENZODIAZEPINES Alprazolam (Xanax) Chlordiazepoxide (Librium) Clonazepam (Klonopin) Diazepam (Valium) Flurazepam (Dalmane) Lorazepam (Ativan) Midazolam (Versed) Nitrazepam (Mogadon) Oxazepam (Serax) Prazepam (Centrax) Temazepam (Restoril) Triazolam (Halcion)	200	50-100**	14 hours to 16 days (short- vs long-acting)	<ul style="list-style-type: none"> • IAs may detect some benzodiazepines only at toxic, not therapeutic, levels. • Consider confirmation of screens < cutoff. • Refer to Table 2 for benzo metabolic profiles

DRUG CLASS OR DRUG	CUTOFF Concentration (ng/mL)		DURATION OF POSITIVE RESULT *	COMMENTS
	Screen	Confirmation		
BUPRENORPHINE Buprenex® Subutex® Suboxone® (buprenorphine with naloxone)		5	Up to 2 to 4 days after use	<ul style="list-style-type: none"> In cases of maintenance treatment for opioid dependence, buprenorphine is monitored for compliance. Metabolized to norbuprenorphine which is pharmacologically active. Results showing only parent buprenorphine with little to no metabolite suggest spiking of urine and noncompliance.
CANNABINOIDS 11-Nor-delta-9-THC-9-carboxylic Acid. 11-OH-delta-9-THC Cannabinol Marinol	20	3**	0 to 21 days (depends on frequency of use and quality of product).	<ul style="list-style-type: none"> Target analyte: Δ^9COOH-THC Peak plasma concentrations reached within 10 minutes of inhalation. Passive inhalation is unlikely to be detected by the screening assay. Hemp seed ingestion may produce a positive result. Marinol® is detected. Ibuprofen and Protonix® do NOT cross-react with current screening assay.
COCAINE METABOLITE Benzoyllecgonine Cocaine Ecgonine Cocaethylene	150	50**	2-3 days after use. May be positive longer with chronic high-dose use.	<ul style="list-style-type: none"> Target analyte: benzoyllecgonine Highly specific assay Cocaine has a half-life of 30-60 minutes. Blood cocaine levels do not guide management. In the presence of ethanol, cocaine is transesterified to form cocaethylene, a more cardiotoxic agent than cocaine.
METHADONE	300	100**	3-16 days.	<ul style="list-style-type: none"> Target analyte: methadone Methadone is NOT detected with the opiate screening or confirmation assays. Methadone is metabolized to EDDP, which is measured by confirmation methods. Results showing only parent morphine with little to no EDDP metabolite suggest spiking of urine and noncompliance.

DRUG CLASS OR DRUG	CUTOFF Concentration (ng/mL)		DURATION OF POSITIVE RESULT*	COMMENTS
OPIATES (Opioids) Codeine Morphine Heroin metabolite (6-acetyl morphine, 6-AM, 6-MAM)) Hydrocodone Hydromorphone Oxycodone Oxymorphone	300	50	<ul style="list-style-type: none"> • 1 to 5 days after use. • Heroin metabolite (6-AM) present only 2-8 hours post heroin use. 	<ul style="list-style-type: none"> • Target analyte: morphine • See Table 3 for opiate/opioid metabolic pathways • Methadone, naloxone, naltrexone, and tramadol do NOT cross-react to produce a positive result. • Oxycodone, hydrocodone, hydromorphone, oxymorphone do not cross react 100%. Consider confirmation testing if screen is <cutoff. • Poppy seed ingestion may cause a positive result. The urine concentration of morphine and codeine from poppy seeds peaks within 2-4 hours, and may be positive up to 72 hrs. Concentrations are usually <2000 ng/mL but depends on food product. • Heroin use: 6-AM if collected within 2-8 h of use, morphine is also present. Codeine may also be present if heroin is contaminated with acetylcodeine.
PHENCYCLIDINE Sernylan (PCP) and metabolites	25	25**	<ul style="list-style-type: none"> • 5-7 days after use 	<ul style="list-style-type: none"> • Sent to MML for testing • Dextromethorphan, dextrophan, diphenhydramine, chlorpromazine, meperidine and mesoridazine may produce false positive results with some screening assays, but confirmation will produce a definitive result.

* Estimates only and depends upon dose, metabolism and hydration state of patient.

** Confirmation testing sent to Mayo Medical Laboratories (MML) contact Referral Testing (6-2361)

Table 2. BENZODIAZEPINES METABOLIC PROFILES

PARENT COMPOUND	METABOLITES
Alprazolam	α -OH alprazolam + 4-OH alprazolam
Chlordiazepoxide	nordiazepam + oxazepam
Clonazepam	7-aminoclonazepam
Diazepam	temazepam + nordiazepam + oxazepam
Flurazepam	N-OH ethylglucuronide
Flunitrazepam	7-aminoflunitrazepam
Lorazepam	lorazepam glucuronide
Oxazepam	oxazepam glucuronide
Temazepam	oxazepam

Table 3. Metabolic Profiles for OPIATES and OPIOIDS

PARENT	METABOLITES	NOTES
Heroin	6-acetylmorphine + morphine	Cases with 6-AM only and not producing morphine have been reported (RARE).
Morphine	normorphine + glucuronides and sulfates	Hydromorphone <4-6% may be found and reflects a minor metabolic pathway. <0.03% codeine reported as pharmaceutical contaminant.
Codeine	morphine + norcodeine	
Hydrocodone	hydromorphone (\rightarrow hydromorphol) + norhydrocodone + hydrocodol (\rightarrow hydromorphol)	

October 18, 2011

Hydromorphone	hydromorphol	
Oxycodone	oxymorphone (→ oxymorphol) + oxycodol + noroxycodone	<0.1% hydrocodone reported as pharmaceutical contaminant
Oxymorphone	oxymorphol	